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Provide a context or background for the study (i.e.,the nature of the problem and its significance). State the specific purpose or research objective, or hypothesis tested the study or observation; the research objective is often more sharply focused when stated as a question. Both the main and secondary objectives should be made clear and any pre-specified subgroup analysis should be described. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

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Present your results in logical sequence in the text, tables and illustrations, giving the main or most important findings first.

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Cook NR, Rosner BA, Hankinson SE, Colditz GA. Mammographic screening and risk factors for breast cancer. American Journal of Epidemiology. 2009 Dec;170(11):1422-32. doi: 10.1093/aje/kwp304.

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Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

ACKNOWLEDGEMENT

Provide the list of individuals who contributed in the work and grant details where applicable.

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ISSN (E) 2790-9352
ISSN (P) 2790-9344

PJHS
Pakistan Journal of Health Sciences

Published by:
CrossLinks International Publishers

VOLUME 04 ISSUE 11

PJHS
Pakistan Journal of Health Sciences

ISSN (E) 2790-9352
ISSN (P) 2790-9344

Published by:
CrossLinks International Publishers

ISSN (E) 2790-9352
ISSN (P) 2790-9344

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Published by:
CrossLinks International Publishers

DOI: https://doi.org/10.54393/pjhs.v4i11.1202

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Unveiling the Health Crisis of Urban Smog

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ARTICLE INFO

How to Cite:

Naveed, M. A. (2023). Beyond Haze: Unveiling the Health Crisis of Urban Smog. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1202

With the industrial growth and urbanization in large cities of Pakistan, the smog has become a lurking adversary amidst the haze impacting millions of people every winter season. Pakistan ranks at number 3 in the countries with poor air quality as of 2019, the main reason of which is the persistent smog. It is formed the presence of severe atmospheric pollutants suspended in air which gives it a yellowish black dense appearance. These pollutants mainly originate from industries due to the burning of fuels in industries, and from automobile exhausts due to the release of harmful gases such as ozone, nitrogen oxides and sulfur oxide along with the particulate matter such as dust and volatile compounds in air. It not only reduces visibility and obscures the skyline but is known to have serious implications for human health. Various studies associate smog with the respiratory and eye infections, allergies, and lungs cancer. The particulate matter present in the smog such as PM10 reach the lower levels of the respiratory tract and is responsible for irritation and allergies. Moreover, they carry other harmful materials, such hydrocarbons and poisonous gases with them as well that enter the blood stream via gaseous in alveoli [1]. The constituents in smog have been reported to elevate the risk of adenocarcinoma and squamous cell carcinoma in lungs in the people with chronic respiratory conditions. People from all age groups are affected with the youngest and immunocompromised individuals more susceptible to perilous effects of smog depending upon the time of exposure. Apart from respiratory system, there are various reports which link smog with the cardiovascular system issues as well. Researchers from the US Environmental Protection Agency (EPA) have proved the long-term exposure to PM2.5 can result in myocardial infarction and decreased life expectancy [2]. A number of multifaceted strategies are required to address this health crisis. Regulatory policies for the controlled emission of harmful matter in the air, and plans for the introducing cleaner technologies may prove beneficial to mitigate this risk and improve the overall air quality. Public awareness is equally critical to equip general masses with the knowledge about the adverse effects of smog and ways to prevent them. Smog is not merely an environmental concern, it's a public health emergency which demands urgent attention. It's a collected responsibility of policy makers and communities to revitalize the urban environments steering towards healthier tomorrows.

REFERENCES

[1] Naureen I, Saleem A, Aslam S, Zakir L, Mukhtar A, Nazir R *et al.* Potential Impact of Smog on Human Health. Haya: The Saudi Journal of Life Sciences. 2022 Mar; 7(3): 78-84.

[2] United States Environmental Protection Agency. Air Pollution and Cardiovascular Disease Basics. 2023. [Last Cited: 27th Nov, 2023]. Available at: https://www.epa.gov/air-research/air-pollution-and-cardiovascular-disease-basics

DOI: https://doi.org/10.54393/pjhs.v4i11.821

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Review Article

A Critical Glance to Non-Pharmacological Management of Novel COVID-19 Infection

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ARTICLE INFO

Key Words:
COVID-19, Pandemic, NPIs

How to Cite:
Saleem, A., Davis, M., Rafique, S., Meer, S., Qader, A., & Aslam, M. N. (2023). A Critical Glance to Non-Pharmacological Management of Novel COVID-19 Infection: Non-Pharmacological Management of COVID-19 Infection. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.821

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Received Date: 3rd June, 2023
Acceptance Date: 2nd November, 2023
Published Date: 30th November, 2023

ABSTRACT

Our study aim was to enhance awareness about the management of COVID-19 infection. Human health and way of life have been severely disrupted by corona virus disease-19 (COVID-19), a severe global public health emergency. While vaccines and cures are still being developed, the pandemic is still spreading. The main tools used to combat the COVID-19 infection are known as non-pharmacological interventions (NPIs), which have an impact on almost every aspect of social functioning. This review concentrated on identifying successful NPIs. Effective NPIs include isolation and quarantine, physical separation, and good hand hygiene. They should also be put into practice in light of the socioeconomic and cultural makeup of the population. UV light and public spraying of the outdoors are examples of ineffective NPIs. The optimum way to apply these measures is to apply them simultaneously or in combination. According to the findings, they have to be implemented early in the pandemic and for extended periods. The least amount of morbidity and mortality was achieved when vaccination was paired with strict NPI adherence. It has also been noticed that closing schools only work to contain COVID-19 when it is combined with thorough contact tracking. Determining how limiting NPIs will affect the number of cases and the categorization of COVID-19-related deaths is difficult. The design of the evidence for hygiene precautions like face masks is more solid and offers reliable information on COVID-19 infection prevention. These findings provide proof to support policy decisions about NPIs to prevent the COVID-19 pandemic from spreading.

INTRODUCTION

Nearly 250 million confirmed cases and 5 million deaths associated with SARS-CoV-2 infection have been reported globally as of November 2021 [1]. To stop the pandemic, numerous non-pharmacological interventions (NPIs) were used worldwide [1, 2]. NPIS was advised for usage in influenza pandemics at any degree of severity by the World Health Organization (WHO), which included hand washing, face masks for symptomatic and asymptomatic people, isolation of ill people, travel guidance, and surface or object cleaning [2]. School closures and the public wearing face masks are advised as additional measures when the severity is high [3]. In the event of symptomatic individuals isolating themselves, we predicted that these interventions would have an impact on the frequency of interpersonal interaction as well as the relative infectiousness of those who are clinically ill (but not those who are preclinically or sub clinically infected). Based on survey information gathered in Great Britain in 2006, distinct contact matrices were created for encounters made at home, at work, at school, and in other situations

DOI: https://doi.org/10.54393/pjhs.v4i11.821

(such as leisure, transportation, and other places)[4]. Even if people do not exhibit any symptoms, practicing social distancing in both indoor and outdoor settings is crucial to prevent the spread of COVID-19. It is vital to note the distinction between quarantine and isolation, even if the public press frequently uses the terms interchangeably. While isolation is appropriate for someone who has been diagnosed with the virus, quarantine keeps someone who may have been exposed to the virus away from other people. Self-quarantine and self-isolation, as the terms are used, can take place at the person's house [5]. The participants who always wore masks, practiced social distancing and used hand sanitizer or hand washing were represented by 47.1%, 37.8%, and 68.8%, respectively. Only less than 10% of the population does not follow non-pharmacological therapies [6]. These combined therapies have been demonstrated to be beneficial and have an enormous impact on reducing the transmission of the disease, preventing the collapse of the healthcare system, and preventing death as shown in figure 1.

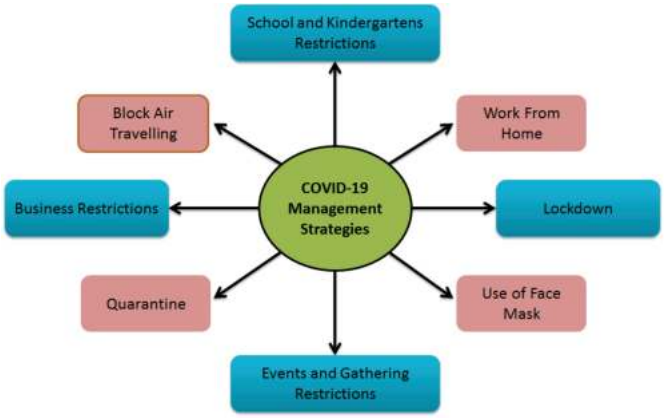

Figure 1: Elaborating the non-pharmacological management of COVID-19 infection

Restriction on school and kindergartens

Both observational and modeling studies have demonstrated that school closure can reduce the rate of seasonal influenza transmission [7]. However, for COVID-19, children and adults both have assault rates. Therefore, it is unknown if closing schools would reduce the transmission, given that most children with COVID-19 either experience moderate symptoms or show no symptoms at all [8]. Contrarily, a study conducted in the USA found that closure was linked to a considerable drop in SARS-CoV-2 circulation and associated clinical issues [9]. The opening of schools for specific grade levels, staggered timetables, an alternation between remote and on-site teaching modes, limiting class sizes, improved hand hygiene, wearing face masks, keeping distance from people, ventilation of rooms, as well as respiratory etiquette and policies for sick students and staff to stay at home, were among the non-pharmaceutical interventions and hygiene measures implemented after the reopening of schools [10]. Students from low-income families sometimes lack the financial means to purchase necessary infection prevention and control (IPC) supplies like face masks and hand sanitizers [11]. For instance, the government of Uganda has promised to give all residents older than six years old free masks [12]. The spread of numerous infections in these facilities would be significantly, positively, and over time reduced in all school restrooms and hand washing locations with enough soap dispensers and paper towels [13]. In Australia, testing of contacts linked to 12 children and 15 adults in 15 schools (students aged six and older) and ten kindergartens/nurseries (students aged six weeks to 5 years) revealed an attack rate of 0.3% between children, 1% between children and adults, 1.5% between adults and children, and 4.4% between adults and adults. Out of 35 contact cases, only one suffered an epidemic, which resulted in six adults and seven children getting sick [1]. Greater community transmission, inadequate physical separation, poor ventilation, and a lack of masking are all linked to larger school epidemics. Schools that used transmission mitigation strategies (even in European nations) do not appear to have significantly increased the virus's ability to spread within the surrounding area [14]. School closures have major negative consequences, including harm to children's learning and mental health, a heavy load on parents, and decreased economic productivity, even though they may help control the epidemic [15]. However, many schools have continued to impose food prohibitions, either voluntarily or due to accommodations made under the federal disability statute, in response to requests from parents of children with food allergies and to avoid spreading infection [16].

Businesses restrictions

Business closures result in job losses and economic damage, which may therefore harm health. Almost all states have restricted or shut down the functioning of establishments like bars, restaurants, theatres, gyms, and shopping centers [17]. From March 14 to August 8, 2020, over 52 million Americans filed unemployment insurance claims. As of August 22, 2020, more than 15 million Americans filed for Pandemic Unemployment Assistance, which is available to workers in the unorganized sector who are self-employed, looking for part-time work, or otherwise would not be eligible for regular unemployment compensation [18]. Ontario initially generated a binary variable to represent whether non-essential firms were closed on each day of the timeline owing to limitations before constructing the business closure variable [19]. Due to the decline in demand, disruptions in the supply chain,

DOI: https://doi.org/10.54393/pjhs.v4i11.821

and production slowdowns brought on by unsafe workplaces, the COVID-19 pandemic has presented small businesses and their owners with hitherto unheard-of obstacles [20]. Small firms are the most vulnerable in Russia, especially those in the service industry, where the danger of "contact" infection is greatest [21]. The impact of company closings on the COVID-19 fatalities in Italy. They compile a sizable dataset from 222 local labor markets across 4,000 Italian towns. The percentage of employees who are not performing any critical tasks as a result of COVID-19 is how they define a business shutdown. Additional controls include factors like the percentage of women of working age, the percentage of high school graduates, and population density. According to their research, business closure, particularly in the retail and hotel industries, dramatically lowers the COVID-19 death rate. The outcomes also show that implementing closure limitations one week sooner could prevent 25% of the fatalities in Italy [22]. The workers whose jobs could not be performed remotely (e.g., by working from home) may have suffered disproportionate employment and health losses as a result of the COVID-19 epidemic. In non-remote jobs, it is more difficult to avoid social contact [23]. According to statistics, 75% of companies without a continuity strategy fail three years after a tragedy or crisis [24].

Restriction on events and gatherings

The COVID-19 pandemic has had a significant effect on the events sector [25]. Canceling public activities is the most efficient sort of containment technique for reducing COVID-19 infections and has the least negative effects on the economy [26]. According to many super-spreading occurrences, including the Austrian ski resort of Ischgl, the number of confirmed cases soon doubled globally. Through community transmission, the infection rate increased from there, and by April 15, confirmed cases had surpassed 2 million (with over 125,000 deaths) in more than 200 countries [27]. The almost 10 million Muslims who congregate in Makkah and Medina during the Umrah and Hajj seasons are anticipated to have an impact on the epidemiology of respiratory viruses in KSA [28]. In June 2020, Saudi Arabia declared that it would ban foreign travelers for the 2020 Hajj pilgrimage to Mecca and the domestic population with chronic ailments and those 65 years of age and older to contain the COVID-19 pandemic and prevent super spreader events [29]. In general, many factors, such as the type of event and anticipated size, duration, and spatial distribution; expected origin and recent travel patterns of participants; level of infectious disease activity or pressure in the host country at the time of the event; level of public attention; and event-related activities during, before, and after the event, may have an impact on the risk of disease spreading and outbreaks during an event [30]. The definition of MG events includes public and private celebrations, religious meetings and pilgrimages, sporting and tourism events, political events, and festivals. Travel and movement patterns on a local, national, or international scale linked to MGs may worsen the spread of infectious diseases in a variety of geographic situations [31]. The Sri Petaling mass gathering, which took place from February 27 to March 1, 2020, is directly responsible for more than 35% of the COVID instances in Malaysia. More than 19,000 individuals, including 1500 visitors from India, South Korea, Brunei, China, Japan, and Thailand, are present at the Sri Petaling gathering, a Muslim missionary activity [32]. A community in Barnstable County, Massachusetts, hosted numerous summer activities and sizable public gatherings from July 3–17, 2021, drawing thousands of visitors from all around the country. On July 10, reports of a spike in COVID-19 cases among residents of or recent visitors to Barnstable County— including those who are fully immunized—were sent to the Massachusetts Department of Public Health (MA DPH). People with COVID-19 reported going to indoor and outdoor events that were quite crowded in places like pubs, restaurants, lodging facilities, and rental homes [33]. Scenarios aboard large cruise ships also fulfill the concept of mass gatherings because there are more people there than is typical in other settlements on land. With 2000 to 4000 passengers, large cruise ships like the Diamond Princess, which was quarantined in Japan owing to the COVID-19 epidemic, make it nearly impossible to maintain social distancing [34]. Since the beginning of March 2020, all significant sports leagues and competitions have been postponed or canceled because of COVID-19 [35]. The study on the Prevention of SARS-CoV-2 Transmission in a large Indoor Gathering (SPRING) trial was designed to test the hypothesis that a method that included medical mask use, systematic antigen screening within three days of the event, and optimized ventilation could stop SARS-CoV-2 from spreading during a sizable indoor gathering without requiring physical separation [36].

Restriction on movement of people or lockdown

Lockdown measures have helped the pandemic and have been successful in lowering the number of COVID-19 cases in the nations where they have been used. Looking at the European example in particular, its Effectiveness starts to lower COVID-19 infections about three weeks after the lockout and continues for another 20 days [37]. As a first step in containing the spread of the disease, the Indian government enforced the Janata Curfew for 24 hours. This was followed by a lockdown under the Disaster Management Act 2005 for 21 days beginning on March 24, 2020 [38]. The United Nations Educational, Scientific, and Cultural Organization (UNESCO) has calculated that 1.6

DOI: https://doi.org/10.54393/pjhs.v4i11.821

billion (90.2%) students are currently not enrolled in primary, secondary, or tertiary education (henceforth schools) as a result of the global COVID-19 lockdown, with nationwide school closures currently in effect in 191 countries [39]. The limitation of inter-individual physical interaction is known as social lockdown. To avoid interaction with (asymptomatic) infected individuals in the outside world, it is advised not to leave the house [40]. The onset of COVID-19 was estimated to occur on December 4. Wuhan City and the major cities in Hubei, China, were put under lockdown on the 23rd and 24th of January, respectively [41]. On March 23, 2020, the province of Sindh in Pakistan ordered a lockdown, which was then followed by the other provinces and towns in the nation. Unquestionably, the pandemic-driven lockdown has resulted in significant losses on a global scale in terms of both money and lives, in addition to ongoing hardships and a wide range of challenges [42]. On March 23, the South African government ordered a rigorous lockdown that would last for three weeks, beginning on March 26. At that point, there were officially 554 positive cases but no fatalities [43]. Greece was the nation that implemented the COVID-19 lockdown at the earliest [44]. As a result, Greece had the third-lowest 30-day mortality rate per million people, trailing only Norway and Finland, which had made significant investments in the growth of their public health systems [45]. Numerous service sectors were severely impacted by the COVID-19 epidemic and the lockdown, with healthcare services being one of them. Following the lockdown, many locations closed their outpatient clinics, and patients with COVID-19 infections could only access emergency services or clinics designed explicitly for them [44]. The people stayed at home, which has resulted in a dramatic improvement in air quality over the past several months, especially in hard-hit locations like Wuhan, northern Italy, and many American metropolises [46]. A more extended period of total lockdown has unknown consequences for the number of people infected with COVID-19 and the number of fatalities. Comparing countries with different lockdown lengths, those with a shorter lockdown period (about 15 days) are related to lower average levels of confirmed cases per population (%) but with a higher average variation of confirmed cases per population (%) [47]. The issues relating to "long-covid" and other non-mortality expenditures that lockdown can minimize [48]. Global economic activity ceased as nations went into lockdown. Due to the lockdown, among many other industries, the transport industry has been hardest hit. Due to travel restrictions or reluctance, air and ground transit has ceased [49]. Since the lockdown that completely shut down all activity in response to the COVID-19 pandemic, anthropogenic air pollution has been seen to decrease. NO2 concentrations in eastern and central China at the beginning of 2020 were 10–30% lower than those in comparable periods in 2019, according to NASA Earth Observatory satellite data [50]. Lockdown procedures have caused extraordinarily pure air in urban areas in many parts of the world, and news is rife with accounts of exceptionally blue skies and excellent visibility [51]. The primary sources of carbon emissions are the use of fossil fuels by industry, thermal power plants, air travel, and vehicle traffic. Since industrial sectors were closed during the lockdown, the level of carbon concentration decreased [52].

Restriction on international air traveling

The fast expansion of cases throughout the world, notably in the United States, Europe, and Asian nations, was expedited by domestic and international human migration [53]. Affected the most by the advent of SARS-CoV-2/COVID-19 is the travel industry. Millions of people worldwide were impacted by the abrupt enactment of domestic and international travel prohibitions. In addition to travelers, airline firms also suffered a rapid decline in revenue. Travelers are thought to have spread COVID-19 cases throughout the world, mostly via air travel [54]. The results of Wuhan's travel ban and the international travel restrictions enacted by many nations in early February 2020 [55]. The United States government shut the border with Canada on March 18 and banned inbound planes from Europe (the Schengen Area) on March 14 [56]. Between January and June 2020, COVID-19 importations into Australia were reduced by 87.68% (83.39-91.35) as a result of international travel restrictions [57]. When travel restrictions were put in place for a group of 120 countries, three out of every four of those nations had more than 50 confirmed cases [58]. As countries apply limitations on international travel to stem the sudden spread of the novel Coronavirus disease 2019 or COVID-19, cross-border population mobility has largely ceased. More than 90% of the world's population, or over 7.1 billion people, will be living in nations that impose entry restrictions on travelers who are neither citizens nor residents as of March 31, 2020 [59]. The flight restrictions into and out of China have further decreased the quantity of exported cases [60]. When assuming no reduction in travel volumes (i.e., with 2019 travel volumes), imported cases are likely to have contributed more than 10% of total incidence in 102 (95% credible interval 63-129) of 136 countries in May 2020 and 74 countries (33-114) when assuming estimated 2020 travel volumes. When assuming no decreases in travel numbers, imported cases in September 2020 would have made up little more than 10% of overall incidence in 106 (50-140) of 162 countries and less than 1% in 21 countries (4-71) [61]. According to a study that evaluated the impact of human

DOI: https://doi.org/10.54393/pjhs.v4i11.821

mobility and control measures in China, travel limitations are more helpful in the early stages of an outbreak before the disease spreads widely [62]. The importation of COVID-19 depends heavily on mass transportation (such as buses and trains). The frequency of buses, trains, and planes from affected cities is positively correlated with the importation of cases [63]. All travel arrangements, including tourist excursions departing from China (to other countries), were canceled, and non-urgent corporate travel for both inbound and outbound journeys was drastically limited [64]. The Chinese government's COVID-19 travel restriction rules, which included a complete ban on travel outside of the province, restricted the movement of more than five million people in Hubei Province, including during the 2020 Spring Festival [65]. Some nations have implemented travel restrictions akin to a cordon sanitaire, either to stop the spread of diseases from a primary disease epicenter (like Wuhan in January 2020) or both [66]. The travelers are required to abide by any safety precautions that are deemed necessary by the country of origin, the country of destination, and the transporter, particularly airlines. Concerning the possibility of SARS-CoV-2 transmission, there needs to be more clarity. Airlines take precautions against the danger of infection during flights or at the airport, including the use of filters, surveillance, and passenger testing. Governments implement policies like travel restrictions and quarantine to reduce the risk of bringing infectious passengers into the country from abroad or within [67]. In the 135 study nations or territories, we calculated that as of May 31, 2020, there were 15 million (IQR (11-20) million) COVID-19 cases undergoing travel and physical distancing therapies. By June 30, 2020, we predicted that 983 million (808-1169) infections would have been avoided and only 20 million (15-27) cases may have arisen if levels of travel and contact restrictions remained constant [68].

Work from home

Decreasing infection rates while working from home is immensely effective [69]. A home office is a very effective tool for lowering infection rates: Regions with fewer workers who can work from home due to the nature of their occupation and industry composition have seen higher COVID-19 infection rates and fatalities; the financial costs of confinement are also significantly higher in regions where a smaller percentage of jobs can be done in a home office [70]. The widespread use of WFH practices is shown in the US, where studies reveal that in May 2020, 35.2% of the workforce did so, up from 8.2% in February. Additionally, 71.7% of the workers whom WFH assessed could perform their jobs well [71]. The ability to work from home (WFH) has gained ample significance because it allows workers to continue earning a living, employers to continue providing services and income, and overall reduces the danger of virus spread and pandemic recessive effects [72]. In COVID-19, schools switched to online instruction. The change to online adoption of online learning and teachers' level of comfort with working in a virtual classroom are closely related [73].

Quarantine and self–isolation or physical distancing:

Twenty-four hours following the commencement of symptoms, self-isolation was put into place. Social distancing techniques include wearing masks, maintaining a safe distance from other people, and forbidding trips to hospitals or other facilities [74]. The pandemic curve has been flattened by governments all over the world issuing rules and directives to establish physical distance [75]. Physical separation is a key component of control strategies for COVID-19, although it is uncertain in which situations and for how long physical separation and contact are safe. Regulations that call for a fixed physical separation of 1 or 2 meters between people to minimize the spread of the COVID-19-causing virus SARS-CoV-2 are founded on an outmoded, binary understanding of respiratory droplet size [76]. Physical separation effectively halted the exponential spread of COVID-19 at its inception, avoiding the oversaturation of healthcare personnel and saving many lives, according to multiple studies [77]. Although strictness in policy interventions has gained widespread acceptance, there are differences in how governments respond to policies that call for phased implementation and a reduction in physical distance. Sweden moved quite slowly in its pursuit of voluntarily separating its populations physically. However, stricter guidelines for physical separation were implemented by countries like Germany, South Korea, and Hong Kong, among others [78]. With just over 6,000 confirmed cases as of March 23, the UK Government enacted stringent physical separation policies, ordering people to stay inside and refrain from leaving the house aside from necessary tasks, engage in one form of exercise each day, and purchase necessities like food and medications. This came after the previous week's cancellation of athletic events, schools, restaurants, pubs, gyms, and other places of entertainment or hospitality, as well as a rise in social isolation among the populace that had been going on for a few days before the announcement [79]. MMR vaccination numbers were 19.8% lower (95% CI: 20.7 to 18.9) in the first three weeks of physical separation in England compared to the same time in 2019 [80]. Physical distance can lower the pandemic's death toll. However, it can also come at a high cost to society, as evidenced by the US's sharp declines in GDP and employment in the months after physical distance measures were implemented. This shows that adjusting the degree and timing of physical distance constraints

DOI: https://doi.org/10.54393/pjhs.v4i11.821

might result in significant benefits [81]. Even though physical distancing has significantly disrupted society and economies, it is essential to limit the resurgence in the absence of a viable vaccine [82]. The breathing and coughing simulations indicate a physical distance of 1-2 m to be effective when there is no wind. The physical distance suggestion of 2 m was shown to be ineffective when sneezing was present; rather, a distance of 2.8 m and larger was found to be more beneficial in lowering the exposure to respiratory droplets. In each case, the assessment of the ambient wind conditions called for a greater degree of physical separation. The advice for physical separation was changed from 2 meters to 4.5 meters or more in the situation where respiration was recorded with a soft wind, yielding a gap of 1.1 meters. It was thought to be unhealthy to sneeze when there was a light breeze [83]. The term "self-quarantine" refers to the prohibition on travel for those who are deemed to have been exposed to a contagious disease but are not ill, either because they did not contract the illness or because it is still in the incubation period, which is generally 6.4 days but can range from 2.1 to 11.1 days [84]. A worsened COVID-19 prognosis might result from weight gain via COVID-19 self-quarantine [85]. Being in quarantine is frequently a miserable experience since it can have negative impacts on one's independence, health, and level of boredom. The potential advantages of mandated mass quarantine must be carefully evaluated against any potential long-term detrimental consequences for the burden of cardiovascular risk [86]. Additionally, it might be unpleasant to hear or read about the epidemic nonstop while under quarantine. As a result, stress causes people to overeat, usually turning to sweet "comfort foods [87].

Use of face masks

Face masks are now routinely used in China and other Asian nations, including South Korea and Japan, following the emergence of the Coronavirus disease 2019 (COVID-19), also known as the severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2). In several Chinese provinces and towns, wearing a face mask in public is required [88]. Many specialists cautioned against the general population using facemasks at the start of the pandemic because they believed that there would be hazards associated with doing so, such as the possibility of self-contamination, that outweighed any possible advantages and that widespread usage would deplete the supply needed for healthcare personnel. Then, experts changed their perspective on the possible advantages of masks to include safeguarding people against SARS-CoV-2 infection (source control), much like surgical masks safeguard patients in operating rooms [89]. The use of masks to reduce the transmission of illness has been the subject of several investigations by various academics, technicians, and scientists. The light-scattering experiment is one such investigation that was conducted by scientists from the National Institutes of Health (NIH). In this experiment, researchers illuminated the droplets using lasers and counted them. They also counted the quantities of spit droplets released into the air by people wearing and not wearing face masks [90]. This study shows how the virus spreads through droplets. The fact that a piece of fabric is obstructing the drops is obvious. About half of COVID-19 is spread by people who have no symptoms and are unaware that they are ill. According to this study, COVID-19 can be transmitted by asymptomatic and pre-symptomatic people. These studies highlight the fact that people can spread the virus before they even feel unwell and that donning a mask in public may prevent an infected person from dispersing contagious droplets. The epidemic had an especially big impact on face-to-face contact. Face masks were required as a vital precaution to stop the virus's transmission, but this had a significant negative impact on how people interacted with one another. Facial expressions and gestures greatly aid the conveyance of desired messages and interpersonal communication. Face masks reduced the effect of conveyed content because they made it harder to observe and comprehend others' facial expressions during interactions [91]. Under tidal breathing and coughing situations, medical masks were potentially very successful as both source control and primary prevention in manikin experiments, with better grade masks (such as an N95 respirator vs. a surgical mask) providing more protection [92]. According to research, masks serve two crucial purposes. First, they reduce the amount of quick, turbulent aerosol jets that are directed at people or the environment by preventing the creation of gas clouds during coughing and sneezing. Second, the aerosol is filtered by the layer in the mask, which keeps it from reaching the nasopharynx [93]. When persons are unable to maintain a distance of two meters between them or when they are in an enclosed environment, the Department of Health suggests the use of a cloth face covering and releases patterns so that anyone may make face masks at home and utilize them [94]. A surgical mask is intended to be used just once. Consider the circumstances of usage and integrity, and replace it as soon as it gets wet and no later than every 4 hours at most. The CE (Conformity Europe) certification is required for surgical mask packaging [95]. Regardless of the COVID-19 epidemic, individuals in Japan have a cultural tradition of using surgical masks. Every day, many individuals in Japan use medical masks, especially when the flu is prevalent [96].

DOI: https://doi.org/10.54393/pjhs.v4i11.821

Personnel hygiene

In a medical context, hand hygiene, which includes washing hands with soap and water or using alcohol-based hand sanitizers, is widely acknowledged as the cornerstone of infection control [97]. It is crucial to practice good hand hygiene, and one of the finest suggestions from the WHO is too often wash and sanitize your hands with soap or >60% alcoholic hand sanitizer, respectively. To sensitize hands and lessen coronavirus dissemination and infectivity, which recommended two alcohol-based formulations for hand hygiene in healthcare [98]. When compared to conventional soaps, the use of antibacterial hand soaps results in a quicker decrease in the number of microorganisms. Additionally, alcohol-based sanitizers limit the spread of viruses by precipitating the coronavirus surface proteins that break the chain of transmission. The WHO also advises healthcare workers (HCWs) to use gloves when providing direct patient care during the COVID-19 pandemic. Various polymers, such as latex, nitrile rubber, polyvinyl chloride, polyurethane, and neoprene, are used to make medical gloves [99]. Even in the absence of a worldwide pandemic, the danger of contacting surfaces or items that might recontaminate hands after hand rubbing or washing is often disregarded. This is true whether gloves are used or not. During this pandemic, infection control is crucial, and preventing hand recontamination is crucial to maintaining the safety of patients and HCWs at all times [100].

CONCLUSIONS

In this review paper, we discovered that school closures were the most successful NPIs for preventing the spread of COVID-19, followed by workplace closures, company and venue closures, and public event prohibitions. The number of COVID-19 instances and fatalities can be decreased with an immediate response and a combination of particular social isolation techniques. At the individual level, hygiene precautions like wearing a face mask seem more successful at preventing infection spread. Mass vaccination to achieve herd immunity represents the only long-term intervention to keep illness and mortality rates low because the adverse socioeconomic effects of limiting NPIs at the community level are ultimately unsustainable. Even after receiving the immunization, wearing a face mask is still recommended for personal protection against COVID-19. To adjust decision-making, NPI effectiveness must be continuously monitored.

Authors Contribution

Conceptualization: AS, SM, AQ
Writing-review and editing: MD, SR, AQ, MNA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Macartney K, Quinn HE, Pillsbury AJ, Koirala A, Deng L, Winkler N, *et al*. Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. The Lancet Child & Adolescent Health. 2020 Nov; 4(11): 807-16. doi: 10.1016/S2352-4642(20)30251-0.

[2] Lordan R, FitzGerald GA, Grosser T. Reopening schools during COVID-19. Science. 2020 Sep; 369(6508): 1146-. doi: 10.1126/science.abe5765.

[3] Yuan P, Aruffo E, Gatov E, Tan Y, Li Q, Ogden N, *et al*. School and community reopening during the COVID-19 pandemic: a mathematical modelling study. Royal Society Open Science. 2022 Feb; 9(2): 211883. doi: 10.1098/rsos.211883.

[4] Starr M. Back to school: safe for children with underlying medical conditions. Australian Journal of General Practice. 2020 May; 49(21):1-2. doi: 10.31128/AJGP-COVID-21.

[5] Hirt J, Janiaud P, Hemkens LG. Randomized trials on non-pharmaceutical interventions for COVID-19: a scoping review. BMJ Evidence-Based Medicine. 2022 Dec; 27(6): 334-44. doi: 10.1136/bmjebm-2021-111825.

[6] World Health Organization. Non-pharmaceutical public health measures for mitigating the risk and impact of epidemic and pandemic influenza: annex: report of systematic literature reviews. World Health Organization. 2019. Available at: https://apps.who.int/iris/bitstream/handle/10665/329439/WHO-WHE-IHM-GIP-2019.1-eng.pdf.

[7] Copeland DL, Basurto-Davila R, Chung W, Kurian A, Fishbein DB, Szymanowski P, *et al*. Effectiveness of a school district closure for pandemic influenza A (H1N1) on acute respiratory illnesses in the community: a natural experiment. Clinical Infectious Diseases. 2013 Feb; 56(4): 509-16. doi: 10.1093/cid/cis890.

[8] Esposito S, Cotugno N, Principi N. Comprehensive and safe school strategy during COVID-19 pandemic. Italian Journal of Pediatrics. 2021 Jan; 47(1). doi: 10.1186/s13052-021-00960-6.

[9] Chaabane S, Doraiswamy S, Chaabna K, Mamtani R, Cheema S. The impact of COVID-19 school closure on child and adolescent health: a rapid systematic review. Children. 2021 May; 8(5): 415. doi: 10.3390/children8050415.

DOI: https://doi.org/10.54393/pjhs.v4i11.821

[10] Lo Moro G, Sinigaglia T, Bert F, Savatteri A, Gualano MR, Siliquini R. Reopening schools during the COVID-19 pandemic: Overview and rapid systematic review of guidelines and recommendations on preventive measures and the management of cases. International Journal Of Environmental Research And Public Health. 2020 Dec; 17(23): 8839. doi: 10.3390/ijerph17238839.

[11] Walker PGT, Whittaker C, Watson OJ, Baguelin M, Winskill P, Hamlet A, *et al*. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. Science. 2020 Jul; 369(6502): 413-22. doi: 10.1126/science.abc0035.

[12] Sikakulya FK, Ssebuufu R, Mambo SB, Pius T, Kabanyoro A, Kamahoro E, *et al*. Use of face masks to limit the spread of the COVID-19 among western Ugandans: Knowledge, attitude and practices. PLoS One. 2021 Mar; 16(3): e0248706. doi: 10.1371/journal.pone.0248706.

[13] Vardoulakis S, Oyarce DA, Donner E. Transmission of COVID-19 and other infectious diseases in public washrooms: A systematic review. Science of The Total Environment. 2022 Jan; 803: 149932. doi: 10.1016/j.scitotenv.2021.149932.

[14] World Health Organization WHO. Key messages and actions for COVID-19 prevention and control in schools. 2020. [Last Cited: 12th Jun 2023]. Available at: https://www.who.int/docs/default-source/coronaviruse/key-messages-and-actions-for-covid-19-prevention-and-control-in-schools-march-2020.pdf.

[15] Kumar V, Alshazly H, Idris SA, Bourouis S. Evaluating the impact of covid-19 on society, environment, economy, and education. Sustainability. 2021 Dec; 13(24): 13642. doi: 10.3390/su132413642.

[16] Walger P, Heininger U, Knuf M, Exner M, Popp W, Fischbach T, *et al*. Children and adolescents in the CoVid-19 pandemic: Schools and daycare centers are to be opened again without restrictions. The protection of teachers, educators, carers and parents and the general hygiene rules do not conflict with this. GMS Hygiene and Infection Control. 2020 Dec; 15: 1-18.

[17] Gostin LO and Wiley LF. Governmental public health powers during the COVID-19 pandemic: stay-at-home orders, business closures, and travel restrictions. Jama. 2020 Jun; 323(21): 2137-8. doi: 10.1001/jama.2020.5460.

[18] Song H, McKenna R, Chen AT, David G, Smith-McLallen A. The impact of the non-essential business closure policy on Covid-19 infection rates. International Journal of Health Economics and Management. 2021 Dec; 21: 1-40. doi: 10.3386/w28374.

[19] Chum A, Nielsen A, Bellows Z, Farrell E, Durette PN, Banda JM, *et al*. Changes in public response associated with various COVID-19 restrictions in Ontario, Canada: observational infoveillance study using social media time series data. Journal of Medical Internet Research. 2021 Aug; 23(8): e28716. doi: 10.2196/28716.

[20] Kim OS, Parker JA, Schoar A. Revenue collapses and the consumption of small business owners in the early stages of the COVID-19 pandemic. National Bureau of Economic Research. 2020 Nov: 1-56. doi: 10.3386/w28151.

[21] Tkach DV, Kurpayanidi KI. Some Questions About The Impact Of The Covid-19 Pandemic On The Development Of Business Entities. Theoretical & Applied Science. 2020 Nov; 11(91): 1-4. doi: 10.15863/TAS.2020.11.91.1.

[22] Zamanzadeh A and Cavoli T. The effect of nonpharmaceutical interventions on COVID-19 infections for lower and middle-income countries: A debiased LASSO approach. PLoS One. 2022 Jul; 17(7): e0271586. doi: 10.1371/journal.pone.0271586.

[23] Angelucci M, Angrisani M, Bennett DM, Kapteyn A, Schaner SG. Remote work and the heterogeneous impact of COVID-19 on employment and health. National Bureau of Economic Research; 2020 Aug: 1-34. doi: 10.3386/w27749.

[24] Fabeil NF, Pazim KH, Langgat J. The impact of Covid-19 pandemic crisis on micro-enterprises: Entrepreneurs' perspective on business continuity and recovery strategy. Journal of Economics and Business. 2020 May 28;3(2): 1-9. doi: 10.31014/aior.1992.03.02.241.

[25] Janiszewska D, Hannevik Lien V, Kloskowski D, Ossowska L, Dragin-Jensen C, Strzelecka M, *et al*. Effects of COVID-19 infection control measures on the festival and event sector in Poland and Norway. Sustainability. 2021 Nov; 13(23): 13265. doi: 10.3390/su132313265.

[26] Deb P, Furceri D, Ostry JD, Tawk N. The economic effects of COVID-19 containment measures. Open Economies Review. 2022 Feb; 33(1): 1-32. doi: 10.1007/s11079-021-09638-2.

[27] Gössling S, Scott D, Hall CM. Pandemics, tourism and global change: a rapid assessment of COVID-19. Journal of Sustainable Tourism. 2020 Oct; 29(1): 1-20. doi: 10.1080/09669582.2020.1758708.

[28] Hoang VT, Gautret P, Memish ZA, Al-Tawfiq JA. Hajj and Umrah mass gatherings and COVID-19 infection. Current Tropical Medicine Reports. 2020 Dec; 7: 133-

DOI: https://doi.org/10.54393/pjhs.v4i11.821

40. doi: 10.1007/s40475-020-00218-x.
[29] Memish ZA, Ahmed Y, Alqahtani SA, Ebrahim SH. Pausing superspreader events for COVID-19 mitigation: International Hajj pilgrimage cancellation. Travel Medicine and Infectious Disease. 2020 Jul; 36: 101817. doi: 10.1016/j.tmaid.2020.101817.
[30] Heese H, Marquis A, Diercke M, Markus I, Böhm S, Metz J, *et al*. Results of the enhanced COVID-19 surveillance during UEFA EURO 2020 in Germany. Epidemiology & Infection. 2022 Mar; 150:1-. doi: 10.1017/S0950268822000449.
[31] Alahmari AA, Khan AA, Alamri FA, Almuzaini YS, Habash AK, Jokhdar H. Healthcare policies, precautionary measures and outcomes of mass gathering events in the era of COVID-19 pandemic: Expedited review. Journal of Infection and Public Health. 2023 Mar: 1-7. doi: 10.1016/j.jiph.2023.03.026.
[32] Che Mat NF, Edinur HA, Abdul Razab MK, Safuan S. A single mass gathering resulted in massive transmission of COVID-19 infections in Malaysia with further international spread. Journal of Travel Medicine. 2020 Apr; 27(3): taaa059. doi: 10.1093/jtm/taaa059.
[33] Brown CM, Vostok J, Johnson H, Burns M, Gharpure R, Sami S, *et al*. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. Morbidity and Mortality Weekly Report. 2021 Aug; 70(31): 1059. doi: 10.15585/mmwr.mm7031e2.
[34] Ebrahim SH and Memish ZA. COVID-19–the role of mass gatherings. Travel Medicine and Infectious Disease. 2020 Mar; 34: 101617. doi: 10.1016/j.tmaid.2020.101617.
[35] Toresdahl BG and Asif IM. Coronavirus Disease 2019 (COVID-19): Considerations for the Competitive Athlete. Sports Health. 2020 May; 12(3): 221-4. doi: 10.1177/1941738120918876.
[36] Delaugerre C, Foissac F, Abdoul H, Masson G, Choupeaux L, Dufour E, *et al*. Prevention of SARS-CoV-2 transmission during a large, live, indoor gathering (SPRING): a non-inferiority, randomised, controlled trial. The Lancet Infectious Diseases. 2022 Mar; 22(3): 341-8. doi: 10.1016/S1473-3099(21)00673-3.
[37] Alfano V and Ercolano S. The efficacy of lockdown against COVID-19: a cross-country panel analysis. Applied Health Economics and Health Policy. 2020 Aug; 18: 509-17. doi: 10.1007/s40258-020-00596-3.
[38] Ambikapathy B and Krishnamurthy K. Mathematical modelling to assess the impact of lockdown on COVID-19 transmission in India: Model development and validation. JMIR Public Health and Surveillance. 2020 May; 6(2): e19368. doi: 10.2196/19368.
[39] Sheikh A, Sheikh A, Sheikh Z, Dhami S. Reopening schools after the COVID-19 lockdown. Journal of Global Health. 2020 Jun; 10(1): 010376. doi: 10.7189/jogh.10.010376.
[40] Paital B, Das K, Parida SK. Inter nation social lockdown versus medical care against COVID-19, a mild environmental insight with special reference to India. Science of the Total Environment. 2020 Aug;728: 138914. doi: 10.1016/j.scitotenv.2020.138914.
[41] Lau H, Khosrawipour V, Kocbach P, Mikolajczyk A, Schubert J, Bania J, *et al*. The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China. Journal of travel medicine. 2020 May; 27(3): 1-7. doi: 10.1093/jtm/taaa037.
[42] Ali G, Abbas S, Qamer FM, Wong MS, Rasul G, Irteza SM, *et al*. Environmental impacts of shifts in energy, emissions, and urban heat island during the COVID-19 lockdown across Pakistan. Journal of Cleaner Production. 2021 Apr; 291: 125806. doi: 10.1016/j.jclepro.2021.125806.
[43] Stiegler N and Bouchard JP. South Africa: Challenges and successes of the COVID-19 lockdown. InAnnales Médico-psychologiques, revue psychiatrique. Elsevier Masson. 2020 Sep; 178(7): 695-8. doi: 10.1016/j.amp.2020.05.006.
[44] Moris D and Schizas D. Lockdown during COVID-19: the Greek success. in vivo. 2020 Jun; 34(3 suppl): 1695-9. doi: 10.21873/invivo.11963.
[45] Grover S, Mehra A, Sahoo S, Avasthi A, Tripathi A, D'Souza A, *et al*. State of mental health services in various training centers in India during the lockdown and COVID-19 pandemic. Indian Journal of Psychiatry. 2020 Jul; 62(4): 363. doi: 10.4103/psychiatry.IndianJPsychiatry_567_20.
[46] Khan I, Shah D, Shah SS. COVID-19 pandemic and its positive impacts on environment: an updated review. International Journal of Environmental Science and Technology. 2021 Feb; 18: 521-30. doi: 10.1007/s13762-020-03021-3.
[47] Coccia M. The relation between length of lockdown, numbers of infected people and deaths of Covid-19, and economic growth of countries: Lessons learned to cope with future pandemics similar to Covid-19 and to constrain the deterioration of economic system. Science of The Total Environment. 2021 Jun; 775: 145801. doi: 10.1016/j.scitotenv.2021.145801.
[48] Allen DW. Covid-19 lockdown cost/benefits: A critical assessment of the literature. International Journal of the Economics of Business. 2022 Jan; 29(1): 1-32. doi:

DOI: https://doi.org/10.54393/pjhs.v4i11.821

10.1080/13571516.2021.1976051.

[49] Muhammad S, Long X, Salman M. COVID-19 pandemic and environmental pollution: A blessing in disguise?. Science of the Total Environment. 2020 Aug; 728: 138820. doi: 10.1016/j.scitotenv.2020.138820.

[50] Vultaggio M, Varrica D, Alaimo MG. Impact on air quality of the covid-19 lockdown in the urban area of palermo (Italy). International Journal of Environmental Research and Public Health. 2020 Oct; 17(20): 7375.0 doi: 10.3390/ijerph17207375.

[51] Baldasano JM. COVID-19 lockdown effects on air quality by NO2 in the cities of Barcelona and Madrid (Spain). Science of the Total Environment. 2020 Nov; 741: 140353. doi: 10.1016/j.scitotenv.2020.140353.

[52] Mzoughi H, Urom C, Uddin GS, Guesmi K. The effects of COVID-19 pandemic on oil prices, CO 2 emissions and the stock market: Evidence from a VAR model. 2020 Apr: 1-8. doi: 10.2139/ssrn.3587906.

[53] Murano Y, Ueno R, Shi S, Kawashima T, Tanoue Y, Tanaka S, *et al*. Impact of domestic travel restrictions on transmission of COVID-19 infection using public transportation network approach. Scientific Reports. 2021 Feb; 11(1): 1-9. doi: 10.1038/s41598-021-81806-3.

[54] Sharun K, Tiwari R, Natesan S, Yatoo MI, Malik YS, Dhama K. International travel during the COVID-19 pandemic: implications and risks associated with 'travel bubbles'. Journal of Travel Medicine. 2020 Dec; 27(8): taaa184. doi: 10.1093/jtm/taaa184.

[55] Chinazzi M, Davis JT, Ajelli M, Gioannini C, Litvinova M, Merler S, *et al*. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. Science. 2020 Apr; 368(6489): 395-400. doi: 10.1126/science.aba9757.

[56] Suzumura T, Kanezashi H, Dholakia M, Ishii E, Napagao SA, Pérez-Arnal R, *et al*. The impact of COVID-19 on flight networks. In2020 ieee international conference on big data (big data). IEEE. 2020 Dec: pp. 2443-52. doi: 10.1109/BigData50022.2020.9378218.

[57] Liebig J, Najeebullah K, Jurdak R, Shoghri AE, Paini D. Should international borders re-open? The impact of travel restrictions on COVID-19 importation risk. BMC Public Health. 2021 Dec; 21: 1-9. doi: 10.1186/s12889-021-11616-9.

[58] Keita S. Air passenger mobility, travel restrictions, and the transmission of the covid-19 pandemic between countries. Covid Economics. 2020 Apr; 9: 77-96.

[59] Zhu P and Tan X. Evaluating the effectiveness of Hong Kong's border restriction policy in reducing COVID-19 infections. BMC Public Health. 2022 Dec; 22(1): 1-9. doi: 10.1186/s12889-022-13234-5.

[60] Grépin KA, Ho TL, Liu Z, Marion S, Piper J, Worsnop CZ, *et al*. Evidence of the effectiveness of travel-related measures during the early phase of the COVID-19 pandemic: a rapid systematic review. BMJ Global Health. 2021 Mar; 6(3): e004537. doi: 10.1136/bmjgh-2020-004537.

[61] Russell TW, Wu JT, Clifford S, Edmunds WJ, Kucharski AJ, Jit M. Effect of internationally imported cases on internal spread of COVID-19: a mathematical modelling study. The Lancet Public Health. 2021 Jan; 6(1): e12-20. doi: 10.1016/S2468-2667(20)30263-2.

[62] Girum T, Lentiro K, Geremew M, Migora B, Shewamare S, Shimbre MS. Optimal strategies for COVID-19 prevention from global evidence achieved through social distancing, stay at home, travel restriction and lockdown: a systematic review. Archives of Public Health. 2021 Aug; 79(1): 150. doi: 10.1186/s13690-021-00663-8.

[63] Rahman MM, Thill JC, Paul KC. COVID-19 pandemic severity, lockdown regimes, and people's mobility: Early evidence from 88 countries. Sustainability. 2020 Nov; 12(21): 9101. doi: 10.3390/su12219101.

[64] Anzai A, Kobayashi T, Linton NM, Kinoshita R, Hayashi K, Suzuki A, *et al*. Assessing the impact of reduced travel on exportation dynamics of novel coronavirus infection (COVID-19). Journal of Clinical Medicine. 2020 Feb; 9(2): 601. doi: 10.3390/jcm9020601.

[65] Zhang Z, Fu D, Liu F, Wang J, Xiao K, Wolshon B. COVID-19, traffic demand, and activity restriction in China: A national assessment. Travel Behaviour and Society. 2023 Apr; 31: 10-23. doi: 10.1016/j.tbs.2022.11.001.

[66] Quilty BJ, Diamond C, Liu Y, Gibbs H, Russell TW, Jarvis CI, *et al*. The effect of travel restrictions on the geographical spread of COVID-19 between large cities in China: a modelling study. BMC Medicine. 2020 Aug; 18(1): 259. doi: 10.1101/2020.04.16.20067504.

[67] Bielecki M, Patel D, Hinkelbein J, Komorowski M, Kester J, Ebrahim S, *et al*. Reprint of: Air travel and COVID-19 prevention in the pandemic and peri-pandemic period: A narrative review. Travel Medicine and Infectious Disease. 2020 Nov; 38: 101939. doi: 10.1016/j.tmaid.2020.101939.

[68] Lai S, Ruktanonchai NW, Carioli A, Ruktanonchai CW, Floyd JR, Prosper O, *et al*. Assessing the effect of global travel and contact restrictions on mitigating the COVID-19 pandemic. Engineering. 2021 Jul; 7(7): 914-23. doi: 10.1016/j.eng.2021.03.017.

[69] Fadinger H and Schymik J. The effects of working

DOI: https://doi.org/10.54393/pjhs.v4i11.821

from home on covid-19 infections and production a macroeconomic analysis for germany. Covid Economics. 2020 Apr; 9(24): 107-39.

[70] Morikawa M. Productivity of working from home during the COVID-19 pandemic: Evidence from an employee survey. Covid Economics. 2020 Sep; 49: 123-39.

[71] Vyas L and Butakhieo N. The impact of working from home during COVID-19 on work and life domains: an exploratory study on Hong Kong. Policy Design and Practice. 2021 Jan; 4(1): 59-76. doi: 10.1080/25741292.2020.1863560.

[72] Bonacini L, Gallo G, Scicchitano S. Working from home and income inequality: risks of a 'new normal'with COVID-19. Journal of Population Economics. 2021 Jan; 34(1): 303-60. doi: 10.1007/s00148-020-00800-7.

[73] Almazova N, Krylova E, Rubtsova A, Odinokaya M. Challenges and opportunities for Russian higher education amid COVID-19: Teachers' perspective. Education Sciences. 2020 Dec; 10(12): 368. doi: 10.3390/educsci10120368.

[74] Nader IW, Zeilinger EL, Jomar D, Zauchner C. Onset of effects of non-pharmaceutical interventions on COVID-19 infection rates in 176 countries. BMC Public Health. 2021 Dec; 21(1): 1-7. doi: 10.1186/s12889-021-11530-0.

[75] Tria JZ. The COVID-19 pandemic through the lens of education in the Philippines: The new normal. International Journal of Pedagogical Development and Lifelong Learning. 2020 May; 1(1): 2-4. doi: 10.30935/ijpdll/8311.

[76] Jones NR, Qureshi ZU, Temple RJ, Larwood JP, Greenhalgh T, Bourouiba L. Two metres or one: what is the evidence for physical distancing in covid-19? BMJ. 2020 Aug; 370: m3223. doi: 10.1136/bmj.m3223.

[77] Gollwitzer A, Martel C, Brady WJ, Pärnamets P, Freedman IG, Knowles ED, *et al*. Partisan differences in physical distancing are linked to health outcomes during the COVID-19 pandemic. Nature Human Behaviour. 2020 Nov; 4(11): 1186-97. doi: 10.1038/s41562-020-00977-7.

[78] Vaid S, McAdie A, Kremer R, Khanduja V, Bhandari M. Risk of a second wave of Covid-19 infections: using artificial intelligence to investigate stringency of physical distancing policies in North America. International Orthopaedics. 2020 Aug; 44: 1581-9. doi: 10.1007/s00264-020-04653-3.

[79] Jarvis CI, Van Zandvoort K, Gimma A, Prem K, Klepac P, Rubin GJ, *et al*. Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK. BMC Medicine. 2020 Dec; 18(1): 1-10. doi: 10.1186/s12916-020-01597-8.

[80] McDonald HI, Tessier E, White JM, Woodruff M, Knowles C, Bates C, *et al*. Early impact of the coronavirus disease (COVID-19) pandemic and physical distancing measures on routine childhood vaccinations in England, January to April 2020. Eurosurveillance. 2020 May; 25(19): 2000848. doi: 10.2807/1560-7917.ES.2020.25.19.2000848.

[81] Newbold SC, Finnoff D, Thunström L, Ashworth M, Shogren JF. Effects of physical distancing to control COVID-19 on public health, the economy, and the environment. Environmental and Resource Economics. 2020 Aug; 76: 705-29. doi: 10.1007/s10640-020-00440-1.

[82] Huang B, Wang J, Cai J, Yao S, Chan PK, Tam TH, *et al*. Integrated vaccination and physical distancing interventions to prevent future COVID-19 waves in Chinese cities. Nature Human Behaviour. 2021 Jun; 5(6): 695-705. doi: 10.1038/s41562-021-01063-2.

[83] Chea B, Bolt A, Agelin-Chaab M, Dincer I. Assessment of effectiveness of optimum physical distancing phenomena for COVID-19. Physics of Fluids. 2021 May; 33(5): 051903. doi: 10.1063/5.0046429.

[84] Suppawittaya P, Yiemphat P, Yasri P. Effects of social distancing, self-quarantine and self-isolation during the COVID-19 pandemic on people's well-being, and how to cope with it. International Journal of Science and Healthcare Research. 2020 Jun; 5(2): 12-20.

[85] Zeigler Z. COVID-19 self-quarantine and weight gain risk factors in adults. Current Obesity Reports. 2021 Sep; 10: 423-33. doi: 10.1007/s13679-021-00449-7.

[86] Mattioli AV, Ballerini Puviani M, Nasi M, Farinetti A. COVID-19 pandemic: the effects of quarantine on cardiovascular risk. European Journal of Clinical Nutrition. 2020 Jun; 74(6): 852-5. doi: 10.1038/s41430-020-0646-z.

[87] Wang Y, Shi L, Que J, Lu Q, Liu L, Lu Z, *et al*. The impact of quarantine on mental health status among general population in China during the COVID-19 pandemic. Molecular Psychiatry. 2021 Sep; 26(9): 4813-22. doi: 10.1038/s41380-021-01019-y.

[88] Feng S, Shen C, Xia N, Song W, Fan M, Cowling BJ. Rational use of face masks in the COVID-19 pandemic. The Lancet Respiratory Medicine. 2020 May; 8(5): 434-6. doi: 10.1016/S2213-2600(20)30134-X.

[89] Schünemann HJ, Akl EA, Chou R, Chu DK, Loeb M, Lotfi T, *et al*. Use of facemasks during the COVID-19 pandemic. The Lancet Respiratory Medicine. 2020 Oct; 8(10): 954-5. doi: 10.1016/S2213-2600(20)30352-0.

[90] Kantrowitz-Gordon I. A New Normal After the COVID-19 Pandemic. Journal of Midwifery & Women's

DOI: https://doi.org/10.54393/pjhs.v4i11.821

Health. 2021 May; 66(3): 293. doi: 10.1111/jmwh.13247.
[91] Mheidly N, Fares MY, Zalzale H, Fares J. Effect of face masks on interpersonal communication during the COVID-19 pandemic. Frontiers in Public Health. 2020 Dec; 8: 582191. doi: 10.3389/fpubh.2020.582191.
[92] Eikenberry SE, Mancuso M, Iboi E, Phan T, Eikenberry K, Kuang Y, *et al*. To mask or not to mask: Modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic. Infectious Disease Modelling. 2020 Jan; 5: 293-308. doi: 10.1016/j.idm.2020.04.001.
[93] Karmacharya M, Kumar S, Gulenko O, Cho YK. Advances in facemasks during the COVID-19 pandemic era. ACS Applied Bio Materials. 2021 Jan; 4(5): 3891-908. doi: 10.1021/acsabm.0c01329.
[94] O'Dowd K, Nair KM, Forouzandeh P, Mathew S, Grant J, Moran R, *et al*. Face masks and respirators in the fight against the COVID-19 pandemic: A review of current materials, advances and future perspectives. Materials. 2020 Jul; 13(15): 3363. doi: 10.3390/ma13153363.
[95] Lepelletier D, Grandbastien B, Romano-Bertrand S, Aho S, Chidiac C, Géhanno JF, *et al*. What face mask for what use in the context of the COVID-19 pandemic? The French guidelines. Journal of Hospital Infection. 2020 Jul; 105(3): 414-8. doi: 10.1016/j.jhin.2020.04.036.
[96] Matusiak Ł, Szepietowska M, Krajewski P, Białynicki-Birula R, Szepietowski JC. Inconveniences due to the use of face masks during the COVID-19 pandemic: a survey study of 876 young people. Dermatologic Therapy. 2020 Jul; 33(4): e13567. doi: 10.1111/dth.13567.
[97] Roshan R, Feroz AS, Rafique Z, Virani N. Rigorous hand hygiene practices among health care workers reduce hospital-associated infections during the COVID-19 pandemic. Journal of Primary Care & Community Health. 2020 Jul; 11: 2150132720943331. doi: 10.1177/2150132720943331.
[98] Mahmood A, Eqan M, Pervez S, Alghamdi HA, Tabinda AB, Yasar A, *et al*. COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. Science of the Total Environment. 2020 Nov; 742: 140561. doi: 10.1016/j.scitotenv.2020.140561.
[99] Tabary M, Araghi F, Nasiri S, Dadkhahfar S. Dealing with skin reactions to gloves during the COVID-19 pandemic. Infection Control & Hospital Epidemiology. 2021 Feb; 42(2): 247-8. doi: 10.1017/ice.2020.212.
[100] Gon G, Dancer S, Dreibelbis R, Graham WJ, Kilpatrick C. Reducing hand recontamination of healthcare workers during COVID-19. Infection Control & Hospital Epidemiology. 2020 Jul; 41(7): 870-1. doi: 10.1017/ice.2020.111.

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Review Article

A Narrative Review on Management of Cyanosis in Neonates

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ARTICLE INFO

Key Words:
Cyanosis, Etiology, Evaluation, Management

How to Cite:
Fayyaz, M., & Shahbaz, S. (2023). A Narrative Review on Management of Cyanosis in Neonates: Management of Cyanosis in Neonates. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1106

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Received Date: 10th September, 2023
Acceptance Date: 5th November, 2023
Published Date: 30th November, 2023

ABSTRACT

A bluish coloring of the skin or mucous membrane that is characteristic of the medical condition cyanosis can be visible around the lips, fingers, and toes. It is one of the indications of respiratory distress in infants that can be brought on by inadequate circulation and low levels of oxygenated blood. There are two basic causes of cyanosis, cardiac and pulmonary. Medical professionals are constantly very concerned about accurately diagnosing and treating newborns with congenital heart disease (CHD), despite the fact that prenatal diagnostic methods have significantly improved. Although they are physiologically entirely different from one another, ductus dependent congenital cardiac abnormalities can be divided into the ductus dependent systemic or pulmonary sickness. When developing the treatment plan, the clinical state and cardiac abnormalities must be taken into consideration. Many life-threatening conditions may not show signs right away after delivery, and the majority of clinical and physical symptoms are ambiguous, which makes a diagnosis difficult. Careful evaluation is required, and when clinical data, electrocardiograms, and chest X-rays are used. The newborn must be identified as being at such high risk right once, and prompt medical attention is essential to reducing mortality and morbidity.

INTRODUCTION

Cyanosis is a bluish-purple blotch confined to the skin, for instance the area around the lips fingers and toes. When the actual amount of reduced hemoglobin in the capillaries exceed 3g/dl cyanosis develops [1]. Cyanosis is one of the most prominent indicators of newborn respiratory distress. Most of the research point out that if a baby's skin or lips becomes blue, it is most often related with lack of deoxygenation of blood that leading to hypoxia. In this condition, the apparent color of the blood goes from a brilliant red to a darker blue [2]. The main oxygen messenger in the blood is hemoglobin, which consist of four smaller components two alpha and beta polypeptide chain. Iron containing heme group is situated in the center. The potential of the blood to deliver oxygen is seriously hampered by presence of aberrant hemoglobin. This may develop tissue hypoxia, which may be clinically observed as cyanosis [3]. Although the oxygen level improved about 85-95% within 10 minutes of delivery, newborns generally experience central cyanosis after childbirth. So this should be treated and assessed as early as possible. This can be associated with potentially fatal illness due to cardiac, infectious, metabolic, parenchymal and non-parenchymal disease [4]. Central, peripheral, differential and acrocyanosis are four basic types of cyanosis. Central cyanosis causes mucosal layers to prominently turn blue-purple as a result of low level of oxygen in the blood, as a consequence of circumstances that increase the amount of deoxygenated Hb or divergent Hb. Peripheral cyanosis is a condition in which extremities develop a distinctive bluish contusion on the distal extremities because they are

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

not receiving enough oxygenated blood. Peripheral cyanosis is rarely serious medical condition. Differential cyanosis causes the hands and feet to turn blue in color that is unsymmetrical. It usually means that there are substantial underlying cardiopulmonary diseases [5]. Acrocyanosis often seen surrounding the lips or upper and lower limbs, commonly occurring in healthy neonates. It is a gentle disorder produced by vasomotor alterations that can cause vasoconstriction and enriched tissue oxygen extraction [6]. Cyanosis typically happens when Hb has very minimal amount of oxygen. There are two physical conditions in which oxygen is transported in the blood. Only 2% of the total oxygen carried in the blood is dissolved directly in the plasma; the majority, around 98%, is linked to hemoglobin [7]. Absence of adequate oxygen supply to the peripheral tissues might be identified by the appearance of cyanosis. The higher oxygen intake by peripheral tissues possibly a contributing factor. Several factors are crucial for the transportation of oxygen to the internal organs. The amount of the oxygen delivered depends on heart rate and arterial oxygen level. The preload, after-load and contractility are factors that affects heart rate. High level of deoxygenated Hb probably makes cyanosis highly visible. Jaundice, skin tone, the environment, or lighting may influence the detection of cyanosis. Anemia or polycythemia can have a significant impact on cyanosis. When Hb concentration is insufficient, it is more complicated to detect cyanosis. In other word, in a patient with severe anemia, cyanosis cannot be made clinically visible [8]. A comprehensive clinical assessment and detailed history help the doctor to diagnose the cause of the cyanosis. The clinical indications are verified by laboratory test reports such as CBC, pulse oximetry, chest radiography, arterial blood gas and echo-cardiographs [9].

Etiology

Heart failure, genetically inherited heart disease (right-to-left shunting), and valvular heart disorder, for example, complete transposition of the great arteries (TGA), coarctation of the aorta (CoA), critical pulmonary and aortic valvular stenosis/atresia, tricuspid atresia (TA), hypoplastic left heart syndrome (HLHS), arterial septal defect (ASD), patent ductus arteriosus (PDA) might be unnoticed for a long time before manifesting as severe acidosis, cyanosis, shock, or death. Chronic heart diseases are categorized into two types: ductus dependent cardiac lesions and non-ductus dependent cardiac lesions [10]. The predominance of congenital cardiac abnormalities are involved in 10% of all occurrences of cyanosis in children over the age of one year. Fallot syndrome is characterized by four defects: right ventricular hypertrophy, ventricular septal defect, pulmonary stenosis, and aortic dextroposition [11]. Respiratory depression can arise as a result of a central nervous system illness. There is acute alveolar hypoventilation when central nervous system illness manifests as cyanosis [12]. A temperature less than 36.5C is normally referred as neonatal hypothermia, it is correlated with neonatal mortality and morbidity especially in premature and low birth weight babies. Hypothermia is infrequently a direct cause of death. It also does play a significant role in mortality due to asphyxia, prematurity, infection as well as intraventricular hemorrhage [13]. In polycythemia and hyper viscosity blood flow reduced in brain, lungs, heart and intestine. Although renal plasma is impacted, there is no reduction in renal blood flow, which lowers glomerular filtration rate. A higher arterial oxygen content is associated with higher Hb and hematocrit levels. The higher arterial oxygen content, not hyper viscosity, is fully responsible for the diminished blood flow to the brain and heart [14]. Hyperventilation, COPD (chronic obstructed pulmonary disease), bronchiolitis, bronchospasm, and pulmonary hypertension are a few examples of pulmonary illnesses that are indicated by poor alveolar-arterial diffusion and ventilation perfusion mismatches [15]. When pulmonary vascular resistances (PVR) leftover excessively high after birth, blood shunts right to left across fetal circulatory pathway that provoke persistent pulmonary hypertension in a newborn (PPHN). As a consequence, severe hypoxia develops that may or may not response to conventional respiratory support in a newborn. PPHN is expected to impact 1.9 per 1000 live births [16]. Three main categories can be used to classify the reason of persistent pulmonary hypertension in newborn PPHN. The most common form of PPHN is driven by parenchymal disorders such as pneumonia, severe respiratory distress syndrome, and meconium aspiration syndrome (MAS). This is mostly caused by inadequate entry into the alveolar space, especially in cases of MAS with airway obstruction. PPHN patients with congenital hernia have decrease blood vessel thickness, a smaller cross- section of the pulmonary vasculature and higher pulmonary vascular resistance [17]. When the iron in hemoglobin transforms from Fe^{2+} to Fe^{3+} state, it results in methemoglobinemia, a disorder that leads to congenital acquired cyanosis. In this condition only 2 percent hemoglobin is present. The skin tone might be taken on a bluish tinge when methemoglobin is present. This disorder can brought on by contact with the topical anesthetic such as dapsone, nitroglycerine or other strong oxidizing substances. Genetically inherited methemoglobinemia type I or II is caused by a mutagenicity in the gene encoding the cytochrome b5 reductase enzyme. This ailment does not occur frequently. When cytochrome b5 reductase is not enzymatically active, methemoglobin reduction is restricted [18]. Peripheral cyanosis can be caused by a variety of factors, including heart failure and

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

shock, benign vasoconstriction caused on by cold exposure, and regional ischemia from arterial blockage brought on by peripheral vascular disease [19]. Peripheral cyanosis occurs when the body continues to fail providing oxygen-rich blood to the peripheral tissues. Vasoconstriction induces ischemic peripheral cyanosis by reducing blood flow to the extremities. During peripheral cyanosis, arterial saturation is completely natural; but, due to vascular constriction and decreased blood flow, the peripheral tissues in the capillary receive more oxygen. Since there is more de-oxygenated blood on the venous side of the capillary bed, there seems to be a significant difference in saturation between venous and arterial blood [20].

Evaluation

The evaluation should be carefully done by examining the infant's airways, lungs and heart. Risk factors for pregnancy, labor pains and the birth of the baby should be assessed as the part of history. Maternal diabetes increases the chance of polycythemia, which can cause respiratory distress as well as congenital heart problems. Polyhydramnios may signify bronchial, esophageal or neurological disorders and the occurrence of oligohydramnios may reveal renal issues linked to hypoplastic lungs. It is essential to keep in consideration that infection is still possible even if the prenatal culture for group B streptococcus was negative when examining for reports findings for cervical infection. A history of complicated birth may produce cerebral bleeding or phrenic nerve paralysis [21]. Clinical diagnosis should be done once the infant has prepped. It is important to monitor the growth parameters of the infant because babies who are large or little according to the weeks of pregnancy are at a higher risk of developing polycythemia. Common indications of respiratory insufficiency are pulmonary disease including meconium aspiration, persistent pulmonary hypertension, fast breathing, retractions and nasal flaring [22]. Because of hypoventilation, neurologic disorders are possible potential reason of cyanosis and may be associated with lethargic or irregular breathing rate. Additionally it is crucial to assess the infant's activity, tone and irregular respiration. An Erb's palsy or harsh cry are instance of birth trauma signs that may be identified during assessment [23]. The newborn's oxygenation and pulse rate must be closely monitored during the cardiac assessment. The S2 heart sound, which will be continuous and narrow split in pulmonary hypertension, transposition, and pulmonary atresia, should be the major focus of heart auscultation [24]. Blood oxygenation refers to the amount of hemoglobin that has been chemically bonded with oxygen, or the fraction of blood containing oxygen. An ideal non-surgical and persistent method of measuring oxygen saturation is pulse oximetry. The first finger of the right hand should be used for pulse oximetry. In many micro sample blood gas analyzers, the examination of lactate now gives additional, crucial data on global perfusion and oxygenation [25]. A chest X-ray is a crucial aspect of assessment of the baby with cyanotic CHD. In order to find out situs inversus and dextrocardia, the placements of the stomach, liver, and heart should be recognized. While investigating the lungs, one might identify parenchymal lungs illness or abnormalities including cystic adenomatous malformation. Any hemi-diaphragm that is inflated more than two intercostal spaces may be an indication of phrenic nerve damage related to diaphragmatic paralysis. Frequently, lobar emphysema appear with hyper inflated lungs field. Reduced pulmonary vascular markings are a sign of pulmonary stenosis or pulmonary atresia with inappropriate ductal shunting in infants with idiopathic severe pulmonary hypertension. Certain medical signals can be provided by the size and form of the heart, such as the TOF (boot shape) heart, the impression of transposition (like an egg on a string), and the recognizable massive cardiomegaly of Ebstein's anomaly (Figure 1) [26]. Evaluation of newborns with significant conditions like transposition usually benefits from an ECG. A notable example is a newborn with left axis deviation induced by left ventricular hypertrophy [27]. When medical findings is combined with ECG and chest X-ray (CXR) readings, it is typically easy to distinguish between a cardiac and respiratory cause of cyanosis. Unfortunately, some problems remain tough, and in these cases, a hyperoxia test may be useful. Instead of a pulse oximeter, ABG (arterial blood gas) testing should be employed for this test. At room temperature, ABGs are commonly done through the right radial artery. After 10 minutes of 100% oxygen levels, the ABG is performed. Partial pressure of oxygen should raise greatly in the absence of a left-to-right shunt [28].

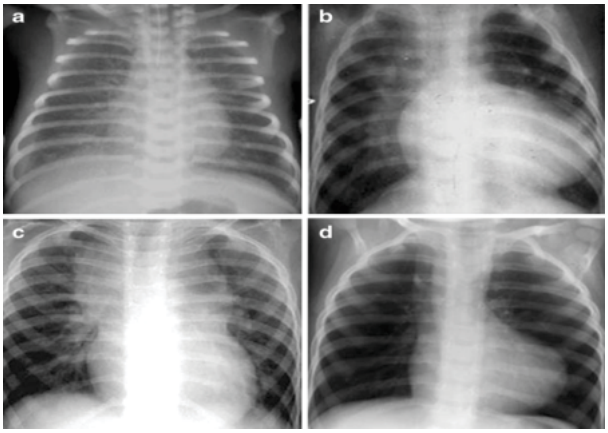

Figure 1: Chest X-ray in numerous cases of cyanotic CHD, **A:**

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

Occluded TAPVC showing no cardiomegaly and extreme pulmonary veins high blood pressure, **B:** Harmonic progression of Great Arteries- cardiac hypertrophy, narrow pedicle with pulmonary plethora, e.g., egg on side elegance, **C:** Supra cardiac TAPVC characteristic snowman look, and **D:** Tetralogy of Fallot, no cardiomegaly, oligemic[26].

Management

Complete transposition of the great arteries (TGA)

The procedure often used for cure of TGA is termed as balloon arterial septostomy. In this procedure, medical specialist inserts a device with a balloon tip into left atrium through the oval fossa. To rupture the fragile atrial septum, the balloon is inflated and dragged back into the right atrium. For this treatment to be effective, the final ASD (atrial septal defect) width must exceed than 5 mm, along with an improvement in O_2 concentration. This method is efficient for developing reliable inter-atrial connectivity. High oxygen rates should be resisted because they can induce ductal closer, have a negative effect on inter-circulatory mixing, and also cause intense alveolar inflation when used with an extremely high ventilator mode like, positive inspiratory pressure (PIP) and positive end expiratory pressure (PEEP) [29]. Reconstructive surgery with an arterial switch is the suggested treatment to achieve total anatomical and physiological repair[30].

Tetralogy of Fallot

The entire surgical treatment of the disease with the lowest possible rate of death and morbidity is the aim of care for patients with TOF. It seeks to treat any side effects that TOF and other cyanotic cardiac problems may cause. Hyper-cyanotic episodes are a disorder that affects children with TOF and causes them to weep uncontrollably, breathe deeply quickly, and become blue and pale. The following is a detailed explanation of how to handle hyper cyanotic episodes. To increase systemic arterial resistance, which encourages pulmonary flow, the infant should be positioned with the knees to the chest. In order to breathe humid oxygen, put on a face mask. To end the trance, subcutaneous morphine sulphate 0.1 mg/kg is needed. At this stage, it is necessary to address metabolic acidosis, fluid transfusion-induced anemia, and sodium bicarbonate-induced dehydration. Propranolol can also be gently administered intravenously in a solution of 0.1 mg/kg combined with 50 ml of water and 5% dextrose. Surgery should be done if none of the aforementioned therapies improve the infant's condition. Many physicians conducted balloon pulmonary valvuloplasty in TOF patients to increase respiratory blood flow as well as allow for the establishment of the left ventricle and pulmonary artery system[31].

Pulmonary circulatory lesions that depend on the ductus

A typical characteristic of right-sided lesions such TOF and its variants is central cyanosis. The stability of the ductus would determine the extent of cyanosis. It is straightforward to differentiate between cardiac and respiratory origin utilizing an arterial blood gases hyperoxia test [32]. As ductal tissues tighten, cyanosis could exacerbate. These newborns must start receiving PGE1 injections immediately. Keeping the ductus arteriosus completely open, up to the Blalock taussing shunt surgery, which aids in improving respiratory flow for pulmonary atresia. PGE1 infusions are essential for stabilizing the airways because they reduce pulmonary vascular resistance, enhance left to right shunting, and ultimately increase respiratory blood flow. PGE1 is first administered at 0.05 g/kg/min. Increase the dosage by 0.1 g/kg/min once the infant's condition has stabilized and there hasn't been any improvement. The dosage should then be adjusted to 0.025 g/kg/min. maintaining the patient's airway is essential for determining whether or not they have septic shock because of its complicated side symptoms, which would include apnea, bradycardia, hypotension, fluid electrolyte imbalance, and pyrexia. PGE1 is not harmful for CHD, but it can lead to limited atrial septal rupture, transposition of the great arteries, and complete atypical pulmonary vascular return (TAPVR)[33].

Ductus dependent systemic circulatory lesions

Therapy for this patient should concentrate on improving metabolic acidosis, which could be harmful to the patient's operative status, and increasing systemic oxygenation. The way in which these people are treated is based on two key concepts. Initially, keep the ductus open. For survival, PGE1 must be supplied. The flow balance between the systemic and pulmonary circulation should be considered when ductal patency has been achieved. When pulmonary blood flow rises, systemic and coronary blood flow are reduced. Oliguria, metabolic acidosis, and cardiovascular failure are signs of inadequate perfusion. To reduce pulmonary over circulation, ventilation techniques are employed to improve pulmonary vascular resistance. The systemic and myocardium systems can both get appropriate perfusion when two competing circulations are kept equal. By carefully adjusting the PEEP (4-6 cm H_2O), regulating the inspiratory rate, pressure, and peak flow to sustain an arterial CO_2 pressure of 5-6 kpa, minimize unnecessary O2 delivery, retaining the systemic arterial concentration at around 80%, and preventing respiratory alkalosis. Low or high partial pressures of CO_2 have the potential to overload the pulmonary circulation with volume and cause heart failure by reducing the pulmonary vascular resistance to blood flow [34]. Neonatal who develop tachypnea from shock require morphine sedation; in this situation, a muscle relaxant should be taken into consideration. Utilizing vasodilators will provide the

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

greatest possible systemic perfusion. If poor cardiac output persists despite all of these attempts, the availability of PGE1 infusions, intravascular volume, and anemia should be reevaluated. If the blood pressure is manageable, metabolic acidosis can be treated with a modest dose of nitroprusside infusion [35].

CONCLUSIONS

When an infant with cyanosis shows up at the emergency room, prompt evaluation, diagnosis, and treatment is necessary. Technology, resources, a lack of time, and a lack of competence are all factors that prevent a baby with suspected cyanosis from receiving a prompt postnatal diagnosis. When diagnosing newborn cyanosis, a methodical and logical approach is crucial. The emergency department practitioner will be able to determine whether the underlying cause is related to airway obstruction, parenchymal disease, hypoventilation due to CNS disease or apnea, or due to cardiac disease by having a thorough understanding of the normal transitional physiology and how diseases of the airway, lung, and circulatory system may disrupt these processes. The clinical diagnosis, careful consideration of hemodynamic stability, prudent oxygen supply, and referral to the most suitable inpatient hospital setting form the basis of management. Although the prognosis varies depending on the diagnosis, it is typically favorable with early detection and treatment.

Authors Contribution

Conceptualization: MF
Writing-review and editing: MF, SS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Lees MH. Cyanosis of the newborn infant: recognition and clinical evaluation. The Journal of Pediatrics. 1970 Sep; 77(3): 484-98. doi: 10.1016/S0022-3476(70)80024-5.

[2] Azmi NF, Delbressine F, Feijs L. Conceptual determination and assessment of cyanosis. Int. J. Bioscience, Biochemistry and Bioinformatics. 2016 Jul; 6(3): 75-83. doi: 10.17706/ijbbb.2016.6.3.75-83.

[3] Adeyinka A and Kondamudi NP. Cyanosis. StatPearls Publishing; 2018.

[4] Eichenwald E and Kim M. Overview of cyanosis in the newborn. UpToDate. 2021 Apr; 2.

[5] Pahal P and Goyal A. Central and peripheral cyanosis. StatPearls publishing; 2021.

[6] Sasidharan P. An approach to diagnosis and management of cyanosis and tachypnea in term infants. Pediatric Clinics. 2004 Aug; 51(4): 999-1021. doi: 10.1016/j.pcl.2004.03.010.

[7] Lundsgaard C. Studies on Cyanosis: I. Primary Causes of Cyanosis. The Journal of Experimental Medicine. 1919 Sep; 30(3): 259-69. doi: 10.1084/jem.30.3.259.

[8] Lees MH and King DH. Cyanosis in the newborn. Pediatrics in Review. 1987 Aug; 9(2): 36-42. doi: 10.1542/pir.9-2-36.

[9] Hiremath G and Kamat D. Diagnostic considerations in infants and children with cyanosis. Pediatric Annals. 2015 Feb; 44(2): 76-80. doi: 10.3928/00904481-20150203-12.

[10] Mutlu B, Keskin EY, Oliveira AC, Relvas L, Bento C. A Rare Cause of Cyanosis since Birth: Hb M-Iwate. Turkish Journal of Hematology. 2019 Dec; 36(4): 299. doi: 10.4274/tjh.galenos.2019.2019.0123.

[11] Wilson R, Ross O, Griksaitis MJ. Tetralogy of fallot. BJA Education. 2019 Nov; 19(11): 362. doi: 10.1016/j.bjae.2019.07.003.

[12] Benson JM and Therrell Jr BL. History and current status of newborn screening for hemoglobinopathies. Seminars in Perinatology. 2010 Apr; 34(2): 134-44. doi: 10.1053/j.semperi.2009.12.006.

[13] Horn EP, Bein B, Steinfath M, Ramaker K, Buchloh B, Höcker J. The incidence and prevention of hypothermia in newborn bonding after cesarean delivery: a randomized controlled trial. Anesthesia & Analgesia. 2014 May; 118(5): 997-1002. doi: 10.1213/ANE.0000000000000160.

[14] Jyotsna M, Srinivas B, Lalita N. Cyanosis–Part 1. Indian Journal of Cardiovascular Disease in Women-WINCARS. 2016 Dec; 1(04): 069-74. doi: 10.1055/s-0038-1656488.

[15] Sattar SBA, Sharma S, Headley A. Bacterial Pneumonia(Nursing). StatPearls Publishing; 2021.

[16] Stark AR and Eichenwald EC. Persistent pulmonary hypertension of the newborn. UpToDate. 2018; 10.

[17] Teng RJ and Wu TJ. Persistent pulmonary hypertension of the newborn. Journal of the Formosan Medical Association. 2013 Apr; 112(4): 177-84. doi: 10.1016/j.jfma.2012.11.007.

[18] Taleb M, Ashraf Z, Valavoor S, Tinkel J. Evaluation and management of acquired methemoglobinemia associated with topical benzocaine use. American Journal of Cardiovascular Drugs. 2013 Oct; 13: 325-30. doi: 10.1007/s40256-013-0027-2.

[19] McMullen SM and Patrick W. Cyanosis. The American

DOI: https://doi.org/10.54393/pjhs.v4i11.1106

Journal of Medicine. 2013 Mar; 126(3): 210-2. doi: 10.1016/j.amjmed.2012.11.004.
[20] Das S and Maiti A. Acrocyanosis: an overview. Indian Journal of Dermatology. 2013 Nov; 58(6): 417. doi: 10.4103/0019-5154.119946.
[21] Steinhorn RH. Evaluation and management of the cyanotic neonate. Clinical Pediatric Emergency Medicine. 2008 Sep; 9(3): 169-75. doi: 10.1016/j.cpem.2008.06.006.
[22] Geggel RL. Diagnosis and initial management of cyanotic heart disease in the newborn. UpToDate. 2021.
[23] Murty VY and Ram KD. Phrenic nerve palsy: a rare cause of respiratory distress in newborn. Journal of Pediatric Neurosciences. 2012 Sep; 7(3): 225. doi: 10.4103/1817-1745.106487.
[24] Geggel R and Armsby C. Cardiac causes of cyanosis in the newborn. UpToDate. 2021 Apr; 11.
[25] Movahedian AH, Mosayebi Z, Sagheb S. Evaluation of pulse oximetry in the early detection of cyanotic congenital heart disease in newborns. The Journal of Tehran University Heart Center. 2016 Apr; 11(2): 73.
[26] Kitterman JA. Cyanosis in the newborn infant. Pediatrics in Review. 1982 Jul; 4(1): 13-23. doi: 10.1542/pir.4-1-13.
[27] Gupta SK. Clinical approach to a neonate with cyanosis. The Indian Journal of Pediatrics. 2015 Nov; 82: 1050-60. doi: 10.1007/s12098-015-1871-7.
[28] Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care. Lippincott Williams & Wilkins; 2008.
[29] Schieppati A, Henter JI, Daina E, Aperia A. Why rare diseases are an important medical and social issue. The Lancet. 2008 Jun; 371(9629): 2039-41. doi: 10.1016/S0140-6736(08)60872-7.
[30] Choi BS, Kwon BS, Kim GB, Bae EJ, Noh CI, Choi JY, *et al*. Long-term outcomes after an arterial switch operation for simple complete transposition of the great arteries. Korean Circulation Journal. 2010 Jan; 40(1): 23-30. doi: 10.4070/kcj.2010.40.1.23.
[31] Rao PS. Diagnosis and management of cyanotic congenital heart disease: part I. The Indian Journal of Pediatrics. 2009 Jan; 76: 57-70. doi: 10.1007/s12098-009-0030-4.
[32] Krishnan US. Approach to congenital heart disease in the neonate. The Indian Journal of Pediatrics. 2002 Jun; 69: 501-5. doi: 10.1007/BF02722652.
[33] Lin AE, Di Sessa TG, Williams RG, Leighton J, Gross K, Wong AL. Balloon and blade atrial septostomy facilitated by two-dimensional echocardiography. The American Journal of Cardiology. 1986 Feb; 57(4): 273-7. doi: 10.1016/0002-9149(86)90904-5.
[34] Barron DJ, Kilby MD, Davies B, Wright JG, Jones TJ, Brawn WJ. Hypoplastic left heart syndrome. The Lancet. 2009 Aug; 374(9689): 551-64. doi: 10.1016/S0140-6736(09)60563-8.
[35] Tweddell JS, Hoffman GM, Fedderly RT, Berger S, Thomas Jr JP, Ghanayem NS, *et al*. Phenoxybenzamine improves systemic oxygen delivery after the Norwood procedure. The Annals of Thoracic Surgery. 1999 Jan; 67(1): 161-7. doi: 10.1016/S0003-4975(98)01266-1.

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Review Article

Combating Metabolic Syndrome through Non-Pharmacological Strategies: A Literature Review

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ARTICLE INFO

Key Words:
Metabolic Syndrome, Non-Pharmacological Management, Diet, Obesity

How to Cite:
Aziz, Z., Shareef, H., Afridi, E., Kashif, M., Hussain, M., Waseem, M., Shahid, T., Khan, M. A., Muntaha, S. T., & Hameed Silro, H. (2023). Combating Metabolic Syndrome through Non-Pharmacological Strategies: A Literature Review: Combating Metabolic Syndrome. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1145

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Received Date: 24th October, 2023
Acceptance Date: 13th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Metabolic syndrome (MetS) represents a constellation of interlinked metabolic abnormalities, encompassing hypertension (HTN), insulin resistance diabetes, obesity, and atherogenic dyslipidemia. It is observed that people suffering from these symptoms of metabolic syndrome are twice as likely to develop cardiovascular diseases (CVDS) and five times more likely to develop Type 2 Diabetes Mellitus (T2DM) during their lifetime. The alarming increase in the incidence of MetS, in population worldwide, has made it an epidemic. In today's world people are more susceptible to MetS due to their sedentary lifestyle, bad eating habits, and various forms of stress. Knowing the socioeconomic burden of disease of MetS on global health throughout the years has brought attention towards its management and therapeutic approach and rightly so, this has also created the need for new, innovative, and non-traditional methods of managing MetS, as the current available treatments of MetS have limited efficacy. In this review, we highlight the prevalence, definition and also summarize the latest non-traditional therapies of MetS worldwide.

INTRODUCTION

Metabolic syndrome, also known as syndrome X or Reaven's syndrome, is a cluster of diseases encompassing cardiovascular diseases (CVDs), Type 2 Diabetes Mellitus (T2DM), and stroke [1, 2]. The risk factors of MetS include abdominal obesity, atherogenic dyslipidemia, hypertension, and insulin resistance [2]. If more than 3 criteria are present then it is called metabolic syndrome [3]. Typical traits of MetS are hyperglycemia, atherogenic dyslipidemia, and hypertension and people with these traits are twice at the risk of developing CVDs and 5 times more for T2DM[4].

Obesity and insulin resistance are believed to be at the core of most cases of metabolic syndrome [4]. The standard of care for managing MetS continues to be pharmaceutical intervention along with dietary and exercise modifications to promote weight loss[5].

Prevalence

In the past, MetS was a disease in Western countries,

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

recent research has shown that over the past decade prevalence of MetS has increased exponentially in urban populations of developing countries [6] and future prediction indicates that it will continue to grow in rural populations too. It is estimated that the global prevalence of MetS is over a billion people (12.5% to 31.4%) with a prevalence of 2.8 % in children and 4.8% in adolescence. It is interestingly, closely associated with the number of incidences of T2DM, obesity, and CVDs [7].

Pathophysiology

It is widely known that in the 1980s, Reaven put forward the idea of MetS, under the term Syndrome X, where he put insulin resistance at the core of the problem leading to CVDs and T2DM [8]. Ever since then, there has been significant research done to understand the mechanism of MetS and the pathophysiology behind it, yet there are still many different points of contention regarding its pathophysiology and definition. Numerous intricate mechanisms make up the pathophysiology of the MetS, many of which are still not fully understood [9]. The question of whether the various MetS components constitute separate pathologies on their own or are part of a single, more general pathogenic process is still up for debate. Some lifestyle and environmental factors, including overeating and lack of physical activity, have been recognized as key contributors to the development of MetS in addition to genetic and epigenetic factors [10]. Since visceral adiposity has been found to be a significant trigger that activates most of the MetS pathways [11], high caloric intake can be attributed to a causal role [6]. Among the suggested pathways, neurohormonal activation, chronic inflammation, and insulin resistance appear to be key players in the development of MetS and associated symptoms [6].

Criteria

Moreover, there are also no set criteria for accessing MetS universally. There are three widely known definitions given by the World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) AND International Diabetes Federation (IDF) as shown in the Table 1A and 1B below.

Table 1A: Dissimilarities in the definition of Metabolic Syndrome as defined by WHO, NCEPATP III and IDF

World Health Organization (WHO)	National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III)	International Diabetes Federation (IDF)
METS patients will have at least two of the following findings: Central obesity, or dyslipidemia, or raised Blood pressure or taking meds for previously diagnosed hypertension as well as hyperinsulinemia, or hyperglycemia.	METS patients will have three or more of the following five conditions:High waist circumference, high Blood pressure, Increased cholesterol, low HDL levels High fasting Blood sugar levels.	People with central obesity & any 2 of the following factors constitute METS:Raised triglycerides, reduced HDL cholesterol, Elevated Blood pressure and Elevated fasting plasma glucose or previously diagnosed T2DM.

World Health Organization (WHO)	National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III)	International Diabetes Federation (IDF)
Waist Circumference greater than 94cm.	Waist circumference greater than 102 cm for men and 88 cm for women.	Waist circumference >90 cm for South & East Asian men &>80 cm for South & East Asian women
Triglycerides levels greater than 140/90 mmHg or HDL cholesterol less than 40 mg/dl.	Fasting Triglyceride levels greater than 150 mg/dl.	Triglycerides>150 mg/dl reduced HDL cholesterol less than 40 mg/dl in men & 50 mg/dl in women.
Blood pressure greater than 140/90 mmHg	Blood pressure greater than 130/85 mmHg.	Blood pressure greater than 130/85 mmHg.
Fasting glucose more than 110 mg/dl.	Fasting glucose more than 100 mg/dl.	Fasting glucose more than 100 mg/dl or previously diagnosed with Type II Diabetes Mellitus.

Table 1B: Similarities between definition of metabolic syndrome as defined by WHO, NCEPATP III and IDF

Organizations	Similarities in Definition
World Health Organization (WHO) National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) International Diabetes Federation (IDF)	**Common Risk Factors:** WHO, NCEPATP III and IDF consider the following risk factors to be the main cause of Metabolic Syndrome which include: 1. Elevated blood pressure and 2. Fasting blood glucose levels, 3. Abdominal obesity 4. Abnormal lipid profiles. **Cardiovascular Risks:** All three of these organizations highlight the necessity of identifying individuals at risk for Metabolic Syndrome as a group of risk factors for cardiovascular diseases.

Interestingly, Eva and colleagues wrote that because of no universally accepted criteria for MetS, there has been a significant focus on finding the right diagnosis rather than assessing existing risk factors of MetS in individuals [12]. Unfortunately, this also takes away from creating criteria and setting a gold standard treatment plan for better management of MetS. However, Saklayen notes in his article that the region-wise differences in definition and criteria of MetS are minor and can be overlooked due to the more grave issue of socioeconomic disease burden that is causing the entire world population and healthcare system to succumb under [13]. It is safe to say that the overall cost of the illness, including medical expenses and lost potential economic output, is in the trillions of dollars. The current trend cannot continue until a miraculous treatment is discovered, or unless significant efforts are made on a global, governmental, and cultural level to alter the way of life that is encouraging it [13].

Management of Metabolic Syndrome according to Types of Diet

Following are different management strategies of Metabolic Syndrome according to diet.

Mediterranean Diet

Over the years, there has been a new approach in preventing MetS and that is with the ancient Mediterranean diet. The Mediterranean diet consists of vegetables, legumes, fruits, nuts, cereals, fish and seafood, monounsaturated fatty acids, dairy products, and

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

moderate alcohol consumption. People consuming this diet do not require salt intake as they supplement it with herbs and spices which not only help in decreasing blood pressure after consumption but also add flavor to the food. The main source of fat in this diet is extra virgin olive oil (EVOO) which has proven to be beneficial in preventing T2DM [14]. In a recent study, 80 patients with new onset diabetes when treated with MedDiet and EVOO showed improved glucose metabolism and a decrease in body weight [15, 16]. The main component of this diet usually consists of polyphenols present in olive oils, red wine, and citrus fruits [17]. This chemical can inhibit the ACE pathway and therefore regulate blood pressure [18]. However, there are a few limitations with the Mediterranean diet, firstly there is a chance of weight gain from eating more than the recommended amount of fat, secondly, there could be chances of anemia due to not consuming an adequate amount of meat, and calcium deficiency due to consumption of fewer dairy products. Also, the Mediterranean diet is overall costly for low socioeconomic populations. Alcohol consumption is restricted in some cultures around the world, this causes a discrepancy in the data provided as different religions prohibit alcohol consumption.

The Vegan Diet

The vegan diet is plant-based specifically excluding all animal-origin foods, unlike vegetarian diets where dairy products, eggs, and honey can be consumed. The vegan diet consists of cereals, vegetables, legumes, seeds, nuts, and vegetable oils. This diet is generally high in alpha-linoleic acid. Alpha-linoleic acid helps in lowering blood pressure, and cholesterol levels and reverses atherosclerosis. A collection of scientific data shows that a vegan diet can promote or restore good health [19]. People adopt this diet due to ethical, health, and environmental reasons, however, in the current trends, the vegan lifestyle should be recommended by healthcare providers due to its positive effects on T2DM, CVDs, and MetS [20]. However, this diet has a few limitations. If it is not consumed in a well-balanced portion, it can cause serious deficiencies in proteins, omega 3 fatty acids, iron, vitamin D, calcium, zinc, and vitamin B12 due to which people are easily susceptible to megaloblastic anemia, kwashiorkor, and marasmus [21]. There is clear evidence that such diets may cause lower bone mineral density and therefore increase the risk of multi-site fractures in consumers [22]. Although research is needed on physiological factors, it is also believed that endocrine profile, BMI, and microbiome may also play a certain role in causing these fractures. Therefore, the use of oral food supplementation along with a vegan diet is required to overcome the above-mentioned nutritional deficiencies [23]. Additionally, athletes following vegan diets may have trouble achieving protein needs for muscle retention, recovery, and increased appetite needs as compared to non-athletic people [24]. Therefore, athletes taking vegan diets once again require additional oral food supplementation. Lastly, another drawback of following a vegan lifestyle is the high cost of sourcing plant based food, in areas where plant-based diets are not commonly found or grown.

Intermittent fasting vs. Calorie restriction diet

Intermittent fasting(IF) also known as alternate-day fasting, other full-day fasting patterns, and time-restricted eating [25] can be defined as consuming 500-700 kcal for 2-4 days/week [26] whereas calorie restriction diet (CR) follows restriction of total calorie intake in a day. Recent studies show that the risk of developing age-related diseases can be decreased by intermittent fasting due to its effect on lowering blood sugar, insulin, fat, and circulating glucose levels [27]. In patients with obesity and type 2 diabetes, clinical trials revealed that 2-day IF significantly reduced body fat mass, improved insulin resistance [28], and improved glycated hemoglobin and glycemic control [28]. Some common pathways that IF intervenes in are autophagy, mitochondrial function, and adaptive cellular response [29]. It also appears to regulate the circadian rhythm of hormones, especially insulin among others [30]. The rising popularity of IF is attributed to its compatibility with human eating patterns as opposed to a continuous restricted diet where several trials have suggested that people had trouble following CR over an indefinite period of time [31]. However, there is still debate concerning IF's long-term negative consequences in people, including hypoglycemia, digestive system harm, and impaired bone metabolism [32]. The lack of data supporting the negative consequences of intermittent fasting regimens is mostly due to the short time frames used to evaluate them (weeks to months). Hypoglycemia, vertigo, and weakness are a few of the often reported negative effects [30].

Coffee and Tea

Coffee and tea are the most commonly consumed beverages in the world. They have become an important part of an average person's diet. It has been discovered that the use of coffee and tea can help in preventing and also combating obesity [33, 34]. Moreover, they can reduce appetite, decrease food consumption, and simultaneously, food absorption in the GIT, as well as increase fat metabolism [35]. It is believed that they exhibit these effects because of the main primary component called caffeine (1,3,7 trimethyl-xanthine) [35]. Tea: The active ingredient in tea is polyphenols [35]. Polyphenols exhibit anti-inflammatory effects on the Gastro-intestinal tract. Moreover, the molecules of tea in the right ratio can also

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

counteract anxiety and stress [36]. According to a study carried out on animals and humans, it was reported that tea reduces the prevalence of metabolic syndrome, cardiovascular diseases, and diabetes [37]. Another study stated that green tea polyphenols can cause reduced glucose blood levels by acting on glucose production in the liver [38]. Most studies support the fact that tea has a positive impact on patients with MetS. However, some studies demonstrate no effect on the concentration of glucose, fatty acids, and triacylglycerols [39, 40]. Coffee: Other than caffeine, the major component of coffee is chlorogenic acid [41]. Chlorogenic acid has antioxidative and anti-inflammatory effects on body cells. These effects show to have preventative and therapeutic influence against diabetes and CVDs [41]. Coffee consumption can also be recommended not only to healthy and young people but also to people with high blood pressure, cholesterol, and blood glucose as well as people with MetS [42]. Many other studies have shown a correlation between the habit of drinking coffee and reduced mortality due to CVDs [43]. However, coffee if consumed in large amounts can cause insomnia, anxiety, and loss of calcium which can further lead to osteoporosis [44]. Coffee can also damage sperm and prolong pregnancy [45].

Curcumin

Curcumin is a yellow pigment found in turmeric. It is a type of polyphenol. It contains (1) anti-inflammatory, (2) anti diabetic, (3) antioxidative, (4) anti atherosclerotic, and (5) hepatoprotective properties. According to a study, it was found that curcumin decreases serum LDL, total cholesterol, and triglyceride levels [46]. It helps to reduce fat production by reducing the expression of PPAR and CCAAT/enhancer binding protein alpha as well as lowering cholesterol levels [47]. Moreover, it also increases insulin secretion by upregulating the gene expression of pancreatic glucose transporter (GLUT-2, GLUT3, GLUT-4)[47]. Once GLUT proteins are expressed on the cell membrane, it allows for the uptake of glucose into the cell, effectively decreasing blood sugar levels in the body. One drawback of a curcumin centered diet is that it is found in low concentrations, in turmeric, which decreases its bioavailability, therefore it is given in the form of supplements for therapeutic purposes [47]. Curcumin can be best given with piperine (a component of black pepper). Some studies have shown that the co-administration of these supplements significantly decreased total cholesterol and LDL levels [48]. Another setback of using curcumin supplementation is gastrointestinal disturbances such as nausea and diarrhea [49]. Also in some studies curcumin, in high doses, has shown to exhibit negative side effects on skin cells where proliferation is inhibited [50].

Capsaicin

Capsaicin is the active constituent in chilli. It works by agonistically binding to transient receptor potential vanilloid channel 1 or TRPV1 [51]. This channel is present on many active tissues in the body, mainly heart, liver, kidney, pancreas, and adipocytes. Therefore, it can be suggestive of the fact that TRPV1 can alleviate symptoms of MetS [52]. TRPV1 works by activating sympathetically mediated brown adipose tissue thermogenesis and consequently reduces body fat [53]. In a meta-analysis of 9 studies and 461 patients, it was concluded that capsaicin supplementation showed a positive result in reducing total cholesterol and LDL levels in the blood [53]. Many other smaller studies have shown that capsaicin may decrease lipid levels among patients with MetS, hence it is a good agent to treat dyslipidemia [53]. Another study showed its effective role in body weight control by regulating lipolysis, increasing the feeling of satiety, and stimulating energy expenditure while reducing energy intake [54]. In fact, three major epidemiological studies conducted in different countries found that regular chili consumers had higher cardiovascular morbidity and mortality than non-consumers [55]. However, there is no convincing evidence that dietary capsaicin can normalize blood sugar levels and/or prevent dyslipidemia [55].

Microalgae

Microalgae are unicellular species found typically in freshwater and contain many bioactive components with therapeutic potential, like dietary fiber, carotenoids, vitamins, polyphenols, sterols, and polyunsaturated fatty acids (PUFAs) [56]. Similarly, long chain polyunsaturated fatty acids (LC-PUFAs) like docosahexaenoic acid (DHA) and eicosapentaenoic acid are also present in fishes and fish oils which have shown preventive impact on metabolic unsettling influences related with obesity and decreased risk of CVDs [57]. The decrease in the number of fishery assets due to increased marine contamination requires an alternate source of LC-PUFAs [57]. In this regard, studies have shown that microalgae might prove to be a good alternative to fish oils as microalgae are less delicate to overwhelming water pollution [57]. Several studies done on male Wistar rats fed with high fructose diet (HF) were given supplements of several microalgae to observe its effect on MetS [57]. Tisochrysis Lutea (Tiso) supplements reported that it decreased fat mass, cholesterol, leptinemia, and plasma tumor necrosis factor-alpha levels[57]. This effect of Tisochrysis Lutea (Tiso) is due to its biochemical tolerance and large amounts of DHA that are responsible for decreasing the risk factors of MetS [57]. Supplements of Diacronemalutheri (D.lutheri) decreased the abdominal fat and epididymal adipose tissue weight/body weight ratios as well [57]. It also decreased triglyceridemia and increased the plasma total cholesterol levels and HDL-C

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

levels as compared to HF rats [57]. Arthrospira maxima and platensis reduced the fat synthesis in white and brown adipose tissues [57]. Ingestion of spirulina (2-6 g/day) reported the improved insulin sensitivity while supplements of chlorella also appear to have antidiabetic, antihyperlipidemic, antihypertensive, and antioxidative impacts [56].

Probiotics, Prebiotics and Synbiotics

The term probiotics is used to describe bacteria that have a beneficial effect on the human body whereas prebiotics are mostly non digestible fibers [58]. Synbiotics are a combination of prebiotics and probiotics. Recent studies have shown that prebiotics, probiotics, and synbiotics work in three distinct mechanisms, namely modulation of gut microbiota composition, regulation of gut metabolites, and improvement of intestinal barrier function [59]. Rat trials have shown that the use of probiotics has had an overall decreasing effect on blood pressure as they stimulated the expression of ACE enzymes in rats [60]. On the other hand, synbiotics have created a new perspective in obesity prevention because when mixed with probiotics, they showed a more definite reduction in hepatic steatosis and lipid accumulation compared to just probiotics alone [61, 62]. Furthermore, oral supplements containing probiotics and synbiotics showed increased lipid metabolism in obese rats [63]. Additionally, there is countless evidence showing that prebiotic consumption may control the level of gut microbial metabolites such as short chain fatty acids (SCFAs) and bile acids, which may have an impact on the metabolic process [64]. All in all many researchers conclude that gut microbacteria play a role in strengthhening the intestinal integrity [59]. Although the US FDA has provided a list of safe probiotics to use commercially, but they are yet to approve the use of probiotics for medical practice [65]. Moreover, various studies also show the negative effects of probiotic use such as sepsis, pathogenic antibiotic resistance, and hypersensitivity reactions [66].

Coenzyme Q10

Coenzyme Q10 is found inside the mitochondria in the inner mitochondrial membrane where it has an essential role in the electron transport chain transferring electrons from complex 1 to complex 3 [67,68]. Additionally, ubiquinol, the active form of CoQ10, acts as a potent antioxidant in the human body which is why it can successfully stop the initial process of lipid peroxyl radical formation [69]. CoQ10 acts directly on the endothelium in the blood vessel as a vasodilator. This, in turn, decreases blood pressure and helps to alleviate symptoms of hypertension [70, 71]. In another random study where CoQ10 was administered for 12 weeks, it was observed that systolic blood pressure had decreased to normal limits in hypertensive patients [72]. Statins are the most effective and safe medication for the treatment of high cholesterol levels in the body [73], however, one of the side effects of long-term statin use is heart failure due to CoQ10 synthesis inhibition [74]. This problem is countered by the use of CoQ10 supplementation, where one study proved that statins had less side effects compared to their therapeutic effects when used in combination with CoQ10 [75]. Some limitations of CoQ10 supplementation therapy are that despite so many desired effects, still more randomized control trials are required and more data is needed to support its efficacy on MetS [76].

CONCLUSIONS

This literature review explores non-pharmacological strategies for combating metabolic syndrome, focusing on dietary management. A personalized, well-balanced diet can improve metabolic health and reduce the risk of complications. However, dietary management should be part of a holistic approach, including physical activity, stress management, and regular health monitoring. Healthcare practitioners and individuals alike should maintain vigilance in remaining current with the latest dietary guidelines and the evolving body of research in this field. The success of dietary strategies depends on patient education, motivation, and long-term adherence. The finding contribute to the growing body of knowledge on metabolic syndrome and has the potential to make a significant impact on public health by reducing the prevalence and burden of metabolic syndrome and its associated complications.

Authors Contribution

Conceptualization: ZA, HS, MH
Writing-review and editing: ZA, HS, EA, MK, MW, TS, MAK, STM, HH

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Reaven GM. Role of insulin resistance in human disease. Nutrition. 1997; 1(13): 65. doi: 10.1016/s0899-9007(96)00380-2 .

[2] Gupta A and Gupta V. Metabolic syndrome: what are the risks for humans? Bioscience Trends. 2010 Oct; 4(5): 204-12.

[3] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, *et al.* Harmonizing the metabolic

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation. 2009 Oct; 120(16): 1640-5. doi: 10.1161/CIRCULATIONAHA.109.192644.

[4] Samson SL and Garber AJ. Metabolic syndrome. Endocrinology and Metabolism Clinics. 2014 Mar; 43(1): 1-23. doi: 10.1016/j.ecl.2013.09.009.

[5] Castro-Barquero S, Ruiz-León AM, Sierra-Pérez M, Estruch R, Casas R. Dietary strategies for metabolic syndrome: a comprehensive review. Nutrients. 2020 Sep; 12(10): 2983. doi: 10.3390/nu12102983.

[6] Rochlani Y, Pothineni NV, Kovelamudi S, Mehta JL. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. Therapeutic Advances in Cardiovascular Disease. 2017 Aug; 11(8): 215-25. doi: 10.1177/1753944717711379.

[7] Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, Nkeck JR, Nyaga UF, Ngouo AT, *et al.* Global, regional, and country estimates of metabolic syndrome burden in children and adolescents in 2020: a systematic review and modelling analysis. The Lancet Child & Adolescent Health. 2022 Mar; 6(3): 158-70. doi: 10.1016/s2352-4642(21)00374-6.

[8] McCracken E, Monaghan M, Sreenivasan S. Pathophysiology of the metabolic syndrome. Clinics in Dermatology. 2018 Jan; 36(1): 14-20. doi: 10.1016/j.clindermatol.2017.09.004.

[9] Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, *et al.* Metabolic syndrome: Updates on pathophysiology and management in 2021. International Journal of Molecular Sciences. 2022 Jan; 23(2): 786. doi: 10.3390/ijms23020786.

[10] Bell PG, Walshe IH, Davison GW, Stevenson E, Howatson G. Montmorency cherries reduce the oxidative stress and inflammatory responses to repeated days high-intensity stochastic cycling. Nutrients. 2014 Feb; 6(2): 829-43. doi: 10.3390/nu6020829.

[11] Shah RV, Murthy VL, Abbasi SA, Blankstein R, Kwong RY, Goldfine AB, *et al.* Visceral adiposity and the risk of metabolic syndrome across body mass index: the MESA Study. JACC: Cardiovascular Imaging. 2014 Dec; 7(12): 1221-35. doi: 10.1016/j.jcmg.2014.07.017.

[12] Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Medicine. 2011 Dec; 9: 1-3. doi: 10.1186/1741-7015-9-48.

[13] Saklayen MG. The global epidemic of the metabolic syndrome. Current Hypertension Reports. 2018 Feb; 20(2): 1-8. doi: 10.1007/s11906-018-0812-z.

[14] D'Alessandro A and De Pergola G. Mediterranean diet pyramid: a proposal for Italian people. Nutrients. 2014 Oct; 6(10): 4302-16. doi: 10.3390/nu6104302.

[15] Salas-Salvadó J, Bulló M, Babio N, Martínez-González MÁ, Ibarrola-Jurado N, Basora J, *et al.* Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes care. 2011 Jan; 34(1): 14-9. doi: 10.2337/dc10-1288.

[16] Salas-Salvadó J, Bulló M, Estruch R, Ros E, Covas MI, Ibarrola-Jurado N, *et al.* Prevention of diabetes with Mediterranean diets: a subgroup analysis of a randomized trial. Annals of Internal Medicine. 2014 Jan; 160(1): 1-10. doi: 10.7326/m13-1725.

[17] Mazzocchi A, Leone L, Agostoni C, Pali-Schöll I. The secrets of the Mediterranean diet. Does [only] olive oil matter? Nutrients. 2019 Dec; 11(12): 2941. doi: 10.3390/nu11122941.

[18] Dayi T and Ozgoren M. Effects of the Mediterranean diet on the components of metabolic syndrome. Journal of Preventive Medicine and Hygiene. 2022 Jun; 63(2 Suppl 3): E56. doi: 10.15167/2421-4248/jpmh2022.63.2s3.2747.

[19] Marrone G, Guerriero C, Palazzetti D, Lido P, Marolla A, Di Daniele F, *et al.* Vegan diet health benefits in metabolic syndrome. Nutrients. 2021 Mar; 13(3): 817. doi: 10.3390/nu13030817.

[20] Gomez-Delgado F, Katsiki N, Lopez-Miranda J, Perez-Martinez P. Dietary habits, lipoprotein metabolism and cardiovascular disease: From individual foods to dietary patterns. Critical Reviews in Food Science and Nutrition. 2021 May; 61(10): 1651-69. doi: 10.1080/10408398.2020.1764487.

[21] Ali O. Lifestyles for the Optimum Quality of Life. Asian Journal of Medicine and Health Science. 2023 Jun; 6(1): 23.

[22] Wakolbinger-Habel R, Reinweber M, König J, Pokan R, König D, Pietschmann P, *et al.* Self-reported Resistance Training Is Associated With Better HR-pQCT–derived Bone Microarchitecture in Vegan People. The Journal of Clinical Endocrinology & Metabolism. 2022 Sep; 107(10): 2900-11. doi: 10.1210/clinem/dgac445.

[23] Bakaloudi DR, Halloran A, Rippin HL, Oikonomidou AC, Dardavesis TI, Williams J, *et al.* Intake and adequacy of the vegan diet. A systematic review of the evidence. Clinical Nutrition. 2021 May; 40(5): 3503-21. doi: 10.1016/j.clnu.2020.11.035.

[24] Rogerson D. Vegan diets: practical advice for

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

athletes and exercisers. Journal of the International Society of Sports Nutrition. 2017 Sep; 14(1): 36. doi: 10.1186/s12970-017-0192-9.

[25] Vasim I, Majeed CN, DeBoer MD. Intermittent fasting and metabolic health. Nutrients. 2022 Jan; 14(3): 631. doi: 10.3390/nu14030631.

[26] Wang X, Li Q, Liu Y, Jiang H, Chen W. Intermittent fasting versus continuous energy-restricted diet for patients with type 2 diabetes mellitus and metabolic syndrome for glycemic control: a systematic review and meta-analysis of randomized controlled trials. Diabetes Research and Clinical Practice. 2021 Sep; 179: 109003. doi: 10.1016/j.diabres.2021.109003.

[27] Teong XT, Liu K, Vincent AD, Bensalem J, Liu B, Hattersley KJ, *et al.* Intermittent fasting plus early time-restricted eating versus calorie restriction and standard care in adults at risk of type 2 diabetes: a randomized controlled trial. Nature Medicine. 2023 Apr; 29: 963-72. doi: 10.1038/s41591-023-02287-7.

[28] Antoni R, Johnston KL, Collins AL, Robertson MD. Intermittent v. continuous energy restriction: differential effects on postprandial glucose and lipid metabolism following matched weight loss in overweight/obese participants. British Journal of Nutrition. 2018 Mar; 119(5): 507-16. doi: 10.1017/s0007114517003890.

[29] Corley BT, Carroll RW, Hall RM, Weatherall M, Parry-Strong A, Krebs J. Intermittent fasting in type 2 diabetes mellitus and the risk of hypoglycaemia: a randomized controlled trial. Diabetic Medicine. 2018 May; 35(5): 588-94. doi: 10.1111/dme.13595.

[30] Joaquim L, Faria A, Loureiro H, Matafome P. Benefits, mechanisms, and risks of intermittent fasting in metabolic syndrome and type 2 diabetes. Journal of Physiology and Biochemistry. 2022 May; 78(2): 295-305. doi: 10.1007/s13105-021-00839-4.

[31] Nowosad K and Sujka M. Effect of various types of intermittent fasting (IF) on weight loss and improvement of diabetic parameters in human. Current Nutrition Reports. 2021 Jun; 10: 146-54. doi: 10.1007/s13668-021-00353-5.

[32] Guo Y, Luo S, Ye Y, Yin S, Fan J, Xia M. Intermittent fasting improves cardiometabolic risk factors and alters gut microbiota in metabolic syndrome patients. The Journal of Clinical Endocrinology & Metabolism. 2021 Jan; 106(1): 64-79. doi: 10.1210/clinem/dgaa644.

[33] Moran-Lev H, Cohen S, Zelber-Sagi S, Mazkeret Mayer E, Anafy A, Yerushalmy-Feler A, *et al.* Effect of coffee and tea consumption on adolescent weight control: an interventional pilot study. Childhood Obesity. 2023 Mar; 19(2): 121-9. doi: 10.1089/chi.2022.0032.

[34] Aziz MA, Millat MS, Akter T, Hossain MS, Islam MM, Mohsin S, *et al.* A comprehensive review on clinically proven medicinal plants in the treatment of overweight and obesity, with mechanistic insights. Heliyon. 2023 Feb; 9(2): e13493. doi: 10.1016/j.heliyon.2023.e13493.

[35] Sirotkin AV and Kolesarova A. The anti-obesity and health-promoting effects of tea and coffee. Physiological Research. 2021 Apr; 70(2): 161. doi: 10.33549/physiolres.934674.

[36] Unno K, Furushima D, Hamamoto S, Iguchi K, Yamada H, Morita A, *et al.* Stress-reducing function of matcha green tea in animal experiments and clinical trials. Nutrients. 2018 Oct; 10(10): 1468. doi: 10.3390/nu10101468.

[37] Yang CS, Wang H, Sheridan ZP. Studies on prevention of obesity, metabolic syndrome, diabetes, cardiovascular diseases and cancer by tea. Journal of Food and Drug Analysis. 2018 Jan; 26(1): 1-3. doi: 10.1016/j.jfda.2017.10.010.

[38] Yang CS, Zhang J, Zhang L, Huang J, Wang Y. Mechanisms of body weight reduction and metabolic syndrome alleviation by tea. Molecular Nutrition & Food Research. 2016 Jan; 60(1): 160-74. doi: 10.1002/mnfr.201500428.

[39] Mielgo-Ayuso J, Barrenechea L, Alcorta P, Larrarte E, Margareto J, Labayen I. Effects of dietary supplementation with epigallocatechin-3-gallate on weight loss, energy homeostasis, cardiometabolic risk factors and liver function in obese women: randomised, double-blind, placebo-controlled clinical trial. British Journal of Nutrition. 2014 Apr; 111(7): 1263-71. doi: 10.1017/s0007114513003784.

[40] Li Y, Wang C, Huai Q, Guo F, Liu L, Feng R, *et al.* Effects of tea or tea extract on metabolic profiles in patients with type 2 diabetes mellitus: a meta-analysis of ten randomized controlled trials. Diabetes/Metabolism Research and Reviews. 2016 Jan; 32(1): 2-10. doi: 10.1002/dmrr.2641.

[41] Islam MT, Tabrez S, Jabir NR, Ali M, Kamal MA, da Silva Araujo L, *et al.* An insight into the therapeutic potential of major coffee components. Current Drug Metabolism. 2018 May; 19(6): 544-56. doi: 10.2174/1389200219666180302154551.

[42] Sarriá B, Martínez-López S, Sierra-Cinos JL, García-Diz L, Mateos R, Bravo-Clemente L. Regularly consuming a green/roasted coffee blend reduces the risk of metabolic syndrome. European Journal of Nutrition. 2018 Feb; 57: 269-78. doi: 10.1007/s00394-016-1316-8.

[43] Khiali S, Agabalazadeh A, Sahrai H, Bannazadeh Baghi H, Rahbari Banaeian G, Entezari-Maleki T. Effect of

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

caffeine consumption on cardiovascular disease: an updated review. Pharmaceutical Medicine. 2023 Mar 30: 1-3. doi: 10.1007/s40290-023-00466-y.

[44] Bhatti SK, O'Keefe JH, Lavie CJ. Coffee and tea: perks for health and longevity? Current Opinion in Clinical Nutrition & Metabolic Care. 2013 Nov; 16(6): 688-97. doi: 10.1097/mco.0b013e328365b9a0.

[45] Ricci E, Viganò P, Cipriani S, Somigliana E, Chiaffarino F, Bulfoni A, *et al*. Coffee and caffeine intake and male infertility: a systematic review. Nutrition Journal. 2017 Dec; 16: 1-4. doi: 10.1186/s12937-017-0257-2.

[46] Azhdari M, Karandish M, Mansoori A. Metabolic benefits of curcumin supplementation in patients with metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. Phytotherapy Research. 2019 May; 33(5): 1289-301. doi: 10.1002/ptr.6323.

[47] Jabczyk M, Nowak J, Hudzik B, Zubelewicz-Szkodzińska B. Curcumin in metabolic health and disease. Nutrients. 2021; 13: 4440. doi: 10.3390/nu13124440.

[48] Hosseini H, Ghavidel F, Panahi G, Majeed M, Sahebkar A. A systematic review and meta-analysis of randomized controlled trials investigating the effect of the curcumin and piperine combination on lipid profile in patients with metabolic syndrome and related disorders. Phytotherapy Research. 2023 Mar; 37(3): 1212-24. doi: 10.1002/ptr.7730.

[49] Reeta V and Kalia S. Turmeric: A review of its' effects on human health. Journal of Medicinal Plants Studies. 2022 May; 10(4): 61-3.

[50] Cianfruglia L, Minnelli C, Laudadio E, Scirè A, Armeni T. Side effects of curcumin: Epigenetic and antiproliferative implications for normal dermal fibroblast and breast cancer cells. Antioxidants. 2019 Sep; 8(9): 382. doi: 10.3390/antiox8090382.

[51] Oka Y, Takahashi K, Ohta T. The effects of vanilloid analogues structurally related to capsaicin on the transient receptor potential vanilloid 1 channel. Biochemistry and Biophysics Reports. 2022 Jul; 30: 101243. doi: 10.1016/j.bbrep.2022.101243.

[52] Panchal SK, Bliss E, Brown L. Capsaicin in metabolic syndrome. Nutrients. 2018 May; 10(5): 630. doi: 10.3390/nu10050630

[53] Jiang Z, Qu H, Lin G, Shi D, Chen K, Gao Z. Lipid-Lowering Efficacy of the Capsaicin in Patients With Metabolic Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Frontiers in Nutrition. 2022 Mar; 9; 812294. doi: 10.3389/fnut.2022.812294.

[54] Elmas C and Gezer C. Capsaicin and Its Effects on Body Weight. Journal of the American Nutrition Association. 2022 Nov; 41(8): 831-9. doi: 10.1080/07315724.2021.1962771.

[55] Szallasi A. Dietary Capsaicin: A Spicy Way to Improve Cardio-Metabolic Health? Biomolecules. 2022 Nov; 12(12): 1783. doi: 10.3390/biom12121783.

[56] Ramos-Romero S, Torrella JR, Pagès T, Viscor G, Torres JL. Edible microalgae and their bioactive compounds in the prevention and treatment of metabolic alterations. Nutrients. 2021 Feb; 13(2): 563. doi: 10.3390/nu13020563.

[57] Mayer C, Richard L, Côme M, Ulmann L, Nazih H, Chénais B, *et al*. The marine microalga, Tisochrysis lutea, protects against metabolic disorders associated with metabolic syndrome and obesity. Nutrients. 2021 Jan; 13(2): 430. doi: 10.3390/nu13020430.

[58] Hutkins RW, Krumbeck JA, Bindels LB, Cani PD, Fahey Jr G, Goh YJ, *et al*. Prebiotics: why definitions matter. Current Opinion in Biotechnology. 2016 Feb; 37: 1-7. doi: 10.1016/j.copbio.2015.09.001.

[59] Li HY, Zhou DD, Gan RY, Huang SY, Zhao CN, Shang A, *et al*. Effects and mechanisms of probiotics, prebiotics, synbiotics, and postbiotics on metabolic diseases targeting gut microbiota: A narrative review. Nutrients. 2021 Sep; 13(9): 3211. doi: 10.3390/nu13093211.

[60] Silva-Cutini MA, Almeida SA, Nascimento AM, Abreu GR, Bissoli NS, Lenz D, *et al*. Long-term treatment with kefir probiotics ameliorates cardiac function in spontaneously hypertensive rats. The Journal of Nutritional Biochemistry. 2019 Apr; 66: 79-85. doi: 10.1016/j.jnutbio.2019.01.006.

[61] Kobyliak N, Falalyeyeva T, Bodnar P, Beregova T. Probiotics supplemented with omega-3 fatty acids are more effective for hepatic steatosis reduction in an animal model of obesity. Probiotics and Antimicrobial Proteins. 2017 Jun; 9: 123-30. doi: 10.1007/s12602-016-9230-1.

[62] Kobyliak N, Falalyeyeva T, Boyko N, Tsyryuk O, Beregova T, Ostapchenko L. Probiotics and nutraceuticals as a new frontier in obesity prevention and management. Diabetes Research and Clinical Practice. 2018 Jul; 141: 190-9. doi: 10.1016/j.diabres.2018.05.005.

[63] Li Y, Liu M, Liu H, Wei X, Su X, Li M, *et al*. Oral supplements of combined Bacillus licheniformis Zhengchangsheng® and xylooligosaccharides improve high-fat diet-induced obesity and modulate the gut microbiota in rats. BioMed Research International. 2020 May; 2020: 9067821. doi: 10.1155/2020/9067821.

[64] Liu Z, Li L, Ma S, Ye J, Zhang H, Li Y, *et al*. High-dietary

DOI: https://doi.org/10.54393/pjhs.v4i11.1145

fiber intake alleviates antenatal obesity-induced postpartum depression: Roles of gut microbiota and microbial metabolite short-chain fatty acid involved. Journal of Agricultural and Food Chemistry. 2020 Nov; 68(47): 13697-710. doi: 10.1021/acs.jafc.0c04290.

[65] Green M, Arora K, Prakash S. Microbial medicine: prebiotic and probiotic functional foods to target obesity and metabolic syndrome. International Journal of Molecular Sciences. 2020 Apr; 21(8): 2890. doi: 10.3390/ijms21082890.

[66] Boyle RJ, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: what are the risks? The American Journal of Clinical Nutrition. 2006 Jun; 83(6): 1256-64. doi: 10.1093/ajcn/83.6.1256.

[67] Deichmann R, Lavie C, Andrews S. Coenzyme q10 and statin-induced mitochondrial dysfunction. Ochsner Journal. 2010 Mar; 10(1): 16-21.

[68] Ayer A, Macdonald P, Stocker R. CoQ10 function and role in heart failure and ischemic heart disease. Annual Review of Nutrition. 2015 Jul; 35: 175-213. doi: 10.1146/annurev-nutr-071714-034258.

[69] Turunen M, Olsson J, Dallner G. Metabolism and function of coenzyme Q. Biochimica et Biophysica Acta (BBA)-Biomembranes. 2004 Jan; 1660(1-2): 171-99. doi: 10.1016/j.bbamem.2003.11.012.

[70] Digiesi V, Cantini F, Oradei A, Bisi G, Guarino GC, Brocchi A, *et al*. Coenzyme Q10 in essential hypertension. Molecular Aspects of Medicine. 1994 Jan; 15: s257-63. doi: 10.1016/0098-2997(94)90036-1.

[71] Ignarro LJ. Biological actions and properties of endothelium-derived nitric oxide formed and released from artery and vein. Circulation Research. 1989 Jul; 65(1): 1-21. doi: 10.1161/01.res.65.1.1.

[72] Burke BE, Neuenschwander R, Olson RD. Randomized, double-blind, placebo-controlled trial of coenzyme Q10 in isolated systolic hypertension. Southern Medical Journal. 2001 Nov; 94(11): 1112-8. doi: 10.1097/00007611-200111000-00015.

[73] Pinal-Fernandez I, Casal-Dominguez M, Mammen AL. Statins: pros and cons. Medicina Clínica (English Edition). 2018 May; 150(10): 398-402. doi: 10.1016/j.medcli.2017.11.030.

[74] Niazi M, Galehdar N, Jamshidi M, Mohammadi R, Moayyedkazemi A. A review of the role of statins in heart failure treatment. Current Clinical Pharmacology. 2020 Apr; 15(1): 30-7. doi: 10.2174/1574884714666190802125627.

[75] Kumar A, Kaur H, Devi P, Mohan V. Role of coenzyme Q10 (CoQ10) in cardiac disease, hypertension and Meniere-like syndrome. Pharmacology & therapeutics. 2009 Dec; 124(3): 259-68. doi: 10.1016/j.pharmthera.2009.07.003.

[76] Zozina VI, Covantev S, Goroshko OA, Krasnykh LM, Kukes VG. Coenzyme Q10 in cardiovascular and metabolic diseases: current state of the problem. Current Cardiology Reviews. 2018 Aug; 14(3): 164-74. doi: 10.2174/1573403X14666180416115428.

DOI: https://doi.org/10.54393/pjhs.v4i11.999

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Association between Achilles Tendon Injury and Daily Activities Performance in Athletes and Non-Athletes after 1 Month of Injury

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ARTICLE INFO

Key Words:
Achilles Tendon Injury, Activities, Athlete, Non-Athlete, Performance

How to Cite:
Tariq, A., Mousavi Zadeh, S. A., Nazarian, S. K., Ismail, A., Waheed, W. bin, & Komitaki, M. B. (2023). Association between Achilles Tendon Injury and Daily Activities Performance in Athletes and Non-Athletes after 1 Month of Injury: Achilles Tendon Injury and Daily Activities Performance. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.999

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Received Date: 18th August, 2023
Acceptance Date: 7th October, 2023
Published Date: 30th November, 2023

ABSTRACT

Achilles tendon injuries are significant because they affect the mobility of the lower extremities, which is important in both sports and daily life. This research aims to shed light on the more general effects of these injuries on people's functional capacities. **Objective:** To determine the association between Achilles tendon injury and daily activities performance in athletes and non-athletes after 1 month of injury. **Methods:** A cross-sectional analytical study was conducted at the university of Lahore and Punjab stadium Lahore over a four months periods from January to April 2019. A total of 30 subjects male were approached by the non-probability convenient sampling method. Fisher exact test was applied to identify the associated factors. P-value ≤ 0.05 counted as significant. **Results:** Results showed symptoms of Achilles tendon injury effect daily activities of athletes and non-athletes. Majority of athletes who participated in study have stiffness in foot as compared to non-athletes. According to results there is association between ankle/foot giving away during strenuous activity (p-value 0.0025), during moderate activity (p-value 0.005) and in light activity (p value-0.006) in both athletes and non -athletes. **Conclusions:** Both athletes and non-athletes were facing difficulties during activities and cause negative impact on activities of participants after one month of injury.

INTRODUCTION

The thickest and strongest tendon in the human body is the Achilles tendon. It is the tendon that ruptures the most frequently despite its size [1]. The most common cause of Achilles tendon rupture (ATR) is tendon overload, which frequently happens in a sporting environment. Achilles tendinopathy manifests acutely as excruciating pain, the inability to carry weight, and weakness; these impairments can last for more than ten years after the initial injury [2]. Achilles tendinopathy is becoming more common everywhere in the world. Elderly people, who are engaging in recreational physical activity more frequently than in the past, are those who are most noticeable for this increase [3]. The effects of Achilles tendon injuries transcend outside of the sports world and into regular life. The Achilles tendon is essential for performing these basic movements, such as walking, getting out of a chair, and climbing stairs. Therefore, when injuries do occur, they may interfere with these activities and result in a lower

DOI: https://doi.org/10.54393/pjhs.v4i11.999

quality of life [4]. Age, level of physical activity, and general health are all factors that can affect how susceptible the Achilles tendon is to damage [5]. Athletes are particularly prone, especially those who participate in sports that call for abrupt acceleration or jumping. As a result of the tendon and surrounding muscles' lack of training, inactive people may also be at danger [6]. Achilles tendon rupture, which can be a crippling injury requiring medical attention, and Achilles tendonitis, which is characterized by inflammation and pain, are both common ailments [7]. Both athletes and non-athletes regularly experience discomfort and incapacity from achilles tendon problems such as tendinopathy and rupture. These injuries are challenging to treat, take a long time to recover from, and recur frequently [8]. The most often injured area of a tendon is its middle; calcaneal insertion ethereal illness is less frequent. The development of tendon disease is influenced by a number of variables, including the impact of exercise, overuse, hereditary predisposition, and aging [9]. While it is well known that inflammatory mediators play a role in the development and progression of tendon disease in the shoulder, the relative importance and function of inflammation in energy-storing tendons like the Achilles, where disease was once frequently labeled as "degenerative," is hotly contested [10]. A thorough history taking and physical examination serve as the main foundations for the diagnosis of acute Achilles tendon rupture [11]. Patients typically present with an abrupt inability to walk and severe pain when running or leaping. They are typically in their third or fourth decade of life. Patients who have an acute rupture of the tendon frequently remember hearing or feeling like they were being kicked in the back of the ankle when their ankle is dorsiflexed at the back of the leg. Plantar flexion weakness, trouble with weight-bearing ambulation, and limping are all indications of a torn tendon [12]. Rest, physical therapy, and, in some circumstances, surgical intervention are all used to treat Achilles tendon injuries [13]. In order to avoid persistent problems and promote optimum healing, early diagnosis and effective treatment are essential [14]. In order to promote preventive and efficient rehabilitation for people with different levels of activity, it is crucial to understand the mechanisms, risk factors, and management techniques linked to Achilles tendon injuries [15]. The purpose of study was to describe the occurrence of disease, rate/frequency of disease and its effects in athletes and non-athletes which will help physicians and physiotherapists to prevent or decrease the ratio of disease in athletes and non-athletes. The finding of this study will rebound to the benefit of society considering that this study will help in prevention of disease. For researcher the study will help them uncover critical areas of the disease. This study will able to train physiotherapists in recognizing the effects of the disease. It will help physiotherapists to improve the performance of athletes and non-athletes.

METHODS

This Observational cross-sectional study was conducted in Lahore among male individuals aged 22 to 30. We employed the Epitool calculator software to determine the sample size required for robust statistical analyses, considering a Confidence Interval Strength of 95%. Total of 30 participants 23 were athletes and 7 were non-athletes recruited from the Punjab stadium. The study was completed within 4 months from January to April 2019. Non-probability Convenient Sampling was used to collect sample size. Achilles tendon injury was identified by looking at participants past health history. Subjects asked questions about activities performed after one month of Achilles tendon injury from a standardized questioner Victorian Institute of Sport Assessment Achilles (VISA.A). Individuals aged 18 to 60 with diagnosed Achilles tendon injuries(such as tendonitis and partial tears)within the past month were eligible. Both athletes and non-athletes were included. Participants with chronic lower limb conditions, recent surgeries, neurological disorders affecting limb function, incomplete data, or significant medication use were excluded. Data were analyzed by SPSS software 24.0 version. Frequency and percentage of Qualitative variables such as age , BMI were analyzed including physical complaints and symptoms, work related concerns, life style activities, attitudes and feeling related to Achilles tendon injury. The Fisher exact test was used to assess the association between variables and parameters. In adherence to ethical standards, this study obtained approval with reference number 161-10-2023, as confirmed by the official letter received on October 16th, 2023.

RESULTS

30 individuals were participated in which there are 7 were non-athletes (23.33%) and 23 athletes (76.67%). The mean age of participants was 24.25 ±3.63 BMI was normal in majority of individuals ranging from 18.2 to 19.4.

Results of table 1 showed that during any strenuous activity like exercise, heavy weight lifting or during any sports did your ankle/foot give way. 3 non-athletes told not at all, 2 said partially, 2 said the ankle/foot gave way fully. In athletes 4 said not at all, 14 said partially gave way, 3 said it gave way completely while 2 said they were not able to do any activity due to that. In this result 53.3 % participant's ankle/foot partially gave way. Fishers exact showed association between foot/ankle give away during strenuous activity. Fisher exact test showed (p-value 0.0025). According to the results there is association between participants Ankle or foot gave way during strenuous activity.

DOI: https://doi.org/10.54393/pjhs.v4i11.999

Table 1: Association between Achilles tendon injury and strenuous activity

Participants	Did not give way at all	Partially gave way	Complete gave way	Could not do the activity	Total	p-value
Non athlete	3(42.9)	2(28.6)	2(28.6)	0	100%	0.00 25
Athlete	4(17.4)	14(60.9)	3(13.0)	2(8.7)	100%	
Total	7(23.3)	16(53.3)	5(16.7)	2(6.7)	100%	

Table 2 shows Results of moderate activities such as physical working like jogging and running which had less side effects as compared to strenuous activities 71.4% 5 patients of not athletes had nothing in doing activities 28.6% (2) patients ankle feet partially gave way. In athletes 13 patients felt nothing 7 patients ankle partially gave away, 2 patients' foot and ankle completely gave way while 1 was unable to continue work. Fisher exact test showed p-value 0.005 and showed there was association in participants Ankle or foot gave way during moderate activity. According to the results there is association between participants Ankle or foot gave way during Moderate activity.

Table 2: Association between Achilles tendon injury and moderate activity

Participants	Did not give way at all	Partially gave way	Complete gave way	Could not do the activity	Total	p-value
Non athlete	5(71.4)	2(28.6)	0	0	7(100%)	0.005
Athlete	13(56.5)	7(30.4)	2(8.7)	1(4.3)	23(100%)	
Total	18(60)	9(30)	2(6.7)	1(3.3)	30(100%)	

Result of table 3 showed that non-athletes showed no symptoms of Achilles tendon injury during light activities on the other hand 82.6% athletes were comfortable in doing work, 3 patient's foot partially gave away whereas 1 patient's foot completely gave way. Fisher exact test showed no association between foot/ ankle gave away during light activities (p-value 0.006). According to the results there is association between participants Ankle or foot gave way during Light activity.

Table 3: Association between Achilles tendon injury and light activity

Participants	Did not give way at all	Partially gave way	Could not do the activity	Total	p-value
Non athlete	7(100)	0	0	7(100%)	0.006
Athlete	19(82.6)	3(13.0)	1(3.3)	30(100%)	
Total	26(86.7)	3(10)	1(3.3)	30(100%)	

DISCUSSION

This study examined the significant association between Achilles tendon injuries and everyday activity performance in both athletes and non-athletes within a month after injury. Our results highlight a strong correlation between Achilles tendon injuries and decreased performance in daily tasks at both activity levels. With a p-value of less than 0.005, this study identified a strong relationship between variables. Achilles tendon injuries significantly influence people's capacity to engage in normal activities regardless of their degree of activity, according to the striking stability of this association across groups of athletes and non-athletes. Our research is consistent with those that have shown a connection between Achilles tendon injury and decreased performance in daily activities. A weakened Achilles tendon presented significant difficulties for athletes, who are known for their higher levels of physical activity and demands on their lower limbs. This result is in line with earlier studies that emphasize the Achilles tendon's critical function in movements like running, jumping, and rotating, which are common in many sports. Our results highlight how severely an Achilles tendon injury affects an athlete's capacity to do even regular tasks in the initial phases of recuperation. We found a similar correlation in the non-athlete group as well, which is interesting because it suggests that the effects of an Achilles tendon injury go beyond only athletics. Even though non-athletes might not exert themselves to the same degree, their daily activities nonetheless strongly depend on appropriate lower limb function. The Achilles tendon plays a universal role in preserving mobility and function across a wide range of populations, as is highlighted by the fact that athletes share this disability. In previous study, patients reported worse Quality of life in the physical aspects of SF-12 and SF-36, and also showed low VISA-A scores [16]. Lower Quality of life was seen in AT patients, with some factors having a more pronounced detrimental effect than others. For instance, age and gender are two demographic factors that affect quality of life [17]. Scores of Quality of life was decreased significantly, particularly in the areas of mobility, typical activities, and pain/discomfort, are linked to Achilles tendon. A low rate of work absences (reported in 9% of patients) and a higher percentage of patients (38%) reported lower productivity at work as a result of AT [18]. Patients with AT frequently had lower job productivity, which had a negative impact on their performance at work [19]. Similarly, our findings are consistent with earlier research in the field when compared to earlier studies in the field. In their study of athletes and non-athletes, Brorsson et al., found a comparable correlation between Achilles tendon injury and decreased performance in daily activities [20]. Additionally, Johns et al., study looked exclusively at the effects of Achilles tendon injuries on athletes [21]. Similar to the results of our investigation, their research showed a significant impairment in athletes' performance in daily activities within the first month after injury.Patients with Achilles Tendonitis are more likely to experience sadness, kinestophobia, and pain catastrophizing. This pessimism may considerably or moderately decrease their ability to do daily tasks. Some studies suggest that factors like fear and self-efficacy may

DOI: https://doi.org/10.54393/pjhs.v4i11.999

have an impact on tendinopathy [22]. Our investigation highlights the complex relationship between Achilles tendon injuries and decreased daily activity performance in both athletes and non-athletes. The significant statistical significance not only supports our findings but also emphasizes the necessity for a thorough knowledge of the wider ramifications of such injuries. This underlines the significance of specialized rehabilitation strategies that take into account the intricate interactions between impairments and functional results.

CONCLUSIONS

In conclusion, our study underscores a significant association between Achilles tendon injuries and compromised daily activities, impacting both athletes and non-athletes. The results reveal a notable vulnerability in ankle and foot stability during light, moderate, and strenuous activities one month post-injury. These findings emphasize the pervasive influence of Achilles tendon injuries on daily activity performance across diverse activity levels.

Authors Contribution

Conceptualization: AT, WBW
Methodology: AT, SAMZ
Formal analysis: AT
Writing-review and editing: SKN, AI, MBK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Maffulli N. Current concepts review-rupture of the Achilles tendon. JBJS. 1999 Jul; 81(7): 1019-36. doi: 10.2106/00004623-199907000-00017.

[2] Holm C, Kjaer M, Eliasson P. A chilles tendon rupture–treatment and complications: a systematic review. Scandinavian Journal of Medicine & Science in Sports. 2015 Feb; 25(1): e1-0. doi: 10.1111/sms.12209.

[3] Erickson BJ, Cvetanovich GL, Nwachukwu BU, Villarroel LD, Lin JL, Bach Jr BR, et al. Trends in the management of Achilles tendon ruptures in the United States Medicare population, 2005-2011. Orthopaedic Journal of Sports Medicine. 2014 Sep; 2(9): 2325967114549948. doi: 10.1177/2325967114549948.

[4] Verges J, Martínez N, Pascual A, Bibas M, Santiña M, Rodas G. Psychosocial and individual factors affecting Quality of Life (QoL) in patients suffering from Achilles tendinopathy: a systematic review. BMC Musculoskeletal Disorders. 2022 Dec; 23(1): 1114. doi: 10.1186/s12891-022-06090-2.

[5] Kongsgaard M, Aagaard P, Kjaer M, Magnusson SP. Structural Achilles tendon properties in athletes subjected to different exercise modes and in Achilles tendon rupture patients. Journal of Applied Physiology. 2005 Nov; 99(5): 1965-71. doi: 10.1152/japplphysiol.00384.2005.

[6] Möller A, Åström M, Westlin NE. Increasing incidence of Achilles tendon rupture. Acta Orthopaedica Scandinavica. 1996 Jan; 67(5): 479-81. doi: 10.3109/17453679608996672.

[7] Gibbon WW, Cooper JR, Radcliffe GS. Sonographic incidence of tendon microtears in athletes with chronic Achilles tendinosis. British Journal of Sports Medicine. 1999 Apr; 33(2): 129-30. doi: 10.1136/bjsm.33.2.129.

[8] Nistor LA. Surgical and non-surgical treatment of Achilles Tendon rupture. A prospective randomized study. JBJS. 1981 Mar; 63(3): 394-9. doi: 10.2106/00004623-198163030-00012.

[9] Bhandari M, Guyatt GH, Siddiqui F, Morrow F, Busse J, Leighton RK, et al. Treatment of acute Achilles tendon ruptures a systematic overview and metaanalysis. Clinical Orthopaedics and Related Research®. 2002 Jul; 400: 190-200. doi: 10.1097/00003086-200207000-00024.

[10] Dakin SG, Newton J, Martinez FO, Hedley R, Gwilym S, Jones N, et al. Chronic inflammation is a feature of Achilles tendinopathy and rupture. British Journal of Sports Medicine. 2018 Mar; 52(6): 359-67. doi: 10.1136/bjsports-2017-098161.

[11] Järvinen TA, Kannus P, Paavola M, Järvinen TL, Józsa L, Järvinen M. Achilles tendon injuries. Current Opinion in Rheumatology. 2001 Mar; 13(2): 150-5. doi: 10.1097/00002281-200103000-00009.

[12] Kvist M. Achilles tendon injuries in athletes. Annales Chirurgiae et Gynaecologiae. 1991 Jan; 80(2): 188-201.

[13] Maffulli N and Ajis A. Management of chronic ruptures of the Achilles tendon. JBJS. 2008 Jun; 90(6): 1348-60. doi: 10.2106/JBJS.G.01241.

[14] Childress MA and Beutler A. Management of chronic tendon injuries. American Family Physician. 2013 Apr; 87(7): 486-90.

[15] Periasamy M, Venkatramani H, Shanmuganathan RS. Management of chronic Achilles tendon injuries—review of current protocols and surgical options. Indian Journal of Plastic Surgery. 2019 Jan; 52(01): 109-16. doi: 10.1055/s-0039-1687923.

[16] Marshall S, Haywood K, Fitzpatrick R. Impact of

DOI: https://doi.org/10.54393/pjhs.v4i11.999

patient-reported outcome measures on routine practice: a structured review. Journal of Evaluation in Clinical Practice. 2006 Oct; 12(5): 559-68. doi: 10.1111/j.1365-2753.2006.00650.x.

[17] López-López D, Becerro-de-Bengoa-Vallejo R, Losa-Iglesias ME, Palomo-López P, Rodríguez-Sanz D, Brandariz-Pereira JM, et al. Evaluation of foot health related quality of life in individuals with foot problems by gender: a cross-sectional comparative analysis study. BMJ Open. 2018 Oct; 8(10): e023980. doi: 10.1136/bmjopen-2018-023980.

[18] Visser TS, Van Der Vlist AC, Van Oosterom RF, Van Veldhoven P, Verhaar JA, de Vos RJ. Impact of chronic Achilles tendinopathy on health-related quality of life, work performance, healthcare utilisation and costs. BMJ Open Sport & Exercise Medicine. 2021 Mar; 7(1): e001023. doi: 10.1136/bmjsem-2020-001023.

[19] Martimo KP, Shiri R, Miranda H, Ketola R, Varonen H, Viikari-Juntura E. Self-reported productivity loss among workers with upper extremity disorders. Scandinavian Journal of Work, Environment & Health. 2009 Jul; 35(4): 301-8. doi: 10.5271/sjweh.1333.

[20] Brorsson A, Grävare Silbernagel K, Olsson N, Nilsson Helander K. Calf muscle performance deficits remain 7 years after an Achilles tendon rupture. The American Journal of Sports Medicine. 2018 Feb; 46(2): 470-7. doi: 10.1177/0363546517737055.

[21] Johns W, Walley KC, Seedat R, Thordarson DB, Jackson B, Gonzalez T. Career outlook and performance of professional athletes after Achilles tendon rupture: a systematic review. Foot & Ankle International. 2021 Apr; 42(4): 495-509. doi: 10.1177/1071100720969633.

[22] Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, Monfort J, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskeletal Disorders. 2019 Dec; 20(1): 1-2. doi: 10.1186/s12891-019-2895-3.

DOI: https://doi.org/10.54393/pjhs.v4i11.1127

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Association between Vitamin D Deficiency and Preeclampsia among Pregnant Females during First Trimester

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ARTICLE INFO

Key Words:
Preeclampsia, Vitamin D, Hypertension

How to Cite:
Syed, S. Z., Fatima, B., Waheed, F., Akhter, N., & Butt, S. (2023). Association between Vitamin D Deficiency and Preeclampsia among Pregnant Females during First Trimester: Vitamin D Deficiency and Preeclampsia. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1127

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Received Date: 14th October. 2023
Acceptance Date: 13th November, 2023
Published Date: 30th November, 2023

ABSTRACT

One of issue during pregnancy among women is vitamin D insufficiency and studies have shown a dose-response relationship between development of preeclampsia and maternal vitamin D levels. **Objective:** To determine any association between vitamin D insufficiency in blood during the first trimester of pregnancy and development of preeclampsia. **Methods:** It was a Case Control study conducted in Department of Obstetrics and Gynecology, Lady Willingdon Hospital Lahore, from September 2019 to August, 2020. 150 women fulfilling selection criteria were enrolled from OPD of Lady Willingdon Hospital, Lahore. Informed consent was taken. Demographic variables e.g. age, gestational age, parity and BMI were recorded. Then females were divided in two groups i.e. cases with preeclampsia and controls without preeclampsia. Then medical record was obtained and vitamin D level during first trimester was noted. If vitamin D <20ng/dl, then vitamin D deficiency was labeled (as per operational definition). Data were entered and analyzed in SPSS version 20.0. Frequency and percentages were calculated for qualitative variables. **Results:** Mean age was 28.01±3.43 years. Mean gestational age was estimated as 32.84±4.75 weeks in cases and 32.24±3.55 in controls, Vitamin D deficiency in blood during the first trimester of pregnancy and development of preeclampsia shows that 90.67% in cases and 82.67% in controls had vitamin D deficiency with odds ratio of 2.03. **Conclusions:** We concluded that there is an association between vitamin D deficiency in blood during the first trimester of pregnancy and development of preeclampsia.

INTRODUCTION

Hypertensive disorders during pregnancy are very prevalent in developing countries with one-quarter of maternal deaths with hypertensive disorders during pregnancy occur in Asia and Africa. Preeclampsia and eclampsia are the major hypertensive disorders that constitute major morbidity and mortality in newborn and mothers [1]. The intrauterine fetal development and infant health later is greatly influenced by Vitamin D status during pregnancy. Among pregnant women vitamin D levels tend to decrease from their normal range and its optimal requirements for the body is also greatly affected for several reasons. This leads to either development of vitamin D insufficiency or deficiency among pregnant women especially in first trimester of pregnancy. This directly affects both the mother and fetus and later in the offspring. However, there is insufficient high-quality data, especially no randomized controlled trials have been done on vitamin D optimal reference range for both mother and neonate to get the most of the health benefits [2]. Christesen *et al.*, in a different study concluded that there is

DOI: https://doi.org/10.54393/pjhs.v4i11.1127

an inverse relationship between maternal vitamin D concentrations and specific pregnancy outcomes such as, preeclampsia, gestational diabetes, and other infertility parameters [3]. Vitamin D status is measured by a specific marker concentration that is 25(OH)D, and data suggest there are valid scientific evidence that levels above 50 nmol/l (>20ng/ml) serum values of 25(OH)D are satisfactory level for a good health status especially in females during pregnancy [4]. In an Indian study, it was reported that about 82.8% females with preeclampsia and 31.25% females without preeclampsia were found deficient in vitamin D (<20ng/dl, p<0.05) [5]. In another Indian study, it was found that almost 100% females with preeclampsia and 92% females without preeclampsia were found to have a deficient in 25(OH)D i.e. <20ng/dl, which was statistically significant. (p>0.05) [6]. However, one American study found that about 11% females with preeclampsia and 10% females without preeclampsia were found deficient in vitamin D (<20ng/dl, p>0.05) [7]. The aim of this study is to evaluate any association between vitamin D deficiency in blood during the first trimester of pregnancy and preeclampsia. Literature reported that in pregnant females who belong to developed country, there is no relationship of vitamin D deficiency with preeclampsia but there is a significant association was found between vitamin D deficiencies in first trimester with preeclampsia in developing countries, also varied data has been retrieved from literature. Vitamin D deficiency and insufficiency are prevalent, particularly in pregnant women, worldwide and also in Pakistan, which is considered an important public health concern. So it can be said that if serum vitamin D level is maintained in pregnant ladies then the ratio of morbidity and mortality can be decreased. So, we want to conduct this study to get local evidence and confirm whether association exists. Therefore, this study will help to get updated and confirmed results and we may be able to implement the screening of pregnant females for vitamin D level in early pregnancy in order to prevent preeclampsia and its consequences. The objective of study was to evaluate any association between vitamin D deficiency in blood during the first trimester of pregnancy and development of preeclampsia.

METHODS

We conducted a case control study at department of Gynecology and Obstetrics out-door patient of Lady Willingdon Hospital, Lahore, Pakistan from September 2019 to August 2020. Sample size of 150 women (75 in Group A (Cases) and 75 in Group B (controls) was calculated with 80% power of study, 5% significance level and taking expected percentage of vitamin D deficiency i.e. 100% in women with preeclampsia and 92% in women without preeclampsia and selected through non-probability, consecutive sampling. Women aged 18-40 years, parity <5, who were enrolled during third trimester (>20 weeks on LMP) for antenatal care. Cases was women with preeclampsia and normotensive women were taken as controls. Un-booked women or women with incomplete antenatal record, women with chronic hypertension, multiple fetuses, previous abortion and women taking vitamin D supplements from first trimester were excluded. Medical record was obtained and vitamin D level during first trimester was noted. If vitamin D <20ng/dl, then vitamin D deficiency was labeled. Data were entered and analyzed in SPSS v 22.0. Numerical variables like age, BMI, gestational age was presented as mean ± SD. Qualitative variables like vitamin D deficiency and parity were presented as frequency and percentage. Association between vitamin D deficiency and preeclampsia was evaluated through Odds ratio with OR > 1 was considered as statistically significant. Data were stratified for confounding variables like age, gestational age, parity and BMI and post-stratification, OR was calculated with p value ≤0.05 was considered as significant.

RESULTS

A total of 150 women (75 in Group A (Cases) and 75 in Group B (controls) were enrolled to determine the association between vitamin D deficiency in blood during the first trimester of pregnancy and development of preeclampsia. 74.67% (n=56) in cases and 73.33% in controls were between 18-30 years of age. Mean age was 28.01±3.43 years in cases and 28.13±3.53 in controls. Mean gestational age was estimated as 32.84±4.75 weeks in cases and 32.24±3.55 weeks in controls. Parity distribution reveals that 57.33% in cases and 62.67% in controls were having 1-2 parity whereas 42.67% (n=32) in cases and 37.33% (n=28) in controls were between 3-4 parity, mean ± SD was 2.40±0.82 in cases and 2.31±0.72 in controls. Body mass index was 29.17±3.52 in cases and 29.19±3.49 in controls (Table 1 and 2).

Table 1: Frequency distribution of age, gestational age and parity of respondents (n=150)

Variables		Cases (n=75)	Controls (n=75)
		Frequency (%)	Frequency (%)
Age (years)	18-30	56 (74.67)	55 (73.33)
	31-40	19 (25.33)	20 (26.67)
G. Age (weeks)	20-37	60 (80)	63 (84)
	>37	15 (20)	12 (16)
Parity	1-2	43 (57.33)	47 (62.67)
	3-4	32 (42.67)	28 (37.33)

DOI: https://doi.org/10.54393/pjhs.v4i11.1127

Table 2: Statistics for age, gestational age and BMI of respondents(n=150)

Variables	Cases (n=75)	Controls (n=75)
Age (years)	28.01 ± 3.43	28.13 ± 3.55
G. Age (weeks)	32.84 ± 4.75	32.24 ± 3.55
BMI	29.17 ± 3.52	29.17 ± 3.52

There were 90.67% (n=68) in cases and 82.67% (n=62) in controls had vitamin D deficiency whereas 9.33% (n=7) in cases and 17.33% (n=13) in controls had no vitamin D deficiency, O.R was calculated as 2.03. (p > 0.05). The data were stratified for age, gestational age, parity and BMI. Post-stratification, OR was calculated to measure association between vitamin D deficiency and preeclampsia for each strata. OR > 1 with p ≤0.05 was taken as significant (Table 3).

Table 3: Cross tabulation for vitamin D deficiency and age, gestational age, parity and BMI of respondents(n=150)

Variables n=150			Cases (n=75)	Controls (n=75)	O.R	p-value
Vitamin D Deficiency		Yes	68	62	2.03	0.155
		No	7	13		
Age (years)	18-30	Yes	51	47	1.73	0.36
		No	5	8		
	31-40	Yes	17	15	2.83	0.25
		No	2	5		
G. Age (weeks)	20-37	Yes	55	50	2.86	0.06
		No	5	13		
	>37	Yes	13	12	0.21	0.33
		No	2	0		
Parity	1-2	Yes	36	39	1.05	0.92
		No	7	8		
	3-4	Yes	32	23	15.21	0.06
		No	0	5		
BMI	Up to 30	Yes	42	39	1.94	0.27
		No	5	9		
	>30	Yes	26	23	2.26	0.37
		No	2	4		

DISCUSSION

Vitamin D insufficiency during pregnancy is significant public health issue among females worldwide but it's more marked in developing countries due to poor diet and nutritional status. There are several risk factors especially in Muslim countries for vitamin D insufficiency that includes low dietary vitamin D intake, extensive skin covering and ethnicity. In developed countries excessive use of sun protection, overweight, obesity and smoking seem to be precipitation factors. There is also a seasonal variation observed at temperate latitudes. Our study was conducted to determine any association between preeclampsia development in the first trimester of pregnancy and vitamin D insufficiency. Several studies done in developed countries have found no relationship of vitamin D deficiency with preeclampsia. On the contrary studies done in developing countries, the vitamin D deficiency in first trimester was found to be significantly associated with preeclampsia; also varied data has been retrieved from literature [7]. This study also attempted to evaluate any association between development of preeclampsia during the first trimester of pregnancy and vitamin D insufficiency. Our data suggest that association between vitamin D insufficiency in blood and development of preeclampsia shows a significant relationship. 90.67% (n=68) of cases and 82.67% (n=62) in controls had vitamin D deficiency (OR 2.03). These findings are supported by an Indian study, where 100% females with preeclampsia and 92% females without preeclampsia were found deficient in vitamin D (<20ng/dl, p>0.05) [6]. There is a conflicting data regarding hypertensive diseases among pregnancy like pre- eclampsia and eclampsia development and Vitamin D insufficiency. Some studies suggest that women with low levels of vitamin D (<50 nmol/l) developed pre-eclampsia and a five- fold increased risk of developing severe pre-eclampsia [8-10]. The risk of developing pre- eclampsia among women with low levels of Vitamin D (<50 nmol/l) in the first half of pregnancy was significant [11] and there is a two-fold increased risk of having vitamin D deficiency (< 37.5 nmol/l) among the neonates of these mothers [12]. Robinson *et al.*, study showed that vitamin D levels <50 nmol/l among pregnant women before 34 weeks of gestation developed severe pre-eclampsia as compared to controls [13]. Additionally, women with early-onset severe pre-eclampsia and with small-for-gestational- age (SGA) neonates have significantly lower vitamin D levels (< 37.5 nmol/l) as compared to women with early-onset severe pre-eclampsia but non-SGA neonates [14]. Ringrose *et al.*, research in their uni-variate analysis showed that pregnant females with low circulating Vitamin D levels (< 37.5 nmol/l) are more likely to have hypertensive disease in pregnancy, but these findings were not substantiated in multivariate analysis [15]. Nevertheless, results of several researchers have shown a weak to non-significant relationship between hypertensive disorders during pregnancy and vitamin D insufficiency [14-16]. A study conducted in 179 patients by Ali *et al.*, concluded that fewer (1.2 %) pre-eclampsia reported in control group having maternal vitamin D level >50 nmol/ml as compared to more pre-eclampsia (8.6%) reported in study group having maternal vitamin D level <50 nmol/ml. Similarly, IUGR was lesser 9.6% and 22.2% respectively [17]. Another study conducted with 172 patients by Shahid S and associates reported significantly lower vitamin D levels (p < 0.001) in pre-eclampsia group as compared to normotensive group. This study found a strong relationship between low vitamin D levels and pre eclamptic manifestation [18]. A case control study

DOI: https://doi.org/10.54393/pjhs.v4i11.1127

conducted by Achkar *et al.*, showed that pre-eclampsia had a significant lower 25(OH) D concentration at 14 weeks gestation as compared women in control group [19]. While another study conducted by Mirzakhani *et al.*, denied with the above said results and reported no reduction in pre-eclampsia incidence in intention to treat paradigm group treated by vitamin D supplementation [20]. Shand *et al.*, was also unable to find any association between gestational hypertension, development of preeclampsia or preterm birth and vitamin D insufficiency [16]. A similar study by Powe *et al.*, also unable to find any association between low vitamin D during first trimester and the consequent development of preeclampsia after controlling BMI [21]. However, two meta- analyses, including 31 studies, demonstrated that there is association between pre-eclampsia and SGA infants and vitamin D insufficiency [21, 22]. A systematic review of several case-control and cross-sectional studies by Purswani *et al.*, have shown as association between vitamin D status and pre-eclampsia [23]. A study by Wei *et al.*, showed that women with circulating 25-hydroxyvitamin D [25(OH)D] level less than 50 nmol/l in pregnancy experienced an increased risk of preeclampsia odds ratio (OR)2.09[24]. In summary, we are of the view that vitamin D insufficiency is very common among pregnant women in this region as our sample size came from a diverse background from different areas in Pakistan. This should be considered a major public health issue among pregnant women especially in first trimester. We recommend that a daily supplementation among women especially during pregnancy oral cholecalciferol or ergocalciferol must be given and that is found to be safe during pregnancy. The NICE guidelines and UK Chief Medical Officers recommendations 2012 suggests that health education must be instituted during pregnancy and among women who are breastfeeding regarding the important role vitamin D plays in fetal and maternal health and a daily recommended allowance of 10 micrograms of vitamin D supplements should be recommended [25, 26]. Women especially pregnant and those who are breast feeding are at high risk of Vitamin D insufficiency and particular care must be taken for them. The NICE guidelines recommend vitamin D supplementation that are based on the established benefits of vitamin D supplementation during stress like pregnancy and lactation among females but many other general actions of vitamin D can also provide additional benefits during and after pregnancy.

CONCLUSIONS

We concluded that there is a significant association between development of preeclampsia during the first trimester of pregnancy and vitamin D deficiency.

Authors Contribution

Conceptualization: SZS, BF
Methodology: FW, SB
Formal analysis: NA
Writing-review and editing: SZS, BF

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] World Health Organization. Nutritional interventions update: vitamin D supplements during pregnancy. 2020. [Last cited: 6th Nov 2023]. Available at: http://www.who.int/elena/titles/vitamind_supp_pregnancy/en/.

[2] Gharaibeh MA and Stoecker BJ. Assessment of serum 25 (OH) D concentration in women of childbearing age and their preschool children in Northern Jordan during summer. European Journal of Clinical Nutrition. 2009 Nov; 63(11): 1320-6. doi: 10.1038/ejcn.2009.99.

[3] Christesen HT, Elvander C, Lamont RF, Jørgensen JS. The impact of vitamin D in pregnancy on extraskeletal health in children: a systematic review. Acta Obstetricia et Gynecologica Scandinavica. 2012 Dec; 91(12): 1368-80. doi: 10.1111/aogs.12006.

[4] Christesen HT, Falkenberg T, Lamont RF, Jørgensen JS. The impact of vitamin D on pregnancy: a systematic review. Acta Obstetricia et Gynecologica Scandinavica. 2012 Dec; 91(12): 1357-67. doi: 10.1111/aogs.12000.

[5] Singh A, Mishra S, Aditya V, Srivastava R. Association of vitamin D deficiency with occurrence of pre eclampsia among inpatients of tertiary care centre, Gorakhpur, Uttar Pradesh, India. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016 May; 5(5): 1304-9. doi: 10.18203/2320-1770.ijrcog20161280.

[6] Goel P, Garg G, Kaur J, Mehra R, Tandon R, Huria A. Association of vitamin D deficiency during pregnancy with preeclampsia and eclampsia. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016 Sep; 5(9): 3046-51. doi: 10.18203/2320-1770.ijrcog20162982.

[7] Flood-Nichols SK, Tinnemore D, Huang RR, Napolitano PG, Ippolito DL. Vitamin D deficiency in early pregnancy. PLoS One. 2015 Apr; 10(4): e0123763.

DOI: https://doi.org/10.54393/pjhs.v4i11.1127

doi: 10.1371/journal.pone.0123763.

[8] Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American college of obstetricians and gynecologists' task force on hypertension in pregnancy. Obstetrics and Gynecology. 2013 Nov; 122(5): 1122-1131. doi: 10.1097/01.AOG.0000437382.03963.88.

[9] ACOG Committee on Obstetric Practice. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. International Journal of Gynaecology and Obstetrics. 2002 Apr; 77(1): 67. doi: 10.1016/S0029-7844(01)01747-1.

[10] Berg CJ, MacKay AP, Qin C, Callaghan WM. Overview of maternal morbidity during hospitalization for labor and delivery in the United States: 1993–1997 and 2001–2005. Obstetrics & Gynecology. 2009 May; 113(5): 1075-81. doi: 10.1097/AOG.0b013e3181a09fc0.

[11] Baker AM, Haeri S, Camargo Jr CA, Espinola JA, Stuebe AM. A nested case-control study of midgestation vitamin D deficiency and risk of severe preeclampsia. The Journal of Clinical Endocrinology & Metabolism. 2010 Nov; 95(11): 5105-9. doi: 10.1210/jc.2010-0996.

[12] Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. The Journal of Clinical Endocrinology & Metabolism. 2007 Sep; 92(9): 3517-22. doi: 10.1210/jc.2007-0718.

[13] Robinson CJ, Alanis MC, Wagner CL, Hollis BW, Johnson DD. Plasma 25-hydroxyvitamin D levels in early-onset severe preeclampsia. American Journal of Obstetrics and Gynecology. 2010 Oct; 203(4): 366-e1. doi: 10.1016/j.ajog.2010.06.036.

[14] Robinson CJ, Wagner CL, Hollis BW, Baatz JE, Johnson DD. Maternal vitamin D and fetal growth in early-onset severe preeclampsia. American Journal of Obstetrics and Gynecology. 2011 Jun; 204(6): 556-e1. doi: 10.1016/j.ajog.2011.03.022.

[15] Ringrose JS, PausJenssen AM, Wilson M, Blanco L, Ward H, Wilson TW. Vitamin D and hypertension in pregnancy. Clinical and Investigative Medicine. 2011 Jun; 34(3): E147-54. doi: 10.25011/cim.v34i3.15187.

[16] Shand AW, Nassar N, Von Dadelszen P, Innis SM, Green TJ. Maternal vitamin D status in pregnancy and adverse pregnancy outcomes in a group at high risk for pre-eclampsia. BJOG: An International Journal of Obstetrics & Gynaecology. 2010 Dec; 117(13): 1593-8. doi: 10.1111/j.1471-0528.2010.02742.x.

[17] Ali AM, Alobaid A, Malhis TN, Khattab AF. Effect of vitamin D3 supplementation in pregnancy on risk of pre-eclampsia–Randomized controlled trial. Clinical Nutrition. 2019 Apr; 38(2): 557-63. doi: 10.1016/j.clnu.2018.02.023.

[18] Shahid S, Ladak A, Fatima SS, Zaidi FA, Farhat S. Association of vitamin D levels with preeclampsia. JPMA. The Journal of the Pakistan Medical Association. 2020 Dec; 70(12(B)): 2390-3.

[19] Achkar M, Dodds L, Giguère Y, Forest JC, Armson BA, Woolcott C, *et al.* Vitamin D status in early pregnancy and risk of preeclampsia. American Journal of Obstetrics and Gynecology. 2015 Apr; 212(4): 511-e1. doi: 10.1016/j.ajog.2014.11.009.

[20] Mirzakhani H, Litonjua AA, McElrath TF, O'Connor G, Lee-Parritz A, Iverson R, *et al.* Early pregnancy vitamin D status and risk of preeclampsia. The Journal of Clinical Investigation. 2016 Dec; 126(12): 4702-15. doi: 10.1172/JCI89031.

[21] Powe CE, Seely EW, Rana S, Bhan I, Ecker J, Karumanchi SA, *et al.* First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. Hypertension. 2010 Oct; 56(4): 758-63. doi: 10.1161/HYPERTENSIONAHA.110.158238.

[22] Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. BMJ. 2013 Mar; 346: f1169. doi: 10.1136/bmj.f1169.

[23] Purswani JM, Gala P, Dwarkanath P, Larkin HM, Kurpad A, Mehta S. The role of vitamin D in pre-eclampsia: a systematic review. BMC Pregnancy and Childbirth. 2017 Dec; 17(1): 1-5. doi: 10.1186/s12884-017-1408-3.

[24] Wei SQ, Qi HP, Luo ZC, Fraser WD. Maternal vitamin D status and adverse pregnancy outcomes: a systematic review and meta-analysis. The Journal of Maternal-Fetal & Neonatal Medicine. 2013 Jun; 26(9): 889-99. doi: 10.3109/14767058.2013.765849.

[25] Davies DSC, Jewell T, McBride M, Burns H. Vitamin D-Advice on Supplements for at Risk Groups. 2021. [Last cited: 6th Nov 2023]. Available at: https://assets.publishing.service.gov.uk/media/5a7c59a3ed915d338141e3af/dh_132508.pdf.

[26] National Institute for Health and Clinical Excellence. Antenatal care for uncomplicated pregnancies. 2019. [Last cited: 6th Nov 2023]. Available at: https://www.nice.org.uk/guidance/cg62.

DOI:http://doi.org/10.54393/pjhs.v4i11.1128

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Efficacy of Ferrous Bis-Glycinate versus Ferrous Sulphate in Children with Iron Deficiency Anemia

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ARTICLE INFO

Key Words:
Iron Deficiency Anemia, Children, Ferrous Sulphate, Bisglycinate

How to Cite:
Khan, A., Muhammad, L., Inayatullah, ., Ali, S., Abdulhaq, A., & Rahman, Z. (2023). Efficacy of Ferrous Bis-Glycinate versus Ferrous Sulphate in Children with Iron Deficiency Anemia: Efficacy of Ferrous Bis-Glycinate versus Ferrous Sulphate. Pakistan Journal of Health Sciences, 4(11).https://doi.org/10.54393/pjhs.v4i11.1128

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Received Date: 17th October, 2023
Acceptance Date: 6th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Iron deficiency anemia is a common pediatric disease and oral iron supplementation is the usual treatment. Newer formulations has been developed to treat iron deficiency anemia in children. **Objective:** To compare the efficacy of ferrous Bis-Glycinate in children with iron deficiency anemia to the conventional therapy with ferrous sulphate. **Methods:** In this open labelled prospective clinical trial was performed in children with iron deficiency anemia. Two groups were made, one group was given ferrous sulphate and the other group ferrous bis-glycinate at a dose of 5 mg/kg/day, single daily dose. Patient were followed 04 weekly till 12 weeks and then baselines reviewed. **Results:** Out of these total 108 children, 64 (59.3%) were male while the remaining 40.7% were female, with mean age was 27.48 in months with SD of 14.1. Iron therapy succefully raised Hb by 3.49 gm/dl as a whole with in Iron Bis -glycinate group as 3.85d/dl while 3.13gm /dl in ferrous sulphate group. The frequency of gastrointestinal adverse symptoms were less in bis-glycinate group. **Conclusions:** It was concluded that ferrous bis-glyicante has better efficacy to ferrous sulphate in term of Hb rising and has less gastrointestinal side effects.

INTRODUCTION

Anaemia, a condition in which the haemoglobin of the blood is lower than normal, is primarily a nutritional problem in most developing countries due to the economic, social, and other negative consequences of this condition [1]. Anaemia results from poor nutritional status of children in Pakistan [2]. Anaemia is caused by a lack of one or more essential nutrients such as iron, vitamin B12, or folic acid. Using haemoglobin levels as a criterion for iron deficiency anaemia, serum haemoglobin levels of 7–10.9 and 7 g/dl represent moderate and severe anaemia, respectively [3]. Iron deficiency is the most frequent malnutrition, affecting up to 20% of the global population, according to the WHO. It occurs when dietary iron fails to meet the body's iron requirements. Reduced iron transport to target areas such as the liver parenchyma, bone marrow, and muscle myoglobin impairs iron-dependent activities like erythropoiesis. A decrease in the quantity of red blood cells may be accompanied by a drop in mean cell size (microcytic anaemia). The net result is decreased oxygen carrying capacity and, as a result, tissue hypoxia [4]. In Pakistan, the prevalence of iron deficiency anemia ranged from 64% to 79% in children aged 5 years [3]. Common causes of iron deficiency include insufficient dietary iron intake, insufficient iron

DOI:http://doi.org/10.54393/pjhs.v4i11.1128

utilization during chronic and inflammatory diseases, impaired iron absorption, or excess iron loss. The cause of iron deficiency anemia is avoidable and reversible in the vast majority of cases by increasing iron supplementation or reducing iron loss [2]. It is common in children during rapid growth and erythroid expansion, particularly in premature or low-birth-weight babies, toddlers, and preschool children, and during adolescence. Iron deficiency anemia is linked to delayed cognitive development in preschool-aged children as well as lower work productivity and cognitive and behavioral issues in adults [5-13]. Although ferrous sulfate is the most often used iron salt for oral delivery, it is known to cause intestinal side effects such as nausea, vomiting, abdominal pain, constipation, and diarrhea in many users. Various novel iron salts are being introduced that are claimed to have minimal gastrointestinal intolerance and thus higher patient compliance [14]. A few of these novel preparations are also reported to boost hemoglobin levels faster and improve iron storage better than traditional ferrous sulfate and ferrous fumarate. Ferrous Bis-glycinate is one of them. Ferrous Bis-glycinate is an amino acid chelate that has shown great efficacy, less gastrointestinal irritation, and its absorption is not hampered by the presence of phytates [2]. A study reported a significant increase in the hemoglobin level from 8.0 g/dl to 10.5 g/dl, a change of 2.5 g/dl with ferrous Bis-glycinate compared to 8.7 g/dl to 10.5 g/dl [15]. In Pakistan, there have been few studies comparing the efficiency of ferrous sulfate. As a result, we will undertake a study to establish the advantages of ferrous Bis-glycinate over ferrous sulfate in terms of change in mean hemoglobin levels after 12 weeks of therapy and gastrointestinal tolerability. The study's findings could provide additional evidence for physicians to use ferrous bis-glycinate as a regular medication for the treatment of iron-deficient anemia in children.

METHODS

It was a Randomized Controlled Trial (RCT) conducted at Lady Reading Hospital's Pediatrics Department in Peshawar for six months following after approval from Institutional Research Board. The sample size was estimated using the WHO sample size calculation using 90% confidence interval, 80% power of test, and mean Hb P2 = 1.86 1.59 (15), Hb P1 = 2.56 1.31 (15). The sample size required each group to have 54 children of iron-deficiency anemia (54 in group 1 and 54 in group 2). Non-probability consecutive sampling was the sampling approach used. Inclusion criteria was a child newly diagnosed with Iron deficiency anemia as per operational definition and has the following features; 1. Age range: 6 to 60 months. 2. Both genders. The following children were excluded from the study; 1. Children with Thalassemia trait. 2. Children with chronic inflammatory disease. 3. Children with renal insufficiency. 4. Children with intestinal surgeries requiring resection. 5. Parents not willing to give informed consent. Before the study conducted, permission from Institutional Research Board was obtained. In order to participate in the study, parents or guardians informed consent was sought. All children aged 6 to 60 months who met the above-mentioned inclusion criteria for iron deficiency anemia presenting to the outpatient department of the hospital were included in the study. A random table generated by a computer for selection of patient to clinical trial group. The enrolled children were randomly assigned to one of two trial groups: ferrous sulfate or ferrous bisglycinate. Group 1 received a daily dose of 5 mg of iron per kilogram of body weight of ferrous sulphate, while group 2 received 5mg/kg of iron of ferrous bisglycinate. Both groups received a daily dose of 5 mg of iron per kilogram of body weight. Characteristics of the population—age and gender—were inquired about and recorded on a specifically developed proforma. Laboratory findings were also recorded in proforma. After every 04 weeks of therapy with ferrous sulphate or ferrous bisglycinate patients were followed in outdoor and checked compliance and adverse effects if they have experienced. After 12 weeks of therapy Hb of all patients were repeated and recorded in the proforma. The difference between the last visit (after therapy) and 1st visit (at the start of therapy) were calculated and recorded. SPSS version 20.0 was used to enter and evaluate the data. Continuous variables, such as age and hemoglobin change were calculated. The frequencies and, for categorical factors such as gender, percentages will be calculated. The Student t test was applied to compare the change in Hb between the two study groups. P-values were calculated. The level of significance p-value < 0.05 was considered. Furthermore, for effect modifiers, comparison will be done by stratifying the child's sex and age. The student t-test was used after stratification.

RESULTS

The total subjects (children with iron deficiency anemia) in this study were 108 divided in two groups equally (54 in either group), one group patients were treated with ferrous sulfate while the other with ferrous Bis-glycinate. Out of these total 108 children (patients), 64 (59.3%) were male while the remaining 40.7% were female, whose mean age was 27.48 in month with SD of 14.1. The frequency of nausea, vomiting and diarrhea after iron therapy were 5(4.6%), 12(11.1%) and 32(29.6%) respectively. After the iron therapy the mean change in Hb level in g/dl as whole was 3.49 with SD of 0.143, while in Group 1 the mean change in Hb level in g/dl was 3.13 with SD of 0.146, while in Group 2

DOI:http://doi.org/10.54393/pjhs.v4i11.1128

the mean change in Hb level was 3.85with SD of 0.140, applying the independent t-test the p value is 0.000001 which is significant. More over the chi-square test was used to compare the adverse effects of either therapy which concluded that only 3 patient had complained of nausea taking FeSO4 while 2 patients reported with nausea treated with ferrous Bis-glycinate (p-vale of 0.647), vomiting was noted in 9 patients who were given FeSO4, while in case of ferrous Bis-glycinate therapy only 3 patient had complained of vomiting (p-value (0.066). Similarly with FeSO4 therapy the diarrhea was reported in 21 patients while diarrhea was noted in 11 patients who had taken ferrous Bis-glycinate with 0.035 p-value. Table 1 shows that total subjects (children with iron deficiency anemia) in this study were 108(54 in either group), out of these 64(59.3%) were male while the remaining 40.7% were female. The frequency of nausea, vomiting and diarrhea after iron therapy were 5(4.6%), 12(11.1%) and 32(29.62%) respectively.

Table 1: Frequency and percentage

Variable		Frequency (%)
Gender	Male	64 (59.3)
	Female	44 (40.7)
	Total	108 (100.0)
Nausea	Yes	5 (4.6)
	No	103 (95.3)
	Total	108 (100.0)
Vomiting	Yes	12 (11.1)
	No	96 (88.9)
	Total	108 (100.0)
Diarrhea	Yes	32 (29.62)
	No	76 (70.37)
	Total	108 (100.0)

Table 2 shows that 54 subjects (children with IDA) the mean change in Hb level in g/dl was 3.85 with SD of 0.140 who were given Ferrous Bis-glycinate, while the remaining 54 subject treated with Feso4 the mean change in Hb level was 3.13 with SD of 0.140, applying the independent t-test the p-value is 0.000001 which is significant.

Table 2: Mean change in Hb

Change in HB	Mean ± SD	t-test for Equality of Means p-value
FeSO4	3.133±0.146	.0000001
Iron Bis-glycinate	3.855±0.140	

Table 3 shows that only 3 patient had complained of nausea taking FeSO4 while nausea was reported in 2 patients treated with ferrous Bis-glycinate (p-vale of 0.0647), vomiting was noted in 9 patients who were given FeSO4, while in case of ferrous Bis-glycinate therapy only 3 patient had complained of vomiting (p-value 0.066) similarly with FeSO4 therapy the diarrhea was reported in 21 patients while diarrhea was noted in 11 patients who had taken ferrous Bis-glycinate with 0.035 p-value.

Table 3: Symptoms after iron therapy

Iron therapy	Mean ± SD	Vomiting	Diarrhea
FeSO4	3	9	21
Ferrous Bis-glycinat	2	3	11
P-value	0.0647	0.066	0.035

DISCUSSION

Iron deficiency anemia is widespread in children and has significant impact on their health and development [16]. A proper history, clinical examination, and baseline work up can lead to diagnosis of iron deficiency anemia. Iron supplementation therapy is a successful treatment technique that has been used for a long time [17]. As science advances, attempts are undertaken to create various iron formulations for the treatment of iron deficiency anemia [18]. Our research is part of an effort to find a better treatment option for iron deficient anemia. We compared traditional iron (ferrous sulphate) therapy to a novel preparation (ferrous Bis-glycinate) in our study. Our study found that ferrous Bis-glycinate was more effective than ferrous sulfate in boosting hemoglobin levels in children with IDA to an average of 3.8 g/dl. With a value of 0.000, the p value was significant. Furthermore, ferrous sulfate was associated with higher adverse effects. Vomiting was more common in the ferrous sulfate group (6 patients, approximately 10%) and occurred in only one patient in the Iron Bis-glycinate group. Similarly, diarrhea was detected in 14 patients receiving ferrous sulfate therapy, while diarrhea was noted in 5 patients receiving ferrous Bis-glycinate with a 0.025 p-value. Yasa *et al.*, did a study identical to ours with 103 children ranging in age from 6 months to 17 years with 42 females and 61 boys and mean age of 29 months [19]. Our study has a similar gender ratio of 71 (58%) males and 51 (42%) girls. Yasa *et al.*, go on to say that long-term compliance in infants and children was challenging and that the gastrointestinal side effects of ferrous sulfate were an additional risk factor for poor compliance. The incidence of nausea or abdominal pain is the same in both the iron polymaltose complex (IPC) and ferrous sulfate groups (09, 09); however, nausea or abdominal pain plus constipation was recorded in 13 children in the ferrous sulfate group and just one child in the iron polymaltose group. Large amounts of research have been conducted to compare traditional iron supplements to newer formulations, with mixed outcomes. Similarly, Toblli *et al.*, performed a meta-analysis and discovered that comparing ferrous sulfate to IPC in adults in equal doses raised hemoglobin levels comparable to IPC, which was determined to have comparable efficacy [20]. However, the adverse effects of IPC were much lower than those of

DOI:http://doi.org/10.54393/pjhs.v4i11.1128

ferrous sulfate, indicating improved tolerance [17]. A similar trial was undertaken in youngsters by Pineda *et al.*, [14]. They compared iron bis-glycinate to FeSO4. For 28 days, they used 5mg/kg/day of both FeSO4 and Iron Bis-glycinate. There was a significant increase in Hb in both groups, but serum ferritin was significantly higher in children treated with Iron Bis-glycinate, with a p-value of 0.005. FeSO4 had an estimated bioavailability of 26.7%, while ferrous Bis-glycinate had a bioavailability of 90.9%. Their research demonstrated a definite advantage for iron bisglycinate. However, this trial had a small number of patients and lasted only 28 days a shorter duration than usually required for IDA [14]. Rosli *et al.*, conducted a comprehensive review and meta-analysis, which revealed that IPC had no advantage over FeSO4 [21]. However, their chosen trials did not include any study that has used Iron Bis-glycinate and did not assess the acceptability of these formulations. In our study, we employed Iron Bis-Glycinate and FeSO4 and found that they were superior to Ferrous sulfate in terms of side effects and tolerability. Our study had limitations in that we conducted it on a hospital-based small sample without interfering with their dietary routines.

CONCLUSIONS

Iron Bis-glycinate has better efficacy in rising haemoglobin (3.8gm/dl) in children with iron deficiency anemia as compared to ferrous sulphate (3.14gm/dl). Similarly tolerability was better for iron Bis-Glycinate as compared to ferous sulphate as diarrhea was not in 9% with ferrous Bis-Glycinate and 26% with ferrous sulphate. So newer iron formulation makes it better treatment option.

Authors Contribution

Conceptualization: AK
Methodology: SA
Formal analysis: I, AA, ZR
Writing-review and editing: AK, LM, I, SA, AA, ZR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Nisar YB, Aurangzeb B, Hazir T. Nutritional status of hospitalized children with nutritional anaemia: a cross sectional study. Annals of Pakistan Institute of Medical Science. 2013; 9(3): 122-5.

[2] Santiago P. Ferrous versus ferric oral iron formulations for the treatment of iron deficiency: a clinical overview. The Scientific World Journal. 2012 Oct; 2012: 846824. doi: 10.1100/2012/846824.

[3] Akhtar S, Ahmed A, Ahmad A, Ali Z, Riaz M, Ismail T. Iron status of the Pakistani population-current issues and strategies. Asia Pacific Journal of Clinical Nutrition. 2013 Jan; 22(3): 340-7.

[4] Zariwala MG, Somavarapu S, Farnaud S, Renshaw D. Comparison study of oral iron preparations using a human intestinal model. Scientia Pharmaceutica. 2013 Dec; 81(4): 1123-40. doi: 10.3797/scipharm.1304-03.

[5] Baird-Gunning J and Bromley J. Correcting iron deficiency. Australian Prescriber. 2016 Dec; 39(6): 193. doi: 10.18773/austprescr.2016.069.

[6] Taghvaei T, Fakheri H, Sartip MA, Mohammadpour RA, Maleki I. Role of upper and lower gastrointestinal endoscopy in investigating the etiologies of iron deficiency anemia in postmenopausal women. Govaresh. 2017 May; 22(2): 119-25.

[7] Rizzo S. Iron requirements in pregnancy. Australian Midwifery News. 2022 Dec; 31(1): 46-7.

[8] Balendran S and Forsyth C. Non-anaemic iron deficiency. Australian Prescriber. 2021 Dec; 44(6): 193. doi: 10.18773/austprescr.2021.052.

[9] Habib MA, Black K, Soofi SB, Hussain I, Bhatti Z, Bhutta ZA, *et al.* Prevalence and predictors of iron deficiency anemia in children under five years of age in Pakistan, a secondary analysis of national nutrition survey data 2011-2012. PloS One. 2016 May; 11(5): e0155051. doi: 10.1371/journal.pone.0155051.

[10] Albaroudi IN, Khodder M, Al Saadi T, Turk T, Youssef LA. Prevalence, diagnosis, and management of iron deficiency and iron deficiency anemia among Syrian children in a major outpatient center in Damascus, Syria. Avicenna Journal of Medicine. 2018 Jul; 8(03): 92-103. doi: 10.4103/ajm.AJM_169_17.

[11] Zahmatkeshan M, Fallahzadeh E, Najib K, Geramizadeh B, Haghighat M, Imanieh MH. Etiology of lower gastrointestinal bleeding in children: a single center experience from southern iran. Middle East Journal of Digestive Diseases. 2012 Oct; 4(4): 216.

[12] Joshi R, Shrestha DB, Shah DR, Khadka S. Iron Deficiency Anemia: A profile of a tertiary care hospital. Journal of Advances in Internal Medicine. 2018 Apr; 7(1): 1-5. doi: 10.3126/jaim.v7i1.19575.

[13] Sarakul O, Kotepui M, Marasa R, Thepwarin W. Anemia and iron deficiency anemia in high school girls in Nakhon Si Thammarat, Thailand. Journal of Health Science and Medical Research. 2018 Aug; 36(3): 197-204. doi: 10.31584/jhsmr.2018.36.3.11.

DOI:http://doi.org/10.54393/pjhs.v4i11.1128

[14] Parveen A, Raja NF, Khan IM, Shaheen H, Imran M, Ahmed RS. Comparison of conventional and newer iron preparations for the treatment of iron deficiency anaemia in children. Journal of Rawalpindi Medical College. 2020 Jun; 24(2): 1160. doi: 10.37939/jrmc.v24i2.1160.

[15] Pineda O and Ashmead HD. Effectiveness of treatment of iron-deficiency anemia in infants and young children with ferrous bis-glycinate chelate. Nutrition. 2001 May; 17(5): 381-4. doi: 10.1016/S0899-9007(01)00519-6.

[16] Natekar P, Deshmukh C, Limaye D, Ramanathan V, Pawar A. A micro review of a nutritional public health challenge: iron deficiency anemia in India. Clinical Epidemiology and Global Health. 2022 Mar; 14: 100992. doi: 10.1016/j.cegh.2022.100992.

[17] Mantadakis E, Chatzimichael E, Zikidou P. Iron deficiency anemia in children residing in high and low-income countries: risk factors, prevention, diagnosis and therapy. Mediterranean journal of hematology and infectious diseases. 2020 Jul; 12(1): e2020041. doi: 10.4084/MJHID.2020.041.

[18] Kontoghiorghes GJ, Kolnagou A, Demetriou T, Neocleous M, Kontoghiorghe CN. New era in the treatment of iron deficiency anaemia using trimaltol iron and other lipophilic iron chelator complexes: historical perspectives of discovery and future applications. International Journal of Molecular Sciences. 2021 May; 22(11): 5546. doi: 10.3390/ijms22115546.

[19] Yasa B, Agaoglu L, Unuvar E. Efficacy, tolerability, and acceptability of iron hydroxide polymaltose complex versus ferrous sulfate: a randomized trial in pediatric patients with iron deficiency anemia. International Journal of Pediatrics. 2011 Sep; 2011: 524520. doi: 10.1155/2011/524520.

[20] Toblli JE and Brignoli R. Iron (III)-hydroxide polymaltose complex in iron deficiency anemia. Arzneimittelforschung. 2007; 57(06): 431-8. doi: 10.1055/s-0031-1296692.

[21] Rosli RR, Norhayati MN, Ismail SB. Effectiveness of iron polymaltose complex in treatment and prevention of iron deficiency anemia in children: a systematic review and meta-analysis. PeerJ. 2021 Jan; 9: e10527. doi: 10.7717/peerj.10527.

DOI: Http://doi.org/10.54393/pjhs.v4i11.1139

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Prevalence of Patellofemoral Pain Syndrome and Its association with Knee Stiffness in Sanitary Workers

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ARTICLE INFO

Key Words:
Stiffness, Patellar, Pendulum Syndrome

How to Cite:
Hussain, G., Rasheed, B. F., Rashid, H. H., Ashraf, M., Manzoor, M., Naeem, Z., Kazmi, S. M., & Qamar, S. (2023). Prevalence of Patellofemoral Pain Syndrome and Its association with Knee Stiffness in Sanitary Workers: Prevalence of Patellofemoral Pain Syndrome. Pakistan Journal of Health Sciences, 4(11).Http://doi.org/10.54393/pjhs.v4i11.1139

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Received Date: 18th October, 2023
Acceptance Date: 7th Nivember, 2023
Published Date: 30th November, 2023

ABSTRACT

Patellofemoral pain syndrome is an overuse injury that causes pain in the front of knee and it's more common in females. Heavy workload and consistent stress on knee especially in labour work is also affecting male population with this syndrome. It can affect quality of life by limiting functions and it has long term effects. **Objective:** To determine the prevalence of patellofemoral pain syndrome in sanitary workers who are facing knee stiffness or knee pain. **Methods:** A sample of 128 participants of age 30-50 years of sanitary workers was included for the survey, according to inclusion criteria. For the selection of participants, convenience sampling was used. Pendulum test, Patellar grind test, and Knee Injury and osteoarthritis outcome score survey for symptoms and pain were used to collect data. An informed consent was signed by the participants stating that personal information of participants is confidential. **Results:** SPSS version 22 was used to define the descriptive and associated analysis of data. Results showed that there is association between Knee injury and osteoarthritis outcome score symptoms and patellar grind test (p>.0001) while there is no association between knee outcome score pain sign and pendulum test (p=.482). 259 participants reported 71% overall prevalence of patellofemoral pain. **Conclusions:** It is concluded that male sanitary workers had high prevalence levels of Patellofemoral pain. Preventative measures such as ergonomics training, physical activity should be taken into consideration to enhance quality of life.

INTRODUCTION

Patellofemoral pain syndrome commonly referred to as runner's knee or anterior knee pain is a common condition characterized by pain in the front of the knee. It primarily affects the area where the patella glides along the groove of the femur (thigh bone) [1]. PFPS often occurs during physical activities that involve repetitive knee movements, such as running, jumping, squatting, or climbing stairs [2]. Patellofemoral pain syndrom is characterized by discomforting pain experienced in the area surrounding or behind the patella (kneecap) and is worsened by engaging in activities that apply pressure to the patella while bearing weight on a bent knee [3]. It is estimated that approximately 1.75 million patients, or roughly 6%, experienced PFPS. 55% of the reported cases were found in women [4]. The South region had the highest proportion of cases at 42%, while the Northeast region had the lowest at 14% following 1,319 physically healthy and active young adults with no prior PFPS history, it was found that 3% developed PFPS over a period of 2.5 years [5]. Additionally, women were more prone to developing the condition compared to men [6]. Pain around or behind the patella is the main symptom of PFPS.

DOI: Http://doi.org/10.54393/pjhs.v4i11.1139

The pain may worsen with activities that involve bending the knee, such as walking downhill, squatting, or sitting for extended periods with knees bent [6]. Work-related tasks like washing, cleaning etc. are performed by sanitation workers. These tasks act as risk factor for patellofemoral pain syndrome which include Activities like prolonged standing, awkward postures, squatting, and kneeling [7]. These positions impart load on joints of sanitary workers which leads to joint pain and tissue damage. That's why sanitary workers are more prone to this disease due to their working patterns [8]. PFPS doesn't involve any structural abnormalities, and diagnostic imaging is not necessary to confirm the condition [9]. Musculoskeletal disorders pose a significant problem for sanitary workers, impacting both their QOL and leading to economic burdens through a combination of reduced productivity [10]. Sanitary workers face an increased risk of PFPS, leading to higher rates of absenteeism and work restrictions [11]. Their health, being highly exposed and vulnerable, is a major concern. Additionally, their job involves handling waste, which necessitates repetitive heavy physical activities like lifting, carrying, pulling, and pushing. These significant occupational issues are prevalent among sanitary workers worldwide [12]. The precise cause of PFPS may not always be evident, but its development is believed to be influenced by various contributing factors. These factors can include: Overuse or repetitive stress, engaging in activities that put excessive stress on the knee joint without allowing sufficient recovery time can lead to PFPS [13]. Weakness or imbalances in the muscles surrounding the knee, such as the quadriceps and hip muscles, can alter the patellar tracking and increase the risk of PFPS [14]. Malalignment of the patella, Flat feet or high arches can affect the alignment of the leg and increase the likelihood of developing PFPS [15]. Common risk factors associated with PFPS involve being female and participating in activities such as running, squatting, and stair climbing [16, 17].

Patellofemoral pain is frequently affecting workers due to uneven load distribution and excessive stress on knee. It possesses a significant challenge to profession that involves labor work and has notable implications on activities of daily living and functioning. The aim of this study was to determine the prevalence of PFPS and its severity in sanitary workers.

METHODS

This was a Cross Sectional study. The aim and objective of the study was to find out the prevalence of Patellofemoral pain and its association with knee stiffness in sanitary workers. Convenience sampling technique was adhered for sample selection. The duration of study after ethical approval was for 6 months from March 2023 to August 2023. Inclusion criteria for sample selection were patients between the ages of 30-50. The patients should be males. The duration of workers employment and experience should be taken into consideration. Sanitary workers who had congenital abnormalities or any other orthopedic condition are to be excluded. Workers who use any assistive devices like crutches, walkers etc. cannot be a part of the study. Self-reported prior surgery in lower extremities. The sample size was estimated as 259 individuals within the age group of 30-50, calculated using WHO calculator to calculate the sample size (). With a confidence level of 95%, a margin of error of 5%, and a population proportion of 13.5%. Data collection tools consisted of patellar grind test to observe prevalence of PFPS, pendulum test to assess knee stiffness and KOOS survey to detect severity of symptoms. Data were collected from private sectors e.g. orange line stations, metro stations and style textile company Lahore. Study participants included male sanitary workers who have working experience of minimum 1 year. The research committee of the University of Management and technology gave approval for research conductance. All participants signed an informed consent form. Every piece of information was kept confidential.

RESULTS

Table 1 displayed the age distribution of participants, ranging from a minimum age of 30 to a maximum age of 50 with the mean age of 41.27 ± 6.13, frequency of working hours of participants in the study. 120(46.3%) participants were working 4-6 hours daily while 139(53.7%) participants were working 6-8 hours daily. There were 68(26.3%) participants have 1-3 year experience, 90(34.7%) have 3-6 years' experience while 101(39%) have 6-9 years' experience. 107(41.3%) participants were working part time while 152(58.7%) were working full time.

Table 1: Demographics

Variable		Mean ± SD
Age	Minimum=30	41.27 ± 6.13
	Maximum=50	
Working hours of participants		Frequency (%)
		4-6 hours (120)
		6-8 hours (139)
Experience of Participants	1-3 years	68 (26.3)
	3-6 years	90 (34.7)
	6-9 years	101 (39.0)
Job Timing of Participants	Part time	107 (41.3)
	Full time	152 (58.7)
Total participants		259 (100.0)

SD is standard deviation

Table 2 table showed the frequency of patellar grind and pendulum test of participants of study. Patellar grind test

DOI: Http://doi.org/10.54393/pjhs.v4i11.1139

was positive for 184(71%) and negative for 75(29%) participants. Pendulum test was positive for 80(30.9%) participants and negative for 179(69.1%) participants.

Table 2: Pendulum and Patellar grind test

Variable		Frequency (%)
Pendulum Test	Positive	80 (30.9)
	Negative	179 (69.1)
Patellar grind test	Positive	184 (71.0)
	Negative	75 (29.0)
	Total	259 (100.0)

Table 3 illustrates the association of KOOS symptoms with patellar grind test and p-value > 0.0001 shows that there is association between KOOS symptoms and patellar grind test.

Table 3: KOOS symptoms association with patellar grind test

Variable		Pendulum Test		Pearson R value	p-value
		Positive	Negative		
KOOS Symptoms	Severe (1-25)	18(16.7%)	90(83.3%)	.18.337	.000
	Moderate (51-75)	19(45.2%)	23(54.8%)		
	Mild (26-50)	37(38.5%)	59(61.5%)		
	No Symptoms (76-100)	6(46.2%)	7(53.8%)		

KOOS is knee injury and osteoarthritis outcome score. R is coefficient correlation

DISCUSSION

The present study was conducted as a cross-sectional investigation with the objective of determining the prevalence of patellofemoral pain syndrome and whether it is associated with knee stiffness or not among sanitary workers. For this purpose convenience sampling technique was used. Sanitary workers with congenital abnormalities and those who used assistive devices were excluded from the study. To check the prevalence, patellar grind test was used. To find out association of knee stiffness with PFPS, pendulum test was used and KOOS survey was obtained to evaluate severity of syndrome. Patellofemoral pain syndrome is a growing disorder among industrial and sanitary workers as the amount of workload and consistent engagement of musculoskeletal unit to do their jobs are making them more susceptible to injury. The current study recorded prevalence of 71% as 184 subjects represented positive to patellar grind test. This is supported by past study of JS Baptista in 2022. According to prior study the economic sector are more prone to PFPS because of numerous numbers of risk factors that affects general health and physical fitness. The past study presented with 30% of prevalence of patella femoral pain in workers. The study concluded that more attention is required to counter patellofemoral disorder [9]. The findings of this study are in consistent by findings from Nilmart *et al.*, where prevalence was evaluated in people suffering from PFPS with low to moderate level of physical activity. The past study illustrated that 72% of participants reported with PFPS tenderness at medial side of patella and 70% with lateral side. This is in similarity with current study where 71% prevalence was determined but in individuals with moderate to high activity levels under stress. The prior study added that patellar facet palpation could be another criteria to diagnose patellofemoral pain syndrome [14]. Through the present study, it is inferred that patellar grind test appeared to be positive in 184 individuals out of 259, highlighting the dangers and risks involved with recurrent loads on knee joint. This is supported by previous study that focused on athlete group. 62.5% weight lifters were found to be diagnosed with PFPS and total 80 participants were found positive with patellar grind test. Hence, concluding that excessive tracking of patella could wear down the cartilage and make the knee joint unstable. This is why people complains about knee giving out during activities of daily living [19]. With regards to different occupations, it was noted that prevalence of PFP was exceptionally higher in people with occupational workload such as automobile industrial workers and garbage carriers. Moreover, there was clear association of deformities like genu varum along with PFP in workers. The results of this previous study supports the findings of current study that pateelofemoral pain syndrome is significantly increasing in sanitary workers and demographic factors such as age and BMI has an impact on it [20]. In people with PFPS, hypermobility of patella is induced. This gives rise to unstable knee joint and increase the risk of falls. All in all, severity of symptoms could disturb the body mechanics and may result in disco-ordination and impaired balance. This makes patella to give away and subject falls down. In the current study to figure out physical activity and Quality of Life in included sample, KOOS survey was obtained. KOOS is a knee specific questionnaire from assessment of knee health according to various factors involved [21]. The current study concluded that 1 to 25 subjects reported severe symptoms and almost 70 to 100 subjects showed normal Activities of daily living. 56 subjects reported moderate symptoms of pain, stiffness and reduced QOL. The study is supported by Lee *et al.*, research that was conducted in 2019. The current study findings are in line with previous study as KOOS score showed reduction in all aspects of physical activity. The worst knee was associated with moderate level of physical activity. In short lifestyle habits of workers could adversely affect their quality of life [22]. The stiffness of knee is a common symptom in all ailments regarding knee. The current studies objective was to calculate knee stiffness in PFPS patients. For this purpose pendulum test was taken as a data collection tool. In this particular test, affected leg is dropped from the position of extension and then the

DOI: Http://doi.org/10.54393/pjhs.v4i11.1139

oscillations were checked. More oscillations means absence of knee stiffness. In current study, no association was observed between patellofemoral pain syndrome and pendulum test. However, this is in contrast with prior study of Bohinc *et al.*, which claimed that knee disorders reduced active and passive range of motion of knee thus causing stiffness and rigidity. Reduction in ROM's of knee results in tightness of surrounding muscles. Tightness further leads to formation of contractures and diminished physical activity but no such association with stiffness was observed in current study [23]. The cross sectional study came to conclusion that there is high prevalence of patellofemoral pain syndrome among sanitary workers and a reduced quality of life.

CONCLUSIONS

This study shows that male sanitary workers had high prevalence levels of patellofemoral pain syndrome. Considering this and the significant levels of disability, PFPS should be a top research priority. Approximately one in ten people currently experience PFPS, making it a widespread condition. Knee pain due to PFPS were commonly reported among male sanitary workers due to their prolonged sitting , standing positions, working in the same awkward and cramped position for long periods of time and doing heavy duty work throughout the day which increases pressure on their knee joint that's why sanitary workers frequently complain of knee discomfort caused by PFPS. Therefore, based on the findings of this study, it is advised to use preventative measures (ergonomics training, physical activity)to enhance QOL.

Authors Contribution

Conceptualization: GH, BFR
Methodology: MA, MM, SMK, SQ
Formal analysis: GH
Writing-review and editing: HHR, ZN

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Willy RW, Hoglund LT, Barton CJ, Bolgla LA, Scalzitti DA, Logerstedt DS, *et al.* Patellofemoral pain: clinical practice guidelines linked to the international classification of functioning, disability and health from the academy of orthopaedic physical therapy of the American physical therapy association. Journal of Orthopaedic & Sports Physical Therapy. 2019 Sep; 49(9): CPG1-95. doi: 10.2519/jospt.2019.0302.

[2] Aldharman SS, Almuhammadi HH, Madkhali AY, Alnami RA, Alkadi MA, Albalawi DM, *et al.* Prevalence of Patellofemoral Pain and Knee Pain in the General Population of Saudi Arabia. Cureus. 2022 Oct; 14(10): e30355. doi: 10.7759/cureus.30355.

[3] Yañez-Álvarez A, Bermúdez-Pulgarín B, Hernández-Sánchez S, Albornoz-Cabello M. Effects of exercise combined with whole body vibration in patients with patellofemoral pain syndrome: a randomised-controlled clinical trial. BMC Musculoskeletal Disorders. 2020 Dec; 21(1): 1-1. doi: 10.1186/s12891-020-03599-2.

[4] Gerberich ME. Reliability and Validity of a Survey to Identify Patellofemoral Pain in an Adolescent Population (Doctoral dissertation, The University of Toledo). 2020. Available at: https://www.proquest.com/openview/d83b5193deb4a7899b475ecb4bd20b18/1?pq-origsite=gscholar&cbl=18750&diss=y.

[5] Rathleff MS, Rathleff CR, Stephenson A, Mellor R, Matthews M, Crossley K, *et al.* Adults with patellofemoral pain do not exhibit manifestations of peripheral and central sensitization when compared to healthy pain-free age and sex matched controls–an assessor blinded cross-sectional study. PLoS One. 2017 Dec; 12(12): e0188930. doi: 10.1371/journal.pone.0188930.

[6] Mujahid A, Afzal A, Dickert FL. An overview of high frequency acoustic sensors—QCMs, SAWs and FBARs—chemical and biochemical applications. Sensors. 2019 Oct; 19(20): 4395. doi: 10.3390/s19204395.

[7] Mohammad WS and Elsais WM. The epidemiology of patellofemoral pain in Majmaah, Saudi Arabia. Asian Journal of Pharmaceutical Research and Health Care. 2021 Feb; 13(1): 43-8. doi: 10.18311/ajprhc/2021/26119.

[8] Singh GK and Srivastava S. Preferential strengthening of VMO muscle during selected biomechanical rehabilitative exercises of automotive workers with patellofemoral pain syndrome. Work. 2018 Jan; 60(1): 135-41. doi: 10.3233/WOR-182723.

[9] Pereira PM, Baptista JS, Conceição F, Duarte J, Ferraz J, Costa JT. Patellofemoral pain syndrome risk associated with squats: A systematic review. International Journal of Environmental Research and Public Health. 2022 Jul; 19(15): 9241. doi: 10.3390/ijerph19159241.

[10] Mujahid A, Afzal A, Dickert FL. An overview of high frequency acoustic sensors—QCMs, SAWs and

DOI: Http://doi.org/10.54393/pjhs.v4i11.1139

FBARs—chemical and biochemical applications. Sensors. 2019 Oct; 19(20): 4395. doi: 10.3390/s19204395.

[11] Lee SH, Shin HS, Park HY, Kim JL, Lee JJ, Lee H, *et al.* Depression as a mediator of chronic fatigue and post-traumatic stress symptoms in Middle East respiratory syndrome survivors. Psychiatry Investigation. 2019 Jan; 16(1): 59. doi: 10.30773/pi.2018.10.22.3.

[12] Reddy EM and Yasobant S. Musculoskeletal disorders among municipal solid waste workers in India: A cross-sectional risk assessment. Journal of Family Medicine and Primary Care. 2015 Oct; 4(4): 519. doi: 10.4103/2249-4863.174270.

[13] M. Pereira P, Amaro J, Duarte J, Santos Baptista J, Torres Costa J. Prevalence of patellofemoral pain syndrome in selective garbage collection workers—cross sectional study. Occupational and Environmental Safety and Health III. 2021 Nov: 337-343. doi: 10.1007/978-3-030-89617-1_30.

[14] Nilmart P, Yodchaisarn W, Vongsirinavarat M. Patellofemoral Pain Syndrome in Young Adult Women With Low to Moderate Physical Activity Levels. Iranian Rehabilitation Journal. 2022 Mar; 20(1): 99-108. doi: 10.32598/irj.20.1.1565.1.

[15] Gaitonde DY, Ericksen A, Robbins RC. Patellofemoral pain syndrome. American Family Physician. 2019 Jan; 99(2): 88-94.

[16] Oza HH, Lee MG, Boisson S, Pega F, Medlicott K, Clasen T. Occupational health outcomes among sanitation workers: A systematic review and meta-analysis. International Journal of Hygiene and Environmental Health. 2022 Mar; 240: 113907. doi: 10.1016/j.ijheh.2021.113907.

[17] Pavone V, Vescio A, Panvini FM, Lucenti L, Caldaci A, Sapienza M, *et al.* Patellofemoral Pain Syndrome in Young Female Athletes: A Case-Control Study. Advances in Orthopedics. 2022 Apr; 2022: 1907975. doi: 10.1155/2022/1907975.

[18] Smith BE, Selfe J, Thacker D, Hendrick P, Bateman M, Moffatt F, *et al*. Incidence and prevalence of patellofemoral pain: a systematic review and meta-analysis. PloS One. 2018 Jan; 13(1): e0190892. doi: 10.1371/journal.pone.0190892.

[19] Gharote GM, Shah SM, Yeole UL, Gawali PP, Adkitte RG. Evaluation of patellofemoral pain syndrome in national level weight lifters with anterior knee pain. Saudi Journal of Sports Medicine. 2016 Sep; 16(3): 192. doi: 10.4103/1319-6308.191337.

[20] Sharifian SA, Chinichian M, HalimiMilani A, Mehrdad R. Prevalence and risk factors of patellofemoral pain in an automobile manufacturing factory. Malaysian Journal of Medicine and Health Sciences. 2020 May; 16(2): 193-7.

[21] Reddy EM and Yasobant S. Musculoskeletal disorders among municipal solid waste workers in India: A cross-sectional risk assessment. Journal of Family Medicine and Primary Care. 2015 Oct; 4(4): 519. doi: 10.4103/2249-4863.174270.

[22] Lee SH, Shin HS, Park HY, Kim JL, Lee JJ, Lee H, *et al.* Depression as a mediator of chronic fatigue and post-traumatic stress symptoms in Middle East respiratory syndrome survivors. Psychiatry Investigation. 2019 Jan; 16(1): 59. doi: 10.30773/pi.2018.10.22.3.

[23] Bohinc K, Vantur N, Torkar D, Lampe T, Hribernik M, Jakovljević M. Knee stiffness and viscosity: New implementation and perspectives in prosthesis development. Bosnian Journal of Basic Medical Sciences. 2017 May; 17(2): 164. doi: 10.17305/bjbms.2017.1765.

DOI: https://doi.org/10.54393/pjhs.v4i11.1142

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Prevalence of Obsessive Compulsive Symptoms in Medical and Dental Practitioners with respect to Gender

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ARTICLE INFO

Dental Practitioners, Medical Practitioners, Obsession

How to Cite:
Ashraf, A., Hassan, S. A., Butt, H., Anjum, M. S., Babary, D. F. ., & Khan, N. R. (2023). Prevalence of Obsessive Compulsive Symptoms in Medical and Dental Practitioners with Respect to Gender : Obsessive Compulsive Symptoms in Medical and Dental Practitioners. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1142

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Received Date: 21st Ocotber, 2023
Acceptance Date: 10th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Obsessive compulsive disorder (OCD) comprises of mental images that provoke anxiety and fear and are recurrent. **Objective:** To find the prevalence of OCD symptoms in medical doctors and dentists with respect to gender. **Methods:** The study design was cross sectional comparative. It was conducted in College of Dentistry, Sharif Medical and Dental College Lahore. All practitioners irrespective of their age and gender were included in the study. Individuals practiced in a clinic or hospital for less than 6 months were excluded from the study. Obsessive compulsive inventory scale was used for data collection. **Results:** Gender of medical doctors and dentists and the symptom of washing (p=0.335, p=0.760 respectively), obsessing (p=0.131, p=0.476 respectively), checking (p=0.620, p=1.000 respectively) and neutralizing (p=0.294, p=1.000 respectively) was not significantly associated. The association between the symptom of ordering and gender of medical practitioners (p=0.05) was statistically significant. The association between gender of dental practitioners with hoarding (p=0.188), ordering (p=0.713) and doubting (p=1.000) was non-significant. **Conclusions:** Among the medical practitioners the symptoms of washing, obsessing, checking and neutralizing were higher in males as compared to the females. Among the dental practitioners the symptom of washing, obsessing and neutralizing were more prevalent in males while the symptom of checking was more prevalent in females. The symptoms of hoarding, ordering and doubting were more prevalent in males in comparison to female medical practitioners. Among the dental practitioners where the prevalence of hoarding was higher in the males while that of ordering and doubting was higher in the females

INTRODUCTION

Obsessive compulsive disorder (OCD) comprises of mental images that provoke anxiety and fear and are recurrent. Once triggered, it leads the patient to undergo a viscous cycle of mentally disturbing and physically exhausting patterns of repetitions of tasks and revising events [1]. It is a psychiatric illness that afflicts 2 to 3 percent of Americans and 2.3% of the world's population. It is amongst the 10 most disabling medical and psychiatric conditions [1]. Brain function impairment can be a consequence of these compulsions and obsessions. It can lead to compulsive behaviors in individuals that lead them to exhaustively repeat a particular task multiple times until they feel it is done rightly [2]. In order to control their thoughts, OCD patients use various techniques which include mentally revising the distressing situation, worrying, distracting themselves, gaining social control and punishments [1, 2]. Out of these methods of thought control the most widely used was punishment and worrying. This has also shown to be an important point of discrimination between patients with and without OCD [1, 2]. OCD is a combination of various mentally distressing abnormalities and is multifaceted [3]. Due a lack of thorough understanding of this psychological ailment, the patients experience long term problems like depression and makes therapy less effective for [4]. An individual can develop it in their childhood as well as in adulthood [5]. OCD

DOI: https://doi.org/10.54393/pjhs.v4i11.1142

is more prevalent among males in childhood and has a higher prevalence in females during the adolescent period [6]. An analysis of the gender differences shows that the higher incidence of OCD in females later in life may be related to the significantly lower duration of education and societal burdens of settling down with a partner [7]. Gender has a very important role to play in determining the personality and psychology of individuals [7]. The incidence of OCD is greater in females in America where as an equal gender distribution is seen in Europe [7]. Development of obsessive or compulsive symptoms in individuals is driven by their gender [7]. Gender has a pivotal role as a mediator in the development of OCD. When developed in males OCD symptoms have an early onset and are very continuous and intense8. In females the development of OCD has risk factors that can not only be identified but treated comparatively easily [8]. Apart from OCD other mental ailments that are more prevalent in females as compared to men include eating disorders. The aim of this study was to find the prevalence of obsessive compulsive symptoms in medical and dental practitioners with respect to gender.

METHODS

The study design was cross sectional comparative. The study took place from December 2022 to September 2023 in College of Dentistry, Sharif Medical and Dental College Lahore on 146 participants. Data were collected after obtaining ethical clearance from ethical committee of Sharif Medical Research Centre (No. SMDC/SMRC/270-22) received on 01.12.22. Inclusion criteria was medical doctors and dentists irrespective of their age and gender. Exclusion criteria was practitioners who practiced for less than 6 months were excluded from the study. Keeping precision 5%, prevalence of obsessive compulsive disorder 10% and confidence level of 95% the sample size was calculated to be 146 [9]. Informed consent prior to the collection of data were taken from participants. Medical doctors and dentists irrespective of their age and gender were included in the study. Practitioners who practiced for less than 6 months were excluded from the study. Obsessive compulsive inventory scale was used for data collection which was a pre-validated scale with a total of 42 questions answered on a five point Likert scale (0 = not at all; 1 = a little; 2 = moderately; 3 = a lot; 4 = extremely), 7 subscales and α= 0.966 [10]. For all the questions answered on five point likert-scale a mean score was calculated for all 7 subscales which gave an overall mean distress score. Any individual with an overall score of 42 or mean score of 2.5 in a subscale was suggestive of OCD [10]. The subscales include washing (performing a cycle of events to purify oneself only due the fear or contamination), obsessing (overwhelming anxiety and stress that renders one unable to carry out day to day activities), checking (the unavoidable urge to check repeatedly and look for errors), neutralizing(an effort to eliminate a disturbing thought that poses a great deal of distress), hoarding (compulsive inability to throw away useless items), ordering (an obsession to put everything in a certain way or manner)and doubting (to remain unsure of a certain event even after repeated going over the situation mentally to the point of exhaustion). Mean and standard deviation was used to present numeric data while percentages and frequencies were used to present nominal data. The statistical analysis was done using Statistical Package for Social Sciences version 23.0. P ≤ 0.05 was considered significant. Fisher exact test was used to assess the association between gender of medical and dental practitioners with the presence of obsessive compulsive disorder symptoms.

RESULTS

The mean age of the participants was 24.81±2.109 years with 20.5% males and 41.1% females and 73 (50%) medical and 73 (50%) dental practitioners. Table 1 shows a statistically non-significant association between the gender of medical and dental practitioners and the symptoms of washing, obsessing, checking and neutralizing. Among the medical practitioners it was seen that the symptoms of washing (50%), obsessing (50%), checking (37.5%) and neutralizing (37.5%) were higher in males as compared to the females. Among the dental practitioners the symptom of washing (22.7%), obsessing (18.2%) and neutralizing (9.1%) were more prevalent in males while the symptom of checking was more prevalent in females as shown in Table 1.

Table 1: Association of washing, obsessing, checking and neutralizing symptoms in medical and dental practitioners with respect to gender

Symptom		Medical practitioners			Dental practitioners		
		Male	Female	p-value	Male	Female	p-value
Washing	Present	4(50%)	2(22.2%)	0.335	5(22.7%)	10(19.6%)	0.760
	Absent	4(50%)	7(77.8%)		17(77.3%)	41(80.4%)	
Obsessing	Present	4(50%)	1(11.1%)	0.131	4(18.2%)	6(11.8%)	0.476
	Absent	4(50%)	8(88.9%)		18(81.8%)	45(88.2%)	
Checking	Present	3(37.5%)	2(22.2%)	0.620	1(4.5%)	4(7.8%)	1.000
	Absent	5(62.5%)	7(77.8%)		21(95.5%)	47(92.2%)	
Neutralizing	Present	3(37.5%)	1(11.1%)	0.294	2(9.1%)	4(7.8%)	1.000
	Absent	5(62.5%)	8(88.9%)		20(90.9%)	47(92.2%)	

Table 2 shows that the symptom of ordering was more prevalent in the males in comparison to the females and its association with gender was significant. There was a non-significant association between the symptom of hoarding and doubting between male and female medical practitioners with all these symptoms being more prevalent in males in comparison to females (62.5% and 25 % respectively). The association between hoarding,

DOI: https://doi.org/10.54393/pjhs.v4i11.1142

ordering and doubting was statistically non-significant with male and female dental practitioners where the prevalence of hoarding (18.2%) was higher in the males while that of ordering (15.7%) and doubting (9.8%) was higher in the females as shown in Table 2.

Table 2: Association of hoarding, ordering and doubting symptoms in medical and dental practitioners with respect to gender

Symptom		Medical practitioners			Dental practitioners		
		Male	Female	p-value	Male	Female	p-value
Hoarding	Present	5 (62.5%)	3 (33.3%)	0.347	4 (18.2%)	3 (5.9%)	0.188
	Absent	3 (37.5%)	6 (66.7%)		18 (81.8%)	48 (94.1%)	
Ordering	Present	5 (62.2%)	1 (11.1%)	0.05	2 (9.1%)	8 (15.7%)	0.713
	Absent	3 (37.5%)	8 (88.9%)		20 (90.9%)	43 (84.3%)	
Doubting	Present	2 (25%)	0 (0%)	0.206	2 (9.1%)	5 (9.8%)	1.000
	Absent	6 (75%)	9 (100%)		20 (90.4%)	46 (30.2%)	

DISCUSSION

Obsessive Compulsive Disorder (OCD) is a psychological condition that impacts a person's standard of life relatively frequently. Its association with severe degrees of societal and vocational impairment underscores the importance of further research in this important clinical domain [11]. According to reports, it ranks as such fourth greatest prevalent psychological condition in the US [12, 3]. Worldwide estimations of OCD frequency fluctuate. According to reports, the annual occurrence of OCD ranges from 1.1 to 1.8% globally and 1.2% within the United States [1]. Surveys conducted in Singapore as well as Iran, two separate Asian countries, found a lifelong frequency of 1.8% and 3%, correspondingly [14, 15]. OCD reported prevalence across South Asian investigations range from 0.28% in India to 3% in Pakistan [16, 17]. In Turkey, OCD affects 3.0% of the general population and 4.2% of university graduates [18, 19]. Regarding the male to female OCD ratios, women amongst Turkish university graduates showed significantly larger prevalence than males (3.3% vs. 2.5%) [19]. According to our study in the medical practitioners the symptoms of washing (50%), obsessing (50%), checking (37.5%) and neutralizing (37.5%) were higher in males as compared to the females. Among the dental practitioners the symptom of washing (22.7%), obsessing (18.2%) and neutralizing (9.1%) were more prevalent in males while the symptom of checking was more prevalent in females. Several psychological problems, particularly OCD, exhibit greater lifelong diagnoses percentages among women. Compared to men, women suffering anxiety and depression had a greater impact of illness [20]. A study done in Pakistan reported that OCD was much more common in the group of people who weren't aware that they had the illness as reported in the statistical data (14.5% vs. 5.9%) [21]. In comparison to figures recorded with in United States (2.3%), Spain as well as Iran (1.8%), Netherlands (0.4%), & Germany (0.39%), the cumulative incidence of OCD was 10.1% [13, 14, 22]. A study by Asghar et al., observed the symptoms of OCD in medical and dental students with regards of gender and he proposed that with the exception of inspecting, greater female subjects in his investigation showed evidence of compulsive cleaning, checking, organizing, and hurting. However, evidence of washing urge was detected in 12% of men and 22% of women, correspondingly. A checking tendency was evident in 15% of the female individuals and 17% of the male subjects [21]. According to our study there was a non-significant association between the symptom of hoarding and doubting between male and female medical practitioners with both these symptoms being more prevalent in males in comparison to females (62.5% and 25 % respectively) but significant with the symptom of ordering with the symptom being more prevalent in the males (62%) in comparison to the females (11.1%). The association between hoarding, ordering and doubting was statistically non-significant with male and female dental practitioners where the prevalence of hoarding (18.2%) was higher in the males while that of ordering (15.7%) and doubting (9.8%) was higher in the females. Likewise, it was noted that OCD manifestations differed by gender, with women reporting much higher levels of decontamination and cleaning than men [23]. This discrepancy may result from the different social obligations that males and girls in society have [24, 25]. Despite the lack of community evidence in Pakistan, incidence of 3% OCD recorded in the general population [17] and the most up-to-date recent numbers depending on hospital records show that a sizable proportion of OCD sufferers need psychiatric assistance. According to research, both men as well as women are similarly susceptible to this condition. Yet, both older and more current studies have reported varying accounts of the prevalence of males or women who appear with OCD. The fact that women are more likely to appear with OCD in Iran [14] and Greece supports this variability [26]. Although a lot of work has been done on Obsessive compulsive disorder there is not an elaborate of body literature that has evaluated the role of gender in its prevalence. Our study evaluated the role of gender in the development of this disorder with reference to the area of practice. Medical doctors and dentists both come in close contact to the body fluids like blood and saliva. The fear of cross infection and contamination can resultantly be very high in them. Our study will help unravel the role that gender has to play in the development of OCD in them and will help provide valuable means to relieve the practitioners of any distress they are facing in the process of care giving. This will eventually make the provision of health care more effective.

CONCLUSIONS

Among the medical practitioners the symptoms of

DOI: https://doi.org/10.54393/pjhs.v4i11.1142

washing, obsessing, checking and neutralizing were higher in males as compared to the females. Among the dental practitioners the symptom of washing, obsessing and neutralizing were more prevalent in males while the symptom of checking was more prevalent in females. The symptoms of hoarding, ordering and doubting were more prevalent in males in comparison to female medical practitioners. Among the dental practitioners where the prevalence of hoarding was higher in the males while that of ordering and doubting was higher in the females.

Authors Contribution

Conceptualization: AA, SAH, HB
Methodology: AA, SAH, HB, NRK
Formal analysis: HB
Writing-review and editing: AA, SAH, HB, MSA, DFB, NRK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Jelinek L, Moritz S, Miegel F, Voderholzer U. Obsessive-compulsive disorder during COVID-19: Turning a problem into an opportunity? J. Anxiety Disorders. 2021 Jan; 77: 102329. doi: 10.1016/j.janxdis.2020.102329.

[2] Guzick AG, Candelari A, Wiese AD, Schneider SC, Goodman WK, Storch EA. Obsessive–compulsive disorder during the COVID-19 pandemic: a systematic review. Current Psychiatry Reports. 2021 Nov; 23: 1-0. doi: 10.1007/s11920-021-01284-2.

[3] Glahn A, Prell T, Grosskreutz J, Peschel T, Müller-Vahl KR. Obsessive-compulsive disorder is a heterogeneous disorder: evidence from diffusion tensor imaging and magnetization transfer imaging. BMC Psychiatry. 2015 Dec; 15(1): 1-0. doi: 10.1186/s12888-015-0535-5.

[4] Benatti B, Girone N, Celebre L, Vismara M, Hollander E, Fineberg NA, et al. The role of gender in a large international OCD sample: A Report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) Network. Comprehensive Psychiatry. 2022 Jul; 116: 152315. doi: 10.1016/j.comppsych.2022.152315.

[5] Riddle M. Obsessive-compulsive disorder in children and adolescents. Obsessive-Compulsive Disorder and Tourette's Syndrome. 2022 Apr: 93-8. doi: 10.4324/9780203822937-10.

[6] Boileau B. A review of obsessive-compulsive disorder in children and adolescents. Dialogues Clin. Neurosci. 2022 Apr; 13: 401-11. doi: 10.31887/DCNS.2011.13.4/bboileau.

[7] Strom NI, Soda T, Mathews CA, Davis LK. A dimensional perspective on the genetics of obsessive-compulsive disorder. Translational Psychiatry. 2021 Jul; 11(1): 1-1. doi: 10.1038/s41398-021-01519-z.

[8] Mathis MA, Alvarenga PD, Funaro G, Torresan RC, Moraes I, Torres AR, et al. Gender differences in obsessive-compulsive disorder: a literature review. Brazilian Journal of Psychiatry. 2011 Dec; 33(4): 390-9. doi: 10.1590/S1516-44462011000400014.

[9] Carmi L, Brakoulias V, Arush OB, Cohen H, Zohar J. A prospective clinical cohort-based study of the prevalence of OCD, obsessive compulsive and related disorders, and tics in families of patients with OCD. BMC psychiatry. 2022 Dec; 22(1): 1-7. doi: 10.1186/s12888-022-03807-4.

[10] Foa EB, Kozak MJ, Salkovskis PM, Coles ME, Amir N. The validation of a new obsessive-compulsive disorder scale: The Obsessive-Compulsive Inventory. Psychological Assessment. 1998 Sep; 10(3): 206. doi: 10.1037/1040-3590.10.3.206.

[11] Edition F. Diagnostic and statistical manual of mental disorders. American Psychiatric Association. 2013;21(21):591643.doi:10.1176/appi.books.9780890425596.

[12] Kim DJ, Mirmina J, Narine S, Wachtel J, Carbajal JM, Fox H, et al. Altered physical pain processing in different psychiatric conditions. Neuroscience & Biobehavioral Reviews. 2022 Feb; 133: 104510. doi: 10.1016/j.neubiorev.2021.12.033.

[13] Veldhuis J, Dieleman JP, Wohlfarth T, Storosum JG, van Den Brink W, Sturkenboom MC, et al. Incidence and prevalence of "diagnosed OCD" in a primary care, treatment seeking, population. International Journal of Psychiatry and Clinical Practice. 2012 Jun; 16(2): 85-92. doi: 10.3109/13651501.2011.617454.

[14] Mohammadi MR, Ghanizadeh A, Rahgozar M, Noorbala AA, Davidian H, Afzali HM, et al. Prevalence of obsessive-compulsive disorder in Iran. BMC Psychiatry. 2004 Dec; 4(1): 1-8. doi: 10.1186/1471-244X-4-2.

[15] Chong SA, Abdin E, Vaingankar JA, Heng D, Sherbourne C, Yap M, Lim YW, et al. A population-based survey of mental disorders in Singapore. Annals of the Academy of Medicine of Singapore. 2012 Feb; 41(2): 49. doi: 10.47102/annals-acadmedsg.V41N2p49.

[16] Nandi DN, Banerjee G, Mukherjee SP, Ghosh A, Nandi

DOI: https://doi.org/10.54393/pjhs.v4i11.1142

PS, Nandi S. Psychiatric morbidity of a rural Indian community: Changes over a 20-year interval. British Journal of Psychiatry. 2000 Apr; 176(4): 351-6. doi: 10.1192/bjp.176.4.351.

[17] Gadit AA. Obsessive compulsive disorder in a fishermen community. Journal of College of Physicians and Surgeons of Pakistan. 2003 Oct; 13(10): 581-3.

[18] CilliÇilli AS, Telcioglu M, Aşkın R, Kaya N, Bodur S, Kucur R. Twelve-month prevalence of obsessive-compulsive disorder in Konya, Turkey. Comprehensive Psychiatry. 2004 Sep; 45(5): 367-74. doi: 10.1016/j.comppsych.2004.06.009.

[19] Yoldascan E, Ozenli Y, Kutlu O, Topal K, Bozkurt AI. Prevalence of obsessive-compulsive disorder in Turkish university students and assessment of associated factors. BMC psychiatry. 2009 Dec; 9(1): 1-8. doi: 10.1186/1471-244X-9-40.

[20] McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. Journal of Psychiatry Research. 2011 Aug; 45(8): 1027-35. doi: 10.1016/j.jpsychires.2011.03.006.

[21] Asghar MA, Rehman AA, Shafiq Y, Siddiq A, Zehravi M, Khan K, et al. Relationship of obsessive-compulsive disorders with religion and psychosocial attitude among local medical college students of Karachi: an epidemiological study. Journal of Pakistan Medical Association. 2020 Sep; 70(9): 1563-67. doi: 10.5455/JPMA.34245.

[22] Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Molecular Psychiatry. 2010 Jan; 15(1): 53-63. doi: 10.1038/mp.2008.94.

[23] Taher TM, Al-fadhul SA, Abutiheen AA, Ghazi HF, Abood NS. Prevalence of obsessive-compulsive disorder (OCD) among Iraqi undergraduate medical students in time of COVID-19 pandemic. Middle East Current Psychiatry. 2021 Dec; 28(1): 1-8. doi: 10.1186/s43045-021-00086-9.

[24] Pinciotti CM, Smith Z, Singh S, Wetterneck CT, Williams MT. Call to action: Recommendations for justice-based treatment of obsessive-compulsive disorder with sexual orientation and gender themes. Behavioral Therapy. 2022 Mar; 53(2): 153-69. doi: 10.1016/j.beth.2021.11.001.

[25] Pinciotti CM, Nuñez M, Riemann BC, Bailey BE. Clinical presentation and treatment trajectory of gender minority patients with obsessive-compulsive disorder. Journal of Cognitive Psychotherapy. 2022 Feb; 36(1): 42-59. doi: 10.1891/JCPSY-D-20-00022.

[26] Skapinakis P, Bellos S, Koupidis S, Grammatikopoulos I, Theodorakis PN, Mavreas V. Prevalence and sociodemographic associations of common mental disorders in a nationally representative sample of the general population of Greece. BMC Psychiatry. 2013 Dec; 13(1): 1-4. doi: 10.1186/1471-244X-13-163.

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Predictors of Outcome in Management of Ruptured Arteriovenous Fistula in Hemodialysis Patients: A Cross-Sectional Study at a Tertiary Care Hospital, Karachi

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ARTICLE INFO

Key Words:
Ruptured Arteriovenous Fistula, Predictors, Salvageability

How to Cite:
Basit, A., Masood, B., Memon, F., Habib, F. A., Zehra, D., & Keen, I. T. (2023). Predictors of Outcome in Management of Ruptured Arteriovenous Fistula in Hemodialysis Patients: A Cross-Sectional Study at a Tertiary Care Hospital, Karachi: Management of Ruptured Arteriovenous fistula. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1152

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Received Date: 26th October, 2023
Acceptance Date: 15th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Bleeding from ruptured arteriovenous fistulae (AVF) is a distressing complication resulting from multiple factors and can lead to life-threatening hemorrhage. **Objective:** To analyze factors that contribute to the development of a bleeding ruptured AVF which could enable us to make decision regarding line of management for saving these AVFs. **Methods:** This cross-sectional study was conducted at Department of Vascular Surgery, Sindh Institute of Urology and Transplant (SIUT), including 52 patients presenting with burst arteriovenous fistula during the time period of six months. Data collection was carried out using a pretested questionnaire which comprised of detailed history regarding pre-operative and per-operative factors related to burst fistula. **Results:** The mean age of the patients was 35.7 ± 19.6 years with gender distribution identified as male (51.9%) and female (48.1%). The major outcome of the study was salvageability of AVF which was observed to be 36.5% among the study cohort. We also analyzed association of AVF salvageavility with pre-operative and intraoperative factors which showed its significant association with risk factors such as fistula age (<40 or > 40 days), area of surrounding inflammation, overlying skin, bleeding AVF before initiation of hemodialysis from fistula, type of cannulation, site of bleeding from AVF and ligation/repair status of fistula. **Conclusions:** Understanding these significantly associated factors could contribute to the early detection and allow measures aimed at averting adverse outcomes, which can span from the loss of vascular access to severe health problems and even, in some cases, prove fatal.

INTRODUCTION

Haemodialysis is recognized as a form of renal replacement therapy which is a measure to sustain acute kidney injury (AKI) or a prolonged, gradual loss in renal function, called chronic kidney disease (CKD), until a kidney transplant can be carried out, or for sustaining those ineligibles for it [1]. Many of the patients who failed to become candidate for renal transplantation remain dependent on HD for lifetime with ultimate long-term need for the development of dialysis access [2]. Haemodialysis patients with central venous catheters have larger mortality secondary to the development of infections while patients with native arteriovenous fistulas (AVFs) tend to experience extended patency and lesser complications. Therefore, AVFs is considered as the most preferred renal replacement methods [3]. National Kidney Foundation Kidney Disease Outcomes Quality Initiative vascular access guidelines correctly rank the arteriovenous fistula (AVF) as the best available access for providing haemodialysis [4]. AV fistula

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

by definition is the autologous arteriovenous access surgically created communications between native artery and vein in an extremity where vein serves as the accessible conduit [5]. Most commonly suggested AVF include radiocephalic fistula, brachiocephalic fistula and basilic vein transposition. The access that is formed is usually used for HD 2-5 times per week [6]. Understanding the potential complications of AVFs may lead to their well-timed detection and enable actions to be taken that might avert damaging consequences that range from loss of vascular access to serious morbidity, and may ultimately be fatal [7]. The potential complications of fistulae for HD are lymphedema, infection, aneurysm, stenosis, congestive heart failure, steal syndrome, ischemic neuropathy and thrombosis. Such fistulas could also result in blood loss due to development of pseudo-aneurysm secondary to repeated punctures for vascular access, stenosis, infection trauma and use of anticoagulant which ultimately led these patients to present in surgical emergency [8]. To better preserve and manage bleeding ruptured arteriovenous fistulas (AVFs), understanding their early causes and associated outcomes is crucial for effective intervention and safeguarding these vital conduits in patients [9].

METHODS

This cross-sectional study was conducted at Department of Vascular Surgery, Sindh Institute of Urology and Transplant (SIUT), a tertiary care hospital after the approval of synopsis from ERC (Ethical review committee) of SIUT (SIUT-ERC-2023/A-437). We enrolled all the patients presenting with burst arteriovenous fistula either before or after initiation of haemodialysis over the time period of six months from March 15, 2023 to August 31, 2023. Data were collected using convenience sampling technique. Inclusion criteria were patients presenting with bleeding from AVF both before and after initiation of haemodialysis from the fistulae while patients undergoing HD presenting with bleeding arteriovenous grafts were excluded. The calculated sample size of the study calculated through OpenEpi, was 52 patients based on the frequency of bleeding/hematoma AVF observed as 16.7% [10] with a margin of error 7 % and 95 % confidence level. Data collection was carried out after taking patient's informed consent using a pretested questionnaire which included socio-demographic details, detailed history regarding pre-operative factors such as age of fistula, time duration since its construction, co-morbidity i.e, DM and HTN, site of fistula, pre-dialysis or post dialysis rupture of fistula and also information about the per-operative/intra-operative findings such as site of bleeding, presence of proximal stenosis, presence of pseudo aneurysm, need for ligation or repair and salvage of fistula for HD. Statistical analysis was done using SPSS version 23.0. Continuous data were shown as mean ± standard deviation (SD) while categorical variables were presented as frequency and percentages. For identification of risk factors associated with salvageability of AVF, a chi-square test was undertaken. A p-value of less than 0.05 was considered significant. Confidentiality of patient data were maintained throughout the study.

RESULTS

In this study, a total of 52 participants presented with burst fistula from March 15, 2023 to August 31, 2023. The gender distribution consisted of 27 participants identified as male (51.9%) and 25 as female (48.1%) with an average age of (35.7 ± 19.1) years. The prevalence of underlying co-morbidities included diabetes mellitus (DM) in 3.8%, hypertension (HTN), the most common co-morbidity accounted for 53.8%. Ischemic heart disease (IHD) constituted 1.9% of the sample. Notably, 9 individuals (17.3%) were found to have both DM and HTN, while only 1 participants (1.9%) presented with the combination of DM, HTN, and IHD. A considerable proportion of the participants, 11 individuals (21.2%), had no co-morbidities as presented in Table 1.

Table 1: Baseline Characteristics

Variable	Patients (N=52)
Age (Years)	35.7 ± 19.6
Gender	
Male	27 (51.9%)
Female	25 (48.1%)
Co-morbidity	
DM	2 (3.8%)
HTN	28 (53.8%)
IHD	1 (1.9%)
DM & HTN	9 (17.3%)
DM, HTN & IHD	1 (1.9%)
None	11 (21.2%)

(DM: Diabetes Mellitus, HTN: Hypertension, IHD: Ischemic Heart Disease)

In our setup, the underlying cause of renal failure in most of the patients was idiopathic (38.5%) followed by hypertension (17.3%), diabetic nephropathy (9.6%) and renal stone disease (7.7%). Some other causes of renal failure like obstetric complications, bladder obstruction and autoimmune disorders were also reported. The frequency of dialysis was also analyzed which showed that twice a week patients were most common (67.3%) followed by thrice weekly (28.8%) and once a week (3.8%) as shown in Table 2.

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

Table 2: Hemodialysis patient characteristics

Variable	Patients (N=52)
Cause of Renal Failure	
Amyloidosis	1 (1.9%)
ARF secondary to obstetric complication	2 (3.8%)
Autoimmune disorder (SLE)	1 (1.9%)
Bilateral medullary nephrocalcinosis	1 (1.9%)
Bladder outflow obstruction	1 (1.9%)
CRF secondary to DM & HTN	1 (1.9%)
CRF secondary to HTN	9 (17.3%)
Diabetic nephropathy	5 (9.6%)
CRF secondary to obstetric complication	1 (1.9%)
CRF secondary to Pre-eclampsia	1 (1.9%)
Idiopathic	20 (38.5%)
Obstructive Uropathy	3 (5.8%)
Posterior urethral valve	1 (1.9%)
Postpartum hemorrhage	1 (1.9%)
Renal stone disease	4 (7.7%)
Frequency of Dialysis	
Once a week	2 (3.8%)
Twice weekly	35 (67.3%)
Thrice weekly	15 (28.8%)

(ARF: Acute Renal Failure, SLE: Systemic Lupus Erythematosus, CRF: Chronic Renal Failure, DM: Diabetes Mellitus, HTN: Hypertension)

During pre-operative assessment of the factors related to the AVF, it was noted that the most preferred side for AVF surgery was found to be the left brachiocephalic (42.3%) followed by left radiocephalic location (19.2%). The proportion of Left basilic vein transposition came out to be 17.3% which was nearly equal to left radiocephalic site. The frequency of age of fistula in less than 40 days AVF was (19.2%) while (80.8%) in more than 40 days AVF. There were total 47 (90.4%) patients who presented with bleeding AVF with surrounding inflammation. In the examined patient cohort, overlying skin induration was observed in 48.1% of cases, while necrosis of the overlying skin was documented in 42.3% of patients. The mean duration of symptoms was 7.6 ± 3.9 days whereas bleeding to intervention time period was spread over 7.8 ± 4.1 days. The predominant technique employed in our study was area technique (42.3%) followed by step ladder technique (32.7%). In 19.2% of the cases, the technique remain unidentified as shown in Table 3.

Table 3: Pre-Operative Characteristics

Variable	Patients (N=52)
Age of Fistula (< 40 or > 40 Days)	
(< 40 Days)	10 (19.2%)
(> 40 Days)	42 (80.8 %)
Site of Fistula	
Left Radiocephalic	10 (19.2%)
Right Brachiocephalic	5 (9.6%)
Left Brachiocephalic	22 (42.3%)
Right Basilic Vein Transposition	3 (5.8%)
Left Basilic Vein Transposition	9 (17.3%)
Left Brachiobasilic	3 (5.8%)
Inflamation area (cm)	
<2 cm	35 (45.5%)
2-4 cm	11 (14.3%)
>4 cm	25 (32.5%)
None	6 (7.8%)
Overlying Skin	
Intact	5 (9.6%)
Indurated	25 (48.1%)
Necrosed	22 (42.3%)
Bleeding AVF before initiation of Hemodialysis from Fistula	
Yes	13 (25%)
No	39 (75%)
Duration of Symptoms (Days)	7.6 ± 3.9
Duration from Bleeding to Intervention (Days)	7.8 ± 4.1
Duration from Admission to Procedure (Days)	1.9 ± 0.7
Type of Cannulation	
Button Hole	3 (5.8%)
Step Ladder	17 (32.7%)
Area Technique	22 (42.3%)
Unknown	10 (19.2%)
Previous Intervention on AVF	
Yes	12 (23.1%)
No	40 (76.9%)
Surgical procedures of previous intervention on AVF	
Outflow Refashioning	1 (1.9%)
Venoplasty	12 (23.1%)
None	39 (75%)

In this study, we observed a distribution of bleeding sites from AVF among the study population, with 19.2% of cases attributed to anastomotic site, 9.6% to side branch, and a majority, 71.2%, were categorized as needling site. AVF were subjected to ligation in 59.6% whereas 40.4% underwent repair of AVF. Clinical evidence of proximal stenosis was found in 55.8% of the cases while bleeding AVF with pseudoaneurysm was documented in 48.1% of the patients. The salvageability of AVF was observed to be 36.5% among the study cohort as presented in Table 4.

Table 4: Per-Operative Factors

Variable	Patients (N=52)
Site of Bleeding from AVF	
Anastomotic site	10 (19.2%)
Side branch	5 (9.6%)
Needling site	37 (71.2%)
AVF ligated/Repaired	
Ligated	31 (59.6%)
Repaired	21 (40.4%)

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

Variable	Patients (N=52)
Clinical evidence of Proximal Stenosis	
Yes	29 (55.8%)
No	23 (44.2%)
Bleeding AVF accompanied with Pseudoaneurysm	
Yes	25 (48.1%)
No	27 (51.9%)
Surgical Treatment for Stenosis/Pseudoaneurysm	
Outflow Refashioning	1 (1.9%)
Outflow Venoplasty	4 (7.7%)
Outflow Refashioning with pseudoaneurysmectomy	3 (5.8%)
Outflow venoplasty with pseudoaneurysmectomy	6 (11.5%)
None	38 (73.1%)
Salvageability of Fistula	
Yes	19 (36.5%)
No	33 (63.5%)

We observed that salvageability of fistula was significantly associated with risk factors such as fistula age (< 40 or > 40 days), bleeding AVF with surrounding inflammation, area of surrounding inflammation, overlying skin, bleeding AVF before initiation of hemodialysis from Fistula, type of cannulation, site of bleeding from AVF and ligation/repair of fistula (Table 5). While factors such as gender, co-morbidity, site of Fistula, frequency of dialysis, previous intervention on AVF, clinical evidence of proximal stenosis and bleeding AVF accompanied with pseudoaneurysm didn't show any significant association with salvageability of fistula.

Table 5: Association of Salvageability of fistula with AVF ligated/Repaired

Parameter		AVF ligated/Repaired		Total	p-value
		Ligated	Repaired		
Salvageability of Fistula	No	31 (93.9%)	2 (6.1%)	33(100.0%)	0.0001
	Yes	0 (0.0%)	19(100.0%)	19(100.0%)	
Total		31 (59.6%)	21 (40.4%)	52(100.0%)	

DISCUSSION

Pakistan has a gross population of 144 million with majority of population (65%) living in rural areas. In Pakistan, chronic renal failure cases are endlessly increasing with an expected incidence of more than 100 new cases per million population annually of end-stage renal disease (ESRD). There is still very inadequate data existing on the gamut of renal diseases culminating in chronic renal failure in Pakistan. In one study conducted at Sindh Institute of Urology and Transplantation (SIUT), a tertiary care center situated in Karachi reported that out of total 874 enrolled patients the largest group of patients were those in whom the aetiology was unknown. Following that, diabetes mellitus (DM) and hypertension (HTN) emerged as the subsequent most prevalent underlying factors. Obstruction both secondary to stone disease and lower tract pathology came out as the fourth commonest cause [11]. Our results also showed alignment with this prior research as most of the patients were idiopathic (38.5%) followed by hypertension (17.3%), diabetic nephropathy (9.6%) and renal stone disease (7.7%). At present, Arteriovenous fistula (AVF) has established itself as the gold standard vascular access; and is reverberated in the renal disease outcomes and quality initiative (KDOQI) guidelines [12, 13]. Both patient related (co-mobidity, gender, age, cause of renal failure) and vascular related factors such as vascular anatomy, surgical procedure, AVF placement, previous complications, techniques employed for the correction of developed complications affect ultimately AVF maturity, patency and possibly result in burst fistulas. Certain other factors have also been identified that affect the AVF are daily care, the cannulation technique used, and the size and angle of the needle inserted [14]. Numerous researches have published the data on various aspects such as AVF patency and maturation but there is extremely limited data available on the incidence of burst AV fistula. At our setup, we encounter the cases of burst fistula frequently. In Pakistan, not a single study has been conducted on the patients presenting with ruptured AV fistula so our study is the first conducted research analyzing various pre-operative and per-operative factors associated with burst fistula. Although the recommendations are for the orderly placement of vascular access for dialysis such as radio-cephalic, brachio-cephalic, basilica-vein transposition followed by AV graft placement as a last resort, but it is evident from previous literature that patient factors majorly affects the preference of fistula sites. One study in this regard conducted in PNS Shifa Islamabad on 726 dialysis dependent patients, reported left brachio-cephalic as the most common site for fistula formation followed by left radio-cephalic site which is also consistent with our results where left brachio-cephalic is the most common site accounting for 42.3% of the cases followed by left radio-cephalic [15]. Proximal stenosis associated with AVF was reported intra-operatively in more than half of the patients in our study. Literature also document stenosis as the most common type of complication accompanied with fistula. One study in this regard reported some of the related findings in patients who developed stenosis such as use of button hole cannulation technique, however it also emphasized that stenosis is influenced by other factors also. On contrary, our study reports area technique as the most frequently employed technique [16]. In our center, we found 48.1% cases of bleeding AVF accompanied with pseudoaneurysm during the study period. Previous literature linked the development of pseudoaneurysms with the cannulation techniques. According to Van Loon *et al.*, the development of both aneurysm and

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

pseudoaneurysms are associated with area puncture and rope ladder technique as compare to buttonhole technique [17]. Mudoni *et al.*, stated that pseudoaneurysms may arise from the anastomosis and reflect leaking of blood outside the lumen either during the perioperative period due to surgical techniques or later as a complication of infection which could even lead to massive hemorrhage [18]. In the case of vascular surgery, infection at the surgical site is thought to be a pronounced risk for massive bleeding due to loose stitches and open wounds which are in direct connection to the arteries [19]. With all of these characteristics, the overall rate of ligated fistulas (59.6%) exceeded that of repair cases [20]. In our study including a total of 31 cases subjected to AVF ligation procedures, 11 cases of brachial artery ligation and 2 cases of radial artery ligation were performed. Noteworthy among our findings is the remarkable absence of any reported occurrences of limb ischemia within our study cohort. This observation underscores the significance of employing precise surgical techniques and careful postoperative care in alleviating the risk of ischemic complications subsequent to AVF ligation procedures.

CONCLUSIONS

In conclusion, our results provide contemporary data on factors associated with salvageability of ruptured AV fistula. However further studies are needed in order to elaborate on these findings and provide a comprehensive understanding of causes and outcomes associated with burst fistulas so that they could be managed effectively.

Authors Contribution

Conceptualization: AB, BM
Methodology: AB, BM
Formal analysis: FAH, DZ, ITK
Writing-review and editing: AB, BM, FM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Murdeshwar HN and Anjum F. Hemodialysis. StatPearls Publishing; 2020.

[2] Rosas SE and Feldman HI. Synthetic vascular hemodialysis access vs native arteriovenous fistula: A cost-utility analysis. Annals of Surgery. 2012 Jan; 255(1): 181. doi: 10.1097/SLA.0b013e31822f4e9b.

[3] Güven C and Uludağ Ö. Proximal arteriovenous fistulas in hemodialysis patients: advantages and disadvantages. Cureus. 2020 Nov; 12(11): e11657. doi: 10.7759/cureus.11657.

[4] Asif A, Roy-Chaudhury P, Beathard GA. Early arteriovenous fistula failure: a logical proposal for when and how to intervene. Clinical Journal of the American Society of Nephrology. 2006 Mar; 1(2): 332-9. doi: 10.2215/CJN.00850805.

[5] Lee T, Mokrzycki M, Moist L, Maya I, Vazquez M, Lok CE, *et al*. Standardized definitions for hemodialysis vascular access. Seminars in Dialysis. 2011 Sep; 24(5): 515-524. doi: 10.1111/j.1525-139X.2011.00969.x.

[6] Stolic R. Most important chronic complications of arteriovenous fistulas for hemodialysis. Medical Principles and Practice. 2013 Nov; 22(3): 220-8. doi: 10.1159/000343669.

[7] Maya ID, Oser R, Saddekni S, Barker J, Allon M. Vascular access stenosis: comparison of arteriovenous grafts and fistulas. American Journal of Kidney Diseases. 2004 Nov; 44(5): 859-65. doi: 10.1016/S0272-6386(04)01085-6.

[8] Joshi A and Agrawal D. Arteriovenous fistula takedown in hemodialysis patients: our experience of 26 cases. Kardiochirurgia i Torakochirurgia Polska/Polish Journal of Thoracic and Cardiovascular Surgery. 2020 Sep; 17(3): 132-6. doi: 10.5114/kitp.2020.99076.

[9] Fokou M, Teyang A, Ashuntantang G, Kaze F, Eyenga VC, Mefire AC, *et al*. Complications of arteriovenous fistula for hemodialysis: an 8-year study. Annals of Vascular Surgery. 2012 Jul; 26(5): 680-4. doi: 10.1016/j.avsg.2011.09.014.

[10] Hossny A. Brachiobasilic arteriovenous fistula: different surgical techniques and their effects on fistula patency and dialysis-related complications. Journal of Vascular Surgery. 2003 Apr; 37(4): 821-6. doi: 10.1067/mva.2003.181.

[11] Rizvi SA and Manzoor K. Causes of chronic renal failure in Pakistan: a single large center experience. Saudi Journal of Kidney Diseases and Transplantation. 2002 Jul; 13(3): 376-9.

[12] Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, *et al*. KDOQI clinical practice guideline for vascular access: 2019 update. American Journal of Kidney Diseases. 2020 Apr; 75(4): S1-64. doi: 10.1053/j.ackd.2020.02.003.

[13] Schmelter C, Raab U, Lazarus F, Ruppert V, Vorwerk D. Outcomes of AV fistulas and AV grafts after interventional stent-graft deployment in haemodialysis patients. Cardiovascular and Interventional Radiology. 2015 Aug; 38: 878-86. doi: 10.1007/s00270-014-1018-7.

[14] Schmidli J, Widmer MK, Basile C, de Donato G, Gallieni

DOI: https://doi.org/10.54393/pjhs.v4i11.1152

M, Gibbons CP, *et al*. Editor's choice–vascular access: 2018 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). European Journal of Vascular and Endovascular Surgery. 2018 Jun; 55(6): 757-818. doi: 10.1016/j.ejvs.2018.02.001.

[15] Azeem SM, Ehsan O, Khan MI. Patency and Complications of Arterio-venous Fistula Created in Pre-and Post-dialysis Settings. Infection. 2022 Apr; 3: 1-67.

[16] Staaf K, Fernström A, Uhlin F. Cannulation technique and complications in arteriovenous fistulas: a Swedish Renal Registry-based cohort study. BMC Nephrology. 2021 Dec; 22(1): 1-2. doi: 10.1186/s12882-021-02458-z.

[17] Van Loon MM, Goovaerts T, Kessels AG, van der Sande FM, Tordoir JH. Buttonhole needling of haemodialysis arteriovenous fistulae results in less complications and interventions compared to the rope-ladder technique. Nephrology Dialysis Transplantation. 2010 Jan; 25(1): 225-30. doi: 10.1093/ndt/gfp420.

[18] Mudoni A, Cornacchiari M, Gallieni M, Guastoni C, McGrogan D, Logias F, *et al*. Aneurysms and pseudoaneurysms in dialysis access. Clinical Kidney Journal. 2015 Aug; 8(4): 363-7. doi: 10.1093/ckj/sfv042.

[19] Al-Jaishi AA, Liu AR, Lok CE, Zhang JC, Moist LM. Complications of the arteriovenous fistula: a systematic review. Journal of the American Society of Nephrology: JASN. 2017 Jun; 28(6): 1839. doi: /10.1681/ASN.2016040412.

[20] Zhang W, Hu R, Zhang L, Zhu H, Zhang H. Outcomes of surgical repair of pediatric coronary artery fistulas. The Journal of Thoracic and Cardiovascular Surgery. 2016 Oct; 152(4): 1123-30. doi: 10.1016/j.jtcvs.2016.04.093.

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Prevalence, Risk Factors and Effects of Low Back Pain on Quality of Life among Healthcare Professionals of Lahore, Pakistan

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ARTICLE INFO

Key Words:
Prevalence, Low Back Pain, Healthcare Professionals, Occupational Risk Factors, Quality of Life

How to Cite:
Rafique, N., Farooq, W., Umer, Z., Tariq, F., Bukht, R., Zeeshan, M., Rukh, M., Zakar, R., & Saleem, J. (2023). Prevalence, Risk Factors and Effects of Low Back Pain on Quality of Life among Healthcare Professionals of Lahore, Pakistan: Effects of Low Back Pain on Quality of Life. Pakistan Journal of Health Sciences, 4(11).
https://doi.org/10.54393/pjhs.v4i11.1133

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Received Date: 17th October, 2023
Acceptance Date: 6th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Low back pain being a prevalent disease is affecting the quality of life. The health care professionals also experience low back pain due to their nature of work. **Objective:** To determine the prevalence of low back pain with its contributing factors and its impact on life's quality of healthcare professionals. **Methods:** The cross-sectional study design was applied to conduct this study. In this study, a total of 384 health care professionals from different hospitals of Lahore, Pakistan were randomly surveyed. Descriptive statistics and Chi square test used to analyze the data (p-value < 0.05). **Results:** The frequency of pain in lower back was 63% among health care professionals. A total of 56% female healthcare professionals had low back pain. Risk factors i.e. smoking behavior, poor posture at work, standing time, working hour per day, sleeping disorder and general stress had significant association with pain intensity rating scale (p-value < 0.05). The quality of life of healthcare professionals measured with Oswestry disability index (ODI) had also significant relation with low back pain (p-value < 0.05). **Conclusions:** In conclusion, the pain in lower back was more prevalent in female healthcare professionals. Occupational risk factors, Smoking behavior, sleeping disorder and general stress were considered as major risk factors. The most useful coping strategy was rest. The quality of life of healthcare professionals were highly effected by low back pain.

INTRODUCTION

Low back pain (LBP) is the sixth-highest burden and is associated with higher impairment globally [1]. The low back pain is also considered as the fifth cause to consult doctors all over the world. It also considered as an issue of health throughout history, dating back to BC 1500 [2]. Low back discomfort affects a lot of people worldwide, and this figure is rising day by day. People from all around the world experience low back pain. China has an 80% prevalence of lower back pain, while Korea has a 90% prevalence [3]. The long working hours, excess load of work, insufficient working staff and instruments, less time of break during work, incorrect work position and road traffic injuries can all be occupational risk factors for LBP in healthcare workers [4, 5]. The activities related to physical work, smoking behavior and household factors such as use of computers and watching television are considered as major risk factors [6]. Several studies have found a number of risk factors connected to LBP in the general population,

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

such as advanced age, alcohol, drug misuse, family history and gender. The frequency of exercise, obesity, incorrect alignment and posture and smoking are also contributing towards low back pain. The professional considerations such as extended sitting and standing; past back injuries; as well as psychological and social concerns are also leading cause of low back pain [7, 8]. The pain in low back among healthcare professionals may interfere with providing quality patient care, result in lost workdays, and increase financial burden [9]. Due to its severity, it is the main reason for job loss, changing work environments, taking leave from job and it effects the resources of healthcare, along with decrease in activities of daily life and social life [10]. The risk factors that can be changed occupation-related issues such bad posture, prolonged sitting, and lifting large loads. Age and a patient with history of pain in lower back are non-modifiable contributing factors while inactivity in life, high BMI and smoking behavior are modifiable factors [11, 12]. Ignoring pain as a musculoskeletal system symptom has major health repercussions, ranging from discomfort to a lower quality of life to injury and disabilities [13]. So, the study aimed to determine the prevalence, risk factors of low back pain and its impact on the quality of life of health care professionals of Lahore, Pakistan.

METHODS

The cross sectional study was designed to find out the prevalence of low back pain and its effects on the quality of life of healthcare professionals. The study was conducted in both public and private hospitals of Lahore, Pakistan. The duration of study was 8 months from December 2022 to July 2023. The study population was healthcare professionals who were working in both public and private selected hospitals of Lahore. Male and female healthcare professionals aged 18-60 years working from more than six months in randomly selected private and public hospitals were included in this study. While participants with pregnancy, degenerative joint disease, arthritis, vertebral fractures and spondylolisthesis were not included in this study. The random sampling technique was used. The size of sample was calculated by following formula in which proportion of population (p) is 50% or 0.5, confidence level (z)=1.96 and margin of error (e) is considered as 5% or 0.05.

$$n = \frac{z^2 p(1 - P)}{e^2}$$

A total of 384 health care professionals were randomly surveyed from selected public and private hospitals of Lahore. Data were collected using a structured self-administered English version questionnaire which consist of three parts. The first part consisted of socio-demographic related questions, the second part consisted of work related questions and the third part consisted of Oswestry Disability Index (ODI) questionnaire developed by Fairbank, Couper, Davies & O'Brien in late 1970, which quantified the effect of disability on quality of life of healthcare professionals . The data were analyzed using descriptive and statistical analysis (Chi square). P-value < 0.05 was considered significant. The confidence interval of 95% was considered to find out prevalence of pain in lower back. Chi square was considered as to find out the consequence of risk factors and to find out the relation between intensity level of low back pain and other variables.

RESULTS

A total of 384 participants were selected from public and private hospitals. The mean age of participants was 31.13±5.82 years. A total of 56% participants were female in this study. The profession of 47%, 25%, 17%, 12% participants were medical doctors, nurses, allied health professionals and dentist respectively. In term of working experience, 55% of the participants had less than 5 years which were majority participants of this study. According to body mass index (BMI), a total of 60% of the participants were with normal weight while 27% of the participants were overweight. A total of 84% of the participants were non-smokers. In term of consumption of tea or coffee, 75% of the participants consume tea or coffee. A total of 77% of the participants did not go for exercise regularly. A total of 37% participants had experienced work related stress and 49% of the participants remained in poor posture at work place. The participants which felt mild to severe pain made up 64 % of this study. About 80% of the participants used the rest technique to handle low back pain while 10% participants used medication to tackle the low back pain. About 3% of the participants did physiotherapy techniques to reduce their back pain. A total of 82% of participants have experienced minimal disability while 15% of participants have experienced moderate disability. Statistical analysis (Chi square) was done between pain intensity rating scale and other variables of low back pain. The nature of hospital, profession and working experience was statistically significant as the p-value was less than 0.05 (Table 1).

Table 1: Statistical analysis between pain intensity rating scale and sociodemographic variables

Categories	Pain intensity rating scale				p-value
	No pain	Mild	Moderate	Severe	
	F (%)	F (%)	F (%)	F (%)	
Nature of hospital					
Public A	33(8.59)	49(12.76)	29(7.55)	9(2.34)	0.000
Public B	17(20.05)	65(16.92)	2(0.52)	16(4.16)	
Private C	48(12.5)	19(4.9)	5(1.30)	0(0)	
Private D	42(10.93)	28(7.29)	2(0.52)	0(0)	
Gender					
Male	68(17.70)	68(17.70)	29(7.55)	11(2.86)	0.786
Female	79(20.57)	93(24.21)	29(7.55)	14(3.64)	

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

Marital status					
Married	61(15.88)	70(18.22)	22(5.72)	8(2.08)	0.317
Unmarried	72(18.75)	91(23.69)	36(9.37)	17(4.42)	
Educational status					
Graduation	88(22.91)	113(29.42)	37(9.63)	21(5.46)	0.232
Master	33(8.59)	32(8.33)	9(2.34)	2(0.52)	
Specialization	18(4.6)	14(3.64)	12(3.12)	2(0.52)	
Profession					
Doctors	53(13.80)	89(23.17)	20(5.20)	15(3.90)	0.005
Nurses	35(9.11)	30(7.81)	24(6.25)	7(1.82)	
Dentists	21(5.46)	19(4.94)	6(1.56)	1(0.26)	
Allied health professionals	31(8.07)	23(5.9)	8(2.08)	2(0.52)	
Working experience					
<5 y	87(22.65)	87(22.65)	30(7.81)	6(1.56)	0.029
5-10 y	37(9.63)	58(15.10)	24(6.25)	14(3.64)	
11-15 y	14(3.64)	11(2.86)	3(0.78)	3(0.78)	
>15 y	2(0.52)	5(1.30)	1(0.26)	2(0.52)	

Body Mass Index (BMI) was not considered as significant as the p value is 0.243. Smoking behavior, sleeping disorder and general stress was considered as significant as p-value is less than 0.05. While BMI, tea or coffee consumption and exercise behavior had p-value more than 0.05 and considered as insignificant (Table 2).

Table 2: Statistical analysis between pain intensity rating scale and risk factors of LBP

Categories	Pain intensity rating scale				p-value
	No pain	Mild	Moderate	Severe	
	F (%)	F (%)	F (%)	F (%)	
BMI					
Underweight	21(5.46)	22(5.72)	5(1.30)	0(0)	0.243
Normal	84(21.87)	91(23.69)	36(9.37)	20(5.20)	
Overweight	35(9.11)	48(12.5)	17(4.42)	5(1.30)	
Smoking behavior					
Smoker	12(3.12)	37(9.63)	8(2.08)	5(1.30)	0.035
Non smoker	128(33.33)	124(32.29)	50(13.02)	20(5.20)	
Consumption of coffee or tea					
Yes	103(26.82)	123(32.03)	46(11.97)	18(4.68)	0.808
No	37(9.63)	38(9.89)	12(3.12)	7(1.82)	
Sleeping disorder					
Not at all	85(21.87)	109(28.38)	19(4.94)	12(3.1)	0.000
A little	54(14.06)	51(13.28)	32(8.33)	13(3.38)	
Severe	1(0.26)	1(0.26)	7(1.82)	0(0)	
General stress					
Not at all to minimum	75(19.53)	52(13.54)	18(4.68)	11(2.86)	0.000
Moderate	62(16.14)	90(23.43)	32(8.33)	14(3.64)	
High	3(0.78)	19(4.94)	8(2.08)	0(0)	
Exercise regularly					
Yes	28(7.29)	43(11.19)	14(3.64)	2(0.52)	0.157
No	112(29.16)	118(30.72)	44(11.45)	23(5.98)	

Physical effort, poor posture, frequent bending or twisting at work and working hour per day were statistically significant. While work stress, working shift, lifting heavy objects, transferring patients, traveling time per day and Leave due to lower back pain were insignificant as the p-value is less than 0.05 (Table 3).

Table 3: Statistical analysis between pain intensity rating scale and work related risk factors

Categories	Pain intensity rating scale				p-value
	No pain	Mild	Moderate	Severe	
	F (%)	F (%)	F (%)	F (%)	
Work stress					
Very low	19(4.94)	23(5.98)	9(2.34)	6(1.56)	0.293
Low	48(12.5)	53(13.80)	20(5.20)	13(3.38)	
Moderate	56(14.58)	66(17.1)	18(4.68)	4(1.04)	
High	17(4.42)	19(4.94)	11(2.86)	2(0.52)	
Physical effort at work					
No/Low	39(10.15)	61(15.88)	13(3.38)	8(2.0)	0.000
Medium	81(21.09)	76(19.79)	23(5.98)	5(1.30)	
High	20(5.2)	24(6.23)	22(5.72)	12(3.12)	
Poor posture at work					
Never to occasionally	58(15.10)	74(19.27)	23(5.98)	6(1.56)	0.004
Regularly	74(19.27)	77(20.05)	26(6.77)	12(3.12)	
Permanent	8(2.0)	10(2.6)	9(2.3)	7(1.82)	
Frequent bending or twisting					
Yes	66(17.18)	68(17.70)	36(9.3)	3(0.78)	0.000
No	74(19.27)	93(24.21)	22(5.72)	22(5.72)	
Lifting heavy objects					
Yes	37(9.63)	57(14.84)	19(4.94)	13(3.38)	0.064
No	103(26.82)	104(27.08)	39(10.15)	12(3.12)	
Transferring patients					
Yes	30(7.81)	37(9.63)	12(3.12)	6(1.56)	0.923
No	109(28.38)	124(32.29)	46(11.97)	19(4.94)	
Overall standing time					
1-4 h	36(9.37)	64(16.66)	31(8.07)	12(3.12)	0.001
5-8 h	55(14.32)	54(14.06)	21(5.46)	10(2.60)	
>8 h	49(12.76)	43(11.19)	6(1.56)	3(0.78)	
Working hour per day					
4-6 h	37(9.63)	85(22.13)	34(8.85)	22(5.7)	0.000
6-8 h	62(16.14)	54(14.06)	10(2.60)	0(0)	
>8 h	41(10.67)	22(5.72)	14(3.64)	3(0.78)	
Traveling time per day					
1-3 h	109(28.38)	135(35.15)	47(12.23)	23(5.98)	0.45
4-6 h	27(7.03)	24(6.25)	11(2.86)	2(0.52)	
>6 h	4(1.04)	2(0.52)	0(0)	0(0)	
Working shift					
Day time	91(23.69)	118(30.72)	31(8.07)	13(3.38)	0.005
Night time	21(5.46)	12(3.12)	4(1.04)	3(0.78)	
Both	28(7.29)	31(8.07)	23(5.98)	9(2.34)	
Leave due to pain					
Yes	37(9.63)	27(7.03)	10(2.60)	3(0.78)	0.115
No	103(26.82)	134(34.89)	48(12.5)	22(5.72)	

The pain intensity rating scale and impact of low back pain on quality of life had showed high significance (p-value 0.05)(Table 4).

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

Table 4: Statistical analysis between pain intensity rating scale and quality of life

Categories	Pain intensity rating scale				p-value
	No pain	Mild	Moderate	Severe	
	F (%)	F (%)	F (%)	F (%)	
Quality of life					
Minimal disability	124(32.29)	138(35.93)	38(9.89)	16(4.16)	0.000
Moderate disability	13(3.38)	22(5.72)	16(4.1)	6(1.56)	
Severe disability	3(0.78)	1(0.26)	4(1.04)	3(0.7)	
Crippled	0(0)	0(0)	0(0)	0(0)	
Bed bound	0(0)	0(0)	0(0)	0(0)	

DISCUSSION

Our study focused on finding the prevalence and risk factors of low back pain and its effect on quality of life among health care professionals of Lahore. Pain in lower back is considered as one of the main issue of public health and its prevalence is high in number in healthcare professionals of both public and private hospitals. Although, the healthcare professionals work at public hospitals are more complaining about private hospitals. Female healthcare professionals have high occurrence of low back pain as comparison to male healthcare professionals. Previous study in Şimşek et al., also has similar findings about the high occurrence of low back pain among females [2]. Smoking behavior, sleeping disorder and general stress are responsible for lower back pain. Work related risk factors are also considered as major reason of low back pain among healthcare professionals. Çınar-Medeni et al., also identified similar risk factors associated with low back pain in healthcare workers [15]. The most useful coping strategy that is used by many healthcare professionals is rest in comparison to other coping strategies. The low back pain has highly effect the quality of life of healthcare professionals because due to low back pain the daily activities of healthcare professionals are disturbed. Spinhoven et al., also suggested that rest is the most useful coping strategy among chronic back pain patients [16]. We find out that the prevalence of low back pain in our study is 63.2%. In comparison to our study Luhur et al., in 2022 conducted a study in Indonesia to find out the prevalence of low back pain and they find that the prevalence of low back pain was 62.7% [17]. The findings of prevalence of low back pain approximately aligns with our study results and might difference is due to difference in sample size, methodology and study designs. In our study, we find out that there is association with low back pain and different risk factors like work related risk factors are the main cause of low back pain. In contrast of our findings Zahra et al., conducted a study in Tabuk, Saudi Arabia in 2020 which also found different risk factors are responsible for the cause of lower back pain like lifting of heavy objects, work with bending position, the wrong positing of body and unstable condition of working [18]. The mean age of health care professionals in our study is 31.13±5.82. In similar to aforementioned findings, a study was conducted by Zahra et al., in Saudi Arabia and find out that the mean age of its study participants was 31.6±8.65. The findings of our study related with the above mentioned study but mild variation was due to difference in study methodology [18]. In our study we find out that there is no correlation between low back pain and obesity but the work related risk factors are major contributors of low back pain. In comparison to our study Ibrahim et al., conducted study in 2019 in Malaysia and find out that obesity and low back pain was highly correlated which was contrary to our study. But the relevance of low back pain with an unfavorable work environment was in accordance of our study [5, 19]. We find in our study results that that perceived stress scores are significantly associated with low back pain. In contrast to our study, Tsuboi et al., reported that high perceived stress was independently associated with a higher prevalence of LBP [20]. The results vary from our study. But in comparison to our study Vinstrup et al., in 2020 find out in his study that low back pain and perceived stress was highly significant correlated which relates with our study findings [21]. Our study indicates that the quality of life of healthcare professionals is highly associated with pain in low back. In comparison to our study Mroczek et al., in 2020 found out that quality of life of healthcare professionals was highly effected by low back pain. The above mentioned study aligns with our study [22]. We find in our study that rest is the most frequent method used by many healthcare professionals. The aforementioned result has similarity with the finding of study conducted by Ibrahim et al., 2019 which determined that rest is more prevalent method used by healthcare professionals to cope with low back pain [19].

CONCLUSIONS

It is concluded that low back pain is considered as one of the main issue of public health and its prevalence is high in healthcare professionals of both public and private hospitals. Low back pain is more prevalent among participants working at public sector hospitals. Female healthcare professionals have high occurrence of low back pain as comparison to male. Healthcare professionals suffering from sleeping disorder had more prevalent low back pain. Stress is indicated as the major risk contributor of low back pain. Occupation related risk factors are also considered as major reason of low back pain among healthcare professionals. The most useful coping strategy that is used by many healthcare professionals was rest. The low back pain is highly effect the quality of life of healthcare

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

professionals.

Authors Contribution

Conceptualization: NR, MW, RZ, JS
Methodology: ZU, FT
Formal analysis: ZU, FT
Writing-review and editing: NR, MW, RB, MZ, MR, RZ, JS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Vujcic I, Stojilovic N, Dubljanin E, Ladjevic N, Ladjevic I, Sipetic-Grujicic S. Low back pain among medical students in Belgrade (Serbia): a cross-sectional study. Pain Research and Management. 2018 Feb; 2018: 8317906. doi: 10.1155/2018/8317906.

[2] Şimşek Ş, Yağcı N, Şenol H. Prevalence of and risk factors for low back pain among healthcare workers in Denizli. Agri. 2017 Apr; 29(2): 71-8. doi: 10.5505/agri.2017.32549.

[3] Mijena GF, Geda B, Dheresa M, Fage SG. Low back pain among nurses working at public hospitals in eastern Ethiopia. Journal of Pain Research. 2020 Jun; 13: 1349-57. doi: 10.2147/JPR.S255254.

[4] Terzi R and Altın F. The prevalence of low back pain in hospital staff and its relationship with chronic fatigue syndrome and occupational factors. Agri. 2015 Jul; 27(3): 149-54. doi: 10.5505/agri.2015.26121.

[5] Farooq MW, Tahir N, Ch NA, Khatara JR. Road Traffic Injuries: Quality of Pre and Post Hospital Care in Pakistan. Journal of Positive School Psychology. 2023 May; 7(4): 1551-64.

[6] Fernandes JA, Genebra CV, Maciel NM, Fiorelli A, Conti MH, De Vitta A. Low back pain in schoolchildren: a cross-sectional study in a western city of São Paulo State, Brazil. Acta Ortopedica Brasileira. 2015 Sep; 23: 235-8. doi: 10.1590/1413-785220152305148842.

[7] Kongsted A, Lancet Low Back Pain Series Working Group. Low back pain: a call for action. Lancet Oncology. 2018 Jun; 391(10137): 2384-8. doi: 10.1016/S0140-6736(18)30488-4.

[8] Koes BW, Van Tulder M, Thomas S. Diagnosis and treatment of low back pain. BMJ. 2006 Jun; 332(7555): 1430-4. doi: 10.1136/bmj.332.7555.1430.

[9] Abolfotouh SM, Mahmoud K, Faraj K, Moammer G, ElSayed A, Abolfotouh MA. Prevalence, consequences and predictors of low back pain among nurses in a tertiary care setting. International Orthopaedics. 2015 Dec; 39: 2439-49. doi: 10.1007/s00264-015-2900-x.

[10] Alnaami I, Awadalla NJ, Alkhairy M, Alburidy S, Alqarni A, Algarni A, *et al.* Prevalence and factors associated with low back pain among health care workers in southwestern Saudi Arabia. BMC Musculoskeletal Disorders. 2019 Dec; 20: 1-7. doi: 10.1186/s12891-019-2431-5.

[11] Ali AA, Haq N, Hussain A, Rafique M, MR MI, Ahmad T, *et al.* Assessment of frequent work related musculoskeletal disorders in patients visiting the physiothrapy OPD of civil hospital Quetta, Pakistan: A cross sectional survey. Indian Journal of Physiotherapy and Occupational Therapy-An International Journal. 2021 Apr; 15: 91.

[12] Nachemson AL. Advances in low-back pain. Clinical Orthopaedics and Related Research (1976-2007). 1985 Nov; 200: 266-78. doi: 10.1097/00003086-198511000-00031.

[13] Parent-Thirion A, Biletta I, Cabrita J, Vargas Llave O, Vermeylen G, Wilczyńska A, *et al.* Sixth European working conditions survey–overview report. 2016 Nov. doi: 10.2806/422172.

[14] Fairbank JC and Pynsent PB. The Oswestry disability index. Spine. 2000 Nov; 25(22): 2940-53. doi: 10.1097/00007632-200011150-00017.

[15] Çınar-Medeni Ö, Elbasan B, Duzgun I. Low back pain prevalence in healthcare professionals and identification of factors affecting low back pain. Journal of Back and Musculoskeletal Rehabilitation. 2017 Jan; 30(3): 451-9. doi: 10.3233/BMR-160571.

[16] Spinhoven P, Ter Kuile MM, Linssen AC, Gazendam B. Pain coping strategies in a Dutch population of chronic low back pain patients. Pain. 1989 Apr; 37(1): 77-83. doi: 10.1016/0304-3959(89)90155-3.

[17] Luhur LJ, Ruma A, Sugianto P. Characteristics of Patients with Low Back Pain among Healthcare Professionals at John Piet Wanane General Hospital: A Cross-Sectional Study. AKSONA. 2022 Jul; 2(2): 72-7. doi: 10.20473/aksona.v2i2.36728.

[18] Zahra N, Sheha EA, Elsayed H. Low back pain, disability and quality of life among health care workers. IJPRPM. 2020 Apr; 9(2): 34-44.

[19] Ibrahim MI, Zubair IU, Yaacob NM, Ahmad MI, Shafei MN. Low back pain and its associated factors among nurses in public hospitals of Penang, Malaysia. International Journal of Environmental Research and Public Health. 2019 Nov; 16(21): 4254. doi: 10.3390/ijerph16214254.

[20] Tsuboi Y, Ueda Y, Naruse F, Ono R. The association

DOI: https://doi.org/10.54393/pjhs.v4i11.1133

between perceived stress and low back pain among eldercare workers in Japan. Journal of Occupational and Environmental Medicine. 2017 Aug; 59(8): 765-7. doi: 10.1097/JOM.0000000000001062.

[21] Vinstrup J, Jakobsen MD, Andersen LL. Perceived stress and low-back pain among healthcare workers: a multi-center prospective cohort study. Frontiers in Public Health. 2020 Aug; 8: 297. doi: 10.3389/fpubh.2020.00297.

[22] Mroczek B, Łubkowska W, Jarno W, Jaraczewska E, Mierzecki A. Occurrence and impact of back pain on the quality of life of healthcare workers. Annals of Agricultural and Environmental Medicine. 2020 Jan; 27(1): 36-42. doi: 10.26444/aaem/115180.

DOI: https://doi.org/10.54393/pjhs.v4i11.1153

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 1 (January 2023)

Original Article

The Comparison of Hearing loss in Otosclerosis Patients in response to Stapedectomy

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ARTICLE INFO

Key Words:
Otosclerosis, Stapedectomy, Post-Operative, Hearing Loss, Pure-Tone Audiometry

How to Cite:
Rasheed, K., Badar, S. A., Khan, M. A., Khan, R. S., Shahid, S., Aslam, M. A., Asif, S., Sadiq, J., Shanawar, M., & Sajjad, A. (2023). The Comparison of Hearing loss in Otosclerosis Patients in response to Stapedectomy : Hearing loss in Otosclerosis Patients . Pakistan Journal of Health Sciences, 4(11 https://doi.org/10.54393/pjhs.v4i11.1153

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Received Date: 30th October, 2023
Acceptance Date: 19th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Otosclerosis patients with remarkable hearing loss are instructed to undergo stapedectomy. Stapedectomy is surgical removal of otosclerosis-damaged stapes, to improve hearing. **Objective:** To compare the hearing loss in otosclerosis patients as the result of stapedectomy. **Methods:** Cross-sectional observational study was conducted to compare hearing loss in patients before and after stapedectomy. Total 25 otosclerosis patients of age 25-45 years, were recruited for study through random sampling technique. Setting was Shaikh Zayed Hospital with duration of 6 months from January 2023 to May 2023. Patients undergoing stapedectomy with co-morbid conditions (vertigo, inflammation at side of operation) were excluded. For data collection of study subjects, well-structured self-constructed data collection form was used. Hearing loss was accessed clinically through pure-tone audiometry (PTA). Data were analyzed statistically through SPSS version 24.0 package. **Results:** Out of 25 patients, 14 (56.0%) were female, while 11 (44.0%) were male. Majority of them (60.0%) were in age group 25-30 years. Out of 25, patients with hearing loss in pre-operative patients with moderate degree 10 (40.0%), mixed degree were 25(100%) and patients in post-operative with moderate degree 14 (56%) and mixed hearing loss were 24 (96.0%) in number. **Conclusions:** This study presents the findings that in pre-operative stapedectomy patients there was moderate to severe degree mixed hearing loss at all frequencies. Whereas, in post-operative stapedectomy patients there was mild degree mixed hearing loss at all frequencies. Stapedectomy proved to be effective in substantially reducing hearing loss in otosclerosis patients.

INTRODUCTION

The capacity to receive sounds via an organ (e.g. as the ear) by identifying vibrations as recurring variations in the amount of pressure of the surrounding environment is known as auditory perception, or hearing [1]. Hearing loss is the term for a partial or complete incapacity to hear [2]. The type of hearing loss depends upon the partway involved in hearing that is damaged [3]. When there is an issue with sound waves being transferred through the middle ear, tympanic membrane, or outer ear, it is known as conductive hearing loss (CHL) [4]. The vestibulocochlear nerve, inner ear, or sensory organ (cochlea and related components) are the primary causes of sensorineural hearing loss (SNHL) [5]. Mixed hearing loss is a combination of CHL and SNHL [4]. A middle ear surgical treatment called a "stapedectomy" is done to increase hearing [6]. CHL results from the stapes footplate being immobile as opposed to normally being mobile [7]. Stapes fixation has two main causes. The first is otosclerosis, a disease process characterized by abnormal mineralization of the temporal bone [8]. The 2nd is a congenital stapes malformation [6]. Success rates for stapedectomy range from eighty to ninety-five percent [9]. Stapedectomy

DOI: https://doi.org/10.54393/pjhs.v4i11.1153

indications include CHL (from stapes fixation), an air-bone gap of a minimum thirty dB intensity, a finding of Carhart's notch in the audiogram of a patient with a relative who has CHL, and good cochlear reserve as determined by the presence of good speech discrimination [10]. The purpose of a stapedectomy is to improve hearing loss [8]. This can significantly improve a person's quality of life [6]. The procedure can also lessen dizziness, enhance balance, and help with vertigo, tinnitus, as well as other otosclerosis symptoms [11]. The "air-bone gap" is effectively closed by a stapedectomy, restoring the best possible conduction of sound through the air to the nerve cells' maximum sensitivity to sound [12]. An audiometer can be used to measure hearing through behavioral tests [11]. Even in unconscious subjects, electrophysiological tests of hearing can accurately measure hearing levels [13]. Researchers found limited data on national level on this topic however there at international level data is available but it will be beneficial to the community because people will undergo stapedectomy surgery for the huge recovery of their hearing loss after surgery. Hence the aim of this study was to compare the hearing loss in otosclerosis patients as the result of stapedectomy.

METHODS

It was prospective observational study. Convenient sampling technique was used. The study was performed at Shaikh Zayed Hospital Lahore, Punjab, Pakistan and ethical approval was taken from research ethics committee of University of Lahore. Duration of the study was 6 months from January 2023 to June 2023. Sample size was 25 adult patients undergoing stapedectomy. Sample size was calculated through online calculator by using formula:

$$n = Z^2_{1-\alpha/2}\frac{p(1-p)}{d^2}$$

on the basis of prevalence of Hearing Impairment 96% with 8% margin of error by using 95% confidence level and 5% confidence interval [14]. Physician diagnosed otosclerosis adult patient age more than 10 years; undergoing stapedectomy and willing to participate in this research project were recruited. Patients who failed to undergo stapedectomy were excluded, patients with age greater than 50 years along with foreign patients (non-Pakistanis) and patients with co-morbid conditions (vertigo and inflammation at the site of operation) were excluded from this study. Moreover, patients unwilling to participate in this study were excluded. Right after their enrollment in the study, patients were required to fill out a data collection form with questions about their diseases and demographics. Patients were asked to complete the form on their own, under the researcher's supervision. The hearing loss was accessed through pure-tone audiometry (PTA), before and after stapedectomy. Using the statistical package for social sciences package (SPSS Inc., version 24.0. ibm.), the collected data were analyzed. Inferential and descriptive statistics were used to compile the outcome variables. The categorical variables were displayed as frequencies and percentages.

RESULTS

Table 1 shows demographics, out of 25 patients, 11 (44%) are male and 14 (56%) are female patients. Majority of the patients 15 (60%) are in age group 25-30 years.

Table 1: Table 1: Demographics

Variables	Categories	N (%)
Gender	Male	11 (44)
	Female	14 (56)
Age	25-30 years	15 (60)
	31-35 years	03 (12)
	36-40 years	07 (28)

Table 2 shows pre-operative type of hearing loss. The results show that all of the pre-operative patients 25 (100%) have mixed hearing loss. There are 10 (40%) pre-operative patients who have moderate degree hearing loss and 15 (60%) pre-operative patients who have severe degree hearing loss.

Table 2: Pre-operative hearing loss in study subjects

Variables	Categories	N (%)
Type of hearing loss	Mixed Hearing loss	25 (100)
	Conductive hearing loss	0.0 (0)
Degree of hearing loss	Moderate	10 (40)
	Severe	15 (60)

Table 3 shows the finding that out of 25 pre-operative air conduction patients, majority of the patient's air conduction 13 (52%) are in intensity range 41-70db at 250 Hz. At 500 Hz majority of the patient's air conduction 16 (64%) are in intensity range 41-70 db. At 1000 Hz majority of the patient's air conduction 21 (84%) are in intensity range 41-70 db. At 2000 Hz majority of the patient's air conduction 19 (76%) are in intensity range 41-70 db. At 4000 Hz majority of the patient's air conduction 19 (76%) are in intensity range 41-70 db. At 8000 Hz majority of the patient's bone conduction 15 (60%) are in intensity range 41-70 db.

Table 3: Hearing loss in pre-operative patients through air conduction

Sound Intensity (db)	Sound Frequency N (%)					
	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
26-40 db	1 (4)	0	0	2 (8)	3 (12)	4 (16)
41-70 db	13 (52)	16 (64)	21 (84)	19 (76)	19 (76)	15 (60)
71-90 db	11 (44)	9 (36)	4 (16)	4 (16)	3 (12)	6 (24)

Table 4 shows the findings of pre-operative bone conduction in patients, majority of the patient's bone conduction 23 (92%) are in intensity range 0-25 db at 250

DOI: https://doi.org/10.54393/pjhs.v4i11.1153

Hz. At 500 Hz majority of the patient's bone conduction 22 (88%) are in intensity range 0-25 db. At 1000 Hz majority of the patient's bone conduction 19 (76%) are in intensity range 0-25 db. At 2000 Hz majority of the patient's bone conduction 15 (60%) are in intensity range 26-40 db. At 4000 Hz majority of the patient's bone conduction 16 (64%) are in intensity range 0-25 db.

Table 4: Hearing loss in pre-operative patients through bone conduction

Sound Intensity (db)	Sound Frequency N (%)				
	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
0-25 db	23 (92)	22 (88)	19 (76)	4 (16)	16 (64)
26-40 db	2 (8)	3 (12)	4 (16)	15 (60)	8 (32)
41-70 db	0	0	2 (8)	6 (24)	1 (4)

Table 5 presents the hearing loss in post-operative patients. Majority of the patients 24 (96%) experienced mixed hearing loss as the result of stapedectomy. Moreover, majority of the patients 14 (56%) experienced moderate degree of hearing loss post stapedectomy.

Table 5: Post-operative hearing loss in study subjects

Variables	Categories	N (%)
Type of hearing loss	Mixed Hearing loss	24 (96)
	Conductive hearing loss	1 (4)
Degree of hearing loss	Mild	9 (36)
	Moderate	14 (56)
	Severe	2 (8)

Table 6 shows that post-operative air conduction of 25 patients, there are majority of the patients 9 (36%) post-operative air conduction are in intensity range 0-25db at 250Hz. At 500 Hz majority of the patients 11(44%) post-operative air conduction are in intensity range 0-25db. At 1000 Hz majority of the patients 11(44%) post-operative air conduction are in intensity range 26-40db. At 2000 Hz majority of the patients 9 (36%) post-operative air conduction are in intensity range 0-25db. At 4000 Hz majority of the patients 10 (40%) post-operative air conduction are in intensity range 26-40db. At 8000 Hz majority of the patients 11 (44%) post-operative air conduction are in 41-70db.

Table 6: Hearing loss in post-operative patients through air conduction

Sound Intensity (db)	Sound Frequency N (%)					
	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
0-25 db	9 (36)	11 (44)	8 (32)	9 (36)	6 (24)	1 (4)
26-40 db	8 (32)	6 (24)	11 (44)	8 (32)	10 (40)	10 (40)
41-70 db	7 (28)	7 (28)	5 (20)	8 (32)	9 (36)	11 (44)
71-90 db	1 (4)	1 (4)	1 (4)	0 (0)	0 (0)	3 (12)

25db. At 2000 Hz majority of the patients 13 (52%) post-operative bone conduction are in intensity range 0-25db. At 4000 Hz majority of the patients 15 (60%) post-operative bone conduction are in intensity range 0-25db25db. At 2000 Hz majority of the patients 13 (52%) post-operative bone conduction are in intensity range 0-25db. At 4000 Hz majority of the patients 15 (60%) post-operative bone conduction are in intensity range 0-25db.

Table 7: Hearing loss in post-operative patients through bone conduction

Sound Intensity (db)	Sound Frequency N (%)				
	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz
0-25 db	22 (88)	22 (88)	21 (84)	13 (52)	15 (60)
26-40 db	3 (12)	3 (12)	2 (8)	9 (36)	9 (36)
41-70 db	0 (0)	0 (0)	2 (8)	3 (12)	1 (4)

DISCUSSION

Stapedectomy is a surgical procedure to remove otosclerosis damaged stapes (small U-shaped bone in the middle ear) to improve hearing [6]. It is a rare surgical procedure as there are a limited number of otosclerosis patients who are willing to undergo Stapedectomy [15]. To the best of the writer's knowledge, this is the first study of its kind to be conducted on otosclerosis patients from north-east of Pakistan, undergoing stapedectomy to compare the hearing loss as the result of stapedectomy. The findings of the recent study showed that out of 25 otosclerosis patients, (56.0%) 14 patients were female, while (44.0%) 11 patients were male i.e., majority of the recruited patients were female. Similarly, a study from Massachusetts, recruited 39 patients undergoing Stapedectomy, among which majority of the patients 24 (61.5%) were female patients and 5 (12.8%) were male patients aged between 31-70 years [16]. Similarly, another research study conducted on patients from the state of California, the United States, recruited a total of 134 stapedectomy undergoing patients, among which majority of the patients 65.1% were female patients [13]. In contrast, a research study was conducted upon 31 patients from Chennai, India had majority male patients (61.3 %) whereas, With ages ranging from 21 to 69 years, 38.7% of the patients were female, with a mean age of 43.67. 5.96 years on average; SD of 6.188 was the period of the symptoms. The two most prevalent initial symptoms were tinnitus (48.4 %) and hearing loss (96.5 %) [14]. The results of current study presented that all of the 25 pre-operative patients had mixed hearing loss. A study conducted in Mayo Clinic School of Medicine, Rochester, Minnesota upon stapedectomy patients, presented that it caused SNHL. This study focuses at 71 stapedectomies that resulted in sensorineural hearing loss and were followed by a revision stapedectomy due to the possibility of an oval window fistula developing. Two primary stapedectomy techniques were used: a wire prosthesis with Gelfoam and a stainless steel Robinson prosthesis on a vein graft. The wire

DOI: https://doi.org/10.54393/pjhs.v4i11.1153

prosthesis' fistula rate was 10 times higher than the Robinson prosthesis'; the wire prosthesis' length was found to be excessive in 21% of cases where it was used, but not in any cases where the Robinson prosthesis was used, dizziness was reduced in 20 percent of patients in the Robinson prosthesis group but 60 percent of those in the wire prosthesis group after revision stapedectomy. The procedure for performing a revision stapedectomy following sensorineural hearing loss is described [3]. Another study conducted in London. A retrospective case series investigation was conducted. Hearing outcomes improved significantly between the six-week postoperative visit (mean air-bone gap 6 dB) and the six-month hearing outcome (mean air-bone gap 3.3 dB)(p 0.01). This improvement was sustained at twelve months (mean air-bone gap 3.1 dB), despite the fact that individual patients' hearing outcomes improved or worsened during this time. Air-bone gap measurements improved in tandem with advances in AC thresholds [17]. The result of current study shows that out of post-operative air conduction of 25 patients, there were majority of the patients 9 (36%) post-operative air conduction were in intensity range 0-25db at 250Hz. At 500 Hz majority of the patients 11(44%) post-operative air conduction were in intensity range 0-25db. At 1000 Hz majority of the patients 11(44%) post-operative air conduction were in intensity range 26-40db. At 2000 Hz majority of the patients 9 (36%) post-operative air conduction were in intensity range 0-25db. At 4000 Hz majority of the patients 10 (40%) post-operative air conduction were in intensity range 26-40db. At 8000 Hz majority of the patients 11 (44%) post-operative air conduction were in 41-70db. Moreover, out of 25 post-operative bone conduction patients. At frequency 250 Hz and 500 Hz majority of the patients 22 (88%) post-operative bone conduction were in intensity range 0-25db. At 1000 Hz majority of the patients 21 (84%) post-operative bone conduction were in intensity range 0-25db. At 2000 Hz majority of the patients 13 (52%) post-operative bone conduction were in intensity range 0-25db. At 4000 Hz majority of the patients 15 (60%) post-operative bone conduction were in intensity range 0-25db. Similarly, a study performed in Italy about otosclerosis surgery effectiveness. The average post-operative air-bone gap was 14.78 dB as a result of revision surgery. An average post-operative air-bone gap of less than 10dB occurred in 24 patients (54.5 %), 14 patients (31.5 %) between 11 and 20 dB, 5 patients (11.5 %) between 21 and 30 dB, and one patient (2.5 %) greater than 30 dB [18]. Another study conducted in Sweden. The data for the study came from the Swedish Quality Register for Otosclerosis Surgery (SQOS). A total of 156 revisions with both preoperative and postoperative audiometry data were available for investigation. One year following revision surgery, 75% of patients reported improved to very improved hearing. In seventy-seven percent of the patients, an air bone gap of 20 dB was seen postoperatively. 4% reported hearing loss of 20 dB PTA4 AC. One year after surgery, 11% had exacerbated or newly formed tinnitus, five percent experienced taste disturbance, and three percent had dizziness. There was no difference in pre-operative and post-operative hearing between patients operated on in university vs. county clinics [19]. A prospective observational study performed in New Zealand, recruited 39 participants including 11 males and 28 females (mean age = 49.2 years). It was carried out on high frequency SNHL following stapedectomy. It was discovered that mean bone conduction thresholds at 4,000 Hz deteriorated by 6 dB after 4 to 6 weeks and improved by 3 dB after 9 months. At 4 to 6 weeks, there was an 8-dB average loss at 8,000 Hz air conduction, followed by a 4-dB gain at 9 months. When preoperative thresholds were held constant, patients over the age of 40 were four times more likely to experience early loss at 4,000 Hz bone conduction. The late outcome for hearing loss was determined more by the preoperative threshold than by the patient's age. The preoperative hearing threshold was a predictor of early and late hearing loss at 8,000 Hz air conduction [20]. Moreover, another retrospective study conducted upon seventy patients from Minnesota, US for a long-term evaluation presented. There was no significant difference between early and late post-operative AC-PTA (41 vs. 49 dB; $p > 0.05$) or early and late post-operative BC-PTA (29 vs. 37 dB; $p > 0.05$). AC at 8 kHz (65 vs. 78 dB; p 0.05) and BC at 2 and 4 kHz (28 vs. 40 dB and 45 vs. 58 dB, respectively; p 0.05) showed a significant difference. To the best of our knowledge, this is the extended mean follow-up time in the literature. A slight decrease in both air conduction and bone conduction thresholds is to be expected, with sensorineural decay being more pronounced at higher frequencies. Subjective hearing symptoms and overall sound perception were both acceptable [10].

CONCLUSIONS

The results of the current study shows that in pre-operative stapedectomy otosclerosis patients there was a moderate to severe degree mixed hearing loss at all frequencies whereas in post-operative stapedectomy patients, there was a mild degree mixed hearing loss at all frequencies. There was a need for further studies with larger sample size. Moreover, the study area should be extended to country wide, to generalized the results to whole nation.

Authors Contribution

Conceptualization: MAK
Methodology: KR, MAA, AS
Formal analysis: SS, SA, JS
Writing-review and editing: KR, SAB, RSK, MS

DOI: https://doi.org/10.54393/pjhs.v4i11.1153

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Moore BC. Hearing. Companion Encyclopedia of Psychology. 2019 Jan: 202-223. Routledge. doi: 10.4324/9781315002897-12.

[2] Fang Y, Chen KG, Zhao Y, Menon NA, Scholp AJ, Shu Y, et al. Relationship between short-term and mid-term hearing outcomes after stapedotomy in patients with otosclerosis: an investigation. Acta Oto-Laryngologica. 2021 Jun; 141(6): 603-7. doi: 10.1080/00016489.2021.1909748.

[3] Carlson ML, Van Abel KM, Pelosi S, Beatty CW, Haynes DS, Wanna GB, et al. Outcomes comparing primary pediatric stapedectomy for congenital stapes footplate fixation and juvenile otosclerosis. Otology & Neurotology. 2013 Jul; 34(5): 816-20. doi: 10.1097/MAO.0b013e318280db7b.

[4] Quaranta N, Besozzi G, Fallacara RA, Quaranta A. Air and bone conduction change after stapedotomy and partial stapedectomy for otosclerosis. Otolaryngology-Head and Neck Surgery. 2005 Jul; 133(1): 116-20. doi: 10.1016/j.otohns.2005.03.011.

[5] Massey BL, Kennedy RJ, Shelton C. Stapedectomy outcomes: titanium versus teflon wire prosthesis. The Laryngoscope. 2005 Feb; 115(2): 249-52. doi: 10.1097/01.mlg.0000154727.85539.76.

[6] Lescanne E, Bakhos D, Metais JP, Robier A, Moriniere S. Otosclerosis in children and adolescents: a clinical and CT-scan survey with review of the literature. International Journal of Pediatric Otorhinolaryngology. 2008 Feb; 72(2): 147-52. doi: 10.1016/j.ijporl.2007.10.017.

[7] Tucker RP, Peterson CA, Hendaoui I, Bichet S, Chiquet-Ehrismann R. The expression of tenascin-C and tenascin-W in human ossicles. Journal of Anatomy. 2016 Sep; 229(3): 416-21. doi: 10.1111/joa.12496.

[8] Massey BL, Hillman TA, Shelton C. Stapedectomy in congenital stapes fixation: are hearing outcomes poorer? Otolaryngology—Head and Neck Surgery. 2006 May; 134(5): 816-8. doi: 10.1016/j.otohns.2005.10.063.

[9] Robinson M. Partial stapedectomy. Elsevier; 2021.

[10] Totten DJ, Marinelli JP, Spear SA, Bowe SN, Carlson ML. With the incidence of otosclerosis declining, should stapedectomy remain a key-indicator case for otolaryngology residents? Otolaryngology–Head and Neck Surgery. 2020 Dec; 163(6): 1070-2. doi: 10.1177/0194599820941836.

[11] Sparano A, Leonetti JP, Marzo S, Kim H. Effects of stapedectomy on tinnitus in patients with otosclerosis. International Tinnitus Journal. 2004 Jan; 10: 73-7.

[12] Van de Heyning P, Claes J, Brokx J, Declau F, Boudewyns A, Hamans E, et al. Surgical management of hearing impairment in audiological medicine. Textbook of Audiological Medicine, London, Martin Dunitz. 2002 Jul; 36: 603-41. doi: 10.1201/b14730-40.

[13] House HP, Hansen MR, Dakhail AA, House JW. Stapedectomy versus stapedotomy: comparison of results with long-term follow-up. The Laryngoscope. 2002 Nov; 112(11): 2046-50. doi: 10.1097/00005537-200211000-00025.

[14] Kolo ES and Ramalingam R. Hearing results in adults after stapedotomy. Nigerian Medical Journal: Journal of the Nigeria Medical Association. 2013 Jul; 54(4): 236. doi: 10.4103/0300-1652.119617.

[15] Meyer TA and Lambert PR. Primary and revision stapedectomy in elderly patients. Current Opinion in Otolaryngology & Head and Neck Surgery. 2004 Oct; 12(5): 387-92.

[16] Meyer SE and Megerian CA. Patients' perceived outcomes after stapedectomy for otosclerosis. Ear, Nose & Throat Journal. 2000 Nov; 79(11): 846-56. doi: 10.1177/014556130007901108.

[17] Nash R, Patel B, Lavy J. Changes to hearing levels over the first year after stapes surgery: an analysis of 139 patients. Otology & Neurotology. 2018 Aug; 39(7): 829-33. doi: 10.1097/MAO.0000000000001854.

[18] Puxeddu R, Ledda GP, Pelagatti CL, Salis G, Agus G, Puxeddu P. Revision stapes surgery for recurrent transmissional hearing loss after stapedectomy and stapedotomy for otosclerosis. Acta Otorhinolaryngologica Italica. 2005 Dec; 25(6): 347.

[19] Pauli N, Finizia C, Lundman L, Björsne A, Dahlin-Redfors Y. Are there differences in revision stapes surgery outcomes between university and county clinics? A study from the quality register for otosclerosis surgery in Sweden. European Archives of Oto-Rhino-Laryngology. 2023 May; 280(5): 2247-55. doi: 10.1007/s00405-022-07737-5.

[20] Gillard DM and Harris JP. Cost-effectiveness of stapedectomy vs hearing aids in the treatment of otosclerosis. JAMA Otolaryngology–Head & Neck Surgery. 2020 Jan; 146(1): 42-8. doi: 10.1001/jamaoto.2019.3221.

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Diagnostic Accuracy of Harbinger Score by Comparing It with Glasgow Blatchford (GBS) for Prediction of Early Endoscopic Intervention Need in Patients with Upper Gastrointestinal Bleed (UGIB)

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ARTICLE INFO

Key Words:
Upper Gastrointestinal Bleeding (UGIB), Harbinger Score, Glasgow-Blatchford Score (GBS), Endoscopic Intervention, Diagnostic Accuracy

How to Cite:
Rehan, B., ul Haq, M. M., & Wadwa, R. K. (2023). Diagnostic Accuracy of Harbinger Score by Comparing It with Glasgow Blatchford (GBS) for Prediction of Early Endoscopic Intervention Need in Patients with Upper Gastrointestinal Bleed (UGIB): Diagnostic Accuracy of Harbinger Score. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1165

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Received Date: 4th November, 2023
Acceptance Date: 24th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Accurate risk assessment techniques are crucial to aid in clinical decision-making on the need for early endoscopic intervention in patients with upper GI bleed. The Glasgow-Blatchford Score and the Harbinger Score are two popular scoring systems; however, it is uncertain how accurate their comparative diagnostic abilities are. **Objective:** To evaluate and compare the diagnostic precision of the Harbinger Score and the Glasgow-Blachford Score in determining the need for early endoscopic intervention among patients experiencing upper gastrointestinal bleeding (UGIB). **Methods:** 278 UGIB patients who came to the Department of Gastroenterology, Liaqat National Hospital, Karachi, between July 2022 and June 2023 were enrolled. Demographic, clinical information and scores for Harbinger and Glasgow-Blatchford rating systems were derived for each patient. Outcome measure was the requirement for early endoscopic intervention. Diagnostic accuracy was determined and contrasted for both scoring systems. **Results:** 192 (69.06%) were male, 86 (30.93%) female. Age ranged from 16 to 80 years, with a mean of 65.5±16.4. 117 patients (42.08%) presented with dyspepsia and heartburn and syncope in 6 (2.15%). Mortality AUC was 0.761 for GBS and 0.532 for Harbinger score, p-value <0.002. Both Harbinger and GBS scored >14 and 1. GBS specificity was 88% and Harbinger 54%, while susceptibility was 80% (90% CI: 35.9-95.8) for both scores. The intensive care AUC was 0.769 for GBS and 0.531 for Harbinger score, with a p-value <0.002. **Conclusions:** According to this study, Harbinger score had better sensitivity than GBS for predicting upper GI bleeding.

INTRODUCTION

Upper gastrointestinal bleeding is a serious medical disorder with high morbidity and mortality (UGIB). To get the best results, patients needing early endoscopic intervention must be identified promptly [1]. Different risk assessment scoring methods have been created to help doctors decide when to conduct endoscopy on UGIB patients [2]. The Glasgow-Blatchford and Harbinger scores are popular scoring systems used for this [3]. Peptic ulcers, esophageal varices, Mallory-Weiss rips, and other underlying gastrointestinal disorders may lead to UGIB, a common medical emergency [4]. Endoscopic timely and suitable intervention may locate the bleeding source, promote hemostasis, and lower the risk of rebleeding and related consequences [5]. Age, vital signs, comorbidities, and laboratory results are among the clinical and laboratory factors the Harbinger Score integrates to classify patients into risk groups. The Glasgow-Blatchford Score, on the other hand, evaluates the necessity for endoscopy by combining clinical and endoscopic data, including hemoglobin levels, melena, and active bleeding. Despite the widespread usage of these scoring systems, study is still being done to determine their comparative diagnostic efficacy and capacity to foretell the need for early endoscopic intervention [6, 7]. We compared the

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

sensitivity, specificity, and AUC-ROC of the Harbinger and Glasgow-Blatchford scores to get clinical insights. These results help clinical practice guidelines and healthcare practitioners make more accurate and timely UGIB treatment choices.

METHODS

This descriptive validation study was carried out at the department of Gastroenterology, Liaqat National Hospital, Karachi during the period between July 2022 and June 2023. This study consisted of 278 male and female patients in age range 16 to 80 years with UGIB. UGIB was defined as patient complaining of hematemesis or melena accompanied by drop in hemoglobin concentration by more than 2gm/dl from the baseline. Patients with history of proton pump inhibitors (PPIs) intake in the last 2 weeks, patients with history of corrosive intake, patients complaining of UGIB after any medical procedures, patients with history of gastric malignancy and patients taking antiplatelets or anticoagulants were excluded. Participants were recruited using non-probability consecutive sampling technique. The sample size was determined using WHO sample size calculator using 5% margin of error at 95% confidence interval. Detailed history was taken from all patients followed by medical examination. Patient age, gender, vital signs at the time of admission (blood pressure, heart rate, respiration rate), laboratory results (hemoglobin levels, platelet count, international normalized ratio), comorbidities, clinical presentation (melena, hematemesis), and endoscopic findings were all recorded. Patients had upper gastrointestinal endoscopy as part of their diagnostic workup, had full data available for both the Harbinger and Glasgow-Blatchford scoring systems, and presented with signs and symptoms indicating UGIB. The main outcome measure was the requirement for early endoscopic intervention, defined as an upper gastrointestinal endoscopy carried out within 24 hours after admission. The patient features were summarized using descriptive statistics. The calculation of the Glasgow-Blachford Score (GBS) included the allocation of points to several criteria, including hemoglobin levels, melena, and active bleeding, in accordance with established rules. The cumulative score for the Harbinger Score was determined in a similar manner, taking into account factors including age, vital signs, laboratory results, and comorbidities. The statistical analysis was conducted using SPSS 26.0. The patient features were summarized via descriptive statistics. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the receiver operating characteristic curve (AUC-ROC) were used to evaluate the diagnostic accuracy of both scores. A comparative study was performed on the two scoring systems using suitable statistical techniques. The statistical significance of discrepancies in diagnostic accuracy was assessed using paired t-tests or their non-parametric counterparts. This study followed ethical guidelines and obtained under reference number CPSP/REU/GAS-2019-192-1032, dated February 25, 2022. The confidentiality of patient data was maintained in compliance with data protection legislation.

RESULTS

In this study, a total of 278 patients were included. Among these patients, 192 (69.06%) were male, while 86 (30.93%) of the study population were female. The age distribution of the patients ranged from 16 to 80 years, with a general mean age of 65.5±16.4. When we examined the mean ages separately by gender, the average age for male patients was 55.6±18.9, whereas the female patients had an average age of 64.2±15.7 (Table 1).

Table 1: Demographic Parameters

Parameter	Frequency (%)/ Mean ± SD (n=278)
Gender	
Male	192 (69.06)
Female	86 (30.94)
Age (Range: 16-80 years)	
Overall	65.5 ± 16.4 years
Male	55.6 ± 18.9 years
Female	64.2 ± 15.7 years

Dyspepsia and heartburn were the most common symptoms in 117 (42.08%). Sixty-seven patients (24.10%) reported stomach pain, 55 (9.78%) nausea/vomiting, 8 (2.87%) dizziness, and 6 (2.15% syncope). 135 (48.56%) were diabetic, 139 (50%) were hypertensive, 13 (4.67%) were asthmatic, and 37 (13.30%) were suffering from ischemic heart disease. Melena was the most prevalent bleeding in 164 (58.99%) cases and hematemesis in 192 (69.06%). Hematemesis occurred in ten patients (3.59%). The study additionally examined the patients' bleeding history. One hundred eighty-five patients (66.54%) had none. Eighty-one patients did not take any medication (29.13%). Some patients used particular medicines, such as antiplatelet agents 9 (3.23%), anticoagulants 15 (5.39%), new generation anticoagulants 11 (3.95%), non-steroidal anti-inflammatory drugs 8 (2.87%), and 38 (13.66%). These findings provide information on the patient group (Table 2).

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

Table 2: Patient complaints, bleeding types and Medication parameters

Parameter	Number of Patients (%) n=278
Patient Complaints at Admission	
Dyspepsia and Heartburn	117 (42.08)
Abdominal Pain	67 (24.10)
Nausea/Vomiting	55 (19.78)
Dizziness	8 (2.87)
Syncope	6 (2.15)
Diabetes	135 (48.56)
Hypertension	139 (50)
Asthma	13 (4.67)
IHD	37 (13.30)
Bleeding Types	
Melena	164 (58.99)
Hematemesis	192 (69.06)
Hematemesis and Active Bleeding	10 (3.59)
History of Bleeding	
No History	185 (66.54)
Medication Use	
No Medication	81 (29.13)
Antiplatelet Agents	9 (3.23)
Anticoagulants	15 (5.39)
New Generation Anticoagulants	11 (3.95)
Non-Steroidal Anti-Inflammatory Drugs	8 (2.87)
Other Drugs	38 (13.66)

GBS and Harbinger patients were assessed using numerous critical factors. First, systolic blood pressure (BP) was divided into three ranges: 1 for 100–160 mmHg, 2 for 80–99, and 3 for below 80. The shock index, which assesses heart rate and systolic blood pressure, scored 1 for values between 0.5 and 1.32. Urea levels, which indicate renal function, were classified into four groups. Patients with urea levels between 6.5 and 10 mmol/L scored 2, whereas those with 10–20 scored 3. Urea levels between 20 and 25 mmol/L were rated 4, while those beyond 25 were awarded 6. The kidney function marker urea/creatinine ratio scored 1 for levels above 130. Anemia was determined by hemoglobin concentration, which was divided into three categories. Scores were 1 for hemoglobin levels between 14 and 14.7 gr/dL, 3 for 12–13.9 gr/dL, and 6 for below 12 gr/dL. Proton pump inhibitor (PPI) usage was also recorded, with scores of 1 and 2 indicating 1-2 uses per week. If the heart rate was 90 beats per minute or above, it was scored 1. The risky symptom syncope scored 6. Hepatic illness and melena (black tarry stool) scored 1 and 2. Final score: 4 for cardiac failure. These parameter-point connections in the GBS and Harbinger scoring systems help doctors evaluate patient gastrointestinal bleeding severity and risk, guiding medical actions and management options (Table 3).

Table 3: The attributes of scoring systems

GBS		HARBINGER	
Parameters	**Point**	**Parameters**	**Point**
Systolic BP mmHg	1 (100-160) 2 (80-99) 3 (<80)	Shock index	1 (.5-1.32)
Urea mmol/L	2 (6.5-10) 3 (10-20) 4 (20-25) 6 (>25)	Urea/creatinine	1 (≥130)
Hemoglobin gr/dL	1 (14-14.7) 3 (12-13.9) 6 (<12)	PPI use (in a week)	1-2
Heart rate	1 (≥90)	-	-
Syncope	6	-	-
Hepatic disease	1	-	-
Melena	2	-	-
Cardiac failure	4	-	-

The mean ± SD and median (IQR20-85) values for systolic blood pressure were 120.5±15.7 mmHg and 110 (120-130) mmHg, respectively. For diastolic blood pressure, 42.02±14.3 mmHg and 50 (54-75) mmHg, respectively. Respiratory rates were 11.3±8.5 /min and 16 (0-20) /min. For heart rate, the values were 95.8±20.4 bpm and 90 (85-139) bpm. Values for hospitalization were 105.3±138.6 hours and 75 (25-78) hours. Blood transfusions were 1.6±1.4 and 1 (0-2) units, respectively. Values for GBS were 8.7±4.6 and 6 (5-12), respectively. For the Harbinger score, the mean ± SD and median values were 1.6±0.8 and 1 (1-2), respectively (Table 4).

Table 4: The measurement of vital signs and the calculation of score averages

Variables	units	Mean ± SD	median (IQR20-85)
Systolic Blood Pressure	mmHg	120.5±15.7	110 (120-130)
Diastolic Blood Pressure	mmHg	42.02±14.3	50 (54-75)
Respiratory rate	/min	11.3±8.5	16 (0-20)
Heart rate	Bpm	95.8±20.4	90 (85-139)
Hospitalization	Hours	105.3±138.6	75 (25-78)
Blood Transfusion	number	1.6±1.4	1 (0-2)
GBS	Score	8.7±4.6	6 (5-12)
HARBINGER	Score	1.6±0.8	1 (1-2)

GBS and Harbinger scores were evaluated for mortality, critical care, rebleeding, and transfusion. Mortality AUC was 0.761 for GBS and 0.532 for Harbinger score, p-value <0.002. Both Harbinger and GBS scored >14 and 1. GBS specificity was 88% and Harbinger 54%, while susceptibility was 80% (90% CI: 35.9-95.8) for both scores. The intensive care AUC was 0.769 for GBS and 0.531 for Harbinger score, with a p-value <0.002. The cut-off values for GBS and Harbinger scores were >12 and <2, respectively. Harbinger score sensitivity was 96.3% and GBS 64.5% (90% CI: 44-86.5). GBS specificity was 84.6% (95% CI: 74.1-85.2) and Harbinger score 14.01%. Rebleeding had a p-value of

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

0.011, GBS AUC of 0.695, and Harbinger score of 0.490. The cut-off values for GBS and Harbinger scores were >11 and <1, respectively. Harbinger score sensitivity was 1% and GBS 64.4% (90% CI: 34.2-81.6). Harbinger score was 96.6%, and GBS specificity was 67.8% (95% CI: 62.4-78.4). GBS AUC was 0.767, Harbinger score 0.510, p-value 0.281 for transfusion. Both Harbinger and GBS scored >6 and >2. Harbinger score sensitivity was 57.2% [45.6-65.2], whereas GBS was 75.6% (90% CI: 65.8-83.2). GBS specificity was 84.55% (95% CI: 73.7-85.4), and Harbinger scored 58.2% (Table 5).

Table 5: All risk score ROC values for clinical outcome prediction and diagnostic accuracy

Variables		GBS	HARBINGER	*p-value*
	AUC	0.761	0.532	<0.002
	Cut-off	>14	>1	
	Sensitivity (90% CI)	80 35.9-95.8	80 35.9-95.8	
Mortality	Specificity (95% CI)	88 84.7-94	54 45.6-60.8	
Intensive care	AUC	0.769	0.531	<0.002
	Cut-off	>12	>2	
	Sensitivity (90% CI)	64.5 44-86.5	96.3 77.3-98.6	
	Sensitivity (95% CI)	84.6 74.1-85.2	14.01 6.5-17.2	
Rebleeding	AUC	0.695	0.490	0.011
	Cut-off	>11	>1	
	Sensitivity (90% CI)	64.4 34.2-81.6	1 1-22.6	
	Sensitivity (95% CI)	67.8 62.4-78.4	96.6 92.4-96.4	
Need for transfusion	AUC	0.767	0.510	0.281
	Cut-off	>6	>2	
	Sensitivity (90% CI)	75.6 65.8-83.2	57.2 45.6-65.2	
	Sensitivity (95% CI)	84.55 73.7-85.4	58.2 44.6-67.4	

DISCUSSION

This study showed that the Harbinger score outperformed other measures in predicting the requirement for intensive care in upper GI hemorrhage. The primary purpose of using UGIB risk scores is to identify persons who are at a low risk for UGIB. The development of tools that can effectively categorize high-risk patients is essential due to the crucial nature of the clinical screening process [8]. In previous studies, the primary stage in the provision of healthcare to patients was evaluating the extent of haemorrhaging [9]. Systemic arterial hypotension often arises as a prevalent consequence in cases of severe bleeding, especially when a substantial loss of 20-25% of the intravascular volume occurs, leading the patient to experience hypovolemic shock [10]. Gastrointestinal bleeding is well recognized as a primary etiological factor contributing to the development of hypovolemic shock [11]. The shock index, which is calculated by dividing the heart rate by the systolic blood pressure, serves as a reliable measure of blood loss sensitivity. Consequently, it may be used as a prognostic tool for predicting the outcomes of patients with hypovolemia [12]. Moreover, it is the most crucial aspect of the Harbinger score. Based on several studies, it has been shown that the shock index lacks clinical use in prognosticating outcomes in cases of upper gastrointestinal haemorrhage, since its predictive capacity is limited to short-term adverse consequences [13, 14]. According to the findings of the study, the Harbinger score shown efficacy in low-risk people. However, the shock index did not exhibit utility in predicting unfavorable outcomes after hospitalization for patients with upper gastrointestinal haemorrhage, as per the research [15]. According to this study, the GBS was determined to be the best predictor of the requirement for intensive care (AUC=0.531) (p0.002). The observed phenomenon may be attributed to the demographic characteristic of upper gastrointestinal bleeding patients, who often consist of older individuals afflicted with chronic ailments. The mean age in our group of participants was 65.5 ± 16.4 years, a finding consistent with previous research [16]. A significant proportion of the patient, used medicine to manage their chronic illnesses effectively. In previous research endeavors, hypertension emerged as the prevailing chronic ailment, but in our investigation, it manifested in 50% of the patient cohort [17, 18]. Antihypertensive medications have the potential to mask or alter pulse and blood pressure readings, hence influencing shock index values and subsequent clinical results. It is noteworthy to mention that both the GBS and Harbinger scores include heart rate and blood pressure measurements. While age does not directly contribute to the scoring system, several studies have provided evidence indicating that advanced age has an impact on both the duration of intensive care unit (ICU) stays and fatality rates [19]. GBS >14, AUC 0.761, and statistically significant difference (p=0.002) were found in our investigation. No research has determined the GBS score cut-off for intensive care. Greater area under the curve (AUC) values, even when using lower cut-off values, signify the superior predictive capability of the GBS score in relation to the Harbinger score for intensive care prognosis. Albumin is a GBS score factor. GI blood loss is a major cause of hypoalbuminemia [20]. The GBS score predicted upper GI bleeding mortality without statistical significance. The GBS score had a superior area under the curve (AUC) value of 0.761 compared to the Harbinger score, which showed no predictive capability for death. The GBS score

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

demonstrated a suboptimal predictive ability for re-bleeding, as shown by its position below the curve. Furthermore, there was no statistically significant disparity seen. The GBS predicted blood transfusions better and had a larger AUC (0.767) area (p=0.281). For in-hospital adverse events, the Harbinger score solely predicted blood transfusion (AUC =0.510).

CONCLUSIONS

The technique used in this study enabled an in-depth evaluation of the Harbinger Score and the Glasgow-Blatchford Score in their ability to predict the need for early endoscopic intervention in patients with upper gastrointestinal bleeding (UGIB). Harbinger score showed better sensitivity than GBS for predicting the need for early endoscopic intervention.

Authors Contribution

Conceptualization: MMUH
Methodology: BR, MMUH, RKW
Formal analysis: BR
Writing-review and editing: BR, RKW

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Kurien M and Lobo AJ. Acute upper gastrointestinal bleeding. Clinical Medicine. 2015 Oct; 15(5): 481-5. doi: 10.7861/clinmedicine.15-5-481.

[2] Yaka E, Yılmaz S, Özgür Doğan N, Pekdemir M. comparison of the glasgow-blatchford and aims 65 scoring systems for risk stratification in upper gastrointestinal bleeding in the emergency department. Academic Emergency Medicine. 2015 Jan; 22(1): 22-30. doi: 10.1111/acem.12554.

[3] Custovic N, Husic-Selimovic A, Srsen N, Prohic D. Comparison of Glasgow-Blatchford Score and Rockall Score in Patients with Upper Gastrointestinal Bleeding. Medical Archives. 2020 Aug; 74(4): 270-4. doi: 10.5455/medarh.2020.74.270-274.

[4] Cremers I and Ribeiro S. Management of variceal and nonvariceal upper gastrointestinal bleeding in patients with cirrhosis. Therapeutic Advances in Gastroenterology. 2014 Sep; 7(5): 206-16. doi: 10.1177/1756283X14538688.

[5] Jung K and Moon W. Role of endoscopy in acute gastrointestinal bleeding in real clinical practice: An evidence-based review. World Journal of Gastrointestinal Endoscopy. 2019 Feb; 11(2): 68. doi: 10.4253/wjge.v11.i2.68.

[6] Schembre DB, Ely RE, Connolly JM, Padhya KT, Sharda R, Brandabur JJ. Semiautomated Glasgow-Blatchford Bleeding Score helps direct bed placement for patients with upper gastrointestinal bleeding. BMJ Open Gastroenterology. 2020 Nov; 7(1): e000479. doi: 10.1136/bmjgast-2020-000479.

[7] Mokhtare M, Bozorgi V, Agah S, Nikkhah M, Faghihi A, Boghratian A, et al. Comparison of Glasgow-Blatchford score and full Rockall score systems to predict clinical outcomes in patients with upper gastrointestinal bleeding. Clinical and Experimental Gastroenterology. 2016 Oct; 9: 337-43. doi: 10.2147/CEG.S114860.

[8] Gayet-Ageron A, Prieto-Merino D, Ker K, Shakur H, Ageron FX, Roberts I, et al. Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40-138 bleeding patients. Lancet. 2018 Jan; 391(10116): 125-32. doi: 10.1016/S0140-6736(17)32455-8.

[9] Frith D, Goslings JC, Gaarder C, Maegele M, Cohen MJ, Allard S, et al. Definition and drivers of acute traumatic coagulopathy: clinical and experimental investigations. Journal of Thrombosis and Haemostasis. 2010 Sep; 8(9): 1919-25. doi: 10.1111/j.1538-7836.2010.03945.x.

[10] Benedeto-Stojanov D, Bjelaković M, Stojanov D, Aleksovski B. Prediction of in-hospital mortality after acute upper gastrointestinal bleeding: cross-validation of several risk scoring systems. Journal of International Medical Research. 2022 Mar; 50(3): 03000605221086442. doi: 10.1177/03000605221086442.

[11] Seo DW, Yi H, Park B, Kim YJ, Jung DH, Woo I, et al. Prediction of Adverse Events in Stable Non-Variceal Gastrointestinal Bleeding Using Machine Learning. Journal of Clinical Medicine. 2020 Aug; 9(8): 2603. doi: 10.3390/jcm9082603.

[12] Horibe M, Iwasaki E, Bazerbachi F, Kaneko T, Matsuzaki J, Minami K, et al. Horibe GI bleeding prediction score: a simple score for triage decision-making in patients with suspected upper GI bleeding. Gastrointestinal Endoscopy. 2020 Sep; 92(3): 578-88.e4. doi: 10.1016/j.gie.2020.03.3846.

[13] Dhir V and Shah R. Scoring systems for upper gastrointestinal bleeding: Which one scores better? Indian Journal of Gastroenterology. 2019 Apr; 38: 95-7. doi: 10.1007/s12664-019-00945-8.

[14] Cheng DW, Lu YW, Teller T, Sekhon HK, Wu BU. A

DOI: https://doi.org/10.54393/pjhs.v4i11.1165

modified Glasgow Blatchford Score improves risk stratification in upper gastrointestinal bleed: a prospective comparison of scoring systems. Alimentary Pharmacology & Therapeutics. 2012 Oct; 36(8): 782-9. doi: 10.1111/apt.12029.

[15] Sasaki Y, Abe T, Kawamura N, Keitoku T, Shibata I, Ohno S, et al. Prediction of the need for emergency endoscopic treatment for upper gastrointestinal bleeding and new score model: A retrospective study. BMC Gastroenterology. 2022 Dec; 22: 337. doi: 10.1186/s12876-022-02413-8.

[16] Taşlidere B, Biberci Keskin E, Özdemir S, Atsiz A, Sönmez E. Comparison of Glasgow Blatchford and New Risk Scores to Predict Outcomes in Patients with Acute Upper GI Bleeding. Bezmialem Science. 2023 Jan; 11(1): 100-7. doi: 10.14235/bas.galenos.2022.80299.

[17] Cazacu SM, Alexandru DO, Statie RC, Iordache S, Ungureanu BS, Iovănescu VF, et al. The Accuracy of Pre-Endoscopic Scores for Mortality Prediction in Patients with Upper GI Bleeding and No Endoscopy Performed. Diagnostics (Basel). 2023 Mar; 13(6): 1188. doi: 10.3390/diagnostics13061188.

[18] Tang Y, Shen J, Zhang F, Zhou X, Tang Z, You T. Scoring systems used to predict mortality in patients with acute upper gastrointestinal bleeding in the ED. The American Journal of Emergency Medicine. 2018 Jan; 36(1): 27-32. doi: 10.1016/j.ajem.2017.06.053.

[19] Ko IG, Kim SE, Chang BS, Kwak MS, Yoon JY, Cha JM, et al. Evaluation of scoring systems without endoscopic findings for predicting outcomes in patients with upper gastrointestinal bleeding. BMC Gastroenterology. 2017 Dec; 17: 1-8. doi: 10.1186/s12876-017-0716-4.

[20] Cúrdia Gonçalves T, Barbosa M, Xavier S, Boal Carvalho P, Firmino Machado J, Magalhães J, et al. Optimizing the risk assessment in upper gastrointestinal bleeding: comparison of 5 scores predicting 7 outcomes. GE-Portuguese Journal of Gastroenterology. 2018 May; 25(6): 299-307. doi: 10.1159/000486802.

DOI: https://doi.org/10.54393/pjhs.v4i11.1168

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Comparative Efficacy of Topical Tacrolimus 0.1% and Clobetasol Propionate 0.05% in the Treatment of Alopecia Areata (AA)

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ARTICLE INFO

Key Words:

Alopecia Areata, Clobetasol Propionate, Tacrolimus

How to Cite:

Sajjad, D., Muzaffar, B., Siddiqui, M. A., Hussain, M., Aslam, S., & Farid, H. (2023). Comparative Efficacy of Topical Tacrolimus 0.1% and Clobetasol Propionate 0.05% in the Treatment of Alopecia Areata (AA) : Efficacy of Tacrolimus and Clobetasol Propionate in the Treatment of Alopecia Areata . Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1168

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Received Date: 6th November, 2023
Acceptance Date: 26th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Alopecia areata patients can choose from a variety of therapy methods. Each method has advantages and limitations, and its suitability varies for each patient. The medical usefulness of topical corticosteroids in AA is yet debatable. **Objective:** To assess the effectiveness of topical tacrolimus 0.1% vs. topical clobetasol propionate 0.05% while treating alopecia areata. **Methods:** Randomized-controlled trial (Double blind) conducted in Dermatology Department, CMH-Abbottabad, from November 2022 to April 2023. The seventy (70) patients with alopecia areata who attended to OPD of CMH Abbottabad between the ages of 20 and 50 were included. The non-probability consecutive sampling method was used. For up to 3 months, patients in Group A used clobetasol propionate 0.05% twice daily, while patients in Group B used topical tacrolimus 0.1% twice daily. Patients were evaluated at the start of each session, four weeks later, eight weeks later, and twelve weeks later. The SALT score was used to estimate hair loss at presentation and during the 3-month follow-up. The degree of response has been characterized by following hair re-growth as excellent (>75%), marked (51-75%), moderate (26-50%), or mild (25%). A p-value of <0.05 was considered significant. **Results:** When the efficacy was compared, 26 (74.3%) patients in group-A (mean age 35.23+7.87 years) shown excellent response, while 14 (40%) patients in group-B (mean age 34.29+7.87 years) with significant p-value was 0.028. **Conclusions:** Clobetasol propionate 0.05% was more efficacious as a therapy choice for stimulating hair re-growth in patients.

INTRODUCTION

An autoimmune disorder called alopecia areata (AA) causes non-scarring hair loss in areas [1]. It also has impact on psychological well-being and daily life [2]. The majority of patients describe a sudden start of one or more well-defined, one to four cm circular regions of scalp hair loss. The presence of broken "exclamation-mark" hairs and short hairs that taper proximally is a typical trait [3]. Some Alopecia areata patients also have nail pitting [4]. The condition can affect any hair-bearing region, although the scalp, brows, eyelashes, and beard are the most usually affected. Hair loss can be spotty or widespread [5]. The severity of alopecia areata is classified into four categories by the National Alopecia Areata Foundation Guidelines Committee: none (S0), 1 to 24 percent (S1), 25 to 49 percent (S2), 50 to 74 percent (S3), 75 to 99 percent (S4), and 100%. The SALT SCORE is a global severity score that considers hair percentage. The scalp is split into four regions based on its surface area. The top of the scalp provides 40%, the posterior of the scalp 24%, the right side of the scalp 18%, and the left side of the scalp 18% [6]. Although the cause of Alopecia areata is uncertain, most evidence suggests that the illness is immunologically mediated [7]. AA is a frequent yet difficult problem to treat in dermatology [8]. Intralesional corticosteroid treatment is being investigated for limited scalp AA and specialists recommend it as the medicine of choice. Corticosteroids applied topically has been shown to be beneficial for moderate-to-severe AA. Folliculitis is a frequent

DOI: https://doi.org/10.54393/pjhs.v4i11.1168

complication of topical corticosteroids. Telangiectasia and atrophy are uncommon. However, the primary downsides of these techniques are their limited effectiveness, local and systemic adverse effects, particularly in long-term therapy [9]. Tacrolimus might be an effective therapeutic option of management of inflammatory dermatological diseases, including alopecia areata [10]. Alopecia areata patients can choose from a variety of therapy methods. Each method has advantages and limitations, and its suitability varies for each patient. The medical usefulness of topical corticosteroids in AA is yet debatable. This literature on this topic is limited that is why this study is conducted with objective of to compare clobetasol with tacrolimus while treating AA. This study will also help to assess relative effectiveness of clobetasol and tacrolimus in treatment of alopecia areata.

METHODS

A RCT study was conducted in dermatology dept of the CMH, Abbottabad from November 2022 to April 2023 after Ethical Review Board approval dated 01-Nov-2022 (Reg#CMHAtd-ETH-56-Derma-22) and RCT (Reg#ClinicalTrials.gov Identifier NCT05885269). The seventy (70) patients who were 20-50 years of age diagnosed as alopecia areata on clinical grounds, confirmed by consultant dermatologist and further examination of plucked hair was done under a microscope. An inform consent was taken. The method of non-probability consecutive sampling was applied. The sample size was estimated using WHO sample size calculator by taking a 95% confidence interval, an 80% power of study, and an expected cure rate of 44.82% for Tacrolimus and 79.31% for Clobetasol propionate. The calculated sample size was 62, with 31 in each group, however a sample size of 70 (35 in each group) was used to boost the study's validity [11]. The study included patients aged between 20-50 years, both gender, who attended the dermatology out-patient department of CMH Abbottabad, had an ailment lasting less than 2 months, and had never had any treatment before. On the other hand, Patients with history of more than 2 months alopecia areata, atypical AA (e.g., Alopecia universalis), a history of hypersensitivity to drugs such as topical corticosteroids and tacrolimus, patients on systemic immune-suppression, and females who are pregnant or on lactation were excluded. Patients' randomization was done by lottery method. Those in Group-A treated clobetasol propionate 0.05% twice a day, whereas those in Group-B treated topical tacrolimus 0.1% two times a day for up to 3 months. A thorough medical history and physical examination, together with an inspection of all hair-bearing regions and nails, were performed at the patient's initial appointment. Patients were given full information on the disease as well as the lapsing nature of AA. The information is also provided on prognosis, and risk/benefit ratio options, in an Urdu or local language, an informed written consent was also obtained. Face-to-face interviews were used to collect data. The effectiveness of therapy was assessed using photos of patients before and after the trial, as well as clinical examination of patients. The clinical response was assessed four weeks, eight weeks, and twelve weeks following the conclusion of therapy. The clinical comparisons were made at every follow-up appointment and at the end of the treatment clinically by me and by consultant dermatologist. All patients' findings were assessed at 4th, 8th, and 12th week duration of following therapy completion. The hair re-growth score was determined using the SALT score at presentation and the SALT score (0 to 4) during the 3-month follow-up as follows: 0 (10% re-growth), 1 (11-25% re-growth), 2 (26-50%), 3 (51-75%), and 4 (>75% re-growth). The response was categorized on examining hair re-growth which was labelled excellent upon (>75%), Marked (51% to 75%), moderate (26% to 50%), or slight (≤ 25%). The statistical program for social sciences (SPSS) version 23.0 was used for analysis. Mean ± SD was determined for continuous data, while frequency percentages were calculated for categorical variables. To evaluate statistical significance for treatment efficacy evaluation, the chi-square test was utilized, with a p-value of 0.05 considered significant.

RESULTS

In group-A mean age was 35.23±7.87 years, and in group-B mean age was 34.29±7.87 years. The two groups were well-evaluated in terms of pre-treatment clinical parameters there was significant relations between gender (p=0.034) and number of lesions (p=0.015) in group-A and Group-B. The majority 46(65.7%) patients were greater than 31 years of age, hence 50(71.4%) were males between both groups of Alopecia areata. The 42(60%) patients of single lesions were effectively treated by both the treatment groups (Table 1).

Table 1: Clinical Parameters of both treatment Groups (n=70)

Variables		Categories	Group-A N (%)	Group-B N (%)	Total N (%)	p-value
Age (years)	20-30	Early Adulthood	11 (31.4%)	13 (37.1%)	24 (34.3%)	0.615
	31-50	Middle Adulthood	24 (68.6%)	22 (62.9%)	46 (65.7%)	
Gender		Mean ± SD	35.23±7.87	34.29±7.87	-	
		Male	21(60%)	29(82.9%)	50(71.4%)	0.034
		Female	14(40%)	6(17.1%)	20(28.6%)	
Number Of Lesions		Single	16(45.7%)	26(74.3%)	42(60%)	0.015
		Multiple	19(54.3%)	09(25.7%)	28(40%)	

In Table 2, while comparing the efficacy, in group-A

DOI: https://doi.org/10.54393/pjhs.v4i11.1168

26(74.3%) patients showed excellent response as compared to 14(40%) patients in group-B ($p<0.05$). whereas remaining patients of Group A showed 5 (14.3%) marked, 3(8.6%) moderate, 1(2.8%) slight dose response. The rest of group B showed marked, moderate and slight response to the dose as 15(42.9%), 4(11.4%) 2(5.7%) respectively. There is significant relationship between both the treatment group which showed that clobetasol propionate of group A had significant difference than the group B topical Tacrolimus 0.01% ($p=0.028$).

Table 2: Treatment efficacy between both Groups at end of treatment(n=70)

Variables		Group A vs. Group B		p-value
		Group A	Group B	
Grades of response	Excellent (>75% re-growth)	26(74.3%)	14(40%)	0.028
	Marked (51-75% re-growth)	5 (14.3%)	15(42.9%)	
	Moderate (26-50% re-growth)	3(8.6%)	4(11.4%)	
	Slight (≤25% re-growth)	1(2.8%)	2(5.7%)	
Total		35(100%)	35(100%)	

DISCUSSION

In our study, topical clobetasol propionate 0.05% was used to treat 35 patients in group-A while topical tacrolimus 0.1% was used to treat 35 patients in group-B. In terms of age distribution, both groups included a majority of people who were 31 to 50 years of age. The duration of sickness was essentially comparable across the two groups as majority of the patients had less than 2 months of illness duration. The study showed that topical clobetasol propionate 0.05% had 74.3% excellent response as compared to the topical tacrolimus 0.1% i.e., 40% which is similar to the study conducted in 2022 by Ullah et al., [11]. Sotiriou et al., studied the effect of topical tacrolimus 0.1% as 45% for active patchy alopecia areata which is quite close to our 40% excellent response in adult patients [12]. Thus, another study by Rokhsar et al., find out 70% topical efficacy of clobetasol propionate while treating alopecia areata but in this study we find out 74% efficacy which is better than the study conducted by Rokhsar et al., [13]. In this study only 4 (11.43%) patients treated with clobetasol propionate Vs. 6(17.14%) patients treated with Tacrolimus 0.1% reported less than 50% improvement during this trial, opposed to 79.4% patients treated with clobetasol and 76.5% patients in the study of Hossain et al., [14, 15]. The determinants of the study were age, gender and number of lesions. There was insignificant difference for age [16] between both groups except gender, number of lesions which showed significant difference which is similar to the study conducted by You et al., [17]. On the contrary, in a meta-analysis suggests that AA is also associated with systemic and psychiatric diseases also. Therefore, Physicians are highly encouraged to assess and manage co-morbidities to get better outcomes [18, 19]. Chanprapaph et al., studied that gender male was the risk factor of alopecia areata which is similar to our study in which most of the patients were male and statistically significant difference was seen as p-value 0.034 [20], but in some studies reported that both genders are equally diagnosed with AA. In group-A 28(40%) patients suffered multiple number of lesions as compared to group-A 09(25.7%) patients. Despite large number of patients suffering multiple lesions in group-A, Clobetasol propionate's efficacy is markedly more than the topical tacrolimus to treat multiple lesions effectively. This comparative efficacy advantage of using clobetasol is more support use of in clinical practice in severe AA. Thereby this study was conducted to compare the efficacy of both groups in order to better treat alopecia (AA) patients and provide informed treatment by following evidence-based practice.

CONCLUSIONS

Topical clobetasol propionate 0.05% was more efficacious as a therapy choice for stimulating hair re-growth among patients of alopecia areata. It also treats multiple lesions effectively as compared to tacrolimus. The treatment is compliant to all patients.

Authors Contribution

Conceptualization: DS, BM
Methodology: SA, HF
Formal analysis: DS, MAS, MH
Writing-review and editing: DS, SA, HF

All authors have read and agreed to the published version of the manuscript.

Acknowledgement

This study was supported by Nutrition Division of NIH and we are thankful to Chief Nutrition Division of NIH and Executive Director of NIH.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Gharib K and Elsayed A. Serum level of interleukin-17A in patients with alopecia areata and its relationship to age of patients and disease recurrence. Egyptian Journal of Dermatology and Venerology. 2021 Jul; 41(2): 83. doi: 10.4103/ejdv.ejdv_24_20.

[2] Rehman S and Jameel R. Appearance anxiety and loneliness: the mediating role of rejection sensitivity in patients with alopecia areata in Lahore Pakistan.

DOI: https://doi.org/10.54393/pjhs.v4i11.1168

JPMA. The Journal of the Pakistan Medical Association. 2023 Apr; 73(4): 800-3. doi: 10.47391/JPMA.6302.

[3] Malakar S, Banerjee U, Mehta P, Mukherjee S, Sardar S, Malakar S, et al. Trichoscopy. Atlas of Dermatology, Dermatopathology and Venereology: Cutaneous Anatomy, Biology and Inherited Disorders and General Dermatologic Concepts. 2021 Oct: 295-322. doi: 10.1007/978-3-319-53811-2_93.

[4] Al-Hamamy HR and Al-Ani GN. Nail Changes in Alopecia Areata and Their Correlation with Disease Severity. Iraqi Postgraduate Medical Journal. 2021; 20(2): 128-35.

[5] Zhou C, Li X, Wang C, Zhang J. Alopecia areata: an update on etiopathogenesis, diagnosis, and management. Clinical Reviews in Allergy & Immunology. 2021 Dec; 61(3): 403-423. doi: 10.1007/s12016-021-08883-0.

[6] Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al. Alopecia areata investigational assessment guidelines-Part II. Journal of the American Academy of Dermatology. 2004 Sep; 51(3): 440-7. doi: 10.1016/j.jaad.2003.09.032.

[7] Simakou T, Butcher JP, Reid S, Henriquez FL. Alopecia areata: A multifactorial autoimmune condition. Journal of Autoimmunity. 2019 Mar; 98: 74-85. doi: 10.1016/j.jaut.2018.12.001.

[8] Fukuyama M, Ito T, Ohyama M. Alopecia areata: Current understanding of the pathophysiology and update on therapeutic approaches, featuring the Japanese Dermatological Association guidelines. The Journal of Dermatology. 2022 Jan; 49(1): 19-36. doi: 10.1111/1346-8138.16207.

[9] Meah N, Wall D, York K, Bhoyrul B, Bokhari L, Sigall DA, et al. The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata. Journal of the American Academy of Dermatology. 2020 Jul; 83(1): 123-30. doi: 10.1016/j.jaad.2020.03.004.

[10] Umar BU, Rahman S, Dutta S, Islam T, Nusrat N, Chowdhury K, et al. Management of Atopic Dermatitis: The Role of Tacrolimus. Cureus. 2022 Aug; 14(8): e28130. doi: 10.7759/cureus.28130.

[11] Ullah F, Dawood M, Noor N, Hameed S. Efficacy of Topical Clobetasol Propionate 0.05% Ointment and Topical Tacrolimus 0.1% Ointment in Treatment of Alopecia Areata.: RCT. Pakistan Journal of Medical & Health Sciences. 2022 Jun; 16(06): 133. doi: 10.53350/pjmhs22166133.

[12] Sotiriou E, Patsatsi A, Fotiadou C, Sotiriadis D, Panagiotidou D. Tacrolimus ointment 0.1% in the treatment of active patchy alopecia areata of childhood. European Journal of Pediatric Dermatology. 2007 Dec; 17(4): 227-30.

[13] Rokhsar CK, Shupack JL, Vafai JJ, Washenik K. Efficacy of topical sensitizers in the treatment of alopecia areata. Journal of the American Academy of Dermatology. 1998 Nov; 39(5): 751-61. doi: 10.1016/S0190-9622(98)70048-9.

[14] Hossain MS, Miah MT, Khan MZ, Khondker L, Hasan MR. Efficacy of topical tacrolimus 0.1% and clobetasol propionate 0.05% in the treatment of alopecia areata. Journal of Pakistan Association of Dermatologists. 2015; 25(3): 197-201.

[15] Shakhawat H, Titu M, Zulfiqur Hossain K, Lubna K, Rashidul H. Efficacy of topical tacrolimus 0.1% and clobetasol propionate 0.05% in the treatment of alopecia areata. Journal of Pakistan Association of Dermatologists. 2016 Nov; 25(3): 197-201.

[16] Alshahrani AA, Al-Tuwaijri R, Abuoliat ZA, Alyabsi M, AlJasser MI, Alkhodair R. Prevalence and clinical characteristics of alopecia areata at a tertiary care center in Saudi Arabia. Dermatology Research and Practice. 2020 Mar; 2020: 7194270. doi: 10.1155/2020/7194270.

[17] You HR and Kim SJ. Factors associated with severity of alopecia areata. Annals of Dermatology. 2017 Oct; 29(5): 565-70. doi: 10.5021/ad.2017.29.5.565. .

[18] Lee S, Lee H, Lee CH, Lee WS. Comorbidities in alopecia areata: a systematic review and meta-analysis. Journal of the American Academy of Dermatology. 2019 Feb; 80(2): 466-77. doi: 10.1016/j.jaad.2018.07.013.

[19] Mian M, Silfvast-Kaiser A, Paek S, Kivelevitch D, Menter A. A review of the most common dermatologic conditions and their debilitating psychosocial impacts. International Archives of Internal Medicine. 2019 Jul; 3: 18. doi: 10.23937/2643-4466/1710018.

[20] Chanprapaph K, Mahasaksiri T, Kositkuljorn C, Leerunyakul K, Suchonwanit P. Prevalence and risk factors associated with the occurrence of autoimmune diseases in patients with alopecia areata. Journal of Inflammation Research. 2021 Sep; 14: 4881. doi: 10.2147/JIR.S331579.

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Common Complications of Mini PCNL in Renal Stones more than 3.0cm

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ARTICLE INFO

Key Words:
Mini Percutaneous Nephrolithotomy (mPCNL), Renal Stones, Complications

How to Cite:
Farooq, K., Ahmed, A., Hameed, H., Zahoor, I., Hameed, N., & Khan, I. A. (2023). Common Complications of Mini PCNL in Renal Stones more than 3.0 cm: Complications of Mini PCNL in Renal Stones. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1171

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Received Date: 7th November, 2023
Acceptance Date: 27th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Mini PCNL (mPCNL) procedures now often employ miniature nephroscopes that were originally created to treat paediatric kidney stones. There is scarcity of knowledge regarding complications of mPCNL in renal stones larger than 3 cm. **Objective:** To determine the common complications of mini PCNL performed for renal stones larger than 3.0cm. **Methods:** This descriptive case series study was conducted over a period of one year from November 2022 to October 2023 registered patients aging 4 to 14 years undergoing mPCNL with renal stones >3cm. The patients underwent mini PCNL and patients were followed over a period of 4 weeks for early (occurring within 48 hours of procedure) and late complications (occurring after 48 hours). **Results:** A total of 86 cases were analyzed. The age of the participants ranged from 4 years to 14 years. The mean age of the patients was 9.19±2.49 years. Majority of the participants were in the age group 10-14 years 57 (66.3%). Male to female ratio was 1.2: 1. Among the early complications, the most commonly reported was post-pain reported by 24 (28.0%) patients, followed by hematuria in 15(17.4%). Surgical site infection was the most common late complications observed in 9 patients (10.4%) followed by re-do surgery for 2 patients (2.3%) and none of the patient suffered renal dysfunction among our participants. **Conclusions:** MPCNL can be offered as a safe and secure surgical option with excellent results and manageable side effects for treating nephrolithiasis larger than 3cm in children.

INTRODUCTION

The phrase "mini-perc" is often used in scientific publications to refer to a procedure that involves the use of an access sheath with a size ranging from 11 to 20 Fr [1]. The treatment is conducted via an 11 French peel-away vascular access kit. A small needle for access is placed into the target calyx, and afterwards a wire to guide it is inserted. The covering and trocar are advanced along the guidewire under fluoroscopic supervision. After the trocar is removed, the sheath is carefully peeled down in order to get the desired working length [2]. The essential instruments required for mini-percutaneous nephrolithotomy (mini-PCNL) consist of a 7.0 French rigid paediatriccystoscope and a 9.5 French flexible ureterorenoscope. In the context of stone disintegration, two viable options are the use of a holmium laser or a lithoclast. Fragments may be eliminated by the use of irrigation and suction techniques, or alternatively, by using a grabbing device [3]. In a recent research including a cohort of 1368 patients, it was shown that mini-percutaneous nephrolithotomy (mini-PCNL) yielded a substantial stone-free rate (SFR) of 82% when using a 16 French (Fr) tract [4]. In contrast to standard percutaneous nephrolithotomy (PCNL), there was a lower incidence of serious bleeding problems (1.4%) [5]. In comparison to retrograde intrarenal surgery (RIRS), mini-percutaneous nephrolithotomy (mini-PCNL) demonstrated a statistically significant improvement in stone-free rate (SFR) and overall procedural efficiency [6]. Can mini-percutaneous nephrolithotomy (mini-PCNL), a

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

less invasive procedure, be considered as a viable substitute for standard percutaneous nephrolithotomy (PCNL) in managing renal stones larger than 3 cm in diameter, given that extracorporeal shock wave lithotripsy (ESWL) and retrograde intrarenal surgery (RIRS) seem to have lower efficacy rates compared to PCNL in this context [7, 8]. Researchers have conducted comprehensive comparisons between percutaneous nephrolithotripsy and different tract sizes [9]. Nevertheless, the quality of the evidence provided was below standard, hence requiring the acquisition of further reliable data derived from randomised controlled trial (RCT) studies [10]. Furthermore, a comparative meta-analysis was not conducted on persons with substantial kidney stone burdens to assess the differences between conventional percutaneous nephrolithotomy (PCNL) and mini-PCNL [11]. Hence, the primary focus of this research was to compare surgical procedures used for the treatment of renal stones above 3 cm in size and the study assessed the safety profile of mini PCNL for kidney stones measuring over 3 cm. Additionally, subgroup analyses were conducted to provide more realistic recommendations for clinical practitioners.

METHODS

The descriptive case series study was carried out at Medical teaching hospital lady reading hospital Peshawar, from November 2022 till October 2023. The study population consisted of 94 individuals diagnosed with renal stones measuring over 3cm. The study included individuals who were aging 4 to 14 years, had normal renal function, had kidney stones larger than 30 mm, and had a documented history of past extracorporeal shock wave lithotripsy (ESWL) treatment failure. Patients with unresolved bleeding diathesis, an active urinary tract infection (UTI), those who had previously had transplant or urinary diversion procedures, and those with congenital anomalies were excluded. Patients were recruited using consecutive (non-probability) sampling technique. Sample size was estimated using WHO sample size calculator. Permission for the conduct of the study was taken vide no. 218/LRH/MTI, dated: 31/10/2022. Comprehensive demographic information of the recruited participants, such as age, sex, body mass index (BMI), and concurrent medical conditions, was collected subsequent to obtaining informed written permission. The preparatory assessment before surgery often involved several diagnostic procedures, including as ultrasonography, plain abdomen and pelvic X-ray (known as KUB), and excretory urography. These tests are primarily used to identify lucent stones and may also include a low-dose non-contrast CT scan with reconstruction confined to the kidneys. Additionally, blood cell counts, assessment of renal function by the measurement of blood urea nitrogen and creatinine levels, as well as urine analysis and culture, were conducted. Patients with positive cultures were given adequate antibiotics and admitted with sterile urine prior to the surgical procedure. All patients were hospitalized six hours before to the surgical procedure and were given parenteral hydration along with a single dose of prophylactic antibiotic. The treatment was performed with general anaesthesia. In the lithotomy or supine position with abducted thigh, a ureteral catheter of either 3 Fr or 4 Fr was introduced into the kidney and secured. Subsequently, the patient underwent a transition to the prone position. Following the appropriate application of padding, the patient's body was finally draped. Subsequently, a contrast solution was administered through a ureteral catheter, and the pelvicalyceal system was visualized. An 18-gauge Chiba needle was used to perform an insertion into the desired calyx. Subsequently, a 0.035 guide wire was introduced through the needle. The procedure of tract dilation was executed via telescopic dilatation devices with a maximum diameter of 18 French. The procedure of nephroscopy was conducted. The lithotripsy procedure was performed using a pneumatic lithoclast, and subsequent removal of the lithotripsy particles was accomplished via forceps. The absence of stones was assessed postoperatively using fluoroscopy and ultrasonography. The outcomes of the study were in terms of early and late complications which were measured as: 1) Early Complications: Complications occurring within 48 hours following the procedure were called early complications. Early complications included hematuria, pain and urosepsis/DIC. 2) Late Complications: Complications occurring between day 3 and 28 following the procedure were called late complications. Late complications included surgical site infection, renal dysfunction and re-do procedure. Means and standard deviation were used to describe continuous variables. Frequencies and percentages were used to illustrate categorical data. The student t test was used to compare the means of continuous variables when the data were normally distributed. The chi-square test and contingency tables were used to compare the categorical data. IBM SPSS version 24.0 was used for all statistical analyses.

RESULTS

A total of 94 patients were enrolled during the study period. 08 patients were lost to follow up. Hence the final sample size comprised of 86 participants. Analysis of 86 patients is presented. As illustrated in Table 1, post-op pain was reported by 24 patients (28.0%) rendering it as the most the common complication, followed by hematuria in 15 patients (17.4%) while urosepsis/DIC was recorded in 04 participants (4.6%). The most common late complication

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

was surgical site infection in 09 participants (10.5%) followed by re-do procedure in 2 patients (2.3%). None of the patients included in our study suffered renal dysfunction as presented in Table 1.

Table 1: Frequencies and percentages of common complications (n = 86)

Complications	Types	Frequencies (%)
Early	Post op pain	24 (28.0)
	Hematuria	15 (17.4)
	Urosepsis/DIC	04 (4.6)
Late	Surgical site infection	09 (10.5)
	Re-do procedure	02 (2.3)
	Renal dysfunction	00 (0.0)

The mean age of the patients was 9.19 years with standard deviation of 2.49. Most of the participants were in the age group 10 to 14 years, comprising of 57 (66.3%) patients. The rest of 29 participants (33.7%) had age in the range of 4 to 9 years as shown in Table 2. In the age group 4-9 years (29 patients), the frequencies and percentages of early complications recorded were, post-op pain (07, 24.1%), hematuria (04, 13.8%) and urosepsis in one patient (3.4%). Regarding the late complications, surgical site infection was recorded in 2 patients (6.9%). None of the patient experienced re-do procedure and renal dysfunction in this age group. Among the 57 participants of the age group 10 to 14 years, post-op pain was the most common recorded for 17 participants (29.8%), hematuria in 11 participants (19.3%) and 03 patients experienced urosepsis (5.3%). The observations about late complications were surgical site infection (07, 12.3%) and re-do procedure among two participants (3.5%) as illustrated in Table 2.

Table 2: Subgroup analysis of common complications with age

Age groups (years)	Early Complications	Frequency (%)	Late complications	Frequency (%)
4 – 9 (n = 29)	Post-op pain	07 (24.1%)	Surgical site infection	02 (6.9%)
	Hematuria	04 (13.8%)	Renal dysfunction	0 (0.0%)
	Urosepsis	01 (3.4%)	Re-do procedure	0 (0.0%)
10–14 (n = 57)	Post-op pain	17 (29.8%)	Surgical site infection	07 (12.3%)
	Hematuria	11 (19.3%)	Re-do procedure	02 (3.5%)
	Urosepsis	03 (5.3%)	Renal dysfunction	0 (0.0%)

As shown in Table 3, the number of male participants in the study was 48 (55.8%). The male to female ratio was 1.2: 1. The distribution of early and late complications among the male participants were post-op pain (12, 25.0%), hematuria (09, 18.8%), urosepsis/DIC (2, 4.2%), surgical site infection (04, 8.3%) and re-do procedure was performed in one patient (1, 2.0%). The frequencies and percentages of early and late complications among female participants were post-op pain (12, 31.6%), hematuria (06, 15.8%), urosepsis (2, 5.3%), surgical site infection (5, 13.1%) and re-do procedure was performed in 02 patients (5.3%).

Table 3: Subgroup analysis of common complications with gender

Gender	Early Complications	Frequency (%)	Late complications	Frequency (%)
male (n = 48)	Post-op pain	12 (25.0%)	Surgical site infection	04 (8.3%)
	Hematuria	09 (18.8%)	Renal dysfunction	01 (2.0%)
	Urosepsis	02 (4.2%)	Re-do procedure	0 (0.0%)
Female (n = 37)	Post-op pain	12 (31.6%)	Surgical site infection	05 (13.1%)
	Hematuria	06 (15.8%)	Re-do procedure	02 (5.3%)
	Urosepsis	02 (5.3%)	Renal dysfunction	0 (0.0%)

The mean stone size of the patients was 3.97 cm with standard deviation of 0.59. 51 patients (59.3%) had stone size less than 4.5cm and the remaining 35 patients (40.7%) had stone size above 4.5cm. Complication rate increased as stone size increased. Patients with stone size more than 4.5cm had 13 patients (37.1%) who experienced more post-op pain, followed by hematuria (9, 25.7%), DIC/sepsis (2, 5.7%), surgical site infection in 06 (17.1%), and 1 patient underwent re-do procedure (2.8%). Out of the total 51 participants with stone size less than 4.5 cm, 11 patient experienced excessive post-op pain (21.6%), hematuria in 06 patients (11.7%), sepsis in 02 patients (3.9%). Late complications included surgical site infection 03 patients (5.9%) while one patient had re-do procedure (1.9%) (Table 4). The number of patients with right kidney stone was 45 (52.3%). Rest of the patients 41 (47.7%) had left kidney stone. The frequencies and percentages of complications in right kidney procedures were post op pain 13 (28.9%), hematuria 8 (17.8%), urosepsis 2 (4.4%), surgical site infection 5 (11.1%) and one patient had re-do procedure (2.2%). Other the other hand, the rate of complications in left kidney were 11 (26.8%), hematuria 07 (17.0%), sepsis 2 (4.9%), surgical site infection 04 (9.7%) and re-do procedure in one patient (2.4%).

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

Table 4: Subgroup analysis of common complications with stone size

Stone size (cm)	Early Complications	Frequency (%)	Late complications	Frequency (%)
≥4.5cm (n = 51)	Post-op pain	13 (37.1%)	Surgical site infection	06 (17.1%)
	Hematuria	09 (25.7%)	Renal dysfunction	1 (2.8%)
	Urosepsis	02 (5.7%)	Re-do procedure	0 (0.0%)
<4.5cm (n = 35)	Post-op pain	11 (21.6%)	Surgical site infection	03 (5.9%)
	Hematuria	06 (11.7%)	Re-do procedure	01 (1.9%)
	Urosepsis	02 (3.9%)	Renal dysfunction	0 (0.0%)

DISCUCSSION

This research shows that the mPCNL technique had a significant complication risk in kids aged 4 to 14 with renal stones larger than 3 centimeters in size. Rather of relying on open surgery as adults do even for nephrectomy, clinicians are increasingly turning to less invasive techniques like ESWL and PCNL, which have developed to ultra-minimally invasive and laparoscopy [12]. Renal stone therapy with PCNL has evolved and improved since it was first used in 1976 [13]. Radiation exposure for the surgeon and the patient has been reduced by switching from pure fluoroscopic to mixed fluoroscopic/ultrasound and pure ultrasound guided for renal access [14]. Bleeding, infection, leaking into the urinary system, issues in the chest, injuries to surrounding viscera, and postoperative discomfort are all possible after PCNL [15]. mPCNL has been shown to be as effective as conventional PCNL with fewer side effects [16]. The SFR results from these two methods are quite similar. Less blood loss, transfusions, and overnight stays are required in mPCNL. mPCNL has a significantly longer running time. There are less cases of infection, fever, postoperative discomfort, renal damage, and other organ damage with mPCNL [17]. Twenty-three children underwent mPCNL by Wah et al., with median stone load of more than 3cm. Their initial SFR was 83.6%, and after treating the leftover pieces, it grew to 90.5%. Hydrothorax ensued in one patient after surgery, while two more had UTIs [18]. Compared to previous research, our early SFR was about 90% and our overall SFR was 95.3%, with just 5.3% of the original stone still present. Farouk et al., conducted a prospective trial comparing mPCNL with ESWL in children with a renal stone size of 1 to 2 cm. After the first surgical session, those who received mPCNL had an SFR of 88.9%, and after a second look at the procedure, they had an SFR of 92.59% [19]. In contrast, the ESWL group had an SFR of 88.89% after three sessions, with 55.6% achieved during the first session [20]. For kids with stones in their upper urinary system, another research evaluated the success rates of super-mPCNL and retrograde intra-renal surgery (RIRS). Patients who received RIRS required considerably more time in the operating room (76.3 vs. 53.9) and in the hospital (4.2 vs. 2.9 days), had a lower success rate (60.0% vs. 94.4%), and were more likely to need re-treatment (20% vs. 0%) [21]. Another research presented experiences of 163 patients. They found postoperative fever rate of 14.6% [22]. One patient with urosepsis was among the 12.5% of patients who had fever following surgery in our research. Twenty-two young patients who received ultra-miniature PCNL were studied by Zhu et al., [23]. Their patients had 18.2% suffered postoperative fever, and 0% had septicemia. Liu et al., conducted a research to determine what variables increase the likelihood of sepsis after mPCNL. Twenty individuals out of 834 in the study got septic shock. Three of these individuals ultimately passed away from complications related to multiple organ failure. Female gender was observed to increase the risk of postoperative septic shock (OR = 1.055, P 0.001), whereas diabetes mellitus increased the risk by a factor of 4.192 (P = 0.0030) [24]. Antibiotic treatment and other non-invasive methods successfully treated all of our patients. Because of the risk of hyponatremia and hypothermia in children, warm saline should be used for irrigation. While saline is the go-to for treating PCNL in adults, there are studies that demonstrate distilled water is just as effective. In our research, none of our patients had experienced these complications

CONCLUSIONS

Our research shows that MPCNL in children has acceptable complication rates and surgical success rates, making it a relatively safe operation. Renal stones greater than 3 cm in size were successfully treated with mini-PCNL, making it a safe and effective alternative to standard PCNL.

Authors Contribution

Conceptualization: KF
Methodology: KF, IZ, NH
Formal analysis: KF, AA, HH
Writing-review and editing: KF, HH, IAK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

REFERENCES

[1] Mahmood SN, Aziz BO, Tawfeeq HM, Fakhralddin SS. Mini-versus standard percutaneous nephrolithotomy for treatment of pediatric renal stones: is smaller enough? Journal of Pediatric Urology. 2019 Dec; 15: 664.e1–e6. doi: 10.1016/j.jpurol.2019.09.009.

[2] Baydilli N, Tosun H, Akinsal EC, Gölbaşi A, Yel S, Demirci D. Effectiveness and complications of mini-percutaneous nephrolithotomy in children: one center experience with 232 kidney units. Turkish Journal of Urology. 2020 Nov; 46: 69-75. doi: 10.5152/tud.2019.19158.

[3] Assimos D, Krambeck A, Miller NL, Monga M, Murad MH, Nelson CP, et al. Surgical management of stones: American urological association/endourological society guideline, PART I. Journal of Urology. 2016 Jan; 196: 1153–60. doi: 10.1016/j.juro.2016.05.090.

[4] Dombrovskiy V and Olweny EO. Percutaneous nephrolithotomy in children: analysis of nationwide hospitalizations and short-term outcomes for the United States, 2001–2014. Journal of Endoscopic Urology. 2018 Nov; 32: 912–8. doi: 10.1089/end.2018.0370.

[5] Guven S, Frattini A, Onal B, Desai M, Montanari E, Kums J, et al. Percutaneous nephrolithotomy in children in different age groups: data from the Clinical Research Office of the Endourological Society (CROES) percutaneous nephrolithotomy global study. British Journal of Urology. 2013 Apr; 111: 148–56.

[6] Tian Y, Yang X, Luo G, Wang Y, Sun Z. Initial prospective study of ambulatory mPCNL on upper urinary tract calculi. Urology Journal. 2020 Sep; 17: 14–8.

[7] Planz VB, Posielski NM, Lubner MG, Li K, Chen GH, Nakada SY, et al. Ultra-low-dose limited renal CT for volumetric stone surveillance: advantages over standard unenhanced CT. Abdomen Radiology. 2019 Mar; 44: 227–33. doi: 10.1007/s00261-018-1719-5.

[8] Hennessey DB, Kinnear NK, Troy A, Angus D, Bolton DM, Webb DR. Mini PCNL for renal calculi: does size matter? British Journal of Urology. 2017 Apr; 119: 39–46. doi: 10.1111/bju.13839.

[9] Agrawal MS and Agrawal M. Tubeless percutaneous nephrolithotomy. Indian Journal of Urology. 2010 Apr; 26: 16. doi: 10.4103/0970-1591.60438.

[10] Tefekli A, Karadag MA, Tepeler K, Sari E, Berberoglu Y, Baykal M, et al. Classification of percutaneous nephrolithotomy complications using the modified clavien grading system: looking for a standard. European Journal of Urology. 2008 Nov; 53: 184–90. doi: 10.1016/j.eururo.2007.06.049.

[11] Ahmed F, Askarpour M-R, Eslahi A, Nikbakht H-A, Jafari S-H, Hassanpour A, et al. The role of ultrasonography in detecting urinary tract calculi compared to CT scan. Research Report in Urology. 2018 Apr; 10: 199. doi: 10.2147/RRU.S178902.

[12] Aminsharifi A, Hosseini M-M, Khakbaz A. Laparoscopic pyelolithotomy versus percutaneous nephrolithotomy for a solitary renal pelvis stone larger than 3 cm: a prospective cohort study. Urolithiasis. 2013 Jan; 41: 493–7. doi: 10.1007/s00240-013-0589-0.

[13] Aminsharifi A, Taddayun A, Niroomand R, Hosseini M-m, Afsar F, Afrasiabi MA. Laparoscopic nephrectomy for non-functioning kidneys is feasible after previous ipsilateral renal surgery: a prospective cohort trial. Journal of Urology. 2011 Dec; 185: 930–4. doi: 10.1016/j.juro.2010.10.075.

[14] Thapa BB and Niranjan V. Mini PCNL over standard PCNL: what makes it better? Surgery Journal. 2020 Aug; 6: e19–23. doi: 10.1055/s-0040-1701225.

[15] Hosseini MM, Hassanpour A, Farzan R, Yousefi A, Afrasiabi MA. Ultrasonography-guided percutaneous nephrolithotomy. Journal of Endourology. 2009 Nov; 23: 603–7. doi: 10.1089/end.2007.0213.

[16] Hosseini MM, Yousefi A, Rastegari M. Pure ultrasonography-guided radiation-free percutaneous nephrolithotomy: report of 357 cases. Springer Plus. 2015 Jun; 4: 1–5. doi: 10.1186/s40064-015-1078-4.

[17] Zeng G, Zhu W, Lam W. Miniaturised percutaneous nephrolithotomy: its role in the treatment of urolithiasis and our experience. Asian Journal of Urology. 2018 Aug; 5: 295–302. doi: 10.1016/j.ajur.2018.05.001.

[18] Wah TM, Kidger L, Kennish S, Irving H, Najmaldin A. MINI PCNL in a pediatric population. Cardiovascular Interventional Radiology. 2013 Dec; 36: 249–54. doi: 10.1007/s00270-012-0460-7.

[19] Farouk A, Tawfick A, Shoeb M, Mahmoud MA, Mostafa DE, Hasan M, et al. Is mini-percutaneous nephrolithotomy a safe alternative to extracorporeal shockwave lithotripsy in pediatric age group in borderline stones? A randomized prospective study. World Journal of Urology. 2018 Apr; 36: 1139–47.doi: 10.1007/s00345-018-2231-9.

[20] Jackman SV, Docimo SG, Cadeddu JA, Bishoff JT, Kavoussi LR, Jarrett TW. The "mini-perc" technique: a less invasive alternative to percutaneous nephrolithotomy. World Journal of Urology. 2022 Dec; 16: 371–4. doi: 10.1007/s003450050083.

[21] Kallidonis P, Panagopoulos V, Kyriazis I, Liatsikos E. Complications of percutaneous nephrolithotomy:

DOI: https://doi.org/10.54393/pjhs.v4i11.1171

classification, management, and prevention. Current Opinions in Urology. 2016 Jan; 26: 88–94. doi: 10.1097/MOU.0000000000000232.

[22] Kyriazis I, Panagopoulos V, Kallidonis P, Özsoy M, Vasilas M, Liatsikos E. Complications in percutaneous nephrolithotomy. World Journal of Urology. 2015 Dec; 33: 1069–77. doi: 10.1007/s00345-014-1400-8.

[23] Zhu W, Liu Y, Liu L, Lei M, Yuan J, Wan SP, et al. Minimally invasive versus standard percutaneous nephrolithotomy: a meta-analysis. Urolithiasis. 2015 Jan; 43: 563–70. doi: 10.1007/s00240-015-0808-y.

[24] Liu B, Jia H, Li J, Zhang P, Yusufu A, Nan Y, et al. Comparison of super-mini-PCNL and flexible ureteroscopy for the management of upper urinary tract calculus (1–2 cm) in children. World Journal of Urology. 2020 Dec; 39: 195–200. doi: 10.1007/s00345-020-03150-x.

DOI:https://doi.org/10.54393/pjhs.v4i11.1177

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

ORIGINAL ARTICLE

Risk Factors of Transient Ischemic Attack in Young Adults in Pakistan

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ARTICLE INFO

Key Words:
Risk Factors, Stroke, Transient Ischemic Attack

How to Cite:
Akbar Jamali, Y., Warsi, J., & Laghari, Z. A. (2023). Risk Factors of Transient Ischemic Attack in Young Adults in Pakistan : Risk Factors of Transient Ischemic Attack. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1177

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Received Date: 9th November, 2023
Acceptance Date: 29th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Transient ischemic attacks precede about 20%-25% of ischemic stroke. These symptoms normally range from a few seconds to several minutes, with a typical duration of less than one hour. **Objective:** To assess the risk factors of transient ischemic attack in young adults. **Methods:** This prospective study was conducted at the People's University of Medical and Health Sciences Hospital, Nawabshah. Patients with stroke admitted to Medical Units I, II, and III from November 2021 to June 2023 were eligible for inclusion. This study eliminated those who were under the age of 18, those who had experienced brain injury, and those who were above the age of 45. The current study included 209 patients, including both male and female participants aged between 18 and 45 years, who exhibited various forms of stroke. For this study, only 14 (6.7%) patients with transient ischemic attack (TIA) were selected. Data on diagnostic tests, medical records, laboratory investigations, and radiological images were obtained for data collection. **Results:** The most prevalent risk factor was diabetes mellitus in nine (64.3%) patients. Seven (50.0%) patients had hypertension. Cardiac disease was seen in six (42.9%) of patients. Smoking and previous stroke history were observed in one (7.1%) patient each. **Conclusions:** The results of this research suggested that diabetes mellitus, hypertension, and heart problems are the predominant risk factors associated with transient ischemic stroke in young individuals.

INTRODUCTION

Transient ischemic attacks precede about 20%-25% of ischemic strokes [1]. These symptoms normally range from a few seconds to several minutes, with a typical duration of less than one hour [2]. The definition of transient ischemic attack (TIA) has undergone revision due to the discovery of brain infarcts on imaging in patients experiencing symptoms lasting longer than 10 minutes. Additionally, the consideration of urgent revascularization is given to patients who present at the hospital within 6 hours of symptom onset. This update challenges the previous time-based definition of TIA, which categorized it based on symptoms lasting less than 24 hours. The current term for TIA has been revised to "tissue-based" in the latest definition. In the context of a transient ischemic attack (TIA), it is important to note that ischemic lesions may not be discernible on brain imaging. Conversely, if a patient exhibits transitory symptoms and presents with even a minute ischemic brain lesion on imaging, medical professionals classify the event as a small ischemic stroke [3-5]. TIA and small ischemic stroke are usually treated the same way, even though scan results can be different. This is why they are considered together in clinical practice [4-6]. Although a number of risk factors and reasons have been identified, most ischemic strokes in younger age groups still do not have known causes. Atherosclerosis, diabetes, high blood pressure, cholesterol, and smoking are known to increase the risk of stroke in older people. Nevertheless, recent research conducted in the United States and Europe has shown a higher prevalence of ischemic stroke in younger individuals [7-10]. Recent

DOI:https://doi.org/10.54393/pjhs.v4i11.1177

statistical data indicates that the incidence of traditional risk factors is much higher among individuals aged 15-55 compared to older age cohorts [9]. However, there is a lack of available data about the frequency of stroke in young populations originating from Eastern Europe and Asia. Most of the existing literature on this topic originates from cohorts in North America and Western Europe. Numerous studies have shown a higher prevalence of ischemic stroke among individuals aged 30 to 45 years [11, 12]. A few hospital-based studies have shown that young Pakistanis are more likely to have a stroke, but there is little statistical research on this group. Syed et al., found that people aged between 35 and 45 years were more likely to have a stroke (26%)[13]. Another study examined a case series and found that thirty-four percent of patients with stroke they studied were younger than 50 years of age [14]. Empirical evidence also shows that more than two-thirds of strokes occur in developing countries. Current estimates place the percentage of stroke cases attributable to young people between 10% and 30% in India but only between 3% and 8.5% in Western countries [15-17]. Young people are more likely to have strokes than older people, which is similar to Pakistan and could have a big effect on the economy. Additionally, it has been established that hypertension is the most prevalent risk factor that young people encounter [18-19]. Furthermore, there are geographical differences in etiological subtyping. To avoid stroke-related impairment and recurrence in younger populations, the evaluation of the factors and origins of stroke in individuals of a younger age group is of utmost importance [18-19].

This study aimed to assess the transient ischemic attack (TIA) risk factors in Pakistan's young population, a demographic that has not been extensively examined in the past.

METHODS

This prospective study was conducted at the People University of Medical and Health Sciences Hospital, Nawabshah. Patients with stroke admitted to Medical Units I, II, and III from November 2021 to June 2023 were eligible for inclusion. This study eliminated those who were under the age of 18, those who had experienced brain injury, and those who were above the age of 45. The current study included 209 patients, including both male and female participants aged between 18 and 45 years, who exhibited various forms of stroke. Only 14 patients (6.7%) with TIA patients were selected for this study. The patients underwent an initial examination conducted by an emergency physician, followed by a subsequent evaluation performed by a neurologist. Data on diagnostic tests, medical records, laboratory investigations, and radiological images were obtained for data collection. After getting ethics approval and permission from the patients or their parents or guardians, detailed demographic information such as age, socioeconomic status, gender, and place of residence was documented on the data collection form. "Complete blood count test" (CBC), "erythrocyte sedimentation rate"(ESR), lipid profile, Hb A1C, "liver function test," and "renal functional tests" were performed initially on all patients. Carotid Doppler, 24-hour ECG recording, and echocardiography were also performed. Upon admission, a computed tomography (CT) scan of the brain was performed for all patients. In instances where it was deemed necessary, a brain MRI with a stroke procedure was also conducted. Operating definitions of hypertension were: An individual is considered to have hypertension if their systolic blood pressure exceeds 140 mmHg, their diastolic blood pressure surpasses 90 mmHg based on two separate measurements prior to the occurrence of a stroke, or if they are already on antihypertensive medication. In addition to the current usage of hypoglycemic drugs, a fasting glucose level of 126 mg/dL or above was diagnostic for diabetes mellitus. Cardiac disease is characterized by a medical history that includes conditions such as valvular heart disease, arrhythmia, and coronary artery disease, among others. The medical records also documented the patient's history of prior transient ischemic attack (TIA), characterized by temporary neurological impairments lasting less than 24 hours, as well as stroke and peripheral angiopathy illness. Cigarette smoking was operationally defined as the act of consuming cigarettes throughout the previous five-year period. The calculation of body mass index (BMI) included dividing weight (in kilograms) by the square of height (in meters). Plasma levels of low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC), apolipoprotein A (ApoA), apolipoprotein B (ApoB) and triglycerides (TG), levels (TG) were evaluated on a subsequent day after admission to the hospital. The tests were done in the morning after not eating or drinking anything all night. They used a Hitachi 7600 automatic analyzer made in Japan by Hitachi Instruments Corporation. All statistical data were analyzed using Excel-365 and SPSS version 26.0. The Chi-square goodness-of-fit test was used to examine the differences across binary categorical variables. To determine if there was a link between the categorical variables, Fisher's exact test was also used. Statistical calculations were performed to determine the variables' percentages, means, and standard deviations. A statistically significant p-value of less than 0.05 was deemed acceptable. The research ensured that all participants, as well as their parents/guardians or legally authorized representatives, provided written informed consent prior to their

DOI:https://doi.org/10.54393/pjhs.v4i11.1177

participation. Ethical approval was obtained from the Advanced Studies and Research Board (ASRB) (No. DRGS/2421, Dated: 2-11-2021) at the University of Sindh, Jamshoro. Code numbers were used in lieu of patients' names to protect confidentiality.

RESULTS

Total transient ischemic attack (TIA) patients were 14 (6.7%) out of 209. Six (42.9%) patients were men and eight (57.1%) were women. Mostly 10 (71.4%) patients were in the age group of 31 – 45 years. The mean ± SD GCS score of TIA patients was 13.4 ± 2.2, which indicates a mild TIA, while the mean ± SD age was 36.1 ± 9.3 years. Seven (50.0%) patients were from middle-class families, and the other seven (50.0%) were from low-income families (Table 1).

Table 1: Baseline characteristic of TIA in young adults

Characteristics	Frequency n (%)
Age (Mean ± SD)	36.1 ± 9.3
GCS score (Mean ± SD)	13.4 ± 2.2
Gender	
Male	6 (42.9%)
Female	8 (57.1%)
Age groups (years)	
18 – 30 years	4 (28.6%)
31 – 45 years	10 (71.4%)
Socio-Eco status	
Middle class	7 (50.0%)
Lower class	7 (50.0%)

The most prevalent risk factor was diabetes mellitus in nine (64.3%) patients. Seven (50%) patients had hypertension. Cardiac disease was seen in six (42.9%) of patients. Smoking and previous stroke history were present in one (7.1%) and one (7.1%) patient each. The patient had no family history of any of the risk factors for TIA (Table 2).

Table 2: Risk factors of transient ischemic attack in young adults

Characteristics	Yes	No	p-value
Diabetes Mellitus	9 (64.3%)	5 (35.7%)	0.285
Hypertension	7 (50.0%)	7 (50.0%)	1.000
Cardiac disease	6 (42.9%)	8 (57.1%)	0.593
Smoking	1 (7.1%)	13 (92.9%)	0.001
Previous Stroke	1 (7.1%)	13 (92.9%)	0.001

Diabetes mellitus was observed in three (50.0%) male and six (75.0%) female patients, with no gender differences. Although hypertension is more observed in five (62.5%) female patients than in two (33.3%) male patients. Cardiac disease in 3 (50.0%) males was slightly higher than in females 3 (37.5%). One (16.7%) patient had a smoking history, and one (12.5%) female patient had a previous stroke history. No significant gender differences were observed between male and female patients' risk factors. Ten (71.4%) patients were aged 31 – 45 years and four (28.6%) were aged 18 – 30. Diabetes mellitus was found in eight (80.0%) patients in the age group 31 – 45 years than in one (25%) of patients age group 18 – 30 years. Hypertension was in three (75.0%) patients aged 18 – 30 compared to 4 (40%) patients aged 31 – 45. All six (60.0%) patients with cardiac disease were 31 – 45 years old. Smoking and a previous stroke history were only found in the age group of 31 – 45 years. No significant differences were observed between age groups (Table 3).

Table 3: Risk factors of TIA in young adults according to gender and age

Risk Factors	Total n = 14 n (%)	Male n = 6		Female n = 8		p-value*	Age 18 – 30 n = 4		Age 31 – 45 n = 10		p-value*
		Yes n (%)	No n (%)	Yes n (%)	No n (%)		Yes n (%)	No n (%)	Yes n (%)	No n (%)	
Diabetes Mellitus	9 (64.3)	3 (50.0)	3 (50.0)	6 (75.0)	2 (25.0)	1.000	1 (25.0)	3 (75.0)	8 (80.0)	2 (20.0)	0.582
Hyper-tension	7 (50.0)	2 (33.3)	4 (66.7)	5 (62.5)	3 (37.5)	0.592	3 (75.0)	1 (25.0)	4 (40)	6 (60.0)	0.559
Cardiac disease	6 (43.9)	3 (50.0)	3 (50.0)	3 (37.5)	5 (62.5)	1.000	0	4 (100)	6 (60.0)	4 (40.0)	0.085
Smoking	1(7.1)	1(16.7)	5 (83.3)	0	8 (100)	0.428	0	4 (100)	1 (10.0)	9 (90.0)	1.000
Previous Stroke	1(7.1)	0	6 (100)	1(12.5)	7 (87.5)	1.000	0	4 (100)	1 (10.0)	9 (90.0)	1.000

*Significant p-value <0.05

All 14 patients survived, with no mortality observed in TIA. Of these, 6 (100%) were male and 8 (100%) were female.

DISCUSSION

In our study, the most prevalent risk factor was diabetes mellitus in nine (64.3%) TIA patients. Previous literature reported lower diabetes mellitus in (11%) of young TIA patients [12]. Another study has documented a lower rate of diabetes mellitus in 7 (9.0%) patients [20]. Seven (50%) had hypertension in our study. These numbers were analogous to the results of Janssen et al. They found a slightly higher rate of hypertension in 56.4% of their population, which was younger (<50 years) [21]. Ji et al., observed a lower frequency of hypertension in (20%) of stroke/TIA patients [12]. Six (42.9%) patients had cardiac disease in the current study. Janssen et al., found a slightly higher incidence of cardiac disease in (47.9%) [21]. A prospective study conducted on the Chinese population observed a lower incidence of cardiac disease in 109 (20.6%) stroke/TIA patients [22]. Our study discovered a smoking history in 1 (7.1%) patient. Giovannoni and Fritz reported a higher smoking history in 37 (49%) patients [20]. Another study reported a higher rate of smoking in 40% of stroke/TIA patients [21]. In our study, eight (57.1%) female patients had transient ischemic attacks. These results were agreed with a survey that found 58.8% of female

DOI:https://doi.org/10.54393/pjhs.v4i11.1177

patients in a previous study [23]. Pregnancy, migraine, and oral contraceptive use all increase the likelihood of having a stroke or TIA at a younger age, which may explain why women make up a disproportionately high percentage of those affected. Women seem to be more vulnerable to these dangers [21]. All patients survived, and no deaths were reported in the current study. Of the 14 patients, six (100%) were male and eight (100%) were women. The acute fatality and recurrence rates of ischemic stroke in young individuals are quite low, particularly in cases where the underlying etiology remains unidentified. The vast majority of people return to work full-time. The intensity of the first stroke is a good indicator of a person's independence [24].

CONCLUSIONS

The study's conclusions showed that diabetes mellitus was the most common risk factor for TIA, followed by heart disease and hypertension, and that female patients between the ages of 18 and 45 had a higher chance of having the condition. Our study's findings highlight the need to manage common risk factors and do a thorough patient work-up to ascertain the cause of strokes among Pakistan's youth. Larger-scale, continuing research is still required to identify the potential causes of strokes in young individuals as well as the risk factors that may apply to them.

Authors Contribution

Conceptualization: YAJ
Methodology: JW
Formal analysis: YAJ
Writing-review and editing: JW, ZAL
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Rothwell PM and Warlow CP. Timing of TIAs preceding stroke: time window for prevention is very short. Neurology. 2005 Mar; 64(5): 817–20. doi: 10.1212/01.WNL.0000152985.32732.EE.

[2] Fisher CM. Transient Ischemic Attacks. New England Journal of Medicine. 2002 Nov; 347(21): 1642–3. doi: 10.1056/NEJMp020129.

[3] Albers GW, Caplan LR, Easton JD, Fayad PB, Mohr JP, Saver JL, et al. Transient Ischemic Attack — Proposal for a New Definition. New England Journal of Medicine. 2002 Nov; 347(21): 1713–6. doi: 10.1056/NEJmsb020987.

[4] Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiova - scular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease: the American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. Stroke. 2009 Jun; 40(6): 2276–93. doi: 10.1161/STROKEAHA.108.192218.

[5] Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, et al. Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2014 Jul; 45(7): 2160–236. doi: 10.1161/STR.0000000000000024.

[6] Linden B. National Institute for Health and Care Excellence NG128 stroke and transient ischaemic attack in over 16s: diagnosis and initial management. British Journal of Cardiac Nursing. 2020 Sep; 15(9): 1-5. doi: 10.12968/bjca.2020.0121

[7] George MG, Tong X, Bowman BA. Prevalence of cardiovascular risk factors and strokes in younger adults. JAMA Neurology. 2017 Jun; 74(6): 695–703. doi: 10.1001/jamaneurol.2017.0020.

[8] Kissela BM, Khoury JC, Alwell K, Moomaw CJ, Woo D, Adeoye O, et al. Age at stroke: temporal trends in stroke incidence in a large, biracial population. Neurology. 2012 Oct; 79(17): 1781–7. doi: 10.1212/WNL.0b013e318270401d.

[9] Kivioja R, Pietilä A, Martinez-Majander N, Gordin D, Havulinna AS, Salomaa V, et al. Risk factors for Early-Onset ischemic stroke: a Case-Control study. Journal of the American Heart Association. 2018 Nov; 7(21): e009774. doi: 10.1161/JAHA.118.009774.

[10] Singhal AB, Biller J, Elkind MS, Fullerton HJ, Jauch EC, Kittner SJ, et al. Recognition and management of stroke in young adults and adolescents. Neurology. 2013 Sep; 81(12): 1089–97. doi: 10.1212/WNL.0b013e3182a4a451.

[11] Béjot Y, Bailly H, Durier J, Giroud M. Epidemiology of stroke in Europe and trends for the 21st century. Presse Médicale. 2016 Dec; 45(12): e391–8. doi: 10.1016/j.lpm.2016.10.003.

[12] Ji R, Schwamm LH, Pervez MA, Singhal AB. Ischemic stroke and transient ischemic attack in young adults:

DOI:https://doi.org/10.54393/pjhs.v4i11.1177

risk factors, diagnostic yield, neuroimaging, and thrombolysis. JAMA Neurology. 2013 Jan; 70(1): 51–7. doi: 10.1001/jamaneurol.2013.575.

[13] Syed NA, Khealani BA, Ali S, Hasan A, Brohi H, Mozaffar T, et al. Ischemic stroke subtypes in Pakistan: the Aga Khan University stroke data bank. Journal of Pakistan Medical Association. 2003 Dec; 53(12): 584.

[14] Vohra EA, Ahmed WU, Ali M. Aetiology and prognostic factors of patients admitted for stroke. The Journal of the Pakistan Medical Association. 2000 Jul;50(7): 234–6.

[15] Smajlović D. Strokes in young adults: epidemiology and prevention. Vascular Health and Risk Management. 2015 Feb; 157–64. doi: 10.2147/VHRM.S53203.

[16] Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapaniemi E et al. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: the Helsinki young stroke registry. stroke. 2009 Apr; 40(4): 1195-203. doi: 10.1161/STROKEAHA.108.529883

[17] Van Tassell BW, Toldo S, Mezzaroma E, Abbate A. Targeting interleukin-1 in heart disease. Circulation. 2013 Oct; 128(17): 1910–23. doi: 10.1161/CIRCULATIONAHA.113.003199.

[18] Chand P, Ibrahim S, Matloob Alam M, Arain F, Khealani B. Acute childhood ischemic stroke: a Pakistani tertiary care hospital experience. Pakistan Journal of Neurological Sciences (PJNS). 2016; 11(1): 3–6.

[19] Tibæk M, Dehlendorff C, Jørgensen HS, Forchhammer HB, Johnsen SP, Kammersgaard LP. Increasing incidence of hospitalization for stroke and transient ischemic attack in young adults: a registry-based study. Journal of the American Heart Association. 2016 May; 5(5): e003158. doi: 10.1161/JAHA.115.003158.

[20] Giovannoni G and Fritz VU. Transient ischemic attacks in younger and older patients. A comparative study of 798 patients in South Africa. Stroke. 1993 Jul; 24(7): 947–53. doi: 10.1161/01.STR.24.7.947.

[21] Janssen AWM, De Leeuw FE, Janssen MCH. Risk factors for ischemic stroke and transient ischemic attack in patients under age 50. Journal of Thrombosis and Thrombolysis. 2011 Jan; 31: 85–91. doi: 10.1007/s11239-010-0491-3.

[22] Tan YF, Zhan LX, Chen XH, Guo JJ, Qin C, Xu E. Risk Factors, Clinical Features and Prognosis for Subtypes of Ischemic Stroke in a Chinese Population. Current Medical Science. 2018 Apr; 38(2): 296–303. doi: 10.1007/s11596-018-1878-1.

[23] Collaborators NMSS, Sacco RL, Boden-Albala B, Gan R, Chen X, Kargman DE, et al. Stroke incidence among white, black, and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. American Journal of Epidemiology. 1998 Feb; 147(3): 259–68. doi: 10.1093/oxfordjournals.aje.a009445.

[24] Ferro JM and Crespo M. Prognosis after transient ischemic attack and ischemic stroke in young adults. Stroke. 1994 Aug; 25(8): 1611–6. doi: 10.1161/01.STR.25.8.1611

DOI:https://doi.org/10.54393/pjhs.v4i11.1174

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Impact of COVID-19 Pandemic on the Quality of Life of Nurses Working in the Public Sector Tertiary Care Hospitals of Karachi

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ARTICLE INFO

Key Words:
CVID-19, Nurses Health, Quality of Life

How to Cite:
Kumar, A., Badil, ., & Shah, S. Y. (2023). Impact of COVID-19 Pandemic on the Quality of Life of Nurses Working in the Public Sector Tertiary Care Hospitals of Karachi : Impact of COVID-19 Pandemic. Pakistan Journal of Health Sciences, 4(11), 92–96. https://doi.org/10.54393/pjhs.v4i11.1174

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Received Date: 9th November, 2023
Acceptance Date: 29th November, 2023
Published Date: 30th November, 2023

ABSTRACT

COVID-19 has a substantial influence related to the quality of life of nurses by increasing the number of patients, which increases the work burden and stress level. **Objective:** To determine the impact of the COVID-19 pandemic on the quality of life of nurses working in the public sector tertiary care hospitals of Karachi. **Methods:** Present an analytical cross-sectional study design was employed to determine the quality of life of working nurses by using a non-probability convenient sampling technique to recruit 240 nurses. The quality of life of nurses was assessed by using the McGill Quality of Life (QoL) revised questionnaire. Results were considered significant at p-value of ≤0.05. **Results:** Out of a total of 240 nurses, most of them 135 (56.2%) were male, 177(73.88%) married, 128, 53.3% Post RN qualification, and 99 (41.2%) 6 to 10 years of working experience. The mean ± SD of the overall QoL of nurses was 6.56 ± 2.53. Based on multiple logistic regression analysis, males had 2.79 times better QOL during the COVID-19 pandemic as compared to females (ORadj=2.79, 95% CI: 1.05 - 7.45, p= 0.04). Similarly, married persons had 3.06 times better QOL during the COVID-19 pandemic as compared to others (ORadj=3.06, 95% CI: 2.14 – 3.34, p= 0.003). **Conclusions:** It is concluded that the COVID-19 pandemic has a significant effect on all aspects of the physical, psychological, existential and social quality of life of nurses working in the public sector tertiary care hospitals of Karachi, Pakistan.

INTRODUCTION

The Coronavirus disease (COVID-19) is a viral disease that evolved in Wuhan, China and was declared by WHO a pandemic on 11th March 2022, which affected the whole world [1]. The median of COVID-19 incubation was 4 days, and it is transmitted from human to human through respiratory droplets [2]. COVID-19 was identified as a family of severe acute respiratory syndrome, and it was transmitted from animals to humans [3]. Furthermore, in this unprecedented situation of a pandemic, it is quite challenging to cope with life-threatening disasters effectively [4]. During the pandemic, a relatively strong campaign with the slogan 'Stay home, stay safe' was used as a public awareness message to limit public meetings pro, promote home quarantine [5], and limit social gatherings of people who come in contact with coronavirus infected persons with close monitoring for appearing any symptoms to prevent others from getting infection [6]. As frontline health workers, the vital responsibility of nurses is to provide proper nursing care to the patient, and in this pandemic in China, 28,679 nurses were sent to the affected provinces as frontline fighters against COVID-19 disease [7]. In the month of April 2020 COVID 19, reported cases were above 2 million worldwide, and this virus caused 2 lac deaths. At the same time, nurses who are working in an infectious environment have a fear of giving the infection to their loved ones, which increases mental distress, anxiety, and depression in the nurses [8]. Nurses working during this pandemic experienced depression, anxiety and stress that can disrupt the quality of life of nurses and reduce the capabilities of nurses in their different roles as well [9]; additionally, when nurses work in high-risk infection environments, which may affect adversely the nurse's

DOI:https://doi.org/10.54393/pjhs.v4i11.1174

mental health [10].

Thus, the present study aimed to determine the impact of COVID-19 on the quality of life of nurses working in tertiary care hospitals in Karachi, Pakistan.

METHODS

An analytical cross-sectional study was conducted among nurses working at Dow University Hospital and Dr. Ruth K.M Pfau Civil Hospital Karachi for the period of four months from August 2020 to December 2020. Nurses working in the Dow University Hospital and Dr. Ruth KM Pfau Civil Hospital Karachi during the COVID-19 outbreak were enrolled for the study. On the other hand, nurses not willing to participate in the study, student nurses, contract nurses and outpatient department (OPD) nurses were excluded from the study. Non-probability convenient sampling method was utilized to access the respondents. Sample size was calculated through PASS version 11, with a 95% confidence interval, 80% power of the test and 5% margin of error. The sample size was calculated by using a 43.61% prevalence of depression seen in the Chinese population [11]. Prior to data collection, written informed consent were obtained. Questionnaires were explicitly explained to all participants. Confidentiality of data was assured by assigning code numbers. The participation of subjects was voluntary. Ethical approval was obtained from Institutional Review Committee (IRC) of Dow Institute of Nursing and Midwifery, Dow University of Health Sciences, Karachi, Ref No: DIONAM/MSN/2020-18/394. A validated and adopted revised version of the McGill Quality of Life questionnaire was utilized for the data collection [12]. The reliability of the MGQOL-R version is 0.94 [13]. The questionnaire comprises 15 items divided into four Parts. Each item uses 0 to 10 scales with anchors at both ends, where 0 for the lowest desire / Worst condition and 10 for the highest desire / Best condition. The questionnaire consists of four parts.

Data was entered and analyzed through SPSS version-24.0. The quantitative data was measured by using mean and standard deviation, and categorical data was measured through percentages. Results were considered significant at p-value of ≤0.05.

RESULTS

Out of a total 240 nurses, a large number of 135(56.2%) were male, 177 (73.88%) married, 128, 53.3%) Post RN qualification, 99 (41.2%) had 6 to 10 years of experience, 46 (19.2%) working in the emergency ward and 52 (21.7 %) working in COVID-19 ward. With regard to age classification, most of them are from 20-27 years 28 (11.7%), 28-35 years 126 (52.5 %), 36-45 years 57 (23.8%) and 46 and above years 29 (12.1%). Table 1 revealed Quality of life according to McGill's Quality of Life revised questionnaire. According to the McGill Quality of Life (QoL) Questionnaire, in part A, the item scale for the overall quality of life section, the mean +SD of the overall QoL of nurses was about 6.56 ± 2.53 which was higher than the middle point, which showed better QOL. Similarly, in Part B of the questionnaire, the overall average of the physical Scale of quality of life was about 6.59 ± 3.19, which also showed a higher score than the middle point, which showed that the physical QOL of nurses was better. In Part C of the questionnaire, the psychological Scale mean ± SD score was about 6.96 ± 2.5, which also showed the better psychological QOL of nurses. The existential Scale mean ± SD score was about 6.63+1.8, which also showed a higher score that indicates better Existential QOL of Nurses working in the public sector tertiary care hospital of Karachi, Pakistan. In Part D of the questionnaire, the social Scale mean ± SD score was about 6.77 ± 2.5, which was also higher than the middle point and indicates better Social QOL of Nurses.

Table 1: Quality of life according to McGill Quality of Life revised questionnaire

Questions Distribution	Questionnaire	Mean ± SD
Part A Overall QoL	1.Considering all parts of my life - physical, emotional, social, spiritual, and financial - over the past two (2) days the quality of my life has been:	6.56±2.53
Part B Physical Scale	1. My physical symptoms (pain, nausea, weariness, and others) throughout the last two days (48 hours) were as follows:	6.89±3.2
	2. I felt the following for the last two days (48 hours):	6.15±3.3
	3. Being physically unable to accomplish what I desired for the previous two days (48 hours) was:	6.73±3.08
Part C Psychological Scale Feelings & thoughts Existential Scale	1. I was distressed for the last two days (48 hours):	7.15±3.0
	2. I felt nervous or concerned over the last two days (48 hours):	7.16±2.94
	3. I've been displeased for the previous two days (48 hours):	7.12±3.02
	4. When I considered the future through -out the last 48 hours, or the previous two days, I was:	6.41±3.17
	5. In the last 48 hours, or the last two days, my life has been:	7.22±2.73
	6. When I think about my whole life, I feel that in achieving life goals, I have:	6.75±2.72
	7. Over the past two days (48 hours), I felt that the amount of control I had over my life was:	5.48±3.40
	8. Over the past two days (48 hours), I felt good about myself as a person:	7.08±2.83
Part D Social Scale	1. Over the past two days (48 hours), communication with the people I care about was:	6.92±2.97
	2. In previous two days (48 hours), I felt my relationship with people I care about were:	6.31±2.96
	3. In previous two days, I perceived support:	7.08±3.05

DOI:https://doi.org/10.54393/pjhs.v4i11.1174

Table 2 depicts the association between total quality score and demographical variables. Based on chi-square analysis, gender (p-value <0.001), age classification (p-value 0.03) and working area (p-value 0.004) were significantly associated with total quality of life as compared to other demographical variables.

Table 2: Association between Total Quality Score and Demographical Variables

Demographical Variable	Poor Quality of Life	Better Quality of Life	Chi-Square p-value
Gender			
Male	32 (82.1%)	103 (51.2%)	<0.001*
Female	7 (17.9%)	98 (48.8%)	
Age			
20-27	5 (12.8%)	23 (11.4%)	0.03*
28-35	26 (66.7%)	100 (49.8%)	
36-45	7 (17.9%)	50 (24.9%)	
46 & above	1 (2.6%)	28 (13.9%)	
Marital Status			
Married	28 (71.8%)	149 (74.1%)	0.817
Unmarried	11 (28.2%)	51 (25.4%)	
Divorce/Widow	0 (0.0%)	1(0.5%)	
Educational Qualification			
Diploma+ Speciallity	11 (28.2%)	78 (38.8%)	0.329
Post RN-BS Nursing	24 (61.5%)	104 (51.7%)	
Generic Nursing	4 (10.3%)	18 (9.0%)	
MS Nursing	0 (0.0%)	1 (0.5%)	
Working Experience (Years)			
<2	2 (5.1%)	14 (7.0%)	0.06
3-5	14 (35.9%)	37 (18.4%)	
6-10	16 (41.0%)	83 (41.3%)	
>10	7 (17.9%)	67 (33.3%)	
Working Area			
ER	11 (28.2%)	35 (17.4%)	0.004*
ICU	12 (30.8%)	40 (19.9%)	
CCU	3 (7.7%)	11 (5.5%)	
NICU	1 (2.6%)	9 (4.5%)	
MW	8 (20.5%)	39 (19.4%)	
SW	0 (0.0%)	19 (9.5%)	
Covid Ward	4 (10.3%)	48 (23.9%)	

Table 3 exhibited the multiple logistic Regression analysis between the total quality score and demographical Variables. Based on multiple logistic regression analysis (adjusted analysis), males were 2.79 times more affected by COVID-19 as compared to females (ORadj=2.79, 95% CI: 1.05-7.45, p= 0.04). Similarly, married persons were 3.06 times more affected by COVID-19 season as compared to others (ORadj=3.06, 95% CI: 2.14-3.34, p= 0.003). Nurses who worked in the ICU were 3.24 times more affected by COVID-19 season as compared to others (ORadj=3.24(0.57-8.49).

Table 3: Multiple Logistic Regression Analysis between Total Quality Score and Demographical Variables

Demographical Variable	Poor Quality of Life	Better Quality of Life	OR_{adj}(95% CI)	p-value
Gender				
Male	32 (82.1%)	103 (51.2%)	2.79 (1.05-7.45)	0.04*
Female	7 (17.9%)	98 (48.8%)	--	--
Age				
20-27	5 (12.8%)	23 (11.4%)	2.06 (0.14-30.34)	0.598
28-35	26 (66.7%)	100 (49.8%)	2.60 (0.24-27.89)	0.429
36-45	7 (17.9%)	50 (24.9%)	1.59 (0.15-16.88)	0.698
46 & above	1 (2.6%)	28 (13.9%)	--	--
Marital Status				
Married	28 (71.8%)	149 (74.1%)	3.06 (2.14-3.34)	0.003
Unmarried	11 (28.2%)	51 (25.4%)	1.60 (1.24-2.89)	0.429
Divorce/Widow	0 (0.0%)	1(0.5%)	--	--
Educational Qualification				
Diploma+ Speciallity	11 (28.2%)	78 (38.8%)	1.50 (2.31-10.74)	0.987
Post RN-BS Nursing	24 (61.5%)	104 (51.7%)	3.98 (3.09-11.54)	0.002
Generic Nursing	4 (10.3%)	18 (9.0%)	2.56 (2.37-5.97)	0.120
MS Nursing	0 (0.0%)	1 (0.5%)	--	--
Working Experience (Years)				
<2	2 (5.1%)	14 (7.0%)	0.39 (0.05-2.87)	0.357
3-5	14 (35.9%)	37 (18.4%)	1.18 (0.32-4.35)	0.793
6-10	16 (41.0%)	83 (41.3%)	0.64 (0.20-2.0)	0.444
>10	7 (17.9%)	67 (33.3%)	--	--
Working Area				
ER	11 (28.2%)	35 (17.4%)	0.15 (0.69-10.12)	2.653
ICU	12 (30.8%)	40 (19.9%)	3.24(0.57-8.49)	0.001
CCU	3 (7.7%)	11 (5.5%)	0.50 (0.31-10.74)	1.826
NICU	1 (2.6%)	9 (4.5%)	0.98 (0.09-11.54)	1.029
MW	8 (20.5%)	39 (19.4%)	0.56 (0.37-5.97)	1.503
SW	0 (0.0%)	19 (9.5%)	0.98 (0.12-5.23)	1.94
Covid Ward	4 (10.3%)	48 (23.9%)	--	--

DISCUSSION

The present study was conducted to determine the impact of COVID-19 on the quality of life of nurses working in tertiary care hospitals in Karachi, Pakistan. In the current study, the established mean±SD of the overall QoL of nurses was 6.56 ± 2.53. In contrast, the highest mean + SD of overall QoL of nurses, 55.57 ± 18.70, was reported in Iran [14]. The present study disclosed that better physical scores among nurses showed improved quality of life of nurses. These results are dissimilar to a study accomplished in Brazil by Meneguin et al., which revealed low scores in the physical domain of quality of life among nurses during the COVID-19 pandemic [15]. Current study findings exhibited considerable social support among nurses, while a study carried out in Canada depicted low social support [16]. This study unveiled relatively better psychological QOL of nurses working during COVID-19. These study findings are more consistent with a research

DOI:https://doi.org/10.54393/pjhs.v4i11.1174

study employed in Italy, which described a lack of insufficient psychological support that can lead to poorer psychological QOL of nurses [17]. Another research study was done China found psychological changes in nurses includes fear, irritation, anxiety and depression [18]. In the present study, gender (p-value <0.001), age classification (p-value 0.03) and working area (p-value 0.004) were significantly associated with total quality. On the other hand, a research study conducted in Iran by Rashidi found no significant association between age, gender, education level, work experience, with quality of life among nurses while working in COVID-19 pandemic [19]. The present study results demonstrated that male nurses were 2.79 times more affected by COVID-19 as compared to females. These findings are dissimilar from a study conducted in China, which showed a higher prevalence of COVID-19 in females [20]. Present study observed married nurses much more affected than unmarried nurses. These study findings are parallel in study conducted in Quetta, Pakistan, showed lower health outcomes in married nurses [21]. Present study demonstrated that the nurses who worked in the ICU more affected by COVID-19 pandemic. This finding is in agreement with a study carried out in Belgium where nurses working in ICUs are more sufferer during COVID-19 outbreak and reported emotional exhaustion, depersonalization, and burnout as well [22].

CONCLUSIONS

It is concluded that the COVID-19 pandemic has had a significant impact on all aspects of the quality of life of nurses, precisely in physical, psychological and social areas. Study assessed male nurses are more affected than female nurses and married nurses are more victim of harmful effect than single nurses. Furthermore, study observed considerable social support from the family.

Authors Contribution

Conceptualization: AK
Methodology: AK
Formal analysis: SYS
Writing, review and editing: AK, B, AQ
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Tarkar P. Impact of COVID-19 pandemic on education system. International Journal of Advanced Science and Technology. 2020 May; 29(9): 3812-4.

[2] Malta M, Rimoin AW, Strathdee SA. The coronavirus 2019-nCoV epidemic: Is hindsight 20/20? E Clinical Medicine. 2020 Mar; 20. doi: 10.1016/j.eclinm.2020 . 100.

[3] Khan S, Ali A, Siddique R, Nabi G. Novel coronavirus is putting the whole world on alert. Journal of Hospital Infection. 2020 Mar; 104(3): 252-3. doi: 10.1016/j.jhin. 2020.01.019.

[4] Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al., The psychological impact of quarantine and how to reduce it: a rapid review of the evidence. The Lancet. 2020 Mar; 395(10227): 912-20. doi: 10.1016/S0140-6736(20) 30460-8.

[5] Tsai J, Wilson M. COVID-19: a potential public health problem for homeless populations. The Lancet Public Health. 2020 Apr; 5(4): 186-7. doi: 10.1016/S2468-2667(20)30053-0.

[6] Arefi MF and Poursadeqiyan M. A review of studies on the COVID-19 epidemic crisis disease with a preventive approach. Work. 2020 Jan 1;66(4):717-29. doi: 10.3233/WOR-203218

[7] Catton H. Global challenges in health and health care for nurses and midwives everywhere. International nursing review. 2020 Mar; 67(1): 4-6. doi: 10.1111/inr. 12578.

[8] Banerjee D. The COVID-19 outbreak: Crucial role the psychiatrists can play. Asian Journal of Psychiatry. 2020 Apr; 50:102014. doi: 10.1016/j.ajp.2020.102014

[9] Roshani D, Saboni K, Amjadian M. The anxiety associated with COVID-19, general health, spiritual health, and job satisfaction in healthcare providers: a cross-sectional study. BMC Psychology. 2023 Aug; 11(1): 240. doi: 10.1186/s40359-023-01283-3.

[10] Niu A, Li P, Duan P, Ding L, Xu S, Yang Y, et al., Professional quality of life in nurses on the frontline against COVID-19. Journal of Nursing Management. 2022 Jul; 30(5): 1115-24. doi: 10.1111/jonm.13620.

[11] An Y, Yang Y, Wang A, Li Y, Zhang Q, Cheung T, et al., Prevalence of depression and its impact on quality of life among frontline nurses in emergency departments during the COVID-19 outbreak. Journal of Affective Disorders. 2020 Nov; 276(9): 312-5. doi: 10.1016/j.jad.2020.06.047.

[12] Bobevski I, Kissane D, McKenzie D, Murphy G, Perera C, Payne I, et al., The Demoralization Interview: Reliability and validity of a new brief diagnostic measure among medically ill patients. General Hospital Psychiatry. 2022 Nov; 79: 50-9. doi: 10.1016/ j.genhosppsych.2022.10.002.

DOI:https://doi.org/10.54393/pjhs.v4i11.1174

[13] Cohen SR, Sawatzky R, Russell LB, Shahidi J, Heyland DK, Gadermann AM. Measuring the quality of life of people at the end of life: The McGill Quality of Life Questionnaire–Revised. Palliative Medicine. 2017 Feb; 31(2): 120-9. doi: 10.1177/0269216316659603.

[14] Sobhani S, Mohammadi Zeidi I, Tabanfar S, Hosseini MS. Relationship between Anxiety and Quality of Life in Nurses Caring for Covid-19 Patients in Different Wards. Journal of Occupational Hygiene Engineering . 2022 Mar; 9(1): 37-45.

[15] Siddiqa M, Zubair A, Kamal A, Ijaz M, Abushal T. Prevalence and associated factors of stunting, wasting and underweight of children below five using quintile regression analysis (PDHS 2017–2018). Scientific Reports. 2022 Nov; 12(1): 20326. doi: 10.1186/s12912-022-01168-7.

[16] Nin VM, Willmund GD, Jungmann SM, Asmundson GJ, Piefke M. Mental health during the COVID-19 pandemic: Stress and strain profiles in the German population. Frontiers in Public Health. 2023 Apr; 11: 990407. doi: 10.3389/fpubh.2023.990407.

[17] Gentil L, Grenier G, Fleury MJ. Profiles of quality of life among residents in permanent supportive housing during the COVID-19 pandemic. Journal of Social Distress and Homelessness. 2023 Oct 19:1-1. doi: 10.3390/healthcare11111641.

[18] Zhang Y, Wei L, Li H, Pan Y, Wang J, Li Q, et al, The Psychological change process of frontline nurses caring for patients with COVID-19 during its outbreak. Issues in mental health nursing. 2020 Jun 2;41(6):525-30. doi: 10.1080/01612840.2020.1752865.

[19] Rashidi R, Anbari K, Mohammadi R. Factors Affecting the Level of Nurses' Quality of Life in Khorramabad (IRAN) Teaching Hospital during the COVID-19 Epidemic, in 2020. Journal of Occupational Health and Epidemiology. 2022 Aug 30. Last cited 18th Nov 2023. Available at: http://eprints.lums.ac.ir/3908/.

[20] Zheng R, Zhou Y, Fu Y, Xiang Q, Cheng F, Chen H, et al., Prevalence and associated factors of depression and anxiety among nurses during the outbreak of COVID-19 in China: A cross-sectional study. International journal of nursing studies. 2021 Feb; 114: 103809. doi: 10.1016/j.ijnurstu.2020.103809.

[21] Nadeem F, Sadiq A, Raziq A, Iqbal Q, Haider S, Saleem F, et al., Depression, anxiety, and stress among nurses during the COVID-19 wave III: Results of a cross-sectional assessment. Journal of Multidisciplinary Healthcare. 2021 Nov: 3093-101. doi: 10.2147/JMDH.S338104

[22] Bruyneel A, Smith P, Tack J, Pirson M. Prevalence of burnout risk and factors associated with burnout risk among ICU nurses during the COVID-19 outbreak in French speaking Belgium. Intensive and Critical Care Nursing. 2021 Aug; 65: 103059. doi: 10.1016/j.iccn.2021.103059.

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Comparison of Dietary Modifications with and without Aerobic Exercises in Improving the Cholesterol Lipid Profile for Treatment of Hyperlipidemia-Naïve Patients

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ARTICLE INFO

Key Words:
Aerobic Exercise Training, Dietary Restriction, Hyperlipidemia-Naïve, cardiovascular disease

How to Cite:
Nazar, Q.- ul- ain, Hamid, F., Javed, A., Ilyas, Z. bin, Nawazish, S., Aleem, M. I., Mubashir, U., & Muhammad Arsalan, H. R. (2023). Comparison of Dietary Modifications with and without Aerobic Exercises in Improving the Cholesterol Lipid Profile for Treatment of Hyperlipidemia-Naïve Patients: Comparison of Dietary Modifications. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1090

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Received Date: 3rd October, 2023
Acceptance Date: 23rd November, 2023
Published Date: 30th November, 2023

ABSTRACT

Hyperlipidemia describes a condition in which an abnormal mass metabolism brought on by a variety of factors raises blood cholesterol levels. According to epidemiological research, there is a strong link between the lipoprotein profile and cardiovascular morbidity and mortality, and those who are physically active have a 30 to 50% lower chance of developing cardiovascular disease. **Objective:** To compare the effect of dietary modifications with and without aerobic exercises in improving the cholesterol lipid profile for treatment of Hyperlipidemia-Naïve patients. **Methods:** The random sampling technique with random allocation done through the Lottery method. Lipid Profile Test was used as measuring tool. Whole procedure went through three steps: Pre-Labs Testing, 10 - Weeks Intervention Sessions, and Post-Labs Testing. 24 patients were randomly divided into two groups i.e., Experimental Group and the Control Group, each with 12 patients. After the intervention plan, results were analyzed, organized and interpreted. **Results:** Normally distributed variables were HDL-C, Cholesterol and VLDL-C with $p > 0.05$. Whereas, Triglycerides and LDL-C were not distributed normally i.e., $p < 0.05$. After the exercise program accomplished as instructed, a statistically significant decrease was observed in the values of Cholesterol, HDL-C, and VLDL-C with the value of $p < 0.05$ for experimental group. However, values of Triglycerides and LDL-C were significantly decreased for the control group. **Conclusions:** The inclusion of aerobic exercises along with dietary changes substantially enhanced the patient's lipid profile, and exercise program's scope was adequate to produce meaningful changes in the body lipid composition of the study volunteers.

INTRODUCTION

Hyperlipidemia describes a condition in which an abnormal mass metabolism brought on by a variety of factors raises blood cholesterol or triglyceride levels [1]. This disorder can occur from food, tobacco use, or genetics, and it can cause serious problems like cardiovascular disease [2, 3]. Hyperlipidemia is one of the cardiovascular risk factors that makes up the metabolic syndrome, and people who have it frequently experience CVS morbidity and death [4]. It is marked by metabolic conditions that alter the amount of circulating lipids [5]. "Low density lipoprotein (LDL) and high-density lipoprotein (HDL) levels are low, and there are high levels of total cholesterol, triglycerides, LDL, and HDL in these anomalies." It has the potential to lead to cerebrovascular disorders like ischemic heart disease and stroke as well as atherosclerotic cardiovascular disease, which affects the arteries in the heart and blood vessels of the body [6-8]. Additionally, hyperlipidemia can harm the blood-brain barrier, which can seriously harm the brain's structures and functioning and impair "hippocampal-dependent learning and memory [1]." Because hyperlipidemia is a serious health problem in today's society, aerobic exercise has become one of the most popular ways to help patients with newly discovered cholesterol problems increase their levels of "serum high density lipoprotein cholesterol (HDL-C)" [9]. Measurements of the fat max intensity of body

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

composition, "glycemic control, lipid profile, and physical ability in young and elder population" will be made with the aid of aerobic exercise training under predetermined conditions [10]. According to studies, hyperlipidemia is one of the key causes that harms the well-being of this population and is more likely to occur in middle-aged and older persons [11]. The term "Lipid Profile" refers to the various levels of lipids in the blood, with "low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides" being the most frequently reported ones [12]. Aerobic exercise has been utilized as one of the standard treatments for raising levels of "serum high density lipoprotein cholesterol (HDL-C)" in patients with newly identified cholesterol difficulties because hyperlipidemia is a significant health problem in today's society [10] . Any physical activity that results in an elevated heart rate and respiratory volume to meet the oxygen demands of the active muscle is referred to as aerobic exercise [13]. According to epidemiological research, there is a strong link between the "lipoprotein profile and cardiovascular morbidity and mortality, and those who are physically active have a 30 to 50% lower chance of developing cardiovascular disease or type 2 diabetes" than people who are sedentary [14]. A balanced diet and a regimen of light physical activity are thought to be essential and helpful for preventing hyperlipidemia and controlling it once it develops. According to reports, regular exercise also lowers the risk of "coronary heart disease" [5]. Additionally, compared to "LDL-C and TG, HDLC levels" have been observed to be more responsive to aerobic activity. But it's important to fully comprehend how different forms of exercise activities, as well as their degree of difficulty, length, and the rate, affect obesity and hyperlipidemia [15]. Vegetable lipids, dietary fiber, and phytonutrients like "phytosterols are specific macro- and micro-components of a diet high in plants. The effects of these ingredients on lowering blood lipids, specifically low-density lipoprotein cholesterol (LDL-C)," and on lowering the risk of cardiovascular disease were described in this review [3]. Clinical intervention trials in recent years have shown that appropriate lifestyle changes in most patients with hyperlipidemia can have a similar therapeutic effect to that of lipid-lowering drugs, and can effectively reduce the occurrence of cardiovascular events while effectively controlling blood lipids [11].

To compare the effects of Dietary Modifications with and without Aerobic Exercises in Improving the Cholesterol Lipid Profile for Treatment of Hyperlipidemia-Naïve Patients.

METHODS

The study design used for this study was randomized clinical trial. The data were collected from the Gyms, Minhaj-ul-Quran Laboratory, and offices with In-House Training Area, Avicenna Hospital and Different Training Institutes of Lahore. The study was conducted under the period of six months. Its starts from 1st January 2022 to 31st June 2022.The total sample size of this study was 24 by using EPI tool. Out of which, 12 allotted in the Group-A which is Experimental Group. Similarly, the remaining 12 allotted to Group-B, which is Control Group. The sample size was calculated by comparing the two means for the values of oil class from the literature by using EPI Tool [16]. The sampling technique used for this research study is Simple Random Sampling Technique. Moreover, the Random Allocating was done through the Lottery Method. Participants had to be able to briskly walk without help, be inclusive of both genders, not have any vision or hearing issues, and agree to be accessible for follow-ups in order to meet the study's inclusion requirements [11]. The study's exclusion criteria encompassed individuals meeting certain conditions, including those currently using lipid-lowering drugs, individuals with a history of diabetes, cardiovascular patients, pregnant females, individuals with musculoskeletal disorders affecting large muscle groups, and those experiencing hypertension or balance problems [5, 11, 17] The entire procedure consisted of three fundamental steps: Pre-Labs Testing, a 10-Week Intervention Session, and Post-Labs Testing. A total of 26 patients were randomly assigned to either the Experimental Group or the Control Group, each comprising 13 patients. The Experimental Group adhered to dietary restrictions coupled with aerobic exercise, while the Control Group followed dietary restrictions alone. For the Experimental Group, the 10-Week Aerobic Exercise Plan included specific activities during each phase. In Weeks 1-3, participants engaged in aerobic exercise four days a week, involving warm-up, on-spot jogging, basic stretches, and a 15-20 minutes walk to achieve a sub-maximal heart rate (40-60% of Max. HR). Weeks 4-6 maintained the same frequency with an increased duration of on-spot jogging and additional 5-10 minutes of jogging. In Weeks 7-10, the aerobic exercise regimen intensified, including 10-15 minutes of on-spot jogging, extended walk and jogging durations, and the incorporation of brisk walking for 5-10 minutes. Both groups followed the same dietary modification plan.

Diet Plan

The Dietary Restriction Plan/Chart was followed by both the groups during the procedure. This plan was provided by Dr. Sameera Mustafa who is working as an Assistant Professor at University of South Asia, Lahore Cantt and a registered clinical dietician. Below provided chart was followed by the control group.

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

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Table 1: Table 1: Diet plan

Days	Breakfast	Mid-morning	Lunch	Evening Snack	Dinner
Monday	Omelet \ egg (1) vegetable ½ Chapati (1) 6inches Low fat milk (1 c)	Fruit any one	Salad (1 bowl) Roti (2) Dal (1 bowl thin)	Nuts (almonds 6-7)	Steamed/ Sautéed vegetable Salad (1 bowl) Roti (1) Dal (1 bowl thin)
Tuesday	Porridge (oats) (1/2 + 1/2c low fat milk) 6-7 almonds/ fruit	Bean salad 1 bowl	Salad (1 bowl) Roti (2) Chicken Curry (1 bowl Thin 1oz chicken piece)	Shami Kabab	Chicken soup (1 bowl) Salad (1 bowl) Roti (1) Chicken Curry (1 bowl thin 1oz chicken piece)
Wednesday	Shami Kabab 2 Brown Bread Slices 2	Corn on cob	Multigrain roti (1) Palak (1 bowl) + Egg/Paneer (1 bowl), 500 gm of steam chicken	Chana Chaat (1 bowl)	Vegetables (2), Red beans (1 bowl) with 1 chapati. 500 gm of steam chicken
Thursday	Omelet \egg (1) vegetable ½ Chapati (1) 6 inches. Low fat milk (1 c)	Pop-corn	Salad bowl (white beans, nuts, cucumber + Vegetables + Beans) (1 big bowl)	Fruits	Rice (1 small bowl) + Dal (1 bowl) + Raita (1 bowl)
Friday	Porridge (oats) (1/2 + 1/2c low fat milk) 6-7 almonds /fruit	2 plain cookies	Rice (1 bowl) * Mix vegetable stir fn,1 (1 bowl) + Beans/Egg/ Chicken (1 bowl)	Pop-corn	Salad (1 bowl) + Soup (1 bowl) * Grilled chicken /fish/paneer (1 bowl)
Saturday	Scrambled egg whites (2) with Chapati (1) Low fat paneer roll (1)		Phulka (2) + Musli ½ cup Cabbage (1 bowl) + Paneer/Dal + Curd (1 bowl)	Plain Rusk/ Cookies	500 gm of steam chicken

The research data were gathered through a questionnaire distributed across various gyms, call centers with in-house training areas, and training institutes in Lahore, targeting young adults as the population of interest. Every participant provided informed consent, and those meeting the inclusion criteria underwent a simple questionnaire covering demographic details (name, age, height, BMI, gender, etc.). Pre-lab testing was conducted to allocate participants to their respective groups, and there was no blinding of the participants. Randomization occurred using the Lottery Method. Adherence to diet modifications was monitored through documentation charts provided to all participants, enabling them to record their dietary choices. Heart rate measurements were taken using a pulse oximeter. After the complete intervention period, post-lab testing for the lipid profile of the patients was carried out.

Lipid Profile Test

Following steps were taken to complete this test:

Get informed Consent from the patient.

Have the Blood-Samples taken for Lipid Profile Test.

Availability of required services.

Variables	Normal Range
Triglycerides	80-150 mg/dl
Cholesterol	Up to 200 mg/dl
HDL-C	35-55 mg/dl
LDL-C	100-140 mg/dl
VLDL-C	10-30 mg/dl

Data were analyzed using Statistical package for social sciences a windows software SPSS, version 25.0.

RESULTS

In this study, 50 participants were tested. Participants that fulfilled inclusion criteria were 32. Out of which, 6 participants excluded themselves from the study. Out of the remaining participants, two did not show up for pre-lab testing and 2 of the participants withdrew in between the study. Data was entered in the software SPSS version 25 was used for analysis. Frequency table, graphs and charts measured descriptive categorical data. Table 2 shows that the mean and standard deviation of 24 participants is 27.13±2.70 years. The mean and standard deviation of weight of total number (24) of participants is 74.46±8.96 kg. Moreover, same for the height of total number of participants is 5.64±0.31 feet.

Table 2: Distribution of Age, Weight, & Height

Variables	Mean±S.D
Age	27.13±2.692
Weight	74.46±8.964
Height	5.6467±0.31332

Out of 24 participants, frequency of males was 20 with 83.3% and frequency of females were 4 with 16.7%. Descriptive statics showed frequency of smokers was 13(54.2%), frequency of married participants was 9(37.3%), frequency of normally weighted participants was 14(58.3%), frequency of participants getting sleep less than 8 hours was 12(50%) and frequency of participants belonging to middle class socioeconomic status were 23(95.8%) as shown in table 3. Table shows that there were 20 (83.3%) male participants and 4 (16.7) female participants and 11 participants were non-smokers and 13 participants were smokers. Moreover, out of a total of 24 participants 1(4.2%) was under weight (<18), 14(58.3%) were normal (18.5-22.9), 5 (20.3%) were overweight (23-24.9), 3 (12.5%) were obese 1 (25-29.9) and 1 (4.2%) was obese 2(>30). It was noted that 9 participants were married and 15

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

participants were unmarried and out of these participants, 23 belonged to middle class background and 1 of lower class. On the other hand, 12 participant's sleep duration was less than 8 hours and 12 participant's sleep duration was more than 8 hours. Out of all the participants, 12 participant's sleep duration was less than 8 hours and 12 participant's sleep duration was more than 8 hours with having an education level i.e., 4 participants were of matriculation, 3 participants were of intermediate, 6 participants were of under-graduate programs and 11 participants were of graduate programs Table 3.

Table 3: Distribution of Gender, Marital Status, BMI, Smoking Status, Education, Socioeconomic Status, and Sleep Duration

Variable	Category	Exercise + Dietary Modification (Group A)	Dietary Modification (Group B)	Total
Gender	Male	11	9	20
	Female	0	4	4
Marital Status	Married	2	7	9
	Unmarried	9	6	15
BMI	Underweight	1	0	1
	Normal Weight	7	7	14
	Overweight	2	3	5
	Obese 1	1	2	3
	Obese 2	0	1	1
Smoker	Yes	8	5	13
	No	3	8	11
Education	Matriculation	1	3	4
	Intermediate	1	2	3
	Undergraduate	4	2	6
	Graduate	5	6	11
Socioeconomic Status	Upper Class	0	0	0
	Middle Class	10	13	23
	Lower Class	1	0	1
Sleep Duration	< 8 hours	5	7	12
	> 8 hours	6	6	12

Between group comparison for normally distributed variables

Normally distributed variables were HDL-C, Cholesterol and VLDL-C with p > 0.05. Whereas, Triglycerides and LDL-C were not distributed normally i.e., p < 0.05. "After the exercise program accomplished as instructed, a statistically significant decrease" was observed in the values of Cholesterol, HDL-C, and VLDL-C with the value of p <0.05 for experimental group. However, values of Triglycerides and LDL-C were significantly decreased for the control group. "After the exercise program accomplished as instructed, a statistically significant decrease was detected in the values of Cholesterol with the value of p <0.000 for experimental group and that for control group was p <0.001, and HDL-C (p <0.033) for experimental group and (p <0.786) values of the control group showing no significant change in it," while no significant change was observed for VLDL-C values (p> 0.05) for the control group and for experimental group (p <0.01). The table Independent T test summarized the comparison of variables which are Cholesterol, HDH-C, and VLDL-C across both groups as shown in table 4.

Table 4: Between group comparison for normally distributed variables

Variables	Groups	Mean±SD	p-Value
Cholesterol Post-Test Lab Values	Experimental Group	187.91±15.706	0.239
	Control Group	174.77±34.965	
HDL(Cholesterol) Post-Test Lab Values	Experimental Group	35.27±5.274	0.278
	Control Group	41.08±5.235	
VLDL Post-Test Lab Values	Experimental Group	31.18±4.045	0.261
	Control Group	28.38±7.534	

Within group comparison for normally distributed variable

This table summarized the comparison of variables which are Cholesterol, HDH-C, and VLDL-C across both groups. Independent Sample T-test was applied as a parametric test which showed significant distribution for the above three variables.

"Normality of data was tested by Shapiro-Wilk test, it showed that data was normally distributed (p >0.05)." Independent Sample T-test was applied as a parametric test which showed significant distribution for the above three variables. Comparison of the normally distributed variables at pre-treatment and post- treatment level in between groups was done by using paired t test. Parametric Independent sample t test was applied to compare between group analysis on outcome variable. The comparison of variables which are Triglycerides and LDL-C across both groups was done through the non-parametric test as these values were not distributed significantly as shown in table 5. Paired t test was applied to compare between group analysis on outcome variable. Comparison of the normally distributed variables at pre-treatment and post- treatment level in between groups was done by using paired t test.

Table 5: Within group comparison for normally distributed variable

Groups	Variables	Mean±SD	p-Value
Experimental Group	Cholesterol (Pre / Post - Test Lab Values)	16.545±10.634	0.000
Control Group		25.231±21.378	0.001
Experimental Group	HDL-C (Pre / Post - Test Lab Values)	-2±2.683	0.033
Control Group		0.154±1.994	0.786
Experimental Group	VLDL-C (Pre / Post - Test Lab Values)	1.091±1.136	0.010
Control Group		-0.385±7.03	0.847

Between group comparisons for variables which are not normally distribute

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

Table 6 summarized the between group comparison of variables which are Triglycerides and LDL-C across both groups. Mann-Whitney test was applied as these values were not distributed significantly.

Table 6: Mann-Whitney Test

Variable	Groups	Median (IQ)	p value
Triglycerides Post-Test Lab Values	Experimental Group	166.5 (26)	0.542
	Control Group		
LDL-C Post-Test Lab Values	Experimental Group	160.5 (16.25)	0.622
	Control Group		

Within group comparison for variables which are not normally distributed:

Wilcoxon Test was applied to compare the within group, post treatment plan lab values across the groups for the above-mentioned two variables Table 7.

Table 7: Wilcoxon Test

Groups	Variable	p value
Experimental group	Triglycerides (Post / Pre -Test Lab Values)	0.003
Control group		0.001
Experimental group	LDL(Cholesterol) (Post / Pre -Test Lab Values)	0.004
Control group		0.000

DISCUSSION

As per the results calculated in the study accomplished, significant results were calculated for the experimental group for the values of HDL-C, VLDL-C and Cholesterol with the value of p <0.05. However, the control group did not show much significant changes. However, in the past study in 2021 calculated that no significant changes were represented for the experimental group following the exercise plan [10]. This study demonstrated significant results were calculated for the experimental group for the values of HDL-C, VLDL-C and Cholesterol with the value of p <0.05. "After the exercise program accomplished as instructed, a statistically significant decrease was detected in the values of Cholesterol" with the value of p <0.000 for experimental group and that for control group was p <0.001, and HDL-C (p <0.033) for experimental group and (p <0.786) values of the control group showing no significant change in it, while no significant change was observed for VLDL-C values (p> 0.05) for the control group and for experimental group (p <0.01). On the other hand, in a study, 2012 results achieved "statistically significant exercise minus control group decrease in non-HDL-C was found for DE (7 ESs, 389 participants, x = −11.1 mg/dL, 95% CI = −21.7 to −0.6, P = 0.04, Q = 2.4, P = 0.88, I2 = 0%), a trend for the D group (7 ESs, 402 participants, x = −8.5 mg/dL, 95% CI = −18.6 to 1.6, P = 0.10, Q = 0.76, P = 0.99, I2 = 0%), and no change for the Exercise group (7 ESs, 387 participants, x = 3.0 mg/dL, 95% CI = −7.1 to 13.1, P = 0.56, Q = 0.78, P = 0.99, I2 = 0%). Overall, there was no statistically significant between-group differences were found (Qb = 4.1, P = 0.12). The present study results showed a significant decrease of Cholesterol to High Density Lipoprotein Ration (Chl/HDL)" [18]. This study has shown that changes were significant for the control group regarding the values for Triglycerides and LDLs, both having the p value of less than 0.05. But significant changes for HDLs, Total Cholesterol and VLDLs were demonstrated in the experimental group following the exercise plan along with the modified dietary plan and representing the value of all having p <0.05. On the other hand, in a past study, it was found that dietary modifications were accepted for accomplishing significant changes for the values of total cholesterol and not for Triglycerides and LDLs having p <0.05 without changes on HDLs and VLDLs [19]. Our study showed that regular exercises had significantly high effects on the levels of total cholesterol, LDL-C and HDL-C with a representation of a significant value of p <0.05. However, in a previous study completed in 2007, it was showed that the aerobic exercises had significant changes on HDL-C levels and aerobic exercise increases HDL-C level when performed regularly. It was noted that a minimum volume of exercise is capable of achieving a significant increase in HDL-C level. However, the most important element to have this change determined was considered to be exercise duration per session of an exercise prescription. Interestingly, it was found in the same study that people with high baseline total "cholesterol levels, low BMIs, or patients who were younger had the best changes in HDL-C levels" [13]. According to the findings of our study, there was a significant difference between the levels of HDL-C before and after the intervention plan, with a value of p 0.05, and the same was true for the levels of total cholesterol and very low-density lipoproteins. However, the changes for the pre and post values for the levels of triglycerides and low-density lipoproteins were not highly significant for the experimental groups. However, a 1998 study found that the therapy group did not experience any appreciable increases in "HDL cholesterol and triglyceride" levels. However, with a value of p 0.05, the serum level of "LDL cholesterol" was dramatically decreased [20].

CONCLUSIONS

The integration of aerobic exercises along with dietary changes substantially enhanced the patient's lipid profile, and it was observed that the physical activity program's scope was adequate to produce meaningful changes in the body lipid composition of the study volunteers.

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

Authors Contribution

Conceptualization: QZ
Methodology: QZ, AJ, ZBI
Formal analysis: SN, MIA, UM
Writing, review and editing: FH, AJ, HRMA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article

REFERENCES

[1] Zhao S, Zhong J, Sun C, Zhang J. Effects of aerobic exercise on TC, HDL-C, LDL-C and TG in patients with hyperlipidemia: A protocol of systematic review and meta-analysis. Medicine. 2021 Mar; 100(10): 25103. doi: 10.1097/MD.0000000000025103.

[2] Varady KA and Jones PJ. Combination diet and exercise interventions for the treatment of dyslipidemia: An effective preliminary strategy to lower cholesterol levels? The Journal of Nutrition. 2005 Aug; 135(8): 1829-35. doi: 10.1093/jn/135.8.1829.

[3] Mann S, Beedie C, Jimenez A. Differential effects of aerobic exercise, resistance training and combined exercise modalities on cholesterol and the lipid profile: review, synthesis and recommendations. Sports Medicine. 2014 Feb; 44: 211-21. doi:10.1007/s40279-013-0110-5.

[4] Yoshida H, Ishikawa T, Suto M, Kurosawa H, Hirowatari Y, Ito K, et al., Effects of supervised aerobic exercise training on serum adiponectin and parameters of lipid and glucose metabolism in subjects with moderate dyslipidemia. Journal of Atherosclerosis and Thrombosis. 2010; 17(11): 1160-6. doi: 10.5551/jat.4358.

[5] Costa RR, Buttelli AC, Coconcelli L, Pereira LF, Vieira AF, Fagundes AD, et al., Water-based aerobic and resistance training as a treatment to improve the lipid profile of women with dyslipidemia: a randomized controlled trial. Journal of Physical Activity and Health. 2019 May; 16(5): 348-54. doi: 10.1123/jpah.2018-0602.

[6] Yang L, Li Z, Song Y, Liu Y, Zhao H, Liu Y, et al., Study on urine metabolic profiling and pathogenesis of hyperlipidemia. Clinica Chimica Acta. 2019 Aug; 495: 365-73. doi: 10.1016/j.cca.2019.05.001.

[7] Su X, Peng H, Chen X, Wu X, Wang B. Hyperlipidemia and hypothyroidism. Clinica Chimica Acta. 2022 Feb; 527: 61-70. doi: 10.1016/j.cca.2022.01.006.

[8] El-Tantawy WH and Temraz A. Natural products for controlling hyperlipidemia. Archives of Physiology and Biochemistry. 2019 Mar; 125(2): 128-35. doi: 10.1080/13813455.2018.1441315.

[9] Mosteoru S, Gaiţă L, Gaiţă D. Sport as Medicine for Dyslipidemia (and Other Risk Factors). Current Atherosclerosis Reports. 2023 Sep; 25(9): 613-7. doi: 10.1007/s11883-023-01133-y.

[10] Hazar K, Polat M, Hazar S, Akyüz T. Effects of Eight-Week Moderate Intensity Aerobic Exercises on Dyslipidemia and Body Composition for Overweight and Obese First-Degree Females. Pakistan Journal of Medical & Health Sciences. 2021; 15(4): 1592-608.

[11] Ngayimbesha A, Bizimana JB, Gakima MS. Effect of eight weeks of exercise training on lipid profile and insulin sensitivity in obese person. International Jornals of Sports Exercise and Medicine. 2019; 5(2): 119-25. doi: 10.23937/2469-5718/1510119.

[12] Doewes RI, Gharibian G, Zaman BA, Akhavan-Sigari R. An updated systematic review on the effects of aerobic exercise on human blood lipid profile. Current Problems in Cardiology. 2023 May; 48(5): 101108. doi: 10.1016/j.cpcardiol.2022.101108.

[13] Kodama S, Tanaka S, Saito K, Shu M, Sone Y, Onitake F, et al., Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Archives of Internal Medicine. 2007 May; 167(10): 999-1008. doi: 10.1001/archinte.167.10.999.

[14] Tay J, Zajac IT, Thompson CH, Luscombe-Marsh ND, Danthiir V, Noakes M, et al., A randomised-controlled trial of the effects of very low-carbohydrate and high-carbohydrate diets on cognitive performance in patients with type 2 diabetes. British Journal of Nutrition. 2016 Nov; 116(10): 1745-53. doi: 10.1017/S0007114516004001.

[15] Iughetti L, Bruzzi P, Predieri B. Evaluation and management of hyperlipidemia in children and adolescents. Current opinion in pediatrics. 2010 Aug; 22(4): 485-93. doi: 10.1097/MOP.0b013e32833ab869.

[16] Luo Q, Jin P, Li H, Cui K, Jiang T. Effects of integrated health education combined with life intervention on patients with coronary atherosclerotic heart disease complicated with hyperlipidemia. American Journal of Health Behavior. 2021 Sep; 45(5): 843-8. doi: 10.5993/AJHB.45.5.4.

[17] Butt NF, Rathore R, Latif H. Effect of atorvastatin on hematological parameters in patients with dyslipidemias. Hypertension. 2018 Jul; 12(3): 1287-90 .

[18] Evans EM, Saunders MJ, Spano MA, Arngrimsson SA, Lewis RD, Cureton KJ. Body-composition changes

DOI: https://doi.org/10.54393/pjhs.v4i11.1090

with diet and exercise in obese women: a comparison of estimates from clinical methods and a 4-component model. The American Journal of Clinical Nutrition. 1999 Jul; 70(1): 5-12. doi: 10.1093/ajcn/70.1.5.

[19] Abdelbasset WK, Nambi G, Alsubaie SF, Elsayed SH, Eid MM, Soliman GS, et al., A Low-Fat Diet Combined with Moderate-Intensity Aerobic Exercise is More Effective than a Low-Fat Diet or Aerobic Exercise Alone on Dyslipidemia and Depression Status in Obese Patients: A Randomized Controlled Trial. Endocrine, Metabolic & Immune Disorders-Drug Targets. 2021 Dec; 21(12): 2289-95. doi: 10.2174/1871530321666210406161226.

[20] Stefanick ML, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. New England Journal of Medicine. 1998 Jul; 339(1): 12-20. doi: 10.1056/NEJM199807023390103.

DOI: https://doi.org/10.54393/pjhs.v4i11.1176

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Adulteration: Supply of Raw Milk and Prevalence of Adulterated / Prepared Milk

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ARTICLE INFO

Key Words:
Raw Milk, Milk Quality, Adulterants, Semi Synthetic Milk

How to Cite:
Ibrahim, T., Wattoo, F. H., Sarwar Wattoo, . M. H., & Mustafa, G. (2023). Adulteration: Supply of Raw Milk and Prevalence of Adulterated / Prepared Milk : Adulteration of Milk. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1176

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Received Date: 6th November, 2023
Acceptance Date: 26th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Raw milk adulteration is one of the food fraud to gain financial benefits by removing fat and cream from whole milk and compensating it by addition of different adulterants to make it near to wholesome milk. **Objectives:** To analyze milk adulterants to not only describe about the prevalence of different milk adulterants but also confirm the sources of adulterants being used for the synthesis of semi synthetic or prepared milk due to their characteristics which they impart to form a sort of wholesome milk. **Methods:** In this regard total of 190 raw milk samples from cow and buffalo sources along with control and in house standards were taken to detect most prevailing adulterants in raw milk samples through automated and/or titration based manual recommended methods. **Results:** The analysis of different adulterants in milk samples showed water in 148(77.89%) raw milk samples, Detergent in 62(32.9%), Cane Sugar 41(21.8%), Caustic Soda 32(16.8%), Sodium Salts 31(16.4%), Starch 21(11.1%), Formalin 18(9.4%), Urea 15(8.05%), Foreign Fat 12(6.4%), Hydrogen Peroxide 04(2.3%), Glucose 02(1.3%), Boric Acid 02(1.1%) and sulfate salts 02(1.1%) in raw milk samples. **Conclusions:** The assessment of quality of fresh milk showed poor quality milk with the provision of different sort of adulterants in 77.89% raw milk samples and alarming sign of semi synthetic milk in 2.63% samples.

INTRODUCTION

Raw milk / Fresh milk is the ideal as well as complete food for infants and children due to presence of all basic nutrients like protein, carbohydrates, fats, vitamins and minerals [1]. It is the normal, clean and pure secretion obtained from the udders of a healthy cow, buffalo, goat or sheep [2]. Milk composition is influenced through various factors like genetic/nutritional status of animals, environmental conditions and stage of lactation. An average milk composition comprises of water 87.00 %, lactose 4.00 % - 5.00 %, protein 3.00 %, lipids 3.00 % - 4.00 %, minerals 0.80 % and vitamins 0.10 % [3]. In Pakistan, there are more than 67.00 million cattle and buffaloes, 89.00 million sheep and goats and 0.20 million camels. Pakistan is blessed with high yielding genetic dairy animals such as Nilli / Ravi buffaloes, Sahiwal Cows, Kajli Sheep and Beetle Goat. Milk is produced throughout the year. However, milk production is extensively reduced during summer months due to heat stress and scarcity of fodder so milk is watered to increase volume. To maintain its composition, starch, flour, urea, cane sugar, vegetable oil etc. are added as chemical adulterants [4]. Adulterants are articles that are not of natural origin, substance, or quality but are claimed to be the part of foreign substance that may degrade the product's quality or which have been combined, coated, or treated with substances that are illegal or whose quality or purity does not meet the required criteria or anything that has a poisonous or otherwise harmful element to human's health [2]. The different sort of adulterants that manipulate the quality of milk are water, sodium carbonate, sodium bicarbonate, caustic soda, formalin, urea, detergents, ammonium sulphate, boric acid, benzoic acid, salicylic acid, hydrogen peroxide,

DOI: https://doi.org/10.54393/pjhs.v4i11.1176

starch, sugars, melamine, skimmed milk powder, reconstituted milk, rice flour, vegetable oil, animal fat and whey powder [5, 6]. Milk is adulterated for financial benefit or to overcome the gaps associated, conditions of sanitary processing, storage, transportation and marketing conditions [6]. Almost 93.00% samples from educational canteen show some of the adulterants like water, urea, formalin, hydrogen peroxide [7]. Water was found to be the most common adulterant in most of the milk samples in Pakistan, followed by detergent 25.00 %, rice flour 22.00 %, caustic soda 18.00 %, salt 17.00 % and cane sugar 14.00 % respectively [8]. Recent studies in Pakistan shows about 80.00 % of sold milk is adulterated [9]. Synthetic / Semi synthetic milk is a sort of adulterated milk contains vegetable oil as a source of milk fat, urea as a nitrogen component, and detergent to make it frothy with a desired specific gravity, which is then mixed with natural milk to create value added milk [10].

METHODS

A prospective study was conducted through collection of samples, sample processing, conducting stability study and analyzing different adulterants. In this context a total 190 numbers of raw milk samples were analyzed to know the presence of different adulterants. 126 out of 190 were collected along with control sample from various sources of milk suppliers like milk collector, milk man as milk distributor or milk retailer, middle man as dhodhie (common name) and end users. 64 samples were received from same sources at the reception of Nutrition Division, NIH. Control sample was self-collected fresh milk sample from healthy buffalo origin having lactation period from 2 – 4 months. Milk samples were collected through recommended method [11] through authorized agent free from infectious disease in the presence of concerned parties in a dry clean container, preserved in cold chain container (2 – 8°C) with proper labeling. A stability study was conducted to know the shelf life of collected fresh milk samples at 02-08°C for 0 to 5 days based upon the quantity and duration of utilization of fresh milk at domestic level. The fall in the concentration of certain important parameters after four days were very negligible like fat decreased from 5.0 % to 4.98 (0.40%), SNF decreased from 8.03% to 7.97% (0.65%) & total solid decreased from 13.03% to 12.95% (0.61%). It means that fresh milk samples remained stable for 04 days at 02-08°C [12]. 250 – 500 ml sample in the form of homogenous milk sample at 20°C through recommended method [13] before analysis. Urea was analyzed by reacting milk samples with p-Dimethyl Amino Benzaldehyde reagent. Appearance of distinct yellow color indicates presence of added urea. Starch was analyzed by adding a few drops of tincture of Iodine or Iodine solution. Formation of blue color indicates the presence of starch. Detergent was analyzed by reacting milk sample with bromocresol purple to get violet blue color in case of presence of detergent as adulterant. Formalin was analyzed by reacting with concentrated sulfuric acid from the sides of the wall without shaking. Appearance of violet or blue ring at the intersection of two layers indicated presence of formalin. Boric acid was analyzed by reacting milk samples with concentrated hydrochloric acid. This mixture converted a yellow strip (filter paper dipped in aqueous turmeric solution) into red strip and even green due to action of one drop of ammonia solution. Neutralizers include Sodium carbonate, Sodium bicarbonate was analyzed by reacting milk samples with rectified spirit and Rosalic acid. The appearance of red color indicated the presence of such compounds while sodium hydroxide was analyzed by alkalinity test. Sodium sulfate was analyzed by reacting milk sample with TCA and barium chloride solution as indicator and formulation of milky white precipitation. Potassium nitrate was analyzed by reacting milk sample with and diphenyl amine sulphate or diphenylbenzidine reagent for the formulation of blue color. Appearance of blue colour indicates the presence of nitrates. Pure milk sample will not develop any color. Hydrogen peroxide was analyzed by reacting milk samples with Vanadium Pentoxide reagent. The appearance of red color indicated Pink or red colour. Glucose gives deep blue color when reacted with modified Barfoed's reagent and heated until boiling, cool and added phosphomolybdic acid. Sucrose/ Sugar reacted with hydrochloric acid and resorcinol. The red coloration indicated the use of sugar in the milk. Sodium chloride was analyzed by reacting milk samples with Silver Nitrate reagent and Potassium Dichromate as indicator. The appearance of yellow color indicated presence of sodium chloride [14, 15]. Edible oil gives the butyro refractive index in the range of vegetable oil (> 43.5) instead of animal origin fat (40 – 43.5) [16, 17]. Milk powder was analyzed by reacting acetic acid treated milk samples with phosphomolybdic acid to get bluish precipitates for presence of milk powder as adulterant [18].

RESULTS

The analysis of 190 fresh milk samples with respect to different adulterants along with supporting physical & chemical quality parameters showed prevalence of water in 148(77.89%), Detergent in 62(32.9%), Cane Sugar 41(21.8%), Caustic Soda 32(16.8%), Sodium Salts 31(16.4%), Starch 21(11.1%), Formalin 18(9.4%), Urea 15(8.05%), Foreign Fat 12(6.4%), Hydrogen Peroxide 04(2.3%), Glucose 02(1.3%), Boric Acid 02(1.1%) and sulfate salts 02(1.1%) as depicted in Figure 1 given below.

DOI: https://doi.org/10.54393/pjhs.v4i11.1176

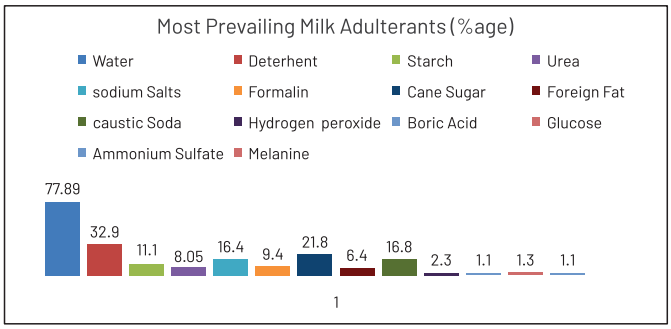

Figure 1: Prevalence of Milk Adulterants

Figure 2 showed an alarming sign of preparation of synthetic/semi synthetic milk, conversion of 01 liter of milk into 50 liters of milk through addition of water and compensatory adulterants to give them original like composition of fresh raw milk. The findings of synthetic milk in above depicted picture showed addition of water in 01 liter of milk followed by substandard milk powder, Detergent, Cane Sugar, Edible Oil, Formalin, Sodium bicarbonate. The identification of such practices have been made through analysis of butyro refractive index value (BR Value at 40°C) which is more than 43.5 in case of addition of foreign fat from plant sources. The prevalence of synthetic milk was 2.63%.

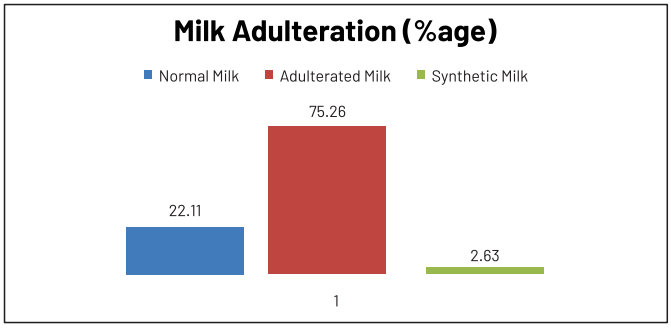

Figure 2: Prevalence of synthetic/semi synthetic Milk

As per Table 1, the analysis of 190 (100 %) fresh milk samples with respect to different adulterants along with supporting physical & chemical quality parameters showed the mean values as per prevalence of water with 0.779 (77.89 %), Detergent with 0.326 (32.90 %), Cane Sugar 0.216 (21.80 %), Caustic Soda 0.168 (16.80 %), Sodium Salts 0.163 (16.40 %), Starch 0.111 (11.10 %), Formalin 0.095 (9.40 %), Urea 0.079 (8.05 %), Foreign Fat 0.063 (6.40 %), Hydrogen Peroxide 0.021 (2.30 %), Glucose 0.011 (1.30 %), Boric Acid 0.011 (1.10 %) and sulfate salts 0.011 (1.10 %).

Table 1: Prevalence of adulterants-one-sample statistics

Parameters (Adulterants)	N (No of Samples)	Mean ± SD (Prevalence of adulterants)	Std. Error Mean
Water in Milk	190	0.779±0.416	0.0302
Detergent in Milk	190	0.326±0.470	0.0341
Starch in Milk	190	0.111±0.314	0.0228
Urea in Milk	190	0.079±0.270	0.0196
Cane Sugar in Milk	190	0.216±0.412	0.0299
Caustic Soda in Milk	190	0.168±0.375	0.0272
Sodium Salts in Milk	190	0.163±0.370	0.0269
Formalin in Milk	190	0.095±0.293	0.0213
Foreign Fat in Milk	190	0.063±0.243	0.0177
Hydrogen peroxide in Milk	190	0.021±0.143	0.0104
Glucose in Milk	190	0.011±0.102	0.0074
Boric Acid in Milk	190	0.011±0.102	0.0074
Sulfates in Milk	190	0.011±0.102	0.0074

DISCUSSION

Multiple studies have been conducted to know the prevalence of different adulterants in milk. To identify the changes in the milk quality which extremely suffer during summer months as described by [4] due to heat stress, scarcity of fodder. To compensate the scarcity of milk, it is unfortunately very easily adulterated and possible reasons behind it may include demand and supply gap, perishable nature of milk, low purchasing capability of customer and lack of suitable detection tests as stated by [1]. This is carried out either for financial gain by [6] or to increase their margin from the sale of milk through its dilution, extraction of valuable components like cream, fat and addition of cheap additives to balance the quality parameters of milk. In recent studies in Pakistan about 80 % of milk sold is adulterated [9]. Almost 93 % samples from educational canteen shows some of the adulterants like water, urea, formalin, hydrogen peroxide [7]. Adulterants in milk mainly include addition of vegetable protein, milk from different species, addition of whey and watering which are known as economically motivated adulteration [19]. Milk adulterants which have been identified in most of the studies are water or water with contaminants, sodium carbonate, sodium bicarbonate, caustic soda, formalin, urea, detergents, ammonium sulphate, boric acid, benzoic acid, salicylic acid, hydrogen peroxide, starch, sugars and melamine. In Pakistan water is the most common milk adulterant as 76.00 % followed by detergent 25.00 %, rice flour 22.00 %, caustic soda 18.00 %, salt 17.00 % and cane sugar 14.00 %. Unfortunately, milk is being very easily adulterated which may affect the quality and safety of milk. This situation is significantly worse in developing and underdeveloped countries due to the absence of adequate monitoring and lack of proper law enforcement system [8]. Milk is transported through a middle man called dhodhie. Such milk is watered to increase volume. To maintain its composition, starch, flour, urea, cane sugar, vegetable oil, etc., are added as chemical adulterants [4]. Synthetic or semi synthetic milk can be identified by reasons that it turns dark yellow in 3-6 hrs, more slippery in touch, bitter in

DOI: https://doi.org/10.54393/pjhs.v4i11.1176

frothy with targeted specific gravity then added in natural milk to form value added milk to get only substantial profit [10]. The analysis of different adulterants in milk samples showed such findings that helped in the discrimination of satisfactory and unsatisfactory milk samples through provided pure raw milk free from adulterants. These findings also supported the previous study of determining possibility of adulteration through physical and chemical quality parameters which showed adulteration possibility of around 76.6% [12].

CONCLUSIONS

The assessment of quality of fresh milk shows poor quality milk with the provision of different sort of adulterants (77.89%) and alarming sign of semi synthetic or prepared milk (2.63). The analysis of milk adulterants confirms the sources of adulterants being used for the synthesis of semi synthetic or prepared milk due to their characteristics which they impart to form a sort of wholesome milk.

Authors Contribution

Conceptualization: TI
Methodology: FHW
Formal analysis: MHSW
Writing-review and editing: GM, MHSW, FHW

All authors have read and agreed to the published version of the manuscript.

Acknowledgement

This study was supported by Nutrition Division of NIH and we are thankful to Chief Nutrition Division of NIH and Executive Director of NIH.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Kamthania M, Saxena J, Saxena K, Sharma DK. Milk Adultration: Methods of Detection &Remedial Measures. International Journal of Engineering and Technical Research. 2014 May; 1: 15-20.

[2] Punjab Food Authority Government of the Punjab. Punjab pure food regulations, 2018. 2018. [16th Nov 2023].Available at: https://food.punjab.gov.pk/system/files/16.%20Punjab%20Pure%20Food%20Regulations%2C%202018%20%28PPFR%2C%202018%29.pdf.

[3] Pereira PC. Milk nutritional composition and its role in human health. Nutrition. 2014 Jun; 30(6): 619-27. doi: 10.1016/j.nut.2013.10.011.

[4] Rabbani M and Chaudhry HR. Laboratory manual quality control of milk: quality control of milk. Amazon; 2015.

[5] Sharma R and Rajput YS. Detection of Adulterants in milk A Laboratory Manual. NDRI Publication; 2012.

[6] Handford CE, Campbell K, Elliott CT. Impacts of milk fraud on food safety and nutrition with special emphasis on developing countries. Comprehensive Reviews in Food Science and Food Safety. 2016 Jan; 15(1): 130-42. doi: 10.1111/1541-4337.12181.

[7] Faraz A, Lateef M, Mustafa MI, Akhtar P, Yaqoob M, Rehman S. Detection of adulteration, chemical composition and hygienic status of milk supplied to various canteens of educational institutes and public places in Faisalabad. Journal of Animal and Plant Sciences. 2013 Jan; 23(Suppl 1): 119-24.

[8] Barham GS, Khaskheli M, Soomro AH, Nizamani ZA. Extent of extraneous water and detection of various adulterants in market milk at Mirpurkhas, Pakistan. IOSR Journal of Agriculture and Veterinary Science. 2014 Apr; 7(3): 83-9. doi: 10.9790/2380-07318389.

[9] Akhtar S. Food safety challenges—a Pakistan's perspective. Critical Reviews in Food Science and Nutrition. 2015 Jan; 55(2): 219-26. doi: 10.1080/10408398.2011.650801.

[10] Mudgil D and Barak S. Synthetic milk: a threat to Indian dairy industry. Carpathian Journal of Food Science Technology. 2013 Jan; 5(1-2): 64-8.

[11] Cunniff P and Association of Official Analytical Chemists. Official methods of analysis of AOAC international. Association of Official Analytical Chemists; 1995.

[12] Ibrahim T, Wattoo FH, Wattoo MH, Hamid S. Assessment of Fresh Milk Quality through Quality Parameters. Pakistan Journal of Health Sciences. 2023 Oct; 4(10): 21-5. doi: 10.54393/pjhs.v4i10.871.

[13] AOAC. International, Official methods of analysis. 16th ed. Vol. II, Dairy Products. Gaithersburg, MD: Association of Official Analytical Chemists. Methods 925.21; 1995.

[14] Azad T and Ahmed S. Common milk adulteration and their detection techniques. International Journal of Food Contamination. 2016 Dec; 3(1): 1-9. doi: 10.1186/s40550-016-0045-3.

[15] AOAC. International, Official methods of analysis. 16th ed. Vol. II, Dairy Products. Gaithersburg, MD: Association of Official Analytical Chemists. Methods 930.28; 1995.

[16] AOAC. International, Official methods of analysis. 16th ed. Vol. II, Dairy Products. Gaithersburg, MD: Association of Official Analytical Chemists. Methods 925.23; 1995.

[17] AOAC. International, Official methods of analysis. 17th ed. Vol. II, Dairy Products. Gaithersburg, MD:

DOI: https://doi.org/10.54393/pjhs.v4i11.1176

Association of Official Analytical Chemists. Methods 905.02; 2000.

[18] Singh P and Gandhi N. Milk preservatives and adulterants: processing, regulatory and safety issues. Food Reviews International. 2015 Jul; 31(3): 236-61. doi: 10.1080/87559129.2014.994818.

[19] Fischer WJ, Schilter B, Tritscher AM, Stadler RH. Contaminants of milk and dairy products: contamination resulting from farm and dairy practices. Encyclopedia of Dairy Sciences. 2011 Jan; 2: 887-97. doi: 10.1016/B978-0-12-374407-4.00104-7.

[20] Bhatt SR, Singh A, Bhatt SM. Assessment of synthetic milk exposure to children of selected population in Uttar Pradesh, India. Indian Journal of Medical Research. 2008; 7: 22-34.

DOI: https://doi.org/10.54393/pjhs.v4i11.825

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Gel Formulation and an In-vitro Kinetic Permeation Release Study of Cefixime Trihydrate and Chlorpheniramine Maleate (CCM)

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ARTICLE INFO

Key Words:
Cefixime Trihydrate, Chlorphenaramine Mleate, CCM Gels, Permeation Parameters

How to Cite:
Rafique, S., Sattar, F., Habib, A., Babar, S., Qader, A., Davis, M., Javed`, S., Ibrahim Khan, M. U., Haris, M., Tariq, H., & Afnan, . (2023). Gel Formulation and an In-vitro Kinetic Permeation Release Study of Cefixime Trihydrate and Chlorpheniramine Maleate (CCM): Cefixime Trihydrate and Chlorpheniramine Maleate (CCM). Pakistan Journal of Health Sciences, 4(11), 109–114. https://doi.org/10.54393/pjhs.v4i11.825

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Received Date: 4th June, 2023
Acceptance Date: 29th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Cefixime is an antibiotic drug used to treat infection. Chlorphenamine, also known as chlorpheniramine, is an antihistamine and used to treat allergic diseases such urticarial infections and rhinitis **Objective:** To formulate a gel by using propylene glycol (PG) along with Polyethylene glycol (PEG) in order to enhance the percutaneous absorption and release of cefixime trihydrate and chlorpheniramine maleate from TDDS (transdermal drug delivery system). **Methods:** Various formulations (G1 to G13) containing cefixime trihydrate and chlorpheniramine maleate gels (CCM gels) were prepared for this purpose with PG and PEG in different ratios. Firstly, gel optimization was estimated from the physical properties of the gels. Later, the diffusion process was carried out through Franz diffusion cells to find out the permeation kinetic parameters of these gel formulations. Only two of the gels (G1 and G3) were selected for further process while the rest were not employed due to stability issues. **Results:** The obtained results were analyzed by using statistical RSM (response surface methodology) and the link between the independent and response variables was depicted using contour plots. The result of the current study of both these gels indicated high values of flux and ER (enhancement ratio) while a reduction in tlag value. However, no significant difference was seen in the values I/R (input ratio) and Kp (permeation constant) with other formulated gels. **Conclusions:** It was concluded that the addition of PG and PEG into gels could enhance the permeation of cifixime trihydrate and chlorphenaramine mleate across membrane.

INTRODUCTION

Cefixime is an antibiotic drug used to treat infection. It belongs to the class of 3rd generation cephalosporin.It is stable to the hydrolysis of β-lactamases [1]. Chlorphenamine, also known as chlorpheniramine, is an antihistamine that is frequently sold in the form of chlorpheniramine maleate (Chlorphen-12). It is used to treat allergic diseases

DOI: https://doi.org/10.54393/pjhs.v4i11.825

such urticarial infections and rhinitis [2]. Intensive research is being conducted to examine alternative ways for improving drug delivery. Various studies are being conducted in order to examine several tactics to facilitate drug delivery [3]. Certain novel ways involve the incorporating drug into microcapsules, niosomes, nanocapsules, emulsion-based systems, liposomes, along with the use of several combinations of chemical enhancer [4]. Chemical enhancers are compounds that weaken the skin's barrier function briefly, allowing for greater medication absorption. Some examples of them include crucial terpenes, fatty acids, and oils. Several in-vitro investigations showed that polyethylene glycol (PEG) when used in combination with propylene glycol (PG) may effectively penetrate the skin, building on their ability as skin permeation enhancers [5]. This study was conducted to assess penetration and release kinetics of medication in the form of CCM gel by using Response Surface Methadology through Franz diffusion cells by using silicone membrane [6]. A technique called Response Surface Methodology (RSM) was adopted in order to develop a CCM gel comprising cefixime trihydrate and chlorphiniramine maleate in various ratios in association with permeation enhancers such as PG as well as PEG [7].Permeation tests were carried out utilising full thickness silicone membrane in modified Franz diffusion cells to study saturation and drug release kinetics from produced gels. Cefixime, a 3rd generation antibiotic is freely soluble in methanol and may quickly traverse the skin or membranes, even when administered in small amounts. In contrast, CPM is freely soluble in both methanol and water, but due to the mixture of organic solvents, both can have a significant influence [8]. Permeation tests were carried out utilising full thickness silicone membrane in modified Franz diffusion cells to study saturation and drug release kinetics from produced gels [9], as a result, this type of gel formulation might become more important and directly apply to topical infections in order to solve this problem. The primary goal to conduct this research study was to formulate a gel with a combination of antibiotic and antihistamine which can be effectively used in topical applications.

METHODS

Cefixime trihydrate (99.9 % purity) was acquired from Merck, Germany. Rest of the chemical substances which includes benzyl alcohol, carbopol 934, polyethylene glycol (PEG 1000), propylene glycol (PG), triethanolamine, rose mery oil, ethylene glycol, and methanol, which were consumed bought from Germany (Merck). UV-Spectro photometer (Spectronic, Genesys 5), Sonicator, Water bath, Weighing balance and Magnetic Stirrer/Hot Plate. CCM gels of cefixime trihydrate and chlorphenira mine maleate having differential ratios of PG & PEG was made by carefully weighing as well as measuring all of the materials, which had variable amounts of each. The CCM gel formulation required taking dilution solution of 5.5mL of methanol in conical flask and dissolving 0.2 g each of cefixime trihydrate and PEG and chlorphinaramine maleate were introduced with constant swirling on a magnetic stirrer with such a magnetic flea until entirely dissolved. In another separate conical flask PG was taken and benzyl alcohol was used to dissolve it. Then add 0.5 g of carbopol-934. Magnetic stirring was continued until the carbopol-934 was lump-free. The prepared form of the 1st conical flask medicines solution was added to the homogenized carbopol-934 preparation in the 2nd conical flask. PG under continuous magnetic stirring adds benzyl ethylene glycol as well as alcohol by portions with continuous stirring and isopropyl alcohol (IPA) was added continuously during preparation and required volume was adjusted through IPA. Finally added rose merry oil for fragrance and later kept it in collapsible tubes for using it later on. The compositions of different gels are mentioned in the following Table 1.

Table 1: Gels constitution

Sr. no	Cefixime trihydrate (g)	CPM (g)	X_1=Propylene glycol (g)	X_2=Poly ethylene Glycol (g)	Carbopol- 934 (g)	Benzyl alcohol (g)	EG (g)	Methanol (g)	Rose mery oil (g)	Volume make up with IPA (g) make 20 gm
Gel_1	0.2	0.2	4.4	1.9	0.5	3.138	0.11	5.9	0.3	3.52
Gel_2	0.2	0.2	4.8	1.9	0.5	3.138	0.11	5.5	0.3	3.352
Gel_3	0.2	0.2	4.4	2.1	0.5	3.138	0.11	5.5	0.3	3.552
Gel_4	0.2	0.2	4.8	2	0.5	3.138	0.11	5.5	0.3	3.25
Gel_5	0.2	0.2	4.2	2	0.5	3.138	0.11	5.5	0.3	3.85
Gel_6	0.2	0.2	5	1.8	0.5	3.138	0.11	5.5	0.3	3.25
Gel_7	0.2	0.2	4.6	2.2	0.5	3.138	0.11	5.5	0.3	3.25
Gel_8	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_9	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_{10}	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_{11}	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_{12}	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_{13}	0.2	0.2	4.6	2	0.5	3.138	0.11	5.5	0.3	3.75
Gel_c	0.2	0.2	0	0	0.5	4.64	0.11	7.86	0.3	6.23

Diffusion research was conducted using Franz diffusion cells with a diffusional area of 0.788 cm2 as well as a receptor phase of volume 5 ml across a silicone membrane. Silicone membrane had been trimmed to size in a circular form and immersed overnight in the methanolic solution. After that, the membrane was put inside the diffusion cells' donor and receptor compartments. The vacuum grease was applied between the surfaces of collar of both the sections before the membrane was put in place to prevent

DOI: https://doi.org/10.54393/pjhs.v4i11.825

it from leakage. Once the donor compartment was placed over the receptor compartment, they were clamped. The arm of the cell was used to inject the receptor fluid into the receptor compartment, which was later withdraw in a bath (ultrasonic) to get rid of any air bubbles and avoid air pockets from accumulating in the receptor phase. In the receptor compartment, a magnetic stirring bar was placed in order to maintain constant mixing of the receptor phase. Then, to prevent evaporation, a parafilm was placed over the donor's perimeter and the receptor's cell arm aperture. The diffusion cells were used to maintain the surface temperature of membrane by placing it on a moving bed that was submerged in water bath set fixed at temperature at 37 °C. After 1 hour, the receptor phase was entirely withdrawn and then completely filled with receptor fluid. Test solution (1ml) placed inside the donor chamber. (cefixime trihydrate and chlorphiniramin maleate, Using a micropipette, sample solution (0.2ml) was taken from the receptor solution at predetermined intervening time of 15 min, 30 min, 45 min, 60 min, 90 min, 120 min and 180 min. To keep the receptor compartment in the sink condition, when every sample was taken then receptor fluid (0.2ml) was added. To determine permeated amount through the silicon membrane, the samples were spectrophotome trically examined at 254 nm and 265 nm. Experiments were conducted in three sets. For solubility analysis, a large quantity of pure cefixime trihydrate was added to three separate glass bottles holding five millilitres each of Phosphate buffer, methanol and distilled water. These combinations were stirred for 48 hours at a constant temperature of 37± 1°C with a thermostatically-controlled stirrer. Centrifugations of mixtures were done for 30 min at 4000 rpm. An aliquot of the supernatant was then removed using a pipette, and the concentration in g/mL was calculated using a UV spectrophotometer at 254 nm. The optimal solvent system for the receptor phase was therefore determined by studying solubility in each solvent. The partition coefficient of Cefixime trihydrate was determined by dissolving it in 10mL of water in separating funnel after shaking it for 10 minutes. Then, after adding 10 mL of octanol solution, the funnel was vigorously shaken for further 10 minutes and then placed it for 1 day. Each layer was separated into two layers, collected in a test tube, and then analyzed it in UV Spectrophotometer to determine the octanol / water ratio. Experiments were conducted in three sets (n=3). Several RSM approaches for this optimization study were executed using Design Expert® software 8.0.1. The most effective gel formulation was found using a computer RSM that used polynomial equations to estimate the impact of formulation factors on drug invasion via membrane as shown in Figure 1. These designs were taken from CCD with α = 2. The ratios of Propylene glycol and Poly ethylene glycol were evaluated at five levels. However, the central point was considered in four times.

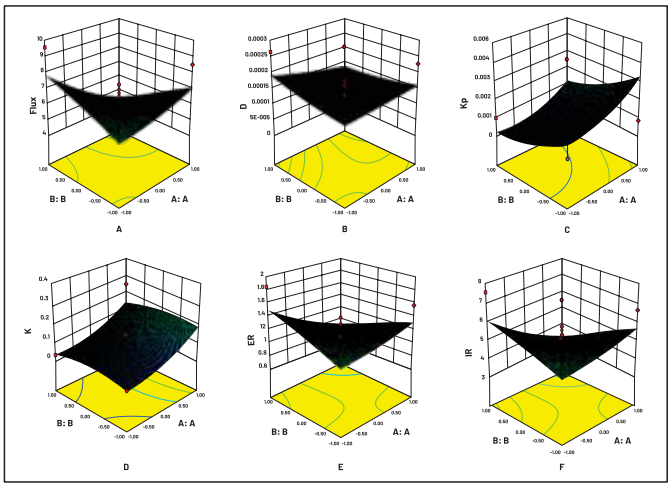

Figure 1: Representing the contour plots of CCM gel formulations obtained by RSM

Parameter like Viscosity was determined through Brookfield viscometer. All the measurements were taken at room temperature at 25°C. pH of CCM gels were calculated at 25 °C by using digital pH meter. Physical traits of formulated CCM gels, such as transparency, precipitation, and homogeneity, were also observed. Overall, 13 experimental turns for CCM gels were created with CCD (two-factor) run for 7 responses as shown in Table 5. We packed CCM gels in collapsible aluminum tubes weighing (5 g) which were exposed so that it can be tested for stability studies at 25 °C at 60 % RH and 40 °C at 65 % RH for 3 months. Specimens were held for the designated amount of time before CCM gels were analyzed for their rheological characteristics, physical appearance, and chemical assays.

RESULTS

Cefixime trihydrate is sparingly soluble in water, however it is easily soluble in two solvents: methanol and IPA. Contrary, CPM was readily soluble in both methanol and water. Two optimized CCM gels, G1 and G3 were used for stability studies which were found stable under specified storage environment. The solubility of CCM gel's in water was 1.28 mg/mL, in methanol 1.95 mg/mL, in PBS (phosphate buffer solution) was 0.821 mg/mL whereas in methanol water (2:1), the solubility reached to 72.15 mg/mL. However, the partition coefficient (Ko/w) was 3.68 ± 0.11 that was associated to log P = 3.80 reported previously. Gels were observed for their physical properties like clarity, precipitation and consistency and were found to have homogenous, transparent and white crystallite appearance. Table 2 showed measured values of drug content, pH, viscosity, spread ability and consistency of CCM gels while Table 3 indicated larger values of flux and ER

DOI: https://doi.org/10.54393/pjhs.v4i11.825

for G1 and G3 whereas the values of tlag were quite minimum. Kp and I/R values were seem to be more prominent. Overall, indicating their ability to cross membrane in less time as compared to other formulated gels. Values of were also more prominent in G1 and G3. We selected both G1 and G3 gels for further in-vitro rat skin permeation studies to authenticate our outcomes. For this purpose, a primary test of skin irritation was conducted for volunteers with no irritation or lesions (erythema, redness and urticarial) seen during 1 month trial. For analysis of stability, the optimized CCM gels were kept for three months in accordance with ICH norms at 25.0 ± 1 °C, at 60 % RH and 40 ± 1 °C, at 75 % of RH and were examined for a change in their appearance.

Table 2: Exhibiting the results of various kinetic parameter study of CCM

Formulation	Gel_1	Gel_2	Gel_3	Gel_4	Gel_5	Gel_6	Gel_7	Gel_8	Gel_9	Gel_{10}	Gel_{11}	Gel_{12}	Gel_{13}
Viscosity in m.poise	44	37	57	42	46	49	41	39	52	56	46	48	46
pH	3.92	3.76	3.84	3.87	3.94	3.94	3.95	3.97	3.94	3.96	3.91	3.94	3.92
Spread ability in cm	3.0	2.8	3.2	2.7	3.1	2.2	2.5	3.4	3.2	2.9	3.0	3.1	3.2
Clarity	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT	YCT
Precipitation	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt	N/ ppt
Drug content (%)	98.5	99.4	98.9	99.9	99.3	98.7	99.5	98.3	98.2	99.1	98.6	98.4	99.2
E/R/U (1st to day 30th)	0	-	0	-	-	-	-	-	-	-	-	-	-

Yellow Crystalline and Transparent (YCT), No precipitation (N/ppt), E: Erythema, R: Redness, U: Urticarial

Table 3: Permeation kinetic parameters of CCM gels through RSM

Sr. no.	t_{lag} (min) ±SD	Flux (µg/cm 2/min) ±SD	$D\times10^{-4}$ (Cm2 / min) ±SD	$K\times10^{-2}$ ±SD	$Kp\times10^{-3}$ (µg/cm 2/min) ±SD	ER ±SD	I/R (µg/ min) ±SD
Gel_1	17.745± 0.937	8.518± 0.026	2.290± 1.21E-05	3.3± 0.001	0.852± 0.002	1.556	6.720± 0.021
Gel_2	7.043± 0.083	5.363± 0.009	0.909± 1.08E-06	5.2 ± 0.001	0.536± 8.54E-07	1.039	4.231± 0.007
Gel_3	20.652± 0.165	9.560± 0.010	2.666± 2.13E-06	3.2± 0.001	0.956± 1.01E-06	1.852	7.543± 0.008
Gel_4	14.902± 0.211	5.015± 0.017	1.92± 2.72E-06	2.3± 0.001	0.502± 1.71E-06	0.971	3.957± 0.013
Gel_5	10.398± 1.464	6.649± 0.019	1.342± 1.89E-05	4.4± 0.001	0.665± 1.86E-06	1.288	5.246± 0.014
Gel_6	8.806± 0.303	5.653± 0.017	1.14± 3.92E-06	43.8± 0.001	5.656± 1.69E-06	1.095	4.463± 0.013
Gel_7	9.931± 0.126	4.804± 0.008	1.263± 1.63E-06	3.30± 0.001	4.804± 8.39E-07	0.931	3.791± 0.007
Gel_8	12.175 ± 0.204	5.116± 0.002	1.57± 2.63E-06	2.9± 0.001	0.512± 2.08E-07	0.991	4.037± 0.002
Gel_9	13.531± 0.147	6.738± 0.014	1.75± 1.9E-06	3.4± 0.001	0.673± 1.4E-06	1.305	5.316± 0.011
Gel_{10}	12.458± 0.266	7.258± 0.008	1.61± 8.08E-07	4.0± 0.001	0.726± 8.08E-07	1.406	5.726± 0.006
Gel_{11}	11.609± 0.489	4.306± 0.007	1.5± 6.32E-06	2.5± 0.001	0.431± 6.93E-07	0.835	3.397± 0.006
Gel_{12}	7.842± 0.243	4.051± 0.008	1.01± 3.14E-06	35.2± 0.001	4.051± 8.08E-07	0.785	3.197± 0.006
Gel_{13}	12.454± 0.263	7.254± 0.002	1.59± 3.4E-06	4.2± 0.011	0.728± 2E-07	1.402	5.695± 0.002

DISCUSSION

The mammalian skin layer stratum corneum selectively behaves as permeable membrane. Lipid molecules can be located to diffuse easily among keratinocytes [10]. These lipid intercellular molecules can be seen to dissolve easily in PG and PEG. PG and PEG affect is concentration dependent. The efficiency of PG is increased by adding more amount of PEG when both are used in combination. So, they have synergistic effect [11]. Earlier studies demonstrated how effectively PEG and PG have used to enhance the skin permeability [12]. In this study, the combined effects of PG and PEG as to increase permeability of skin was investigated, and several gels containing PG and PEG in various ratios were made using cefixime trihydrate and CPM. Free water in the tissue facilitates penetration and alters the drug's solubility in the stratum corneum (SC), which changes the drug's partition value from the vehicle into the membranes [13]. Hydration of SC enhanced the penetration of both hydrophilic and lipophillic chracteristics. An improved SC hydration resulted in the expansion and opening of dense SC structures, which increased drug penetration. Pyrrolidones, sulfoxides (SO), simple terpenes and terpenoids, uread, fatty acids and esters, poly vinyl alcohol(PVA) and essential oils are additional CPEs that resemble glycerides and were once employed in a variety of topical and transdermal treatments [14]. Cefixime trihydrate (an antibiotic drug) while chlorpheniramine maleate (1st generation antihistamine) were used in combination for 1st time to treat the topical infections rhinitis, urticarial, acne, inflammation and redness [15]. This was the simple part of wide-ranging research studies approved to explore numerous methods for supporting drug delivery across skin. CCM gel's solubility in water was 1.28 mg/mL, in methanol 1.95mg/mL, in PBS was 0.821 mg/mL while in methanolic water (2:1), the solubility was 72.15 mg/mL. Partition coefficient (Ko/w) was 3.68, compared with a previous value of log P = 3.80 [16]. CCM gels remained clear, crystalline and transparent. No change in consistency, viscosity, homogeneity was observed. Due to greater flux and ER value, the drug contents were released from gels and permeated through skin. In CCM gels, the values for flux and ER were greater in G1 and G3, whereas tlag values for both gels were least indicating the time required by G1 and G3 to cross the membrane was less in comparison with formulated gels [17]. Kp& I/R also showed projecting values in G1 and G3 [18]. So both the gels G1 and G3 were optimized the best formulation. No skin irritation or lesions (erythema, redness and urticarial) was found upon application of optimized CCM gels (G1& G3) indicating a good sign of its safety. ICH norms were performed for stability testing [19],

DOI: https://doi.org/10.54393/pjhs.v4i11.825

the optimized CCM gels (G1& G3) were provided with 3 months of storage conditions as per criteria (25.00 ± 1 °C, at 60 % RH & 40.00 ± 1 °C, at RH 75 %), but no change in their appearance was analyzed. The greater values of ER, flux and minimum values of tlag while prominent values of Kp, I/R of CCM gels gave protuberant clue that they are able to pass across the human skin barrier easily. A CCD statistical design with 7 responses was chosen for this study using design selected from the previous reported studies of topical formulations [20]. The values of 13 CCM gels responses along with independent variables were also being generated, from where; the independent x-axis variables were PG and PEG while dependent variable responses were on Y1to Y7 in 3 hrs. Improved drug stability and solubility with reduced lag time has also increased the degree of drug delivery to the outer membrane compartment [21]. Further this study also suggested that PG and PEG in combination has enhanced the rate of permeation of CCM gels in different ratios. frothy with targeted specific gravity then added in natural milk to form value added milk to get only substantial profit [10]. The analysis of different adulterants in milk samples showed such findings that helped in the discrimination of satisfactory and unsatisfactory milk samples through provided pure raw milk free from adulterants. These findings also supported the previous study of determining possibility of adulteration through physical and chemical quality parameters which showed adulteration possibility of around 76.6% [12].

CONCLUSIONS

The Poly glycol and Poly ethylene glycol are effective permeation enhancers to be used in combination and the CCM gel formulations can be effectively used because even when taken in modest amounts, cefixime trihydrate is quickly absorbed via the skin or membrane since it is freely soluble in methanol. Despite being easily soluble in both methanol and water, CPM can exhibit significant effects when combined with organic solvents. Especially, considering joint and acne infections, the oral formulation is not helpful in patients with ulcers. In order to overcome this problematic situation, CCM gel can be used effectively by direct application on topical infections.

Authors Contribution

Conceptualization: SR, A, FS, AQ
Methodology: AH, SB
Formal analysis: HT, MUIK
Writing-review and editing: AQ, MD, SJ, MH

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Alfei S and Zuccari G. Recommendations to Synthetize Old and New β-Lactamases Inhibitors: A Review to Encourage Further Production. Pharmaceuticals. 2022 Mar; 15(3): 384. doi: 10.3390/ ph15030384.

[2] Erkoçoğlu M, Kaya A, Civelek E, Özcan C, Çakır B, Akan A, et al. Prevalence of confirmed immediate type drug hypersensitivity reactions among school children. Pediatric Allergy and Immunology. 2013 Mar; 24(2): 160-7. doi: 10.1111/pai.12047.

[3] Sabbagh F and Kim BS. Recent advances in polymeric transdermal drug delivery systems. Journal of Controlled Release. 2022 Jan; 341: 132-46. doi: 10.1016/j.jconrel.2021.11.025.

[4] Hussain Z, Thu HE, Rawas-Qalaji M, Naseem M, Khan S, Sohail M. Recent developments and advanced strategies for promoting burn wound healing. Journal of Drug Delivery Science and Technology. 2022 Feb; 68: 103092. doi: 10.1016/j.jddst.2022.103092.

[5] Szebeni J, Baranyi L, Savay S, Milosevits J, Bunger R, Laverman P, et al. Role of complement activation in hypersensitivity reactions to doxil and hynic PEG liposomes: experimental and clinical studies. Journal of Liposome Research. 2002 Jan; 12(1-2): 165-72. doi: 10.1081/LPR-120004790.

[6] Parhi R and Panchamukhi T. RSM-based design and optimization of transdermal film of ondansetron HCl. Journal of Pharmaceutical Innovation. 2020 Mar; 15: 94-109. doi: 10.1007/s12247-019-09373-9.

[7] Shahzad Y, Afreen U, Nisar Hussain Shah S, Hussain T. Applying response surface methodology to optimize nimesulide permeation from topical formulation. Pharmaceutical Development and Technology. 2013 Dec; 18(6): 1391-8. doi: 10.3109/10837450.2012.723721

[8] Riaz R. Microsponges as Promising Vehicle for Delivery of Antibiotic and Antihistamine for Infectious and Allergic Disorders: Preparation, Characterization and Applications (Doctoral dissertation, Bahauddin Zakariya University Multan). 2019. Available at: http://142.54.178.187:9060 /xmlui/handle/123456789/4527.

[9] Turner D, Levine A, Escher JC, Griffiths AM, Russell RK, Dignass A, et al. Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. Journal of Pediatric Gastroenterology and Nutrition. 2012 Sep; 55(3): 340-61. doi: 10.1097/MPG.0b013e3182662233.

[10] Katari O and Jain S. Solid lipid nanoparticles and

DOI: https://doi.org/10.54393/pjhs.v4i11.825

nanostructured lipid carrier-based nanothera peutics for the treatment of psoriasis. Expert Opinion on Drug Delivery. 2021 Dec; 18(12): 1857 -72. doi: 10.108 0/17425247.2021.2011857.

[11] Baabur-Cohen H, Vossen LI, Krüger HR, Eldar-Boock A, Yeini E, Landa-Rouben N, et al. In vivo comparative study of distinct polymeric architectures bearing a combination of paclitaxel and doxorubicin at a synergistic ratio. Journal of Controlled Release. 2017 Jul; 257: 118-31. doi: 0.1016/j.jconrel.2016.06.037.

[12] Suksaeree J, Simchareon W, Pichayakorn W. Effect of glycols permeation enhancer on the release and permeation of meloxicam-natural rubber film through pig skin. Journal of Drug Delivery Science and Technology. 2021 Dec; 66: 102874.

[13] Kis N, Gunnarsson M, Berkó S, Sparr E. The effects of glycols on molecular mobility, structure, and permeability in stratum corneum. Journal of Controlled Release. 2022 Mar; 343: 755-64. doi: 10. 10 16/j.jconrel.2022.02.007.

[14] Chatterjee B, Reddy A, Santra M, Khamanga S. Amorphization of drugs for transdermal delivery-a recent update. Pharmaceutics. 2022 May; 14(5): 983. doi: 10.3390/pharmaceutics14050983.

[15] World Health Organization. Restrictions in use and availability of pharmaceuticals, 2010-2018. 2020. [Last cited:14thNov2023].Available at: https://www. who.int/publications/i/item/9789240014770.

[16] Breindl A, Beck B, Clark T, Glen RC. Prediction of the n-octanol/water partition coefficient, logP, using a combination of semiempirical MO-calculations and a neural network. Molecular Modeling Annual. 1997 Mar; 3: 142-55. doi: 10.1007/s008940050027.

[17] Jiang Z, Qu J, Tian X, Huo X, Zhang J, Guo X, et al. Sol-gel technique for the preparation of β-cyclodex- trin gold nanoparticles as chiral stationary phase in open-tubular capillary electrochromatography. Journal of Separation Science. 2019 May; 42(10): 1948 -54. doi: 10.1002/jssc. 201900071.

[18] Das SK, Bedar A, Kannan A, Jasuja K. Aqueous dispersions of few-layer-thick chemically modified magnesium diboride nanosheets by ultrasonication assisted exfoliation. Scientific Reports. 2015 Jun; 5(1): 10522. doi: 10.1038/srep10522.

[19] Ioele G, Grande F, De Luca M, Occhiuzzi MA, Garofalo A, Ragno G. Photodegradation of anti-inflammatory drugs: Stability tests and lipid nanocarriers for their photoprotection. Molecules. 2021 Oct; 26(19): 5989. doi: 10.3390/molecules26195989.

[20] Khan MZ, Makreski P, Murtaza G. Preparation, optimi- zation, in vitro evaluation and ex vivo permeation studies of finasteride loaded gel formulations prepared by using response surface methodology. Current Drug Delivery. 2018 Nov; 15(9): 1312-22. doi: 10.2174/1567201815666180502165436 .

[21] da Silva Júnior WF, de Oliveira Pinheiro JG, Moreira CD, de Souza FJ, de Lima ÁA. Alternative technol- ogies to improve solubility and stability of poorly water-soluble drugs. Multifunctional Systems for Combined Delivery, Biosensing and Diagnostics. 2017 Jan: 281-305. doi: 10.1016/B978-0-323-52725-5. 000 15-0.

DOI: https://doi.org/10.54393/pjhs.v4i11.1163

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Grit among Nursing Students at Private Nursing Institute of Karachi Pakistan

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ARTICLE INFO

Key Words:
Grit, Nursing Students, Grit-Focused Interventions

How to Cite:
Bibi, A., Ishaq, M., Khaliq, F., & Ahmad, A. (2023). Grit among Nursing Students at Private Nursing Institute of Karachi Pakistan: Grit among Nursing Students . Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1163

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Received Date: 3rd November, 2023
Acceptance Date: 23rd November, 2023
Published Date: 30th November, 2023

ABSTRACT

Grit is a psychological trait that reflects an individual's perseverance and passion for long-term goals. It involves working strenuously towards challenges, maintaining effort and interest over the years despite failure, adversity, and plateaus in progress. **Objective:** To Evaluate grit among nursing students at the private nursing institute of Karachi, Pakistan. **Methods:** This cross-sectional study was conducted in two nursing institutes in Karachi, Pakistan, from July to September 2023. Moreover, this study adopted a convenient sampling technique to approach the study participants. Furthermore, the Grit Scale, developed by Angela Duckworth for the data collection, measures traits such as Consistency of Interest, Perseverance of Effort, and Ambition. **Results:** The study result shows that among 117 participants, 99.1% are male, and 6.0% are females. Moreover, the grit levels among nursing students, 4.3% had moderate grit, and 95.7% had high grit. **Conclusions:** Based on the findings, an overwhelming majority of nursing students (95.7%) exhibited high levels of grit, with none showing low grit and a small percentage (4.3%) demonstrating moderate grit. Implementing grit-focused interventions or programs within the nursing education curriculum is recommended. These initiatives can further enhance students' resilience and perseverance, equipping them with the necessary mindset to navigate.

INTRODUCTION

Grit is figuring out and wanting to have established goals for the future [1]. Furthermore, it enables students to see a goal through to completion [2]. In addition, it involves using self-control, making decisions, and acting in ways that will eventually lead to success [3]. Moreover, grit, perseverance and passion for long-term goals" have recently been connected to success and achievement in various contexts. Grit may help someone in a collegiate context become more self-aware of their capacity for academic success [4]. Additionally, it realizing and accomplishes important long-term goals while maintaining the flexibility to satisfy those short-term, daily objectives. Grit is more than being strong-willed or tenacious in the face of difficulty. When faced with obstacles, unfavourable comments, failures, or stagnation in their endeavours, more resilient individuals often look for comprehension to keep going and do better—they never stray from their objectives [5]. Moreover, two noncognitive abilities are included in grit: perseverance in effort and consistency in interest. These two skills have received much attention lately in health and general education programs [6]. It has also been demonstrated that grit strongly correlates with other qualities, including consistency, perseverance, and conscientiousness, one of the big five personality traits [7, 8]. Additionally, it is more important in predicting achievement than other traits or factors, such as higher grade point averages and longer employment tenure [5]. Grittier people have been demonstrated to perform better both academically and extracurricularly. They also exhibit higher motivation levels as they look for purpose in their work and strive towards it [9]. Grit was a stronger predictor of individual achievement than talent alone regarding achievement indicators in academic and non-academic domains [9]. In this regard, a descriptive study aims to explore how grit affects nursing students' adaption to clinical practice. Grit was discovered to influence nursing students' clinical practice adaption, accounting for 32.0% of the adaptation. Therefore,

DOI: https://doi.org/10.54393/pjhs.v4i11.1163

initiatives to strengthen grit and the development of clinical practice curricula are required to boost the clinical practice adoption of nursing students [10]. In addition, the data analysis of other studies revealed a positive correlation between the individuals' grit and their self-efficacy and self-esteem [11]. Another study found that grit was the factor that affected nursing students' capacity for self-directed learning the most [12]. Additionally, grit has been identified as one of the most essential ways of coping with mental health stresses. It is crucial to investigate grit to understand better and increase the possibilities of academic success and personal well-being for at-risk students [13]. In addition, it is particularly useful in guiding the kind of instruction that should support nursing students during their clinical rotations [11]. Grit reduced the intention to leave the job and raised job participation. As a result, developing a programme and techniques to strengthen nurses' grit is essential to lowering their intention to leave [14]. As a result, grit is a crucial trait that can help students succeed in nursing programmes and as graduate nurses in clinical settings [15]. Therefore, this study aims to assess the grit among nursing students at a private institute in Karachi, Pakistan. There is currently relatively little study material that describes nursing students' general grit levels and the elements that may influence their grittiness. Understanding the grit levels among nursing students can inform tailored support systems within educational institutions.

METHODS

This cross-sectional study was conducted in two nursing institutes in Karachi, Pakistan, from July to September 2023. Moreover, this study adopted a convenient sampling technique to approach the study participants. The sample size was calculated through Open Epi with a 95% confidence interval with a total population of 200. The calculated sample size was 132, but 15 did not give the data, so the final participants were 117. Furthermore, the Grit Scale, developed by Angela Duckworth [16] for the data collection, measures traits such as Consistency of Interest, Perseverance of Effort, and Ambition. Participants rate themselves on a Likert scale ranging from 1 to 5, where five represents "Very much like me" and one represents "Not like me at all." Consistency of Interest assesses the stability of one's interests, Perseverance of Effort evaluates the ability to maintain motivation despite challenges, and Ambition measures the drive to achieve long-term goals. The tool total score was 85, and this converted into the percentage of those participants who scored (1-28) considered Low Grit, Moderate Grit (29-56) and High Grit (57-85). The tool Cronbach alpha has been calculated on 10% of the total population, and the value is 0.84. Nursing students from 3rd year and 4th years were part of this study. Both males and females were included. Those who were not willing to participate in the study were excluded. The data were collected through Google Forms. Before the data collection, the participants read and understood the consent form, and after they clicked on the consent form, the participants filled out the questionnaire. Before the data collection, consent forms were taken from each participant. Study approval was taken from the relevant institute to maintain the ethical integrity of the study. SPSS version 26.0 was used for the data analysis. Descriptive statistics such as mean, frequency and percentage were used to analyze the data.

RESULTS

Table 1 provides the result of demographic variables in which 99.1% are male, and 6.0% are females. Regarding age, most of the participants, 94% were between 19 and 24. Only a small proportion had ages between 25-29. Concerning their academic year, 47.9% from the 3rd year and 52.1% from the 4th year.

Table 1: Demographic variables n=117

Variables	Frequency (%)
Age	
19-24	110 (94.0)
25-29	7 (6.0)
Gender	
Male	116 (99.1)
Female	1 (0.9)
Academic year	
Year3	56 (47.9)
Year4	56 (47.9)

Table 2 provides the result of levels of grit among nursing students. In which 0% had low grit, 4.3% had moderate grit, and 95.7% had high grit.

Table 2: Level of Grit among Nursing Students

Level of Grit	Frequency (%)
Low Grit (1-28)	0 (0)
Moderate Grit (29-56)	5 (4.3)
High Grit (57-85	112 (95.7)

Table 3 shows the mean of the grit score. The total score was 85, and the mean score was 73.8376.

Table 3: Mean and Standard deviation of total grit score

N	Mean ± SD
117	73.837±10.583

DISCUSSION

It is common knowledge that raising student accomplish-ment levels is crucial for improving individual and organizat-ional performance in the classroom and academic setting.

DOI: https://doi.org/10.54393/pjhs.v4i11.1163

Numerous studies in the present era suggest that students' grit levels significantly positively impact their academic performance [1]. Therefore, this study aims to assess the grit level among nursing students. The present findings show that 95.7% had high grit among the study participants. There are studies reported which suggests higher level of grit among participants [15, 17-19], which is consistant with our data. Grit helps students persevere through challenges and setbacks, keeping them focused on their long-term goals despite difficulties. Gritty students are more likely to achieve their academic goals because they are willing to put in the effort required to master complex subjects and skills [20, 21]. Due to several unfavourable social and personal situations, grit lessens detrimental effects on nursing students' educational experiences. In fact, grit and other protective qualities indirectly influence academic performance and achievement orientation. The consistency of interest is not as crucial as the perseverance of effort. Therefore, academic staff can support their teaching efforts by creating a learning atmosphere emphasizing grit [22, 23]. Students who develop grit and a growth attitude will be better equipped to achieve their objectives and more driven to stay with them [24]. The current findings show that 4.3% had a moderate level of grit. There are studies who also found moderate level of grit among participants [15, 25]. Students with greater grit experience greater academic performance than those with less grit [1]. Another study found that achievement rises with grit level in a student's academic life. According to regression research, grit is a significant predictor of success [1]. A a result, nurse educators ought to support initiatives that strengthen nursing students' grit [26]. Because it is a crucial protective quality that helps nursing students handle the significant stress they encounter in their studies, especially those related to their educational experience [26]. Studies found that 3.27-3.5 out of 5 indicate an average grit level [27-29]. The present study found that the mean grit score is 73.8, indicating a high level of grit. In contrast, studies found opposing results and showed a mean score of 37.62, 27.3 and 41.09 respectively [23, 30, 31]. A research study concluded that knowing a person's grit level can help identify healthcare professionals more likely to experience burnout. Given that grit is correlated with a lower risk of burnout, therapies aimed at enhancing grit via resilience training warrant further investigation. More research is required to understand why healthcare professionals endure higher levels of burnout and how their grit levels evolve over their careers[32].

CONCLUSIONS

Based on the findings, an overwhelming majority of nursing students (95.7%) exhibited high levels of grit, with none showing low grit and a small percentage (4.3%) demonstrating moderate grit. Implementing grit-focused interventions or programs within the nursing education curriculum is recommended. These initiatives can further enhance students' resilience and perseverance, equipping them with the necessary mindset to navigate.

Authors Contribution

Conceptualization: MI, AB
Methodology: FK
Formal analysis: AB, FK
Writing-review and editing: AA
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Beyhan Ö. University students grit level and grit achievement relation. Social Sciences and Education Research Review. 2016 Mar; 3(2): 13-23.
[2] Reed L and Jeremiah J. Student grit as an important ingredient for academic and personal success. Developments in Business Simulation and Experiential Learning: Proceedings of the Annual ABSEL Conference. 2017; 44: 252-56.
[3] Fosnacht K, Copridge K, Sarraf S. Peering into the box of grit: How does grit influence the engagement of undergraduates? Association for the Study of Higher Education Annual Conference. 2017 Nov: 1-36.
[4] Weisskirch RS. Grit, self-esteem, learning strategies and attitudes and estimated and achieved course grades among college students. Current Psychology. 2018 Mar; 37: 21-7. doi: 10.1007/s12144-016-9485-4.
[5] Terry D and Peck B. Factors that impact measures of grit among nursing students: A journey emblematic of the Koi Fish. European Journal of Investigation in Health, Psychology and Education. 2020 Apr; 10(2): 564-74. doi: 10.3390/ejihpe10020041.
[6] Elnaem MH, Barakat M, Mubarak N, KT MS, Abdelaziz DH, Fathelrahman AI, et al. Evaluation of grit and its associated factors among undergraduate pharmacy students from 14 Asian and Middle Eastern countries amid the COVID-19 pandemic. Saudi Pharmaceutical Journal. 2023 Mar; 31(3): 410-6. doi: 10.1016/j.jsps.202

DOI: https://doi.org/10.54393/pjhs.v4i11.1163

3.01.008.
[7] Duckworth AL, Kirby TA, Tsukayama E, Berstein H, Ericsson KA. Deliberate practice spells success: Why grittier competitors triumph at the National Spelling Bee. Social Psychological and Personality Science. 2011 Mar; 2(2): 174-81. doi: 10.1177/1948550610385872.
[8] Credé M, Tynan MC, Harms PD. Much ado about grit: A meta-analytic synthesis of the grit literature. Journal of Personality and social Psychology. 2017 Sep; 113(3): 492. doi: 10.1037/pspp0000102.
[9] Terry D and Peck B. Academic and clinical performance among nursing students: What's grit go to do with it? Nurse Education Today. 2020 May; 88: 104371. doi: 10.1016/j.nedt.2020.104371.
[10] Baek KH and Cho MO. Effect of grit and resilience on clinical practice adaptation of nursing students. Journal of Digital Convergence. 2020 Jun; 18(6): 363-71.
[11] Park JY, Woo CH, Kim JE. Convergence factors affecting the grit of nursing students experiencing clinical practice. Journal of Digital Convergence. 2018 Jan; 16(1): 165-75.
[12] Lee S and Kim J. Growth mindset, grit and self-directed learning ability of nursing students in online education. Journal of the Korean Applied Science and Technology. 2021 Apr; 38(2): 567-78.
[13] Stoffel JM and Cain J. Review of grit and resilience literature within health professions education. American Journal of Pharmaceutical Education. 2018 Mar; 82(2): 6150. doi: 10.5688/ajpe6150.
[14] Jeong JY, Seo YS, Choi JH, Kim SH, Lee MS, Hong SH, et al. The influence of grit on turnover intention of university hospital nurses: The mediating effect of job involvement. Journal of Korean Academy of Nursing. 2019 Apr; 49(2): 181-90. doi: 10.4040/jkan.2019.49.2.181.
[15] Munn AC, George TP, Phillips TA, Kershner SH, Hucks JM. Resilience and GRIT among undergraduate nursing students during the COVID 19 pandemic. International Journal of Nursing Education Scholarship. 2022 May; 19(1): 20220012. doi: 10.1515/ijnes-2022-0012.
[16] Duckworth AL, Peterson C, Matthews MD, Kelly DR. Grit: perseverance and passion for long-term goals. Journal of Personality and Social Psychology. 2007 Jun; 92(6): 1087. doi: 10.1037/0022-3514.92.6.1087.
[17] Burke L, Rebeschi L, Weismuller P, Bulmer S, Kehoe P. Grit levels of graduate nursing students: Why grit is needed in nursing. Journal of Nursing Education. 2022 Apr; 61(4): 197-200. doi: 10.3928/01484834-20220209-05.
[18] Musumari PM, Tangmunkongvorakul A, Srithanavi boonchai K, Techasrivichien T, Suguimoto SP, Ono-Kihara M, et al. Grit is associated with lower level of depression and anxiety among university students in Chiang Mai, Thailand: A cross-sectional study. PloS one. 2018 Dec; 13(12): e0209121. doi: 10.1371/journal.pone.0209121.
[19] Arnold KR. Examining Academic Success Factors and Grit in Baccalaureate Nursing Students. Charleston Southern University; 2022.
[20] Olson JS. Helping first-year students get grit: The impact of intentional assignments on the development of grit, tenacity, and perseverance. Journal of The First-Year Experience & Students in Transition. 2017 Apr; 29(1): 99-118.
[21] Bashant J. Developing grit in our students: Why grit is such a desirable trait, and practical strategies for teachers and schools. Journal for Leadership and Instruction. 2014 Sep; 13(2): 14-7.
[22] Alhadabi A and Karpinski AC. Grit, self-efficacy, achievement orientation goals, and academic performance in University students. International Journal of Adolescence and Youth. 2020 Dec; 25(1): 519-35. doi: 10.1080/02673843.2019.1679202.
[23] Mason HD. Grit and academic performance among first-year university students: A brief report. Journal of Psychology in Africa. 2018 Jan; 28(1): 66-8. doi: 10.1080/14330237.2017.1409478.
[24] Young-Brice A and Dreifuerst KT. Exploring grit among black prelicensure nursing students. Nursing Education Perspectives. 2020 Jan; 41(1): 46-8. doi: 10.1097/01.NEP.0000000000000473.
[25] Abubakar U, Azli NA, Hashim IA, Kamarudin NF, Latif NA, Badaruddin AR, et al. Association between grit and academic achievement among undergraduate pharmacy students in Malaysia. Currents in Pharmacy Teaching and Learning. 2021 May; 13(5): 550-5. doi: 10.1016/j.cptl.2021.01.013.
[26] Alshammari MH and Alboliteeh M. Predictors and correlates of Saudi nursing students' grit and positive thinking amidst the COVID-19 pandemic. Teaching and Learning in Nursing. 2022 Oct; 17(4): 471-6. doi: 10.1016/j.teln.2022.06.012.
[27] Kang SW. Nursing students' grit: A cross-sectional study. Advances in Social Sciences Research Journal. 2018 Oct; 5(10): 127-131. doi: 10.14738/assrj.510.5303.
[28] Jin JI and Kim NC. Grit, academic resilience, and psychological well-being in nursing students. The Journal of Korean Academic Society of Nursing Education. 2017 May; 23(2): 175-83. doi: 10.5977/jkasne.2017.23.2.175.
[29] Martin H, Craigwell R, Ramjarrie K. Grit, motivational

DOI: https://doi.org/10.54393/pjhs.v4i11.1163

belief, self-regulated learning (SRL), and academic achievement of civil engineering students. European Journal of Engineering Education. 2022 Jul; 47(4): 535-57. doi: 10.1080/03043797.2021.2021861.

[30] Yang L and Wu D. Grit and meaning in life of Chinese nurses: the chain mediating effect of social support and hope. Frontiers in Psychology. 2021 Nov; 12: 769707. doi: 10.3389/fpsyg.2021.769707.

[31] Cherian J and Kumari P. Examining the relationship between grit and quality of life: The mediating role of social support among nurses. Journal of Emerging Technologies and Innovative Research. 2021 Jul; 8(7): g62-70.

[32] Halliday L, Walker A, Vig S, Hines J, Brecknell J. Grit and burnout in UK doctors: a cross-sectional study across specialties and stages of training. Postgraduate Medical Journal. 2017 Jul; 93(1101): 389-94. doi: 10.1136/postgradmedj-2015-133919.

DOI: https://doi.org/10.54393/pjhs.v4i11.1101

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Prevalence of Iron Deficiency Anemia among Infants Consuming Cow's Milk

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ARTICLE INFO

Key Words:
Iron Deficiency Anemia, Cow Milk, Infants

How to Cite:
Bai, A., Shaikh, F., Kumar, . S., Ahmed, A., Marium, ., & Shaikh, M. A. (2023). Prevalence of Iron Deficiency Anemia among Infants Consuming Cow's Milk : Prevalence of Iron Deficiency Anemia. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1101

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Received Date: 5th October, 2023
Acceptance Date: 25th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Iron Deficiency Anemia (IDA) in children is a public health issue affecting child morbidity, mortality, and cognitive development. Infants fed cow's milk are at a higher risk of severe IDA due to calcium and iron absorption competition. **Objective:** To determine the frequency of Iron deficiency anemia among Cow Milk Fed Infants. **Methods:** This cross-sectional study was conducted at Peadiatric wards of Liaquat University Hospital Hyderabad and Jamshoro from November 2020 to April 2021. All the full-term infants with age of up to 6 months either gender and having history of cow's milk consumption and clinically diagnosed to have anemia were included. Infants had 3ml intravenous blood samples taken to get a complete blood picture and ferritin level. All the mothers were interviewed regarding duration of cow's milk consumption. Data were collected via a predesigned proforma. **Results:** Total 323 infants were studied to assess the frequency of iron deficiency anemia among cow's milk infants up to 6 months and the mean age of infants was 4.11 ± 1.31 months. Females were 56.3% and males were 43.7%. Overall average of hemoglobin was 8.92 ± 1.09 g/dl, and overall mean of ferritin level was 90.16 ± 17.71 ng/ml. Frequency of iron deficiency anemia was found to be 18.6%. **Conclusions:** As per study conclusion overall frequency of iron deficiency anemia was observed to be 18.6% and cow's milk consumption has been observed as a risk factor of infant's anemia.

INTRODUCTION

Iron deficiency, with or without anemia, impacts around 30% of the global populace, marking it as the most common nutrient deficiency. It negatively affects central nervous functions, leading to delayed cognitive development [1]. Infants on a cow's milk diet face a higher risk of severe Iron Deficiency Anemia (IDA) as calcium in cow's milk competes with iron absorption. Cow's milk consumption has been found to diminish iron stores in infants and toddlers, a fact well-documented across various regions. Numerous factors contribute to iron deficiency in this demographic, with cow's milk's low iron content being a primary one, making it challenging for infants to meet their iron needs for growth. Recent data suggest a 13.5% prevalence of iron deficiency and a 2.7% prevalence of IDA among toddlers aged 1 to 2 in the USA [2]. Iron plays a crucial role in numerous metabolic, oxidation reactions and is fundamental for mitosis. Persistent deficiency during childhood leads to serious health ramifications [3]. A national study revealed that 27% of mothers provided pre-lacteals, with salt water (44%) and cow's milk (26%) being the notable feeds [4]. Observed consequences include delayed psychomotor development, language acquisition challenges, substantial cognitive loss, heightened infection susceptibility, fatigue, and irritability [5, 6]. In Pakistan, the prevalence of IDA in children under five ranges from 40-70% [7, 8]. Pakistani children with IDA show growth retardation, impaired cognition, reduced physical activity, and are speculated to

DOI: https://doi.org/10.54393/pjhs.v4i11.1101

contribute to the nation's high infant mortality rate [7, 9-11]. Serum Ferritin concentrations are utilized to measure iron deficiency due to their high sensitivity and specificity in identifying iron deficiency in individuals [1]. No such studies have been found at local level especially at Sindh on this objective. Therefore, this study has been conducted to determine the frequency of iron deficiency anemia among cow's milk infants up to 6 months of age at LUMHS. AS per high frequency of iron deficiency anemia due to cow's milk, it is recommended that, the cow's milk consumption should be avoided and mother milk should be consumed to decrease the infant's morbidity. This study explored the current knowledge regarding prevalence of iron deficiency anemia among cow's milk consumed infants at local level.

METHODS

This cross-sectional research was conducted in the Pediatric Department of Liaquat University Hospital, Hyderabad & Jamshoro. The study spanned a duration of six months, from November 2020 to April 2021. Sample size was calculated via rao-soft software by taking the proportion of Iron deficiency anemia as 30.8% among children who consumed cow milk [11]. With 5% margin error and 95% confidential level, the sample size was calculated to be 323. The inclusion criteria encompassed all infants up to the age of six months, regardless of gender, provided they were full-term infants with a history of cow's milk consumption. Conversely, the exclusion criteria comprised patients who declined participation in the study, those with a history of preterm birth or severe acute malnutrition, children with any infectious disease or inflammation, children receiving iron therapy, and those on breastfeeding. Upon fulfilling the inclusion criteria, patients were selected for participation through the pediatric outpatient department (Paeds OPD). Written consent was obtained from all participants before proceeding. A thorough medical history was compiled and relevant investigations were conducted for each participant. Infants up to six months of age, having hemoglobin level < 9.5 g/dl and MCV < 74 were labelled as having Iron Deficiency Anemia. The severity of anemia was assessed via levels of serum ferritin. Serum ferritin levels in between 30 ng/dl to 50ng/dl was labelled as having mild anemia, while infants with range between 15ng/dl to 20ng/dl was labelled as having moderate anemia. Severe anemia was labelled when infant had serum ferritin levels less than 15ng/dl [12]. Mothers were interviewed to ascertain the duration of cow's milk consumption for their infants. A 3ml intravenous blood sample was collected from all infants to conduct a complete blood picture and determine ferritin levels. Information such as age, gender, length, weight, Z-score, heart rate, respiratory rate, signs and symptoms, duration of cow's milk consumption, severity of anemia was assessed via levels of ferritin and IDA were meticulously collected using a pre-designed proforma. For data analysis, the acquired data were entered and evaluated using the statistical program SPSS version-20.0. Quantitative variables such as age, length, weight, Hb level, and ferritin level were analyzed to estimate their mean and standard deviation. Qualitative variables like gender, palmar pallor, irritability, severity of anemia, and iron deficiency anemia were assessed through simple frequency and percentage calculations.

RESULTS

Total 323 infants were studied to assess the frequency of iron deficiency anemia among cow's milk infants up to 6 months. Mean age of infants was 4.11 ± 1.31 months, minimum 1 month and maximum 6 months. In this study girls were 56.3% and boys were 43.7. Weight, length, standard deviation as per weight is given in table 1.

Table 1: Gender Distribution Along with Weight and Standard Deviation of Weight by Length (N=323)

Gender Distribution	**Male**	**Female**
	141 (43.7%)	182 (56.3%)
Weight Distribution	**Less than 5 kg**	**More than 5 kg**
	281 (87%)	42 (13%)
Standard Deviation of Weight by Length (Z-Score)	-1	-2
	156 (48.6%)	167 (51.4%)

As per sign and symptoms, 99.1% infants were pale or sallow (yellow) skin with 99.1% exhibited a paler appearance in the lining of the eyelids and nail beds than usual. Irritability was reported among 15.8% of the infants and 25.4% were presented with pale cheeks and lips, respiratory rate and heart rate while 3 infants were without sign and symptoms (Table 2).

Table 2: Signs and Symptoms of Infants (N=323)

Signs and Symptoms	Frequency (%)
Normal	03 (0.9%)
Pale or yellow skin	320 (99.1%)
Pale cheeks and lips	82 (25.4%)
Irritability	51 (15.8%)
Nail bed and conjunctiva look less pink than normal	320 (99.1%)

Most of the cases had moderate anemia 82.4%, 15.8% had mild anemia and 0.9% infants had no anemia and 0.9% had severe anemia. Overall average of hemoglobin was 8.92 ± 1.09 g/dl, minimum 5.50 g/dl and maximum 12.00 g/dl (Table 3).

DOI: https://doi.org/10.54393/pjhs.v4i11.1101

Table 3: Severity of Anemia of the Infants (N=323)

Anemia	Frequency (%)
No	03 (0.9%)
Mild Serum Ferritin (30 ng/dl to 50ng/dl)	266 (82.4%)
Moderate Serum Ferritin (15 ng/dl to 29ng/dl)	51 (15.8%)
Severe Serum Ferritin (< 15ng/dl)	3 (0.9%)

According to the duration of cow milk consumption, most of the infants 63.8% had duration of less than one month, 26.9% had duration of one month 4.6% were under consumption from 1.5 months and 4.6% from 2 months (Table 4).

Table 4: Duration of Cow Milk Consumption (N=323)

Duration (Months)	Frequency (%)
0.5 month	206 (63.8%)
1 month	87 (26.9%)
1.5 months	15 (4.6%)
2 months or more	15 (4.6%)

In this study overall frequency of iron deficiency anemia was found to be 18.6%. Frequency of iron deficiency anemia of the infants was statistically significant according to age (p-0.039). Frequency of iron deficiency anemia of the infants was statistically significant according to gender (p-0.018). Iron deficiency anemia was statistically significant according to Z-score (p-0.001), while statistically insignificant according to weight, length, HR and RR (P≥0.05).

DISCUSSION

The intake of cow's milk (CM) by infants and toddlers negatively impacts their iron stores, a fact extensively documented in various regions. In this study total 323 infants were studied to assess the frequency of iron deficiency anemia among cow's milk infants up to 6 months and the mean age of infants was 4.11 ± 1.31 months, minimum 1 month and maximum 6 months. Similarly, Burke et al., reported that the mean age of the infants was 6.7 ± 0.9 months [13]. In another study of Siddique et al., examined the frequency of iron deficiency anemia in infants under exclusive breastfeeding, fortified milk, and cow milk feeding regimes, encompassing 150 infants—89 males and 61 females, with an average age of 7.77 months. It analyzed the impact of varying feeding regimes on iron status and anemia frequency among infants aged 6 to 9 months, while in this study out of all females were 56.3% and males were 43.7% [14] and Burke et al., also demonstrated that the male infants were 52% and remaining were females [13]. Although Patel et al., also reported that among anemic children males were 57.3% and females were 42.3% with male to female ratio as Male: female ratio was 1.3:1 [15]. In this study as per sign and symptoms, 99.1% infants were pale or sallow (yellow) skin, with 99.1% exhibited a paler appearance in the lining of the eyelids and nail beds than usual. Irritability was among 15.8% of the infants and 25.4% were presented with pale cheeks and lips, while 3 infants were without sign and symptoms. In another study of Joo et al., it is demonstrated that the under-diagnosis of IDA in infants persists due to challenges in infant blood sampling and acquiring adequate blood volume for laboratory identification of IDA [16]. Typically, infants are not subjected to blood tests unless notable clinical events warrant them. Additionally, the symptoms of IDA, such as pallor, irritability, poor feeding, fatigue, lethargy, and pica, are non-specific. In this study most of the cases 82.4% has mild anemia, 15.8% had moderate anemia and 0.9% infants were severely anemic and overall average of hemoglobin was 8.92+1.09 g/dl, minimum 5.50 g/dl and maximum 12.00 g/dl. Similarly, Patel et al., reported that the average hemoglobin level in anemic infants was 9.3 g/dl. Among them, 54 (41.2%) exhibited mild anemia, 66 (50.4%) had moderate anemia, and 11 (8.4%) showed severe anemia [15]. On other hand in the study of Parkin et al., reported that the mean Hb was 55.1+15.2) g/l with a range of 13–79 g/l; and median serum ferritin was 4 (interquartile range 2–8) µg/l [17]. In this study overall frequency of iron deficiency anemia was found to be 18.6%. On other hand Qudisa et al., reported that among all, 113 infants were identified as anemic (75.3%), with iron deficiency attributed to cow milk feeding [18]. Common causes of IDA in infants include inadequate diet, whole cow's milk consumption, early introduction of cow's milk into an infant's diet, reduced total body iron at birth, Pica, and lead poisoning [19]. Above studies showed higher incidence of the anemia among cow milk consumption children as compared to this study and this may because of this has been conducted on limited age range of only 6 months, hence the duration of cow milk consumption is markedly less than other studies as in this study frequency of iron deficiency anemia of the infants was statistically significant according to age. Unmodified cow's milk is recognized for its low iron content and poor iron absorption, alongside a low vitamin C content. Conversely, it has high levels of casein and calcium, which could adversely affect iron absorption and, consequently, hemoglobin synthesis [20-22]. Iron deficiency can lead to a condition that may hinder an infant's mental, motor, and behavioral development, potentially resulting in issues that persist long after iron levels have returned to healthy levels. Infants from developing nations, those born preterm or with low birth weight, or those primarily fed unfortified cow's milk are deemed to be at high risk for iron deficiency [23, 24]. The intake of cow milk during infancy adversely impacts blood indices and serum ferritin levels. A

DOI: https://doi.org/10.54393/pjhs.v4i11.1101

considerable number of uneducated mothers tend to feed their infants cow's milk, which is a significant risk factor for the development of IDA in infants [19].

CONCLUSIONS

As per study conclusion overall frequency of iron deficiency anemia was observed to be 18.6% and cow's milk consumption has been observed as a risk factor of infant's anemia.

Authors Contribution

ptualization: AB
Methodology: AB, FS, SK, MAK
Formal analysis: AB, SK, AA
Writing-review and editing: FS, SK, AA, MAK
All authors have read and 1agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Al Hawsawi ZM, Al-Rehali SA, Mahros AM, Al-Sisi AM, Al-Harbi KD, Yousef AM. High prevalence of iron deficiency anemia in infants attending a well-baby clinic in northwestern Saudi Arabia. Saudi Medical Journal. 2015 Sep; 36(9): 1067. doi: 10.15537/smj.2015.9.11844.

[2] Mantadakis E, Zikidou P, Tsouvala E, Thomaidis S, Chatzimichael A. Severe iron deficiency anemia and anasarca edema due to excessive cow's milk intake. The Turkish Journal of Pediatrics. 2019 Feb; 61(1): 102-6. doi: 10.24953/turkjped.2019.01.016.

[3] Waiswa P, Kemigisa M, Kiguli J, Naikoba S, Pariyo GW, Peterson S. Acceptability of evidence-based neonatal care practices in rural Uganda–implications for programming. BMC Pregnancy and Childbirth. 2008 Dec; 8: 1-9. doi: 10.1186/1471-2393-8-21.

[4] Khan GN, Memon ZA, Bhutta ZA. A cross sectional study of newborn care practices in Gilgit, Pakistan. Journal of Neonatal Perinatal Medicine. 2013 Jan; 6(1):69-76. doi: 10.3233/NPM-1364712.

[5] Lisbôa MB, Oliveira EO, Lamounier JA, Silva CA, Freitas RN. Prevalence of iron-deficiency anemia in children aged less than 60 months: A population-based study from the state of Minas Gerais, Brazil. Revista de Nutrição. 2015 Apr; 28(2): 121-31. doi: 10.1590/1415-52732015000200001.

[6] Braga J, Vitalle MS. Deficiência de ferro na criança. Revista Brasileira de Hematologia e Hemoterapia. 2010 Jun; 32(2): 38-44. doi: 10.1590/S1516-84842010005000054.

[7] Habib MA, Black K, Soofi SB, Hussain I, Bhatti Z, Bhutta ZA et al. Prevalence and predictors of iron deficiency anemia in children under five years of age in Pakistan, a secondary analysis of national nutrition survey data 2011–2012. PloS One. 2016 May; 11(5): e0155051. doi: 10.1371/journal.pone.0155051.

[8] Rahbar MH, Hozhabri S, Wang J. Prevalence of anaemia among children living in five communities in and near Karachi, Pakistan. Toxicological & Environmental Chemistry. 2007 Apr; 89(2): 337–46. doi: 10.1080/02772240601025038.

[9] Ahmed A, Ahmad A, Khalid N, David A, Sandhu MA, Randhawa MA et al. A question mark on iron deficiency in 185 million people of Pakistan: its outcomes 83 and prevention. Critical Reviews in Food Science and Nutrition. 2014 Dec; 54(12): 1617–35. doi: 10.1080/10408398.2011.645087.

[10] Akhtar S, Ahmed A, Ahmad A, Ali Z, Riaz M, Ismail T. Iron status of the Pakistani population-current issues and strategies. Asia Pacific Journal of Clinical Nutrition. 2013 Jan; 22(3): 340-7.

[11] Ahmad MS, Farooq H, Maham SN, Qayyum Z, Waheed A, Nasir W. Frequency of anemia and iron deficiency among children starting first year of school life and their association with weight and height. Anemia. 2018 Apr; 2018: 8906258. doi: 10.1155/2018/8906258.

[12] Yao DC and Fergie J. Iron deficiency and other types of anemia in infants and children. American Family Physician. 2013 Feb; 87(4): 98-104.

[13] Burke RM, Rebolledo PA, Aceituno AM, Revollo R, Iñiguez V, Klein M et al. Effect of infant feeding practices on iron status in a cohort study of Bolivian infants. BMC Pediatrics. 2018 Dec; 18(1): 1-9. doi: 10.1186/s12887-018-1066-2.

[14] Siddique AW, Basheer F, Ashraf T, Naseem S. Comparison of frequency of iron deficiency anemia in infants on exclusive breast feed, fortified milk and cow's milk. Pakistan Armed Force Medical Journal. 2021 Feb; 71(1): 201-05.

[15] Patel AH and Patel PK. Study of anemia in hospitalised infants with special reference to its risk factors. Pediatric Review: International Journal of Pediatric Research. 2019 Oct: 6(10): 527-533. doi: 10.17511/ijpr.2019.i10.06.

[16] Bondi SA and Lieuw, K. Excessive cow's milk consumption and iron deficiency in toddlers. Two unusual presentations and Review. ICAN: Infant, Child, & Adolescent Nutrition. 2009 Jun; 1(3): 133–139. doi: 10.1177/1941406409335481.

[17] Parkin PC, DeGroot J, Maguire JL, Birken CS, Zlotkin

DOI: https://doi.org/10.54393/pjhs.v4i11.1101

S. Severe irondeficiency anaemia and feeding practices in young children. Public Health Nutrition. 2016 Mar; 19(4): 716-22. doi: 10.1017/S1368980015001639.

[18] Qudsia F, Saboor M, Khosa SM, Ayub Q. Comparative analysis of serum iron, serum ferritin and red cell folate levels among breast fed, fortified milk and cow's milk fed infants. Pakistan Journal of Medical Sciences. 2015 May; 31(3): 706. doi: 10.12669/pjms.313.6937.

[19] Yang W, Li X, Li Y, Zhang S, Liu L, Wang X et al. Anemia, malnutrition and their correlations with socio-demographic characteristics and feeding practices among infants aged 0–18 months in rural areas of Shaanxi province in northwestern China: a cross-sectional study. BMC Public Health. 2012 Dec; 12(1): 1-7. doi: 10.1186/1471-2458-12-1127.

[20] Abdurahman A and Gashu D. Level of hemoglobin among cow milk and camel milk consuming young children: A comparative study. Plos one. 2021 Mar; 16(3): e0247572. doi: 10.1371/journal.pone.0247572.

[21] Joo EY, Kim KY, Kim DH, Lee JE, Kim SK. Iron deficiency anemia in infants and toddlers. Blood Research. 2016 Dec; 51(4): 268. doi: 10.5045/br.2016.51.4.268.

[22] Killip S, Bennett JM, Chambers MD. Iron deficiency anemia. American Family Physician. 2007 Mar; 75(5): 671-8.

[23] Hassan FM, El-Gendy FM, Badra HS, Eldin SM, Elsayyad DM. Evaluation of iron-deficiency anemia in infancy. Menoufia Medical Journal. 2016 Apr; 29(2): 269. doi: 10.4103/1110-2098.192412.

[24] Kazal LA. Prevention of iron deficiency in infants and toddlers. American Family Physician. 2002 Oct; 66(7): 1217-25.

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 4, Issue 11 (November 2023)

Original Article

Effects of Soft Tissue Massage Along with Mobilization Technique on Intensity of Symptoms and Functional Status of Carpal Tunnel Syndrome: A Randomized Controlled Trial

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ARTICLE INFO

Key Words:
Median Neuropathy, Compression Neuropathy, Entrapment Neuropathy, Manual Therapy, Soft Tissue Massage

How to Cite:
Syed, H., Ahmed, S. I., Arif, A., Zia, M., Shahbaz, N. N., & Kashif, M. (2023). Effects of Soft Tissue Massage Along with Mobilization Technique on Intensity of Symptoms and Functional Status of Carpal Tunnel Syndrome: A Randomized Controlled Trial : Effects of Soft Tissue Massage . Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs. v4i11. 1144

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Received Date: 20th October, 2023
Acceptance Date: 9th November, 2023
Published Date: 30th November, 2023

ABSTRACT

The median nerve in the wrist is compressed in the carpal tunnel, causing Carpal Tunnel Syndrome (CTS). The symptoms of this condition include numbness, tingling, and pain in the hand and fingers. The effectiveness of soft tissue massage along with mobilization techniques in managing CTS symptoms and improving functional status is an area to explored. **Objective:** To determine the effects of soft tissue massage along with mobilization technique on intensity of pain and functional status in Carpal tunnel syndrome patients. **Methods:** A randomized controlled trial was conducted on 60 patients with mild and moderate carpal tunnel syndrome at Sindh Institute of Physical Medicine and Rehabilitation, Karachi. In group A, soft tissue massage (Medenci hand massage technique) was combined with joint (radiocarpal and inter-carpal) and median nerve mobilization sliders, whereas in group B, only joint and median nerve mobilization sliders were used. A visual analog pain scale, the Boston scale of carpal tunnel syndrome, a dynamometer and a pinch gauge were used to evaluate participant on day 1 and the last treatment session. **Results:** There was no significant difference between group A and B after treatment. However, there was significant improvement ($p<0.05$) in intragroup analysis in all outcome measures after treatment in both groups with $p< 0.05$. **Conclusions:** Soft tissue massage along with joint and nerve mobilization is effective in symptoms severity and functional status. To further validate the findings of this study, similar investigations will need to be undertaken in the future to consider it before surgical intervention in CTS.

INTRODUCTION

Carpal Tunnel Syndrome (CTS) is considered one of the most common work-related musculoskeletal disorders of the upper limb [1]. Presently days, an increment in the usage of computers among the general population influences 1-5 % of the population with Carpal Tunnel syndrome [2]. In Pakistan, the overall prevalence of CTS among computer users is 61.5% which includes 13.5% of females and 48.1 % of males. In the general population, the prevalence rate of carpal tunnel syndrome varies from 7%-19% [3], and it commonly occurs in middle age females with an annual incidence of 1.5 per 1000 as compared to 0.5 per 1000 males [4]. The etiology of this syndrome is idiopathic [5]. It is related to various factors. Non-occupational variables reported to be related to carpal tunnel syndrome

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

includes; chronic diseases like inflammatory disease (rheumatoid arthritis, gout), endocrine disorders (diabetes mellitus, hypothyroidism), inherited defects like anomalous muscles, wrist trauma (fracture), age, female gender, obesity, oral contraceptive use, pregnancy, menopause. Occupational related factors reported in CTS includes vigorous and repetitive hand task, poor ergonomics, mechanical stress at the base of the palm, and prolonged use of vibratory tool [6]. Usually, the patient presents subjectively with unpleasant sensations like pain on CTS, which is known as a factor that influences the psychological status of various musculoskeletal diseases. A previous study suggests that some psychological issues named as depression and pain-related anxiety correlated along with the severity of CTS which may affect the overall outcome of the patient [7]. In addition, other symptoms paresthesia and numbness on the volar side of the hand, three fingers and half fourth finger (radial side), and atrophy of thenar muscles have been noted in the advanced stage [8]. It can be diagnosed based on the clinical presentation of the patient's signs and symptoms, electrodiagnostic tests, and different provocative tests like Phalen, and Tinel's signs [9]. Physical therapy management for CTS includes electrophysical modalities (Transcutaneous Electrical Nerve Stimulation (TENS)), Interferential Current (IFC) [10], Ultrasound, manual therapy, neural mobilization, Kinesio-taping [6], wrist splints, acupuncture [11]. It has been reported in existing evidence that Soft Tissue Massage (STM) is used to promote positive physical, functional and psychological outcomes in clinical health practice [12], but weak base evidence on massage is present. So, there is a need to bridge a gap in research on massage and observed significant outcomes of massage mainly on symptom severity, functional imitation, and also related psychological issues. This study examined the effects of soft tissue massage with mobilization technique on pain intensity and functional status in patients with Carpal Tunnel Syndrome using a Jamar hand-held dynamometer, a pinch gauge, and the Boston Scale. This study aimed to determine the effectiveness of soft tissue massage with mobilization technique versus mobilization technique alone in the management of Carpal tunnel syndrome.

METHODS

This study was conducted at Sindh Institute of Physical Medicine and Rehabilitation (IPMR) and Civil Hospital Karachi at the Neurology Department. This study was approved by the Institutional Review Board of Dow University of Health Sciences with the reference IRB-1992/DUHS/Approval/2021/456.This trial is trial registry clinicaltrials.gov: with Trial registration number NCT05466162. It was conducted using a non-probability purposive sampling technique. A sample size of 48 was calculated through open EPI version-3.0 software. Using 80 % of power and 95% of confidence interval with after intervention mean 1.90 standard deviation 0.62 in Group A and mean 2.55 standard deviation 0.55 in Group B by using Boston Carpal Tunnel-Functional status scale Questionnaire (FSS BCTQ-FSS) [13]. Due to low sample size, we considered 30 subjects in each group. Total sample size of this study is 60, 30 samples in each group. The inclusion criteria were Consultant Physiatrist diagnosed patients of CTS on electro diagnostic test i.e., Nerve Conduction Studies, Mild and moderate severity of CTS, Age from 18-50 years, both gender patients with unilateral involvement of hand. Patients with electrodiagnostic test results or motor or sensory deficits in the ulnar nerve and radial nerve, and other neurological conditions (cervical myelopathy, motor neuron disease such as amyotrophic lateral sclerosis), neoplasm around the affected arm, musculoskeletal problems of the upper quadrant (such as rheumatoid arthritis or fibromyalgia, cervical radiculopathy) or recent upper extremity trauma on the affected side were excluded. Each participant was explained the study purpose and procedure before consent was taken (either in Urdu or English). Medications were continued during the study, prescribed by Physiatrist (figure 1).

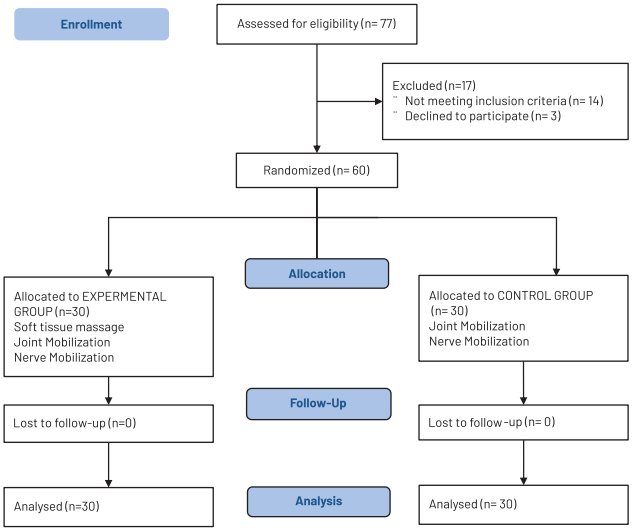

Figure 1: Consort Diagram

An outcome assessor blinded to the intervention performed an assessment at baseline and at the end of the sixth week. Using a Visual Analog Scale, measure the change in pain intensity. The pain level was rated on a 0-10 cm scale, with 0 cm meaning 'no pain' and 10 cm meaning the most excruciating pain. Increasing the number of cm suggests the worst pain [14]. Hand and Pinch Grip strength was quantified in kilogram by using Jamar dynamometer

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

Pinch Gauge. Participants hold it in tested hand, with the arm at right angles and the elbow by the side of the body. Participants were instructed to perform maximum isometric contraction and hold it for 5 seconds. Participants repeated it 3 times with rest period of one minute between two consecutive trials. The best score was recorded. In order to calculate the mean of these readings, measurements were taken three times for each individual [15]. Boston Carpal Tunnel Questionnaire was used to assess changes in symptoms severity and functional status. Each item on the scale of symptom severity contains 11 items and each item on the scale of functional status contains 8 items. Higher scores on both scales indicate greater severity and difficulty. Scores below or equal to 11 are considered asymptomatic, 12-22 are mild, 23-33 are moderate, 24-44 are severe, and 45-55 are very severe. Functional status scale cut-off: less than 8 or 8 = Asymptomatic, 9-16 = Mild, 17-24 = Moderate, 25-32 = Severe, 33-40 = Very Severe [16]. The treatment duration was 30 - 45 minutes, 3 sessions per week in alternate days for 6 weeks. After recruiting CTS patients, participants were randomly assigned to one of two groups (1:1) using www.random.org. A statistician constructed the computer-generated randomization sheet. Following initial screening, the primary investigator intervened, and the participant was assigned to a treatment by the first researcher. As an effort to avoid the interaction between the participants, each intervention was given on a different time window. The outcome assessor was not informed of the allocation and recorded the readings at baseline and after the fourth week. Joint mobilizations and the nerve mobilization was provided to both groups. for the joint mobilization the Patient was lying in a supine position, and affected arm was place in a supination for radiocarpal flexion and in pronation for radiocarpal extension. Therapist was standing at the patient's waist level and side of the table and facing superiorly. For the Radio-carpal flexion Technique; while maintaining joint in traction, from a position midway between flexion and extension, the patient wrist was moved downward towards the floor while the carpus held firmly between therapist's index finger and thumbs, is flexed on radius and ulna. While performing this movement the carpus must be held firmly. For Radio-carpal Extension Technique; with traction, extension movement is produced through a very firm localized grasp with the fingers and thumb while lowering the wrist toward the floor as the wrist is extended. The oscillation is completed by returning the patient's arm to the starting position, while at the same time returning the extended radio-carpal joint to its mid –position. Patient was supine – lying, affected side elbow was flexed to 90 degree and forearm in supination. Therapist was standing at the patient's affected hand and facing toward patient's body for applying inter-carpal horizontal flexion. Therapist changed position and stand beyond patient's flex elbow with supinated forearm and facing across patient's head. For Inter-carpal Horizontal Flexion Technique; the oscillatory movement was provided by opposite pressure through forearm. Therapist's one hand provided a cupping action on the patient's hand around the pivot formed by the therapist's thumb of another hand. For Inter-carpal Horizontal Extension Technique; The oscillatory movement was provided by the thumb pressure against the center of the carpus posteriorly and pulling against the medial and lateral margins of carpus with finger. The action will produce by wrist extension of therapist and will facilitate by pushing the patient's hand away with thumb [17]. The nerve mobilization was provided as described by the Stephanie and colleague [18]. However, the Soft Tissue Massage Technique with Madenci hand massage technique was provided to only experimental group. Patient position was supine – lying with affected arm in supination. The therapist's position was standing at the patient's waist level and side of the table and facing superiorly. Effleurage: On the ventral surface of forearm, scrubbing from distal to proximal in a direction for 30 seconds. Petrissage: Scouring depths on forearm, from distal to proximal direction for 30 seconds. Friction: Slow stroking for sedative effect, from distal to proximal in a clock wise direction, on volar surface of deep tissue for 60 seconds. Shaking: Patient will actively shake his hand for thirty seconds [19]. Data were stored and analyzed using IBM-SPSS version 23.0; Counts with percentages were reported for baseline characteristics and outcomes on VAS, BCTQ (BCTQ-SSS and BCTQ-FSS), scales. Mean with standard deviation were given on age, BMI, mean scores on VAS, BCTQ-SSS and BCTQ-FSS, involved hand grip and pinch strengths. Within group comparison was made using paired sample –test, between group comparisons was done using independent sample t-test, Pearson Chi Square test was used to check the association on qualitative outcomes of scales. P-values less than 0.05 were considered statistically significant.

RESULTS

Table 1 below lists the baseline characteristics of the patients who were being studied. According to the Pearson Chi Square test, there was no significant correlation between baseline characteristics and treatment groups ($p>0.05$).

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

Table 1: Baseline Characteristics of Studied Patients (n=60)

Characteristics		Treatment Group A n (%)	Treatment Group B n (%)	p-value
Age Group	25 - 40 years	14 (46.7)	14 (46.7)	0.99
	41 - 50 years	16 (53.3)	16 (53.3)	
	Mean ±SD	41.7 ± 6.0	40.1 ± 7.1	
Gender	Male	5 (16.7)	7 (23.3)	0.51
	Female	25 (83.3)	23 (76.7)	
BMI (kg/m2)	Normal	7 (23.3)	2 (6.7)	0.19
	Overweight	21 (70.0)	16 (53.3)	
	Obesity	2 (6.7)	2 (6.7)	
	Mean ±SD	26.6 ± 4.1	27.6 ± 4.0	
Involved hand	Right	12 (40)	11 (36.7)	-
	Left	18 (60)	19 (63.3)	
Dominant hand	Right	29 (96.7)	29 (96.7)	0.99
	Left	1 (3.3)	1 (3.3)	
Occupation	House chores	22 (73.3)	18 (60.0)	0.32
	Desktop worker	1 (3.3)	5 (16.7)	
	Field worker	1 (3.3)	2 (6.7)	
	Other	6 (20.0)	5 (16.7)	
Working Hours per day	Less than 2 hours	0 (0.0)	3 (10.0)	0.08
	2-5 hours	17 (56.7)	17 (56.7)	
	6- hours	10 (33.3)	4 (13.3)	
	More than 9 hours	3 (10.0)	6 (20.0)	
CTS classification according to electrophysio-logical test	Mild	9 (30.0)	9 (30.0)	0.99
	Moderate	21 (70.0)	21 (70.0)	

*p-value<0.05 was considered statistically significant

The improvement in VAS after treatment was statistically significant in both groups with p<0.05. However, between group analysis showed no significant mean difference in the VAS scores between treatment both groups after treatment, p>0.05 (table 2). The improvement in BCTQ scores for both BCTQ-SSS and BCTQ-FSS after treatment was also statistically significant within both groups with p<0.05. However same as VAS, the findings had no significant mean differences between treatment A and B after treatment, p>0.05 shows below in table 2.

Table 3: Outcome differences within and between groups

Outcome Measures	Baseline[a]	After treatment[a]	p-value within groups	p-value between groups
VAS (0-10)				0.380
Group A	6.32±1.2	2.83±1.3	<0.01	
Group B	6.07±1.1	3.17±1.5	<0.01	
BCTQ				0.258
BCTQ-SSS				
Group A	32.17±7.96	2.83±1.3	<0.01	
Group B	29.23±64.26	3.17±1.5	<0.01	
BCTQ-FSS				0.105
Group A	23.73±5.22	13.66±2.31	<0.01	
Group B	25.33±4.47	14.66±2.40	<0.01	
Involved HGS				0.784
Group A	23.50±9.65	33.27±12.13	<0.01	
Group B	25.40±13.04	34.17±13.14	<0.01	
Involved HPG				0.889
Group A	8.80±2.39	11.52±3.1	<0.01	
Group B	9.05±3.56	11.38±4.18	<0.01	

VAS=Visual analogue scale, BCTQ= Boston Carpal Tunnel Questionnaire, BCTQ-SSS= Boston Carpal Tunnel Questionnaire Symptom Severity Scale, BCTQ-FSS= Boston Carpal Tunnel Questionnaire, FSS=Functional Status Scale, HGS= Hand Grip Strength, HPG Hand Pinch Grip

[a]Values of mean and standard deviation

[b]Values of mean difference and p-value

DISCUSSION

The study was intended to ascertain the effects of soft tissue massage along with joint and nerve mobilization on symptoms and functional status of CTS. So, purpose was to determine the effect of soft tissue massage along with mobilization technique on intensity of pain and functional status by using Jamar hand-held dynamometer, Pinch Gauge and Boston Scale for carpal tunnel syndrome questionnaire in Carpal tunnel syndrome patients. The findings showed significant improvement before and after treatment in both groups but no significant difference after treatment between both groups. It is observed that that SSS, FSS and strength were improved in both groups though not significant difference observed between groups. In contrast of this study, other study mentioned dominant hand more commonly involved [7]. Symptoms severity and functional status were used to assess by Boston scale of carpal tunnel syndrome questionnaire. BSCTQ contain items that assess uni-manual and bimanual tasks of daily living. These tasks are mainly performed by both hands. Most of the participants in this study have involvement of non-dominant hand i.e., left hand in both groups [8]. Variety of parameters were used to assess usually in studies conducted on CTS were; pain, grip strength and symptoms severity and functional status. For pain measures, mainly VAS used but in another study the patient global assessment and the physician global assessment were used to assess pain. However, it is a self-assessment of overall disease activity in a rheumatoid arthritis [20]. The findings of the present study stated that significant reduction in pain, symptoms as regards VAS and SSS score, and improvement in functions via FSS score, handgrip, and pinch strength after 6 weeks of treatment in both treatments' groups. Similar to this study, various studies show significant improvement in outcome

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

measures after treatment using multimodal manual therapy [9]. Unlike the present study, a series of chronic CTS patient was conducted which assessed pain by Numeric Pain rating scale (NPRS) which reduced, but did not change in pain pressure threshold by using algometer at different sites: mainly over peripheral nerve of the arm (median, radial, and ulnar nerves), C5-C6 zygapophyseal joint, the carpal tunnel, and the tibialis anterior muscle. Also, study applied soft tissue mobilization over anatomical sites of median nerve and neurodynamic slider technique. Nerve mobilization can be used as an adjuvant treatment along with other manual technique. Similarly, to current study findings on pain by using VAS, a randomized control trial compared nerve mobilization with ultrasound and result showed that pain intensity reduces significantly and improve function by following median nerve mobilization. A mark significant mean difference was found pre and post treatment on VAS [6]. Contrary to this, independent effects of nerve mobilization did not assess in this study but previous studies supported it on the basis of facts that increase in nerve strain while extending a joint causing elongation of nerve bed concurrently counteract by reduction in nerve strain while flexing and adjacent joints [11, 21]. Pain reduction was also observed immediately after therapy in manual therapy (MT) and electrical modalities (EM) group on VAS scale conducted by Wolny et al. This study assesses electrophysiology parameters after treatment and found that median nerve sensory conduction velocity enhanced by 34% and the motor conduction velocity increased by 6% in the MT group. However, the sensory and motor conduction velocities of the median nerve remain same in the EM, a reduction in distal motor delay in both groups were analyzed. Moreover, functional status of both groups improved, and subjective CTS symptoms decreased according to BCTQ these were more significantly improved in MT [22]. In contrast to the present study, this study showed improvement in electrophysiological parameters which was not an outcome measurement tool in the current study due to the limited time of trial and accessibility of resources. The present study used electrophysiological test only for diagnostic purpose and did not used as an outcome measure. Author found studies that solely implement joint mobilization, nerve mobilization in CTS. Gunay et al., reported that Carpal bone mobilization improved symptom severity strength, functional status after treatment [17]. Similar techniques were used in the present study and findings were also in agreement with the available literature. On the basis of result author suggest that this multimodal technique including soft tissue massage can be used as conservative management in CTS. It is non-invasive affordable treatment. To further validate the findings of this study, similar investigations will need to be undertaken in the future. The limitations of this study are that the follow-up session has not been conducted so, long term effects of treatment are not known. The pregnant women were not included however, CTS is prevalent among them. Electro diagnostic test was not repeated after treatment so would not analyze effects of treatment on test parameters. However, there is no gender biasness, males are equally included in both groups. Patients were included after confirmation of electro diagnostic and physical test which are standardized.

CONCLUSIONS

The present study concluded that STM along with joint and nerve mobilization is a non-surgical treatment, and it is found in the present study that this treatment was effective in symptom severity and functional status and reduced pain in both groups with mild to moderate CTS. The results indicated statistically significant within groups and non-significant between groups. The findings of the present study stated that there was a significant reduction in pain, and symptoms as regards VAS and SSS score and improvement in functions as measured by the FSS score, handgrip, and pinch strength after 6 weeks of treatment in both treatment groups. As a result, the study findings support the null hypothesis. STM along with joint and nerve mobilization was effective but not superior to the mobilization technique alone. However, to further validate the findings of this study, similar investigations will need to be undertaken in the future to consider them before surgical intervention in CTS.

Authors Contribution

Conceptualization: HS
Methodology: SIA
Formal analysis: AA
Writing-review and editing: MZ, NNS, MK
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Huisstede BM, Hoogvliet P, Franke TP, Randsdorp MS, Koes BW. Carpal Tunnel Syndrome: Effectiveness of Physical Therapy and Electrophysical Modalities. An Updated Systematic Review of Randomized Controlled Trials. Archives of Physical Medicine and Rehabilitation. 2018 Aug; 99(8): 1623-34. doi: 10.1016/j.apmr.2017.08.482.

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

[2] Klokkari D and Mamais I. Effectiveness of surgical versus conservative treatment for carpal tunnel syndrome: A systematic review, meta-analysis and qualitative analysis. Hong Kong Physiotherapy Journal. 2018 Dec; 38(2): 91-114. doi: 10.1142/S1013702518500087.

[3] Cazares-Manríquez MA, Wilson CC, Vardasca R, García-Alcaraz JL, Olguín-Tiznado JE, López-Barreras JA et al. A Review of Carpal Tunnel Syndrome and Its Association with Age, Body Mass Index, Cardiovascular Risk Factors, Hand Dominance, and Sex. Applied Sciences. 2020 May; 10(10): 3488. doi: 10.3390/app10103488.15-0.

[4] Iftikhar S, Javed AM, Kasuri NM. Frequency of Metabolic Syndrome and Its Components in Patients with Carpal Tunnel Syndrome. Journal of the College of Physicians and Surgeons Pakistan. 2016 May; 26 (5): 380-3.

[5] Aboonq MS. Pathophysiology of carpal tunnel syndrome. Neurosciences Journal. 2015 Jan; 20(1): 4-9.

[6] Külcü DG, Bursali C, Aktaş İ, Alp SB, Özkan FU, Akpinar P. Kinesiotaping as an alternative treatment method for carpal tunnel syndrome. Turkish Journal of Medical Sciences. 2016; 46(4): 1042-9. doi: 10.3906/sag-1503-4.

[7] Shin YH, Yoon JO, Kim YK, Kim JK. Psychological Status Is Associated With Symptom Severity in Patients With Carpal Tunnel Syndrome. The Journal of Hand Surgery. 2018 May; 43(5): 484. doi: 10.1016/j.jhsa.2017.10.031.

[8] Koca I, Boyaci A, Tutoglu A, Ucar M, Kocaturk O. Assessment of the effectiveness of interferential current therapy and TENS in the management of carpal tunnel syndrome: a randomized controlled study. Rheumatology International. 2014 Dec; 34(12): 1639-45. doi: 10.1007/s00296-014-3005-3.

[9] Hafez RA, Alenazi MA, Kachanathu JS, Alroumi MA, Mohamed SE. The Effect of Longitudinal Stretching of Muscles and Nerve versus Deep Transverse Friction Massage in the Management of Patients with Carpal Tunnel Syndrome. Open Journal of Therapy and Rehabilitation. 2014 Oct; 2: 199-206. doi: 10.4236/ojtr.2014.24025.

[10] Lewańska M. The bilaterality of idiopathic carpal tunnel syndrome among manual workers. International Journal of Occupational Medicine and Environmental Health. 2020; 33(2): 151-61. doi: 10.13075/ijomeh.1896.01517.

[11] Chung VC, Wong SY, Kung K, Zee CY, Leung WN, Chong KC et al. Electroacupuncture and wrist splinting for carpal tunnel syndrome: A randomized trial. Hong Kong Medical Journal. 2017 Jun; 2(3): 28-31.

[12] Elnady B, Rageh EM, Ekhouly T, Fathy SM, Alshaar M, Fouda ES et al. Diagnostic potential of ultrasound in carpal tunnel syndrome with different etiologies: correlation of sonographic median nerve measures with electrodiagnostic severity. BMC Musculoskeletal Disorders. 2019 Dec; 20(1): 1-8. doi: 10.1186/s12891-019-3010-5.

[13] Ijaz MJ, Karimi H, Ahmad A, Gillani SA, Anwar N, Chaudhary MA. Comparative Efficacy of Routine Physical Therapy with and without Neuromobilization in the Treatment of Patients with Mild to Moderate Carpal Tunnel Syndrome. BioMed Research International. 2022 Jun; 2022: 1-8. doi: 10.1155/2022/2155765.

[14] Begum MR and Hossain MA. Validity and reliability of visual analogue scale (VAS) for pain measurement. Journal of Medical Case Reports and Reviews. 2019 Nov; 2(11).

[15] Latif A, Baig AA, Wajid SA, Ali SS. Frequency of median nerve tightness and its association with upper limb functions among smartphone users of a public sector university, Karachi. JPMA. The Journal of the Pakistan Medical Association. 2022 Aug; 72(8): 1529-34. doi: 10.47391/JPMA.3824.

[16] Spies-Dorgelo MN, Terwee CB, Stalman WA, van der Windt DA. Reproducibility and responsiveness of the Symptom Severity Scale and the hand and finger function subscale of the Dutch arthritis impact measurement scales (Dutch-AIMS2-HFF) in primary care patients with wrist or hand problems. Health and Quality of Life Outcomes. 2006 Dec; 4(1): 1-9. doi: 10.1186/1477-7525-4-87.

[17] Gunay B, Alp A. The effectiveness of carpal bone mobilization accompanied by night splinting in idiopathic carpal tunnel syndrome. Turkish Journal of Physical Medicine and Rehabilitation. 2015 Apr; 61 :45-50. doi: 10.5152/tftrd.2015.70446.

[18] Wise S and Bettleyon J. Neurodynamics Is an Effective Intervention for Carpal Tunnel Syndrome. Journal of Sport Rehabilitation. 2021 Dec; 31(4): 501-4. doi: 10.1123/jsr.2021-0155.

[19] Ng KC and Cohen M. The effectiveness of massage therapy a summary of evidence-based research. RMIT University report for Australian Association of Massage Therapists, Melbourne: Australian Association of Massage Therapists. 2011 Oct.

[20] Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. Sports Medicine. 2005 Mar; 35(3): 235-56. doi: 10.2165/00007256-

DOI: https://doi.org/10.54393/pjhs.v4i11.1144

200535030-00004.

[21] Khosrawi S, Emadi M, Mahmoodian AE. Effectiveness of splinting and splinting plus local steroid injection in severe carpal tunnel syndrome: A Randomized control clinical trial. Advanced Biomedical Research. 2016 Feb; 5: 1-6. doi: 10.4103/2277-9175.175902.

[22] Madenci E, Altindag O, Koca I, Yilmaz M, Gur A. Reliability and efficacy of the new massage technique on the treatment in the patients with carpal tunnel syndrome. Rheumatology International. 2012 Oct; 32(10): 3171-9. doi: 10.1007/s00296-011-2149-7.

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Assessment of Non-Ischemic Chest Pain and its Association with Socio-Demographic Characteristics among Post Percutaneous Coronary Interventions (PCI) Patients

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ARTICLE INFO

Key Words:
Non-Ischemic Chest Pain, Percutaneous Coronary Intervention, Numerical Rating Scale, Tertiary Care Hospital

How to Cite:
Naz, S., Ali, A., Rasheed, A., & Ahmed, T. (2023). Assessment of Non-Ischemic Chest Pain and its Association with Socio-Demographic Characteristics among Post Percutaneous Coronary Interventions (PCI) Patients : Non-Ischemic Chest Pain among Post PCI Patient. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1162

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Received Date: 6th November, 2023
Acceptance Date: 26th November, 2023
Published Date: 30th November, 2023

ABSTRACT

The most common procedure used in cardiovascular medicine is percutaneous coronary intervention (PCI) that can create some physiological complications, such as decreasing heart rate, mechanical issues, and cardiac arrest among patients. **Objective:** To determine the frequency of non-ischemic chest pain and its relation with socio-demographic features amongst post PCI patients in a tertiary care hospital in Karachi. **Methods:** This analytical cross-sectional study was led at National Institute of Cardiovascular Diseases (NICVD) Hospital, Karachi. A total of 195 patients with Post PCI non-ischemic chest pain were recruited by using the Numerical rating scale (NRS). Non-probability purposive sampling technique was used and permission was taken from Institutional Review Board (IRB) of DUHS and Ethical Review Committee (ERC) of NICVD. Data were analyzed by using SPSS Version-26.0. Percentages and frequency were used for categorical variables while, a chi-square test was applied to check the associations of non-ischemic chest pain with demographic features of the patients. **Results:** In this study, 63.60% of the participants were male. Most of the participants (75.4%) were married. Non-ischemic chest pain was found significantly associated with age, gender, marital status, history of disease and drug history with p-values <0.001, 0.001, <0.001, <0.001, <0.001 respectively. The majority of the participants (90.26%) were suffered with non-ischemic chest pain. **Conclusions:** This study revealed that majority of the patients suffered with non-ischemic chest pain and moderate pain level was prevailing in the majority of the post PCI patients.

INTRODUCTION

Chest pain is the most common problem among patients with frequent non-cardiac in origin. Researches show that approximately 50% to 80% patients brought in emergency department with chest pain are discharged without any accurate diagnosis and labeled them as a non-cardiac chest pain (NCCP) [1]. The NCCP is similar to angina pectoris like pain with involvement of coronary artery diseases, during diagnostic evaluation, such as cardiac marker (Troponin-I) and angiography [2]. However, there is a need to work on this significant issue because 44% of patients accepted that they had chest pain one year after negative coronary angiography results, and 50% of patients stated that they were unable to perform their routine tasks due to the chest pain [3]. The most common procedure used in cardiovascular medicine is percutaneous coronary intervention (PCI). According to

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

the American Heart Association report, the average PCI performed in United States is approximately 4,80000 in a year [4]. PCI can create some physiological complications, such as decreasing heart rate, mechanical issues and cardiac arrest among patients with age of more than 75 years and having (ST Elevated Myocardial Infarction) STEMI, as compared to the treatment of fibrinolysis [5]. Despite conflicting evidence concerning its efficacy in stable angina, PCI is the single advised as an adjunct to medical therapy and reduction of the risk in patients with rebellious or continuing angina due to conflicting reports about its advantages in stable angina [6-8]. The number of electoral PCI procedures performed in individuals with stable angina still make up 30–40% of all PCI procedures in patients with coronary artery diseases. This method is becoming more popular as a result of the development of efficient noninvasive coronary imaging [9-10]. Post-PCI chest pain (PPCP) is a typical complication after a coronary artery bypass graft. PPCP has previously been researched mostly in patients with acute coronary syndrome (ACS). Schüepp *et al.*, discovered that 1/3rd of individuals had chest discomfort after an effective PCI procedure [11], and Kini *et al.*, discovered that 35.8% of patients had chest pain following stenting in coronary arteries [12]. The mechanics of PPCP have yet to be fully explored. PPCP can be carried out by an acute thrombosis in the stent, insufficient revascularization, reoccurrence of stenosis, improper vasoconstriction, stretch at stent site, discomfort, and disease progress that does not affect the target arteries [11]. As per the guidelines of the European Society of Cardiology, acute STEMI can be best treated by primary PCI rather than fibrinolysis with the indicated timeframes [13]. The indication of PCI is preferable for patients with significant hemodynamic coronary stenosis in the presence of limiting angina or angina equivalent, which is failure to medical therapy [14]. The objective of this study is to determine the incidence of non-ischemic chest pain and its association with socio-demographic features among post PCI patients in tertiary care hospital Karachi.

METHODS

This cross-sectional analytical study was conducted at the National Institute of Cardiovascular Diseases hospital, Karachi. The duration of this study was from December 2017 to April 2018. The non-probability purposive sampling technique was used for participants selection and sampling. Patients over 18 years of age were recruited from Coronary Care Unit (CCU) after identifying post PCI non-ischemic chest pain. NRS were filled to find out the pain intensity. Those patients who had post PCI complications such as bleeding from insertion site, any change in their ECG and participants who were not willing to take part were exempt from this study. Sample size calculation was performed using Open-Epi online calculator, by using prevalence of non-ischemic chest pain as 18% [15], confidence interval was taken as 90% with 5% margin of error, and the calculated sample size was 160. However, the research team distributed 200 questionnaires to achieve the desired sample size, five incomplete forms were rejected, and hence data were collected from 195 patients. The approval of this study was obtained before starting data collection from Institutional Review Board of Dow University of Health Sciences, Karachi (Ref # IRB: 888/DUHS/Approval/2017/96, 15th September 2017). Permission was granted from the National Institute of Cardiovascular Diseases Karachi (ERC-08/2017, 13th July, 2017). Informed consent in written was obtained prior to data collection from all study participants. Demographic information was taken from the study participants. Moreover, to check the pain intensity, Numerical rating scale (NRS) was used. NRS is a valid tool that had been used in previous studies for the measurement of pain levels [16]. NRS contain 0- 10 score, with the categories of no pain (0 score), mild pain (1-3 score), moderate pain (4-6 score) severe pain (7-10 score) category. Data were analyzed by using SPSS Version-26.0. Overall, percentages were used for categorical variables to find out the relationship between patients' demographic characteristics and non-ischemic chest pain. Moreover, Pearson Chi-square test was also performed. P-Value≤ 0.05 was represented statistically significant.

RESULTS

Table 1 highlighted the socio-demographics characteristic of the study participants and their association with non-cardiac chest pain. In this study, 42.5% of participants belonged to age group of >50 years, and 63.60% were male. The majority (37.9%) of participants with below primary education and 75.4% were married. Most of the study participants (45.6%) earned between 10000-20000 PKRs/month and 50.3% respondents had private jobs. Findings of this study also revealed that major part of the study participants did not have any disease history and drug history with frequency of 70.3% and 75.9% respectively. Furthermore, nearly half (49.2%) of the study participants personal interest was watching T.V, News and Mobile. In this study, non-ischemic chest pain was significantly associated with age, gender, marital status, disease history and drug history with p-value of <0.001, 0.001, <0.001, <0.001 and <0.001 respectively. Furthermore, variables including education level, profession, monthly income, and personal interest showed no significant association with non-ischemic chest pain with p-value 0.133, 0.252, 0.764 and 0.091 respectively.

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

Table 1: Demographic features of the participants and its association with non-ischemic chest pain (n=195)

Variables	Categories	n (%)	p-value
Age	18-35	36 (18.5)	<0.001*
	36-50	76 (39)	
	>50	83(42.5)	
Gender	Male	124(63.6)	0.001*
	Female	71(36.4)	
Educational level	Below Primary	74(37.9)	0.133
	Matric	62(31.8)	
	Others	59(30.3)	
Marital status	Single	48(24.6)	0.000*
	Married	147(75.4)	
Profession	Private	98(50.3)	0.252
	Govt. /Others	97(49.7)	
Monthly income PKRs/Month	Less than 10000	50(25.6)	0.764
	10000-20000	89(45.6)	
	More than 30000	56(28.7)	
Disease history	Yes	58(29.7)	0.000*
	No	137(70.3)	
Drug history	Yes	47(24.1)	0.000*
	No	148(75.9)	
Personal interest	T.V, News & Mobile	96 (49.2)	0.091
	Family & Friends	37(19.0)	
	Others	62(31.8)	

P-value≤ 0.05 was considered significant*

Table 2 displays the frequency of pain level among study participants on NRS. The table highlighted that overall non-ischemic chest was 90.26% among patients in Post PCI assessment. On assessment of pain categories, it was evident that the majority of the participants 49.2% were in moderate pain category, followed by mild pain among 58 (29.7%), severe pain among 22 (11.3%) and no pain was observed only 19(9.7%) among study participants.

Table 2: Assessment of NRS frequency of non-ischemic chest pain (n=195)

Pain Categories	Frequency (%)
No pain	19 (9.74)
Mild pain	58 (29.75)
Moderate pain	96 (49.23)
Severe pain	22 (11.28)
Total	195 (100)

DISCUSSION

Autonomic nervous system either peripheral or central shows a vital part in pain processing, emotional activation, and cardiac outflow to many organs [17]. Individual variations in thresholds may also take part in cardiac pain [18]. Post PCI non-ischemic chest pain is still not fully understood; nevertheless, minimum awareness is available related to the history. Reasons, such as affective, sensory, and cognitive characteristics of this pain causing the problems that contribute post PCI non-ischemic chest pain among patients are not fully identified. Limited literature available related to this topic, especially in Asian countries. This study will be pioneer efforts in Pakistani context and provide base line data about the topic. This study finding revealed that approximately 2/3 of the patients with coronary artery diseases were male. The number of cases of coronary artery diseases was low among female participants. It was noticed that more than 3/4 of the female participants suffered with non-ischemic chest pain. These evidences were opposed by study finding of New York (2016), Canada (2016) and Norway in 2003, where non-ischemic chest pain was on lower side among female participants [15, 19, 20]. In this study, the higher prevalence of non-ischemic chest pain was 42.5% among patients with the age group of more than 50 years. Similar results were seen in a Canadian study conducted in Ontario [9], Suzhou Kowloon Hospital and Wuhan Asia Heart Hospital China [21] and North American centers in 2016 [22]. In contrast, the findings of a study conducted in Germany (2018) reveled that as age increased the level of non-ischemic chest pain decreased [23]. The findings of this study suggested that overall, 90.26% of participants suffered with non-ischemic chest pain. These finding were not supported by the study conducted in Canada (2012) and Norway (2003), where the non-ischemic chest pain was found 74% and 18% respectively [15, 24]. Findings of this study revealed that the majority of the participants (75.4%) were married. These finding supported by the Iran study conducted in 2017 [25]. In addition, this study highlighted that age of the participants was significantly associated with pain. Similar findings were recorded in the study conducted in the US in 2017, where age showed significant link with angina [26]. Finding of our study highlights that there is a significant association of disease history with post PCI non-ischemic pain. Similar kind of finding found in a study, where significant association was identified of disease history with coronary artery diseases [27]. This study highlighted that majority of the participants had their education at below primary level 74 (37.9 %). Study conducted at Changsha China in 2018 showed that most of the participants had primary education 69 (34.2%) [28]. Furthermore, this study showed that monthly income ranges from 10,000 to 20, 000, 89(45.6%) while study from China also support these findings as they had 1001-3000 yuan 76 (37.6%) per month income [28]. Findings of this study showed that mostly participants were doing private job 98(50.3 %), on the other hand, the study conducted in Greece where highlighted participants 55 (55.0%) were Pensioner [29]. Moreover, in this current study ¾ of the participants in drug history was responded "No" by the participants. Study conducted in China (2018) showed that more than half of the participants had taken medication

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

[28]. In this study, moderate pain was reported higher after PCI 96 (49.23%), similar findings were found in study conducted in Amman in 2021 where pain was also on moderate level [30].It could be due to nature of chest pain is non-ischemic.

CONCLUSIONS

The finding of this study indicated that moderate pain level was seen in the majority of the post PCI patients. Marital status, gender, disease history, age and drug history were significantly related to post PCI non-ischemic chest pain.

Authors Contribution

Conceptualization: SN
Methodology: AA
Formal analysis: AA, AR
Writing-review and editing: SN, TA

All authors have read and agreed to the published version of the manuscript.

Acknowledgements

The authors of this study highly appreciated the cooperation of National Institute of Cardiovascular Diseases hospital to give permission to conduct study and thankful for the study participants for taking part in this study.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Bekkouche NS, Wawrzyniak AJ, Whittaker KS, Ketterer MW, Krantz DS. Psychological and physiological predictors of angina during exercise-induced ischemia in patients with coronary artery disease. Psychosomatic Medicine. 2013 May; 75(4): 413. doi: 0.1097/PSY.0b013e31828c4cb4.

[2] Xaplanteris P, Fournier S, Pijls NH, Fearon WF, Barbato E, Tonino PA, *et al*. Five-year outcomes with PCI guided by fractional flow reserve. New England Journal of Medicine. 2018 Jul; 379(3): 250-9. doi: 10.1056/NEJMoa1803538.

[3] Ben-Yehuda O, Kazi DS, Bonafede M, Wade SW, Machacz SF, Stephens LA, *et al*. Angina and associated healthcare costs following percutaneous coronary intervention: a real-world analysis from a multi-payer database. Catheterization and Cardiovascular Interventions. 2016 Dec; 88(7): 1017-24. doi: 10.1002/ccd.26365.

[4] Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, *et al*. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation. 2019 Mar; 139(10): e56-28. doi: 10.1161/CIR.0000000000000659.

[5] Peiyuan H, Jingang Y, Haiyan X, Xiaojin G, Ying X, Yuan W, *et al*. The comparison of the outcomes between primary PCI, fibrinolysis, and NO reperfusion in patients≥ 75 years old with ST-segment elevation myocardial infarction: results from the Chinese acute myocardial infarction (CAMI) registry. PLoS One. 2016 Nov; 11(11): e0165672. doi: 10.1371/journal.pone.0165672.

[6] Gorenoi V, Schönermark MP, Hagen A. Percutaneous coronary intervention with optimal medical therapy vs. optimal medical therapy alone for patients with stable angina pectoris. GMS Health Technology Assessment. 2011 Nov; 7: Doc07. doi: 10.3205/hta000098.

[7] Koziński M and Sukiennik A. Revisiting the role of percutaneous coronary interventions in stable angina: The landscape after the COURAGE trial. Cardiology Journal. 2007; 14(4): 321-5.

[8] Maragiannis D, Lazaros G, Vavuranakis M, Chrysohoou C, Athanassopoulou S, Patialiakas A, *et al*. Chronic stable angina: percutaneous coronary intervention or medication. Hellenic Journal of Cardiology. 2011 May; 52(3): 246-52.

[9] Kozuch M, Kralisz P, Korecki J, Rog-Makal M, Prokopczuk P, Bachorzewska-Gajewska H, *et al*. Early and long-term prognosis of patients with coronary artery disease treated with percutaneous coronary interventions in 2005. Experience of single large-volume PCI center. Advances in Medical Sciences. 2011 Dec; 56(2): 222-30. doi: 10.2478/v10039-011-0029-8.

[10] Tebbe U, Hochadel M, Bramlage P, Kerber S, Hambrecht R, Grube E, *et al*. In-hospital outcomes after elective and non-elective percutaneous coronary interventions in hospitals with and without on-site cardiac surgery backup. Clinical Research in Cardiology. 2009 Nov; 98: 701-7. doi: 10.1007/s00392-009-0045-x.

[11] Schüepp M, Ullmer E, Weinbacher M, Pfisterer M, Scholer A, Ritz R, *et al*. Chest pain early after percutaneous coronary intervention: incidence and relation to ECG changes, cardiac enzymes and follow-up events. The Journal of Invasive Cardiology. 2001 Mar; 13(3): 211-6.

[12] Kini AS, Lee P, Mitre CA, Duffy ME, Sharma SK. Postprocedure chest pain after coronary stenting: implications on clinical restenosis. Journal of the American College of Cardiology. 2003 Jan; 41(1): 33-8.

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

doi: 10.1016/S0735-1097(02)02617-7.

[13] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, *et al*. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal. 2018 Jan; 39(2): 119-77.

[14] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al*. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal. 2019 Jan; 40(2): 87-165. doi: 10.1093/eurheartj/ehy855.

[15] Thong IS, Jensen MP, Miró J, Tan G. The validity of pain intensity measures: what do the NRS, VAS, VRS, and FPS-R measure? Scandinavian Journal of Pain. 2018 Jan; 18(1): 99-107. doi: 10.1515/sjpain-2018-0012.

[16] Ronnevig M, Bjorsvik E, Gullestad L, Forfang K. A descriptive study of early nonspecific chest pain after PTCA: important area for the acute health care personnel. Heart & lung. 2003 Jul; 32(4): 241-9. doi: 10.1016/S0147-9563(03)00024-4.

[17] Cannon RO. Microvascular angina and the continuing dilemma of chest pain with normal coronary angiograms. Journal of the American College of Cardiology. 2009 Sep; 54(10): 877-85. doi: 10.1016/j.jacc.2009.03.080.

[18] Davies RF, Linden W, Habibi H, Klinke WP, Nadeau C, Phaneuf DC, *et al*. Relative importance of psychologic traits and severity of ischemia in causing angina during treadmill exercise. Journal of the American College of Cardiology. 1993 Feb; 21(2): 331-6. doi: 10.1016/0735-1097(93)90671-M.

[19] McGillion M, Arthur HM, Natarajan M, Cook A, Gunn E, Watt-Watson J, *et al*. Nonischemic chest pain following successful percutaneous coronary intervention at a regional referral centre in southern Ontario. Canadian Journal of Cardiology. 2012 Mar; 28(2): S60-9. doi: 10.1016/j.cjca.2011.10.017.

[20] Pohlen M, Bunzemeier H, Husemann W, Roeder N, Breithardt G, Reinecke H. Risk predictors for adverse outcomes after percutaneous coronary interventions and their related costs. Clinical Research in Cardiology. 2008 Jul; 97: 441-8. doi: 10.1007/s00392-008-0647-8.

[21] You B, Zhu B, Su X, Liu F, Wang B. Gender differences among elderly patients with primary percutaneous coronary intervention. Aging and Disease. 2018 Oct; 9(5): 852. doi: 10.14336/AD.2017.1129.

[22] Epps KC, Holper EM, Selzer F, Vlachos HA, Gualano SK, Abbott JD, *et al*. Sex differences in outcomes following percutaneous coronary intervention according to age. Circulation: Cardiovascular Quality and Outcomes. 2016 Feb; 9(2_suppl_1): S16-25. doi: 10.1161/CIRCOUTCOMES.115.002482.

[23] Huynh T, Perron S, O'Loughlin J, Joseph L, Labrecque M, Tu JV, *et al*. Comparison of primary percutaneous coronary intervention and fibrinolytic therapy in ST-segment-elevation myocardial infarction: bayesian hierarchical meta-analyses of randomized controlled trials and observational studies. Circulation. 2009 Jun; 119(24): 3101-3109. doi: 10.1161/CIRCULATIONAHA.108.793745.

[24] Jeremias A, Kutscher S, Haude M, Heinen D, Holtmann G, Senf W, *et al*. Nonischemic chest pain induced by coronary interventions: a prospective study comparing coronary angioplasty and stent implantation. Circulation. 1998 Dec; 98(24): 2656-8. doi: 10.1161/01.CIR.98.24.2656.

[25] Darvishpour A, Javadi-Pashaki N, Salari A, Sadeghi T, Taleshan-Nejad M. Factors associated with quality of life in patients undergoing coronary angioplasty. International Journal of Health Sciences. 2017 Sep; 11(4): 35.

[26] Fanaroff AC, Kaltenbach LA, Peterson ED, Hess CN, Cohen DJ, Fonarow GC, *et al*. Management of Persistent Angina After Myocardial Infarction Treated With Percutaneous Coronary Intervention: Insights From the TRANSLATE-ACS Study. Journal of the American Heart Association. 2017 Oct; 6(10): e007007. doi: 10.1161/JAHA.117.007007.

[27] Radico F, Zimarino M, Fulgenzi F, Ricci F, Di Nicola M, Jespersen L, *et al*. Determinants of long-term clinical outcomes in patients with angina but without obstructive coronary artery disease: a systematic review and meta-analysis. European Heart Journal. 2018 Jun; 39(23): 2135-46. doi: 10.1093/eurheartj/ehy185.

[28] Yang XL, Xie WY, Cai YM, Tang HY, Tao MY, Shen ZM, *et al*. Investigation of the negative emotions exhibited in patients with coronary heart disease after PCI and any influencing factors. Psychology Research and Behavior Management. 2022 Oct; 15: 3027-37. doi: 10.2147/PRBM.S379422.

[29] Tsoulou V, Vasilopoulos G, Kapadochos T, Pavlatou N, Kalogianni A, Toulia G, *et al*. Quality of Life in Patients Undergoing Percutaneous Coronary Intervention. Clinics and Practice. 2023 May; 13(3): 621-37. doi: 10.3390/clinpract13030057.

[30] Abdelhaq MJ, Shajrawi AM, Ismaile S, Al-Smadi AM, Al-Akash HY, Ashour A, *et al*. Predictors of Post-Percutaneous Coronary Intervention Chest Pain

DOI: https://doi.org/10.54393/pjhs.v4i11.1162

Among Coronary Heart Disease Patients. Clinical Nursing Research. 2023 Sep; 32(7): 1010-20. doi: 10.1177/10547738231184085.

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Prevalence of Typhoid Fever among Different Socio-Demographic Groups in District Bahawalnagar, Pakistan

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ARTICLE INFO

Key Words:
Prevalence, *Salmonella typhi*. socio-demography, typhoid fever, water sources.

How to Cite:
Ishtiaq, A., Khalil, S., Khalil, S., Ahmed, F., Ahmad, B., Ghaffar, A., Khalid, M., Azam, S. M., & Imran, M. (2023). Prevalence of Typhoid Fever among Different Socio-Demographic Groups in District Bahawalnagar, Pakistan: Prevalence of Typhoid Fever. *Pakistan Journal of Health Sciences*, 4(11), 138–143. https://doi.org/10.54393/pjhs.v4i11.1063

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Received Date: 23rd September, 2023
Acceptance Date: 13th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Typhoid is an infectious disease caused by a bacterium *Salmonella typhi* and this bacterium spreads so fast in non-hygienic conditions. This disease is abundantly found in areas where hygienic conditions are poor. **Objective**: To evaluate the prevalence of typhoid among different socio-demographic groups and gender from the populace of different tehsils of district Bahawalnagar (Pakistan). **Methods:** The blood samples of suspected patients were collected from the suspected patients belonging various tehsils of Bahawalnagar (Pakistan) during April to July, 2022. A rapid serological test for detection of IgG/IgM against typhoid bacteria was performed using test kit. A questionnaire was also used to collect information from all the suspects with questions related to age, gender, month, socioeconomic status, area, source of water for drinking purpose, and source of food. **Results:** Results showed 66.39% positive cases for *S. typhi* from a total of 360 suspected patients with apparent symptoms of typhoid fever belonged to various regions of district Bahawalnagar (Pakistan). Significant difference was found in gender-based data, showing significantly ($p<0.05$) higher occurrence of typhoid fever in females (51.46%) than males (48.54%). Population consuming homemade food was significantly ($p<0.05$) most affected with the *S. typhi*. **Conclusions:** Higher prevalence of typhoid fever was recorded in the females of district Bahawalnagar (Pakistan). An alarming percentage (54.07%) of positive cases for typhoid fever among the populace was also found, consuming water from the local water-filtration-plants of the studied region.

INTRODUCTION

The estimated global incidence typhoid fever is known to have 11-21 million cases per year, and causing deaths in range of 1,20,000 to 1,60,000 people [1-3]. Earlier it was in the range of 16 million cases with almost 6,00,000 deaths with decreased fatal rate. The cases of suffering patients with typhoid fever are 93% of global episodes occurring in Southeast Asia [4]. According to epidemiological study, this disease is found to be highly prevalent in areas like those parts of South and Central America, India, and Africa where there is not much cleaned water and are very crowded [5]. This fever is predominantly affecting children and its main source of spreading is feces excretion of *typhi*

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

[6]. In 2007, it was reported that most notorious focal points overall the world for typhoid fever are Pakistan, Indonesia, Peru, India, Nepal, Egypt, and Mexico [7]. The commonness of the typhoid fever is very less in the countries, which are highly developed such as the United States and Canada. However, typhoid is a minor problem in developed country the United States [8, 9]. Typhoid fever is abundantly infecting Pakistan as it is a developing country. Children with age above five years suffer most complications as compare to one third of the patients suffering from intestinal fever [10]. A review led in 2003 which described that water borne diseases guarantee two hundred and fifty thousand passings every year in Pakistan among which typhoid fever is the main source [11]. As per concentrate on in 2013 in pediatric patients in Quetta revealed 18.6% patients were positive serologically for typhoid [4]. A study conducted in Islamabad of Pakistan depicted that 48% females and 42% of males were positive for both IgM and IgG of the total tests conducted in 12 months period [12]. Typhoid fever can be a significant mark of financial state of populace like other Asian countries [13]. Intestinal fever is an intense febrile ailment that occur by intake of the bacterium *Salmonella enterica* serotype *Typhi (S. Typhi)* or serotype *Paratyphi* A, B or C, frequently through food or water defiled with human excrement [14, 15]. This bacterium is a gram negative, flagellated, rod shaped that caused typhoid fever. The term "typhoid fever" was termed by Pierre Louis [16]. *Salmonella typhi* find humans as their host [17]. It is an irregular sickness. It can likewise create a periodic point-source pandemic [18]. The typhoid fever starts with common cold. Then the temperature starts to rise up gradually every day that can be as high as 103–104 °F (39–40 °C) and pulse rate starts to be slow [19]. It also leads to dehydration and diarrhea. Shivering and delirium are also observed. It starts with gentle sickness with poor quality fever, uneasiness, dry cough, to extreme clinical signs with stomach uneasiness and numerous inconveniences [20]. It is also observed that the typhoid fever is also associated with many other complications in 10-15% of patients. Most of complications have been studied but most common are typhoid encephalopathy, intestinal perforation, relapse, and gastrointestinal hemorrhage. The patient gets prolonged passiveness, toxemia, myocarditis, anemia, confusion, typhoid intestinal perforation (TIP), gastrointestinal hemorrhage, pneumonia, hepatitis, disorientation, diarrhea, and followed by coma. It can cause damage to various organs in the body if not cured [21-23]. Mouth is the mode of entrance of *Salmonella typhi* infection, via the sources of fecal contaminated food or water [24]. The bacterium gets transferred through ingestion of water or food that has been polluted by dung or less usually, pee of contaminated people [1]. This infectious fever is observed to occur mostly in the months of September, October and in months of July and August after monsoon rains [4]. According to an Indonesian study, improper hygiene is extremely a clear factor of getting typhoid [25]. Therefore, it is addressed in schools that it is necessary to wash hands after stool and urine excretion. Flies are also a major cause of spreading the bacteria to food [26]. Fecal typhi from stool are transferred to the water sewage system through the flushes and toilet pipes and then polluting the ground and surface water [20]. According to research held in South Asia it was observed that typhoid is more common in rural areas of developing South Asia as compared to urban areas. Also, according to this research, both of sexes are affected equally [27]. Typhoid fever is treated with antimicrobial therapy. Before the invention of antibiotics, the mortality rate from infection of typhoid fever was round about 15% all over the world [28]. Typhoid fever can also be treated by vaccination either in injection or in capsule form. World Health Organization (WHO) suggested a programmed utilization of these two vaccines (ViPS and Ty21) for prevention from the outbreak of typhoid in 2008 [29]. As, there was no previous study data available on the prevalence of infection from typhoid fever in the population of District Bahawalnagar in Pakistan. Thus, the purpose of the research was to study the prevalence of typhoid fever among different socio-demographic groups and genders from the populace of different tehsils of district Bahawalnagar (Pakistan).

METHODS

An observational, cross-sectional study was conducted at the Islamia University of Bahawalpur (Bahawalnagar Campus), Bahawalnagar (Pakistan) after taking ethical approval. A total of 360 blood samples were collected from the suspected patients with apparent symptoms of typhoid fever belonged to district Bahawalnagar, Punjab, Pakistan including all its five tehsils i.e., Bahawalnagar, Chishtian, Haroonabad, Minchanabad, and Fort Abbas, during April to July 2022, adopting stratified random sampling technique. Sample size was calculated by using online sample size calculator (www.calculator.net) having confidence level of 95% with 5.2% of margin of error and 50% of population proportion. Both suspected males and females for typhoid fever of any age groups and socio-economic backgrounds having symptoms and signs (like fever > 99° F, relative bradycardia, abdominal discomfort, headache, diarrhea, weakness etc.) from all 5 tehsils of Bahawalnagar were enrolled. While, participants suffering from any other life-threatening disease (like carcinoma) or with multiple comorbid like chronic kidney disease, diabetes mellitus and ischemic heart disease were excluded. Moreover, non-

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

consenting patients were also excluded from the study. A questionnaire, including the information like their gender, age groups, month of infection, their source of water, source of food, economic status, and region, were being filled by them. 5ml of venous blood was withdrawn from participants after obtaining written informed consent by the routine method under septic measures. The blood samples were centrifuged immediately after collection at 4000 rpm for fifteen minutes to get the serum. Obtained clear and non-hemolyzed serum specimens were used to perform tests using a kit (Acu-Check, RAPID Diagnostic Test) following the instructions of the company. One full drop of serum (approximately 30µl) was taken at test kit and one drop of buffer (approximately 40µl) was also added on the serum drop. The results were checked immediately after 15 minutes and interpreted noticing the appeared bands on the kit following the company's instructions.

Statistical Analysis

Percentages and frequencies were used to express the data. Chi-squared test was performed to compare the observed frequencies of positive tests for each parameter against the expected frequencies, using IBM SPSS Statistics 23.0 for Windows.

RESULTS

Results revealed a total of 66.39% positive cases for S. typhi from 360 suspected patients with apparent symptoms of typhoid fever belonged to various regions of district Bahawalnagar, (Pakistan). Table 1 provides the results of analysis of typhoid fever among age groups of all tehsils of Bahawalnagar (Pakistan). No significant difference ($p>0.05$) in prevalence of typhoid fever was observed among different age groups. However, number of suspected individuals with apparent symptoms of typhoid fever were found the highest in the age group being 21-30 years, and hence showing the highest positive cases (28.45%) among different studied age groups.

Table 1: Prevalence of typhoid fever among the population of different age groups from five tehsils of Bahawalnagar, Pakistan

Pain intensity rating scale								
Age groups	Total No. of Tests perfor-med	Bahaw-alnagar	Haroon-abad	Fort-Abbas	Mancha-nabad	Chish-tian	Total No. of Positive tests (%)	p-Value
Less than 1 year	40	5	0	5	5	1	16 (6.70%)	0.6725
1-10 Year	39	9	0	8	3	3	23 (9.62%)	
11-20 years	50	2	8	5	5	14	34 (14.23%)	
21-30 years	90	14	19	10	17	8	68 (28.45%)	
31-40 years	52	11	11	4	9	8	43 (17.10%)	
41-50 +years	38	6	7	4	6	7	30 (12.55%)	
51-60 years	28	5	0	5	4	4	18 (7.53%)	
61-70 years	10	0	0	1	1	0	2 (0.84%)	
>70 years	13	1	0	0	3	1	5 (2.09%)	
Total	360	53	45	42	53	46	239 (66.39%)	

Cumulatively gender wise prevalence of typhoid fever from the population of Bahawalnagar (Pakistan) showed significant higher positive cases (51.46%, $p<0.05$) of typhoid fever in females than males Table 2.

Table 2: Cumulatively gender wise prevalence of typhoid fever from the population of Bahawalnagar (Pakistan)

Gender	Total No. of Positive Tests	Frequency (%)	p-value
Female	239	123 (51.46%)	0.0012
Male		116 (48.54%)	

Monthly prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), during April-July, 2022 is depicted in Table 3. Although, no significant difference ($p<0.05$) was found among frequencies of positive typhoid cases during the studied months, however an increasing trend in number of suspected patients and hence the percentage of positive cases was observed from April to July.

Table 3: Monthly prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), during April-July, 2022

Month	No. of Tests Performed	Frequency of Positive Tests (%)	p-value
April	55	35 (14.64%)	0.2467
May	67	42 (17.57%)	
June	93	68 (28.45%)	
July	145	94 (39.33%)	

In the present study, the highest number of suspected patents were observed in the population belong to lower class, followed by middle and higher class. But no significant difference ($p>0.05$) was found among frequencies of positive cases for typhoid fever among the three studied socioeconomic classes, as showed in Table 4.

Table 4: Prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), depending on socio-economic levels

Socioeconomic Level	No. of Tests . Performed	Frequency of Positive Tests (%)	p-value
Lower Class	147	110 (46.02%)	0.5676
Middle Class	122	90 (37.66%)	
High Class	91	39 (16.31%)	

Prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), depending on urban/rural areas

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

is presented in Table 5, representing no significant difference (p>0.05) between urban and rural population.

Table 5: Prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), depending on urban/rural area

Area	Total No. of Positive Tests	Frequency (%)	p-value
Urban	239	97 (40.5%)	0.1965
Rural		142 (59.40%)	

Significant difference (p<0.05) in the frequencies of positive tests was found among the groups depending on source of drinking water (Mineral water, tap water and Water from local water filtration-plants), as shown in Table 6. Population depending upon local water-filtration-plants (54.07%) was highly affected (p<0.05) than consuming the water from tap water (25.32%) and mineral water (20.60%), in 233 positive tests (excluding six newborn cases from 239 positive cases).

Table 6: Prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), depending on source of drinking water

Source of water	No. of Tests . Performed	Frequency of Positive Tests (%)	p-value
Mineral water	83	48 (20.60%)	0.0002
Tap water	89	59 (25.32%)	
Local Water Filtration-Plant	188	126 (54.07%)	
Total	360	233 (100.0%)	

Table 7 provided the results of prevalence of typhoid fever by source of food from all Tehsils of District Bahawalnagar (Pakistan). In this table percentage was derived from a total of 222 positive tests, as 17 newborn and toddlers' samples were excluded from total of 239 positive samples. Results showing that people consuming homemade food found significantly (p<0.05) the most affected (63.51%) with the S. typhi.

Table 7: Prevalence of typhoid fever among the population of Bahawalnagar (Pakistan), depending on food source

Source of food	No. of Tests . Performed	Frequency of Positive Tests (%)	p-value
Homemade	201	141 (63.51%)	0.0002
Mostly Homemade	71	49 (22.07%)	
Homemade & Hotels	50	18 (8.1%)	
Often Hotels	38	14 (6.30%)	
Total	360	222 (100.0%)	

DISCUSSION

Typhoid fever has been indicated as the most infectious disease of the South Asian Countries like Pakistan as it is causing great level of morbidity and mortality in Pakistan. A number of cases reported every year across the country. It is dominant in those areas, which suffer lack of safe drinking water and the lack of hygienic food. Typhoid fever, like other Asian countries, is dependent on many socio-economic conditions [12]. In the present study, no significant difference (p>0.05) in prevalence of typhoid fever was observed among different age groups. But, higher positive cases of typhoid fever were found in the age group being 11-50 years, representing the occurrence of disease in higher rates usually in school and college going age groups and in jobholders. Among these age groups, age group of 21-30 years was most affected with typhoid fever, and the findings also supported by some other study by Ghosh et al., [30]. It could be due to many reasons as this is age of poor hygienic practices as adults in this age eat junk foods in restaurants and by other ways where hygienic practices are not prioritized. Most of the gender wise studies showed that typhoid is more prevalent in males than females. For instance, according to a study conducted by Medhat and Aljanabay [31] in Iraq, males were affected more than females. It could be due to many reasons like males spend most of the time outside the house than females so they may have greater chance of being affected [32, 33]. On contrary, Butler et al., [34] reported higher prevalence rate of typhoid fever in females. Findings of the present study also revealed that females were affected significantly higher than males. This might be due to the fact that most of the rural region females work outside the homes in the fields to cope with economical demands in the under-developed district. The prevalence rate data obtained according to monthly variation showed no significant difference among the studied months but an increasing trend in positive cases of typhoid fever was observed from April to July, with the highest positive cases during the month of monsoon (July). Due to heavy rains in monsoon season, there is a greater chance of contamination in surface water so people closer to water bodies are at high risk of getting the infection and prevalence rate increases during this duration [35]. Moreover, typhoid is more prevalent in summer as compare to other seasons [4]. It is the fact that Salmonella typhi is typically spread through contaminated food or water. In the present study, statistically higher ration of typhoid fever prevalence in the people consuming home-made food might be related to poor sanitation, unhygienic conditions or use of unsafe water for cooking purpose. Moreover, it was threating to observe that frequency of positive tests was found statistically higher in the populace of the studied region, depending on local water filtration-plants for drinking water, followed by tap water and mineral water. A recent published study conducted by Majeed et al., [36] on safety assessment of water purification plants of Lahore (Pakistan) has also revealed presence of typhoid in the majority of residents of some suburban areas of Lahore as total coliform counts was greater than 20 per 100 ml. As, most of the population of Bahawalnagar (Pakistan) rely on local purification plants for drinking water, hence it is dire need to manage the purification plants properly.

CONCLUSIONS

The study concluded that the most of the typhoid fever cases were reported in people with age between 21 to 30

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

years. Typhoid fever significantly more affected females than males. It was affecting both men and women with significant higher ratio in females in the studied area. Typhoid spread fast in the months of monsoon i.e., July. Its rate was higher in lower class and rural areas than upper class and urban areas respectively in Bahawalnagar district. Moreover, it was more abundant in people who were exposed to unhygienic conditions and often drink unfiltered water. To the best of our knowledge, it is the first study describing the association of water purification plants and prevalence of typhoid fever in Bahawalnagar (Pakistan). Hence, regular maintenance to check the adequate hygiene and contamination status of water purification plants specially from coliform bacteria is recommended, to avoid waterborne infections, including typhoid fever. Further studies are required to study the presence of coliform bacteria, especially *Salmonella typhi*, in water supply of purification plants. Awareness campaigns on water-borne diseases and use of clean drinking water must be launched and proper administration on adequate sanitation system and water management should be emphasized.

Authors Contribution

Conceptualization: AI, AG
Methodology: SK[1], SK[2], FA
Formal analysis: SK[1], BA, MI, SMA
Writing, review and editing: AI, AG, FA, MK, SMA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The author declares no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bulletin of The World Health Organization. 2004 May;82(5):346-53.

[2] Mogasale V, Maskery B, Ochiai RL, Lee JS, Mogasale VV, Ramani E, et al., Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. The Lancet Global Health. 2014 Oct; 2(10): 570-80. doi: 10.1016/S2214-109X(14)70301-8.

[3] Stanaway JD, Reiner RC, Blacker BF, Goldberg EM, Khalil IA, Troeger CE, et al., The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Infectious Diseases. 2019 Apr; 19(4): 369-381.

[4] Siddiqui FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA. Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan. International Journal of Infectious Diseases. 2006 May; 10(3): 215-222. doi: 10.1016/j.ijid.2005.03.010.

[5] White NJ. *Salmonella typhi* (typhoid fever) and S. paratyphi (paratyphoid fever). In: Antimicrobial Therapy and Vaccines. Apple Tree Productions; 2002: 583-603.

[6] Buckle GC, Walker CLF, Black RE. Typhoid fever and paratyphoid fever: systematic review to estimate global morbidity and mortality for 2010. Journal of Global Health. 2012 Jun; 2(1). doi: 10.7189/jogh.01.010401.

[7] Sulaiman K and Sarwari A. Culture-confirmed typhoid fever and pregnancy. International Journal of Infectious Diseases. 2007 Jul; 11(4): 337-341. doi: 10.1016/j.ijid.2006.09.007.

[8] Date KA, Newton AE, Medalla F, Blackstock A, Richardson L, McCullough A, et al., Changing patterns in enteric fever incidence and increasing antibiotic resistance of enteric fever isolates in the United States, 2008–2012. Reviews of Infectious Diseases. 2016 Apr; 63(3): 322-329. doi: 10.1093/cid/ciw232.

[9] Radhakrishnan A, Als D, Mintz ED, Crump JA, Stanaway J, Breiman RF, et al., Introductory article on global burden and epidemiology of typhoid fever. The American Journal of Tropical Medicine and Hygiene. 2018 Sep; 99(3): 4-9. doi: 10.4269/ajtmh.18-0032.

[10] Malik A and Malik R. Typhoid fever in Malaysian children. The Medical Journal of Malaysia. 2001 Dec; 56(4): 478-490.

[11] Shah SM, Yousafzai M, Lakhani NB, Chotani RA, Nowshad G. Prevalence and correlates of diarrhea. The Indian Journal of Pediatrics. 2003 Mar; 70(3): 207-211. doi: 10.1007/BF02725583.

[12] Ayub U, Khattak AA, Saleem A, Javed F, Siddiqui N, Hussain N, et al., Incidence of typhoid fever in Islamabad, Pakistan. American-Eurasian Journal of Toxicological Sciences. 2015; 7(4): 220-223.

[13] Bajracharya D, Khan MI, Pach AP III, Shrestha P, Joshi N, Upreti SR, et al., 25 years after Vi typhoid vaccine efficacy study, typhoid affects significant number of population in Nepal. PLOS ONE. 2014 Jan; 9(1): 77974. doi: 10.1371/journal.pone.0077974.

[14] Hornick R, Greisman S, Woodward T, DuPont H, Hawkins A, Snyder M. Typhoid fever: pathogenesis and immunologic control. New England Journal of Medicine. 1970 Oct; 283(14): 739-746. doi: 10.1056/NEJM197010012831406.

[15] Bhan M, Bahl R, Bhatnagar S. Typhoid and

DOI: https://doi.org/10.54393/pjhs.v4i11.1063

paratyphoid fever. Lancet. 2005 Aug; 366(9487): 749-762. doi: 10.1016/S0140-6736(05)67181-4.

[16] Ashurst JV, Truong J, Woodbury B. *Salmonella typhi*. StatPearls Publishing; 2021. Last cited: 23rd Nov 2023. Available at: https://europepmc.org/books/nbk519002.

[17] World Health Organization (WHO). Manual for the laboratory identification and antimicrobial susceptibility testing of bacterial pathogens of public health importance in the developing world: Haemophilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae, Neisseria gonorrhoea, Salmonella serotype Typhi, Shigella, and Vibrio cholerae. WHO; 2003. Last cited: 23rd Nov 2023. Available at: https://apps.who.int/iris/bitstream/handle/10665/68554/WHO_CDS_CSR_RMD_2003.6.pdf.

[18] Ackers ML, Puhr ND, Tauxe RV, Mintz ED. Laboratory-based surveillance of Salmonella serotype Typhi infections in the United States: Antimicrobial Resistance on the Rise. Jama. 2000 May; 283(20): 2668-2673. doi: 10.1001/jama.283.20.2668.

[19] Gunn JS, Marshall JM, Baker S, Dongol S, Charles RC, Ryan ET. Salmonella chronic carriage: epidemiology, diagnosis, and gallbladder persistence. Trends in Microbiology. 2014 Nov; 22(11): 648-655. doi: 10.1016/j.tim.2014.06.007.

[20] Bekele D and Lata W. Retrospective study on prevalence of typhoid fever infection among patients visiting Ejere health center, west Shawa zone, Ethiopia. Research Square. 2022. doi: 10.21203/rs.3.rs-1426059/v1.

[21] Parry C, Hien T, Dougan G, White N. Typhoid fever. The New England Journal of Medicine. 2002 Nov; 347: 1770-1782. doi: 10.1056/NEJMra020201.

[22] Harrison T and Fauci A. Harrison's principles of internal medicine. Schistosomiasis And Other Trematode Infection. 2008: 1266-1271.

[23] Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive Salmonella infections. Clinical Microbiology Reviews. 2015 Oct; 28(4): 901-937. doi: 10.1128/CMR.00002-15.

[24] Crump JA. Progress in typhoid fever epidemiology. Clinical Infectious Diseases. 2019 Feb; 68(1): 4-9. doi: 10.1093/cid/ciy846.

[25] Gasem MH, Dolmans W, Keuter M, Djokomoeljanto R. Poor food hygiene and housing as risk factors for typhoid fever in Semarang, Indonesia. Tropical Medicine & International Health. 2001 Jun; 6(6): 484-490. doi: 10.1046/j.1365-3156.2001.00734.x.

[26] Soper R and Smith ST. Biology: An integrated approach for East African Schools. Macmillan; 1977.

[27] Sharma J and Malakar M. Distribution of Typhoid fever in different rural and urban areas of Lakhimpur District of Assam. International Journal of Research and Development of Health. 2013; 1(3): 109-114.

[28] Haque S, Swami P, Khan A. S. Typhi derived vaccines and a proposal for outer membrane vesicles (OMVs) as potential vaccine for typhoid fever. Microbial Pathogenesis. 2021 Sep; 158 : 105082. doi: 10.1016/j.micpath.2021.105082.

[29] WHO. Typhoid vaccines: WHO position paper. Weekly Epidemiological Record 2008 Feb; 83(06):49-59.

[30] Ghosh S, Batabyal P, Rajendran K, Palit A. Typhoid Fever in Rural Communities of West Bengal, India–an Age-Wise Perspective. Japanese Journal of Infectious Diseases. 2010 May; 63(3): 219-221. doi: 10.7883/yoken.63.219.

[31] Medhat AR and Aljanabay AAJ. Epidemiology of Typhoid Fever in Balad City, Iraq. International Journal of Health Sciences. 2022; 6(1): 1049-1063. doi: 10.53730/ijhs.v6nS1.4834.

[32] Siddiqui TR, Bibi S, Mustufa MA, Ayaz SM, Khan A. High prevalence of typhoidal Salmonella enterica serovars excreting food handlers in Karachi-Pakistan: a probable factor for regional typhoid endemicity. Journal of Health, Population and Nutrition. 2015 Dec; 33(1): 1-9. doi: 10.1186/s41043-015-0037-6.

[33] F, Hussain SZM, Batool D, Usman A, Khalid U, Yaqoob U, et al., Study of socio-demographic factors affecting the prevalence of typhoid. Morbidity and Mortality. 2019 May; 1(2): 469-71.

[34] Butler T, Islam A, Kabir I, Jones PK. Patterns of morbidity and mortality in typhoid fever dependent on age and gender: review of 552 hospitalized patients with diarrhea. Reviews of Infectious Diseases. 1991 Jan; 13(1): 85-90. doi: 10.1093/clinids/13.1.85.

[35] Dewan AM, Corner R, Hashizume M, Ongee ET. Typhoid fever and its association with environmental factors in the Dhaka metropolitan area of Bangladesh: a spatial and time-series approach. PLOS Neglected Tropical Diseases. 2013 Jan; 7(1): 1998. doi: 10.1371/journal.pntd.0001998.

[36] Majeed A, Shahid S, Ali S, Firdous N. Safety assessment of water purification plants of Lahore. Journal of the Pakistan Institute of Chemical Engineers. 2022; 50(2): 29-44. doi: 10.54693/piche.05023.

DOI: https://doi.org/10.54393/pjhs.v4i11.1196

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Effect of Educational Program on Awareness and Practices Regarding Menstrual Hygiene among Adolescent Girls

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ARTICLE INFO

Key Words:
Awareness, Practices, Menstrual Hygiene, Adolescent Girls

How to Cite:
Rani, N., Mukhtar, M., & Masih, S. (2023). Effect of Educational Program on Awareness and Practices Regarding Menstrual Hygiene among Adolescent Girls: Awareness and Practices Regarding Menstrual Hygiene. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1196

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Received Date: 3rd November, 2023
Acceptance Date: 23rdNovember, 2023
Published Date: 30th November, 2023

ABSTRACT

Menstrual hygiene maintenance is very low cost and reliable in Pakistan for adolescents' girls to prevent any dangerous future consequences. Adolescent girl's good awareness and practices is very important in smooth handling and maintain menstrual hygiene. **Objective:** To assess the effect of educational program on awareness and practices regarding menstrual hygiene among adolescents' girls. **Methods:** This was a quasi-experimental study carried out at high school, named Government Girls High School Kahna Nau, Tehsil Model Town Lahore. Data were collected from overall 110 adolescents' girls were studying at Government Girls High School Kahna Nau Tehsil Model Town Lahore about awareness and practices regarding menstrual hygiene. Data were collected using awareness and practices questionnaire regarding menstrual hygiene. Pre and Post-interventional awareness and practices was assessed using the same questionnaire. SPSS 25.0 was used for data analysis. **Results:** Overall 73.6% of the adolescent's girls had reported poor pre-interventional awareness, which enhanced to excellent awareness (100%) after interventions. Similarly, 79.1% of the adolescent girls were reported unsafe practices in pre-intervention phase while 94.5% of the adolescent girls reported safe practices after interventions. There was significant difference among pre and post-interventional awareness (P<0.001) and practices (P<0.001) of adolescent girls regarding menstrual hygiene. **Conclusions:** Adolescent girls reported poor awareness and unsafe practices regarding menstrual hygiene. The findings of the study showed that educational interventions are the key for enhancing the awareness and practices of adolescents regarding menstrual hygiene.

INTRODUCTION

Adolescent girls make one-fifth of the global female population. Adolescent girls have been recognized as a particular stage of their lives that requires the particular and special care [1]. Adolescent girls who reached puberty are menstruating, naturally shedding blood for 1 to 7 days each month from uterus till menopause [2]. Pakistani girls, the average age at menarche is 11 years [3]. Adolescents need to be aware of the many physical and psychological changes that occur. The body begins to grow and develop into physical maturity throughout this time. The dissemination of knowledge about the physical changes that occur during puberty, family planning, conception, and contraception could give the young women an opportunity to make their own decisions about the reproductive health status [4]. On the other hand, menstrual hygienic practices during menstrual period are essential for reproductive health; lack of awareness results in poor performance, which increases sensitivity to infections of the reproductive tract [5]. Due to taboos and other societal and cultural restrictions, menstruation and menstrual practices are kept hidden, which prevents adolescents from having sufficient understanding of the facts about menstruation and good menstrual hygiene practices [2]. Poor menstrual hygiene awareness and practices cause

DOI: https://doi.org/10.54393/pjhs.v4i11.1196

about 10% of women worldwide to annually be exposed to genital infections, such as urinary tract infections (UTI) and bacterial vaginosis [6]. Lack of awareness about menstruation hygiene creates the possibility of developing infections like candidiasis, reproductive tract infections, and urinary tract infections (UTI). Menstrual hygiene among adolescents must priorities maintaining the structural health of the reproductive system [7]. The female population in Pakistan, which is 21.9% of the total, encounters Secondary infertility, is recognized as a woman's inability to conceive a child due to unsanitary practices during the menstrual or postpartum periods [8]. A research in Pakistan's three distinct provinces found that traditional menstrual hygiene management techniques and ideas regarding menstruation are extremely sensitive and deeply embedded in daily life. As a result, our adolescent respondents are frequently hesitant and reluctant to express their opinions on these issues. Similar to younger females, older women were not used to discussing these issues and, in many cases, had come to accept these practices as the standard [9]. A substantial portion of the global population engages in inadequate menstrual hygiene practices. Addressing this issue requires tailored education that aligns with specific needs and imparts standardized guidelines. The aim is to enhance awareness and promote proper practices among adolescent girls for their well-being and future reproductive health. So that the present study was conducted to evaluate the effect of educational program on awareness and practices regarding menstrual hygiene among adolescent girls in high school setting.

METHODS

This was a quasi-experimental study carried out at high school, named Government Girls High School Kahna Nau, Tehsil Model Town Lahore after the approval from Research Ethics Committee of university of Lahore (REC-UOL-478). Data were collected from overall 110 adolescents' girls were studying at Government Girls High School Kahna Nau Tehsil Model Town Lahore about awareness and practices regarding menstrual hygiene. Consents were taken from all participants. In pre-interventional phase the schedule of sessions was provided to the participants. The participants were educated (intervene) in (08) sessions. Different strategies such as Power Point presentation, lectures, discussion, videos presentation and charts, booklets were used. Post interventional data were collected using the same questionnaire about the awareness and practices of adolescents' girls regarding menstrual hygiene at the last week of intervention from each group with two weeks gap. Data were collected using awareness and practices questionnaire regarding menstrual hygiene. Pre-interventional data were collected and 08-week interventions were applied. Post-interventional awareness and practices was assessed using the same questionnaire. All the adolescent girls studying in high school, who have at least 6-month experience of menses, were enrolled in the study.

RESULTS

The mean age of the participants was 14.75±1.05 years. The majority (38.2%) of the girls of 15 years. This study was conducted on adolescent girls, so from grade 9 we included 50% girls and in the same way from grade 10 we included 50% girls. The majority of the girls were Muslim 99.1%, and only 0.9% from Christianity. 69.1% of the participants had a nuclear family system, 24.5% had a joint family system, and 4.5% were living with single parents. The overall pre-median awareness score among study participants was 07 and the mean awareness score was 13. The post median awareness score was increased from 07 to 13 and the mean awareness score also increased from 6.38 to 12.46. The results revealed that there was a significant difference between pre and post-awareness scores among adolescent girls regarding menstrual hygiene care as evidenced by (p-value <0.05). The overall pre-median practice score among girls was 05 and the mean practice score was 5.52 with an SD of 1.19. While the post median practice scores were increased to 08 and the mean practice score also increased to 8.37. So, the difference between pre and post-practice scores after the educational intervention was 03. The results revealed that there was a significant difference between pre and post-educational intervention, and practice among adolescent girls regarding menstrual hygiene, as evidenced by (p-value <0.05) (Table 1).

Table 1: Comparison of pre and post-awareness and Practices regarding menstrual hygiene

Variables	Pre	Post	p-value	z-value
	(Median) Mean ± SD	(Median) Mean ± SD	p-value	z-value
Awareness Score	(07) 6.38±1.73	(13) 12.46±0.62	<0.001	-9.098
Practice Scores	(05) 5.52±1.19	(08) 8.37±1.00	<0.001	-9.024

Table 2 indicates that the majority of girls (73.6%) had poor knowledge about menstrual hygiene, and 26.4% had awareness about menstrual hygiene before educational intervention. There was a significant increase in awareness knowledge seen in post-intervention, the awareness knowledge was improved in 100% of girls. The practices among adolescent girls regarding menstrual hygiene in pre-interventional were unsatisfactory in 79.1% of girls. On the contrary, in the post-intervention phase, there was a remarkable difference in girls' practices

DOI: https://doi.org/10.54393/pjhs.v4i11.1196

towards menstrual hygiene. Majority of the adolescent girls had satisfied practice (94.5%), and only one 5.5% had unsatisfied practice after intervention.

Table 2: Comparison of pre and post-awareness categories (n=110)

Awareness Knowledge Categories	Pre-intervention f(%)	Pre-intervention f(%)
Aware	29(26.4)	110(100)
Unaware	81(73.6)	0(0)
Practice Categories		
Unsatisfactory	87(79.1)	06(5.5)
Satisfactory	23(20.9)	104(94.5)

DISCUSSION

Menstruation represents a significant pubertal milestone occurring in adolescent females, characterized by a cyclical process of physiological development and maturation [10]. Menstruation holds significant importance in the realm of a young girl's reproductive well-being. Therefore, it is imperative to provide health education on menstrual hygiene to adolescent girls to effectively manage menstruation and uphold proper menstrual hygiene practices. The present study shows that the average age was 14.75±1.051 years, this is comparable with the study reported by Dixit, 2018 [11], where the majority of the girls between the ages 14 to 16 years, and in another study participants age ranges from 10-19 years [12]. The present study revealed that the initial awareness score of 26.4% of adolescent girls was poor before the implementation of the menstrual health education program. However, the program played a significant role in enhancing their knowledge level after its introduction. The participants' awareness has been greatly improved during the post-intervention phase. The findings exhibited consistency with previous research conducted in India, Egypt, and Saudi Arabia [13, 14]. A study conducted in Manipal, India conducted a sample of 550 adolescent school girls, revealing that a mere 34% of them possessed prior awareness [15]. A study conducted in Nigeria reported that poor awareness knowledge before the educational program was 53.3% in their study which is higher than our study [16]. In our study, the level of awareness increased from 26.4% to 100% after educational intervention. In other studies, it was, 44%-60% [17] and in Bangladesh 51%-82.5% [13]. In the current study, the pretest mean ± SD of baseline knowledge was 5.52±1.19, and the median score was 05 which is poor according to El-Mowafy et al., [5]. Similarly, a study conducted on the perception of menstruation and menstrual practices among adolescent girls in high school within a low-resource setting near Bangalore, Karnataka, the average knowledge score was determined 4.04 ± 1.32 [18]. In a study carried out in Ethiopia, a total of 791 adolescent schoolgirls were investigated. The findings revealed that 68.3% of the participants revealed inadequate knowledge regarding menstruation, while 60.3% of the girls displayed substandard menstrual hygiene practices [19]. In the present study, overall practices about menstrual hygiene were unsatisfactory among 79.1% of adolescent girls. After the educational program, it was improved from 79.1% to 94.5%. A study revealed that the practice of using sanitary pads disposal, wrapping pads in either paper (42.8%), or plastic (39.8%), and subsequently discarding it in a designated receptacle, such as a dustbin (77.0%), is a common practice. Concerning personal hygiene practices, it was found that approximately 4.5% of the respondents do not engage in genital hygiene during menstruation, while others solely rely on water for cleansing purposes [20]. This particular approach to hygiene may contribute to the proliferation of bacteria in the genital region, thereby increasing the susceptibility to infections.

CONCLUSIONS

The study revealed that significant differences in awareness levels in pre and post-intervention education programs. Based on the findings of the study, it was determined that adolescent girls indicated a deficiency in adequate understanding regarding menstruation and menstrual hygiene during the pre-program phase. There were substantial improvements in the knowledge and practice of teenagers following the program's implementation. Hence, the educational program demonstrated efficacy in achieving its objectives of effectively altering the understanding and behavior surrounding menstruation.

Authors Contribution

Conceptualization: NR
Methodology: MM
Formal analysis: SM
Writing-review and editing: NR, MM SM
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Devi RU, Sivagurunathan C, Kumar PM. Awareness about menstrual hygiene among adolescent girls in rural area of Kancheepuram District-Tamil Nadu. International Journal of Pharma and Bio Sciences.

DOI: https://doi.org/10.54393/pjhs.v4i11.1196

2016 Jan; 7: 267-9.

[2] Ameade EP and Garti HA. Age at menarche and factors that influence it: a study among female university students in Tamale, Northern Ghana. PloS One. 2016 May; 11(5): e0155310. doi: 10.1371/journal.pone.0155310.

[3] Ahmed SM, Waheed MA, Ahmad F, Danish SH. Factors contributing to early menarche in school girls. JPMA. The Journal of the Pakistan Medical Association. 2016 May; 66(5): 629-33.

[4] Chakre SS. A Study to assess the Effectiveness of Planned Teaching regarding Reproductive Health among adolescent girls in Pune City. Asian Journal of Nursing Education and Research. 2018 Oct; 8(4): 493-7. doi: 10.5958/2349-2996.2018.00101.5.

[5] El-Mowafy RI, Moussa M, El-Ezaby HH. Effect of health education program on knowledge and practices about menstrual hygiene among adolescents girls at orphanage home. IOSR Journal of Nursing and Health Sciences. 2014 Nov; 3(6): 48-55. doi: 10.9790/1959-03614855.

[6] Kanem N. Adolescents: The face of today, the face of the future. Journal of Adolescent Health. 2019 Jul; 65(1): 13-4. doi: 10.1016/j.jadohealth.2019.04.013.

[7] Alva J, Kannappan SR, Joseph G, Upashe S. Hostel Residents' Knowledge on Feminine Hygiene—Effect of Information Booklet. Journal of Health and Allied Sciences NU. 2021 Nov; 12(03): 336-40. doi: 10.1055/s-0041-1739231.

[8] Shahid H, Kamal A, Younas S. Knowledge and Attitudes toward Perceived Causes of Infertility and Adoption of Child among Infertile Couples: A Cross-sectional Descriptive Study. Pakistan Journal of Medical Research. 2020 Nov; 59(3): 106-10.

[9] Mumtaz Z, Sivananthajothy P, Bhatti A, Sommer M. "How can we leave the traditions of our Baab Daada" socio-cultural structures and values driving menstrual hygiene management challenges in schools in Pakistan. Journal of Adolescence. 2019 Oct; 76: 152-61. doi: 10.1016/j.adolescence.2019.07.008.

[10] John J and Nath KR. Knowledge of menstrual hygiene among adolescent girls in a rural area of Kanyakumari District of Tamilnadu. International Journal of Preventive, Curative & Community Medicine. 2019 Dec; 5(1): 22-7. doi: 10.24321/2454.325X.201905.

[11] Dixit AM. A cross-sectional study on menstrual hygiene practices among school going adolescent girls (10-19 years) of Government Girls Inter College, Saifai, Etawah. International Journal of Community Medicine and Public Health. 2018 Oct; 5(10): 4560. doi: 10.18203/2394-6040.ijcmph20184010.

[12] Adebisi AR. Intervention Study on Practice of Menstrual Hygiene among Adolescents in Two Selected Secondary Schools, Lagos State. International Journal of Medicine, Nursing & Health Sciences. 2022 Apr; 3(2): 215-228.

[13] Haque SE, Rahman M, Itsuko K, Mutahara M, Sakisaka K. The effect of a school-based educational intervention on menstrual health: an intervention study among adolescent girls in Bangladesh. BMJ Open. 2014 Jul; 4(7): e004607. doi: 10.1136/bmjopen-2013-004607.

[14] Abushaid F, Ahmad SG, Ashmauey AA, Mohammad HG. Effect of planned health educational program on menstrual knowledge and practices among adolescent Saudi girls. Journal of Nursing and Health Studies. 2017 Oct; 2(3): 16.

[15] Kamath A and Pai RR. Retrospective study of gynaecological malignancies in less than 35 years of age in Southern India. Journal of Clinical and Diagnostic Research. 2012 Jun; 5(6): 1251-5.

[16] Parle J and Khatoon Z. Knowledge, attitude, practice and perception about menstruation and menstrual hygiene among adolescent school girls in rural areas of Raigad district. International Journal of Community Medicine and Public Health. 2019 Jun; 6(6): 2490-7. doi: 10.18203/2394-6040.ijcmph20192310.

[17] Dwivedi R, Sharma C, Bhardwaj P, Singh K, Joshi N, Sharma PP. Effect of peer educator-PRAGATI (PeeR Action for Group Awareness through Intervention) on knowledge, attitude, and practice of menstrual hygiene in adolescent school girls. Journal of Family Medicine and Primary Care. 2020 Jul; 9(7): 3593. doi: 10.4103/jfmpc.jfmpc_309_20.

[18] Shanbhag D, Shilpa R, D'Souza N, Josephine P, Singh J, Goud BR. Perceptions regarding menstruation and practices during menstrual cycles among high school going adolescent girls in resource limited settings around Bangalore city, Karnataka, India. International Journal of Collaborative Research on Internal Medicine & Public Health. 2012 Jul; 4(7): 1353.

[19] Belayneh Z and Mekuriaw B. Knowledge and menstrual hygiene practice among adolescent school girls in southern Ethiopia: a cross-sectional study. BMC Public Health. 2019 Dec; 19: 1-8. doi: 10. 1186/s12889-019-7973-9.

[20] Daniel N, Kejela G, Fantahun F, Desalegn M, Guteta F. Menstrual hygiene management practice and its associated factors among in-school adolescent girls in Western Ethiopia. Contraception and Reproductive Medicine. 2023 Dec; 8(1): 1-2. doi: 10.1186/s40834-022-00196-7.

DOI: https://doi.org/10.54393/pjhs.v4i11.1061

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Frequency of Hypocalcemia among Patients with Moderate to Severe Chronic Plaque Psoriasis

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ARTICLE INFO

Key Words:
Chronic Plaque, Psoriasis, Severity, Hypocalcemia

How to Cite:
Ilyas, S., Mukhtar, R., Bashir, B., Nusrat, W., Ilyas, T., & Malik, L. M. (2023). Frequency of Hypocalcemia among Patients with Moderate to Severe Chronic Plaque Psoriasis: Chronic Plaque Psoriasis. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1061

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Received Date: 22nd September, 2023
Acceptance Date: 12th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Psoriasis is a common skin problem. It is associated with many risk factors including hypocalcemia. It is important to determine serum calcium levels among psoriatic patients that may help in proper management. **Objective:** To determine frequency of hypocalcemia in patients of moderate to severe chronic plaque psoriasis. **Methods:** It was a cross-sectional study that had involved 90 patients of both genders aged between 22-70 years having chronic plaque psoriasis. The patients were evaluated for level of calcium in serum and hypocalcemia was labeled if albumin corrected serum calcium was <8.9 mg/dl. A prior written informed consent was taken from each patient. **Results:** The mean age of the patients was 40.7 ±1 3.9 years. There were 51 (56.7%) male and 39 (43.3%) female patients with a male to female ratio of 1.3:1. The mean duration of disease was 9.2 ± 4.4 years while the mean serum calcium was 8.89 ± 0.79 mg/dl. 59 (65.6%) patients had moderate while 31 (34.4%) patients had severe disease. Hypocalcemia was observed in 35 (38.9%) patients and it was significantly higher in patients with severe disease as compared to moderate disease (58.1% vs. 28.8%; p-value=0.007). **Conclusions:** In this study a substantial proportion of patients with chronic plaque psoriasis had hypocalcemia suggesting potential role of serum calcium in the pathogenesis of psoriasis. Hypocalcemia may also indicate severity of disease. This study advocates routine screening a correction of serum calcium levels among such patients as it leads to timely identification and appropriate management of the disease.

INTRODUCTION

Psoriasis is an immune mediated inflammatory skin condition with a chronic course. It is characterized by erythematous plaques covered with thick scale. It commonly involves elbows, scalp and lower back but it can involve any skin surface. It is associated with many comorbidities including arthritis, cardiovascular, metabolic and psychological problems as a result of which lifespan is reduced [1]. Psoriasis affects both males and females. It has an early onset in females and those having a family history of psoriasis. Its bimodal distribution of age of onset with peaks at 30–39 years. In men age of onset is 60–69 years and 10 years earlier in women [2]. Various epigenetic, genetic, environmental and lifestyle factors are involved in its development. Inflammatory and immune circuits were generated by autoreactive T cells and keratinocytes that cause initiation of the disease process as well as its progression and persistence [3]. Histologically there is inflammation, hyperkeratosis and angiogenesis along with increased epidermal proliferation, abnormal keratinization and shortened maturation time [4]. It is aggravated by infections, stress, alcohol consumption, smoking, obesity, cold weather and drugs e.g. antimalarial, beta blockers and lithium [5]. It causes disfigurement, stigmatization and chronic pruritus leading to development of anxiety in patients of psoriasis. Furthermore, depression and anxiety also trigger psoriasis in a vicious manner [6]. There is increased risk of development of metabolic syndrome, cardiovascular

DOI: https://doi.org/10.54393/pjhs.v4i11.1061

disease, diabetes and non-alcoholic fatty liver disease in these patients. High mortality rate has been noted in patients suffering from severe psoriasis mainly due to cardiovascular disease [2]. There is also development of psoriatic arthritis in around 20-30% of patients suffering from psoriasis which affect quality of life as it alters physical function [7]. It causes in intensifying kinds of disabilities and imposes heavy expenditures to the patients. The best cure for psoriasis is to understand what the underlying cause is in first place [4]. It is important to know the exact underlying pathogenesis of the psoriasis as it is the mainstay of treatment. The skin hyperproliferation is controlled by calcium inside the cells. Low calcium level damages cell adhesion molecules like cadherins causing hyperproliferation of keratinocytes which leads to a development of psoriasis [5]. It has also been observed that if calcium channel blockers like diltiazem has been prescribed to some patients it results in development of psoriasiform rash and these rashes disappear on stopping calcium channel blockers. This also suggests a role of hypocalcemia in development of psoriasis [8]. Serum calcium level particularly ionized calcium level depends on level of serum albumin because 45% of serum calcium binds to serum albumin. So, it is important to measure albumin level while measuring calcium level in serum [4]. Various studies reported hypocalcemia in patients with psoriasis [4, 8, 9]. In a study conducted by Qadim at el hypocalcemia was present in 37.2% psoriatic patients [4]. Whereas it was found to be 33.75 % psoriatic patients in comparison to 7.5% in controls in a study conducted by Jomah et al., Mohammed et al., also observed decreased levels of serum calcium in psoriatic patients [8, 9]. This study was conducted to highlight the importance of hypocalcemia in patients with moderate to severe chronic plaque psoriasis and as no such study is done in Pakistan previously. It helped out in making new management guidelines of psoriasis in future.

METHODS

After approval from ethical review board this cross-sectional study was carried out at department of Dermatology Unit 1, Jinnah Hospital Lahore for a period of 6 months starting from 19 June 2019 to 18 December 2019. Non-probability, consecutive sampling was done and informed written consent was obtained. A total of 90 patients of chronic plaque psoriasis including both males and females of age 22 - 70 years were enrolled in study. Patients of chronic kidney and liver disease, hypoparathyroidism and severe dietary deficiencies were excluded. Serum calcium and albumin levels were measured in laboratory of Jinnah Hospital Lahore. Normal calcium range was taken as 8.9-10.1 mg/dl bearing in mind the available kits. Demographic data pertaining to age, sex, duration and severity of disease was noted on a predesigned structured proforma. The collected data were analysed through SPSS version-17.0.

RESULTS

There was a total of 90 patients, out of these 51 (56.7%) were males and 39 (43.3%) were female patients constituting a male to female ratio of 1.3:1. The mean age was 40.7 ± 13.9 years with age ranging from 22 years to 70 years. The mean duration of disease was 9.2 ± 4.4 years with age ranging from 1 year to 16 years. Fifty-nine (65.6%) patients had moderate while thirty-one (34.4%) patients had severe disease (Table 1). Serum calcium level ranged from 7.1 mg/dl to 10.1 mg/dl with a mean of 8.89±0.79 mg/dl (Table 1).

Table 1: Baseline characteristics of study sample

Characteristics	Participants n=90
Age (years)	40.7±13.9
≤45 years	54 (60.0%)
>45 years	36 (40.0%)
Gender	
Male	51 (56.7%)
Female	39 (43.3%)
Duration of Disease (years)	9.2±4.4
1-8 years	49 (54.4%)
9-16 years	41 (45.6%)
Severity of Disease	
Moderate	59 (65.6%)
Severe	31 (34.4%)
Serum Calcium (mg/dl)	8.89±0.79

Hypocalcemia was seen in 35 (38.9%) psoriatic patients

Table 2: Frequency of Hypocalcemia in patients of Chronic Plaque Psoriasis n=90Table 1: Baseline characteristics of study sample

Hypocalcemia	Frequency (%)
Yes	35(38.9)
No	55(61.1)
Total	90(100)

No statistically significant difference was seen in the frequency of hypocalcaemia across various subgroups depending on age, gender and duration of disease. Statistically significant difference was present among patients with severe and moderate disease. Hypocalcemia was significantly higher in patients of severe psoriasis. It was found to be 58.1% in with severe disease and 28.8% with mid psoriasis (p-value=0.007) as shown in Table 3.

Table 1: Baseline characteristics of study sample

Subgroups	N	Hypocalcemia F (%)	p-value
Age			
≤45 years	54	21 (38.9%)	

DOI: https://doi.org/10.54393/pjhs.v4i11.1061

>45 years	36	14 (38.9%)	1.000
Gender			
Male	51	20 (39.2%)	0.942
Female	39	15 (38.5%)	
Duration of Disease			
1-8 years	49	19 (38.8%)	0.981
9-16 years	41	16 (39.0%)	
Severity of Disease			
Moderate	59	17 (28.8%)	0.007*
Severe	31	18 (58.1%)	

Chi-square test *indicating observed difference was statistically significant

DISCUSSION

Psoriasis is a heterogeneous skin disease which may persist lifelong. It has various types such as plaque, pustular, guttate, flexural and erythrodermic [2]. It causes loss of productivity approximately around 10% and exerts societal impact by influencing financial status of patient as well as by increasing resource use of community [10]. Disturbances in systemic calcium metabolism have been shown in various forms of psoriasis. It has been shown that hypocalcemia is associated with intensification of lesions in most patients and systemic vitamin D and calcium are recommended to treat this condition. It was shown in recent studies that a significant number of patients with chronic plaque psoriasis had hypocalcaemia and these studies recommended correction of decreased calcium levels in psoriatic patients in future practice [4, 8]. However, the existing evidence is scarce and limited number of local studies are available. This leads to necessitation of present study. The mean age of the chronic plaque psoriatic patients was 40.7 ± 13.9 years in this study. This observation is in accordance with that of Haider et al in which the mean age of patients of chronic plaque psoriasis was 40.0 ± 12.6 years [11]. Similar mean age of 43.90 ± 1.11 years among psoriatic patients was reported in a study conducted by Rawat et al., [12]. In other studies, conducted by Chaudhari and Das et al., mean ages of 38.1 ± 15.6 years and 39.7±7.3 years respectively were observed among psoriatic patients [13, 14]. We observed a slight male predominance among patients of chronic plaque psoriasis. The ratio of male to female is 1.3:1 in this study. Shaiq et al., also observed a similar male predominance among psoriatic patients with male to female ratio of 1.4:1 [15]. Haider et al., reported higher male predominance with male to female ratio of 1.6:1 and 2.5:1 respectively among psoriatic patients [11, 12]. In another study conducted by Asim et al., at Dow University Hospital, Karachi equal gender distribution among such patients was observed [16]. While Bijina et al., found it to be 3:1 (male: female) in Indian patients [17]. The mean duration of disease was 9.2 ± 4.4 years in the present study. Choi et al., also observed a similar mean duration of disease among Romanian patients of psoriasis. It was found to be 9.5 ± 10.2 years [18]. In the present study 38.9% of patients of chronic plaque psoriasis had hypocalcemia. Bijina et al., in a similar study in India also observed that 38.0% of the patients with psoriasis had serum calcium level below normal limit (<8.8 mg/dl) which is in line with the present study [17]. Anuja et al., also reported hypocalcemia in 41.0% patients of psoriasis [19]. Our observation is also in accordance with study conducted by Qadim et al., who observed similar frequency of hypocalcaemia. It was found to be 37.2% among Iranian patients of psoriasis [4]. Basha et al., also reported decreased level of serum calcium in patients of psoriasis vulgaris compared with controls which is consistent with the results of the present study [20]. Zhai et al., found significant improvement in patients of psoriasis who were treated with calcium before starting methotrexate [21]. This observation supports that by correcting levels of calcium, psoriasis may get improved. The frequency of hypocalcemia was 58.1% in patients with severe disease as compared to moderate disease in which it was 28.8%. This suggests important role of serum calcium in the pathogenesis of psoriasis. This is supported by observation made by Jomah et al., that serum calcium decreases as PASI score increases [8]. The present study was a unique kind of study conducted in local population and it helps in adding up to already available scarce international research evidence. Hypocalcaemia was observed in considerable number of psoriatic patients and it was found to be statistically higher among patients presenting with severe disease. The strengths of the present study include large sample size along with strict exclusion criteria. There was stratification of results to address different effect modifiers. There was also limitation to the present study as we did not compare treatment response and recurrence of disease in patients with hypocalcaemia versus patients without hypocalcemia. The effect of management of hypocalcemia on the severity and treatment response of disease was also not observed as it could have further cleared the probable role of hypocalcemia in prevention and treatment of patients.

CONCLUSIONS

This study concludes that it is important to do routine screening of serum calcium level among patients of chronic plaque psoriasis as it may lead to timely identification and proper management which may further improve the outcome of such patients in dermatologic practice. It is also suggested to correct serum calcium

DOI: https://doi.org/10.54393/pjhs.v4i11.1061

levels which may improve the condition and helps in preventing progression to severe forms of disease.

Authors Contribution

Conceptualization: SI
Methodology: RM
Formal analysis: BB
Writing-review and editing: SI, BB, WN, TI, LMM
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020 May; 369: m1590. doi: 10.1136/bmj.m1590.

[2] Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clinical Medicine (Lond). 2021 May; 21(3): 170-3. doi: 10.7861/clinmed.2021-0257.

[3] Albanesi C, Madonna S, Gisondi P, Girolomoni G. The Interplay Between Keratinocytes and Immune Cells in the Pathogenesis of Psoriasis. Frontiers in Immunology. 2018 Jul; 9: 1549. doi: 10.3389/fimmu.2018.01549.

[4] Qadim H, Goforousha F, Nejad S, Goldust M. Studying the Calcium Serum Level in Patients Suffering from Psoriasis. Pakistan Journal of Biological Sciences. 2013 Mar; 16(6): 291-4. doi: 10.3923/pjbs.2013.291.294.

[5] Maheswari A and Dutta B. Correlation of hypocalcaemia with severity and type of psoriasis: A cross-sectional study. Indian Journal of Clinical and Experimental Dermatology. 2021 May; 7(2): 164-8. doi: 10.18231/j.ijced.2021.031.

[6] Tampa M, Sarbu MI, Mitran MI, Mitran CI, Matei C, Georgescu SR. The Pathophysiological Mechanisms and the Quest for Biomarkers in Psoriasis, a Stress-Related Skin Disease. Disease Markers. 2018 Jan; 2018: 5823684. doi: 10.1155/2018/5823684.

[7] Ingrasciotta Y, Isgrò V, Ientile V, Tari M, Trifirò G, Guarneri C. Are Patients with Psoriasis and Psoriatic Arthritis Undertreated? A Population-Based Study from Southern Italy. Journal of Clinical Medicine. 2021 Jul; 10(15): 3431. doi: 10.3390/jcm10153431.

[8] Jomah NS, Ismaiel MA, Khadam J. Evaluation of serum Calcium level in psoriatic patients. Journal of Medical and Pharmaceutical Sciences. 2022 Jun; 6(3): 40-51. doi: 10.26389/AJSRP.R051121.

[9] Mohamad SN. Trace elements homeostatic imbalance in mild and severe psoriasis: a new insight in biomarker diagnostic value for psoriasis. Our Dermatology Online. 2013 Oct; 4(4): 449-52. doi: 10.7241/ourd.20134.115.

[10] Häbel H, Wettermark B, Hägg D, Villacorta R, Wennerström ECM, Linder M. Societal impact for patients with psoriasis: A nationwide Swedish register study. JAAD International. 2021 Jun; 3: 63-75 .doi: 10.1016/j.jdin.2021.02.003.

[11] Haider S, Wahid Z, Najam-us-Saher, Riaz F. Efficacy of methotrexate in patients with plaque type psoriasis. Pakistan Journal of Medical Sciences. 2014 Sep; 30(5): 1050-3. doi: 10.12669/pjms.305.4451.

[12] Rawat L, Kothiwala R, Mehra A. India. Serum calcium level in patients suffering from psoriasis and its correlation with severity of psoriasis: A case control study. International Multispecialty Journal of Health (IMJH). 2019: 2395-6291.

[13] Chaudhari S and Rathi S. Correlation of serum calcium levels with severity of psoriasis. International Journal of Research in Dermatology. 2018 Nov; 4(4): 591-4. doi: 10.18203/issn.2455-4529.IntJResDermatol20184467.

[14] Das S, Biswas UK, Kumar A, Roy A. Study of serum carbonic anhydrase activity, uric acid, C-reactive protein levels and lipid parameters in patients with Psoriasis. Nepal Journal of Dermatology Venereology & Leprology. 2013 April; 11(1): 20-7. doi: 10.3126/ njdvl .v11i1.7931.

[15] Shaiq PA, Stuart PE, Latif A, Schmotzer C, Kazmi AH, Khan MS, et al. Genetic associations of psoriasis in a Pakistani population. British Journal of Dermatology. 2013 Aug; 169(2): 406-11. doi: 10.1111/bjd.12313.

[16] Asim SA, Hameed A, Niaz F, Sarwat A. To assess the frequency of raised serum uric acid level in patients with psoriasis and compare it with healthy controls in outpatient of a tertiary care hospital. International Journal of Advance Research. 2016 June; 4(6): 2124-32. doi: 10.21474/IJAR01/728.

[17] Bijina KD, Raghavendra BN, Mohamed M. A study of serum calcium and uric acid levels in psoriasis. Indian Journal of Clinical and Experimental Dermatology. 2018 Dec; 4(4): 342-5. doi: 10.18231/2581-4729.2018.0075.

[18] Choi JW, Kim BR, Seo E, Youn SW. Identification of nail features associated with psoriasis severity. Journal of Dermatology. 2017 Feb; 44(2): 147-53. doi: 10.1111/1346-8138.13565.

[19] Anuja GE and Sarojini PA. Psoriatic arthropathy: a clinical and biochemical study. Indian Journal of

DOI: https://doi.org/10.54393/pjhs.v4i11.1061

Dermatology Venereology & Leprology. 1997 Dec; 63(6): 357-60.

[20] Basha MA, Shehta WA, Gayed IM, El Hagary SB. The value of calcium and high sensitivity Creactive protein serum levels in psoriatic patients. Monoufia Medical Journal. 2021 Mar; 34: 56-60. doi: 10.4103/mmj.mmj_227_19.

[21] Zhai Z, Chen L, Yang H, Yan J, Wang C, Yang J, et al. Can pretreatment serum calcium level predict the efficacy of methotrexate in the treatment of severe plaque psoriasis. Journal of American Academy of Dermatology. 2015 Dec; 73(6): 991-7. doi: 10.1016/j.jaad.2015.08.036.

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Comparison of Intracoronary Tirofiban And Intravenous Tirofiban for Major Adverse Cardiac Events and Cerebrovascular Accident

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ARTICLE INFO

Key Words:
Myocardial Infarction, Cerebrovascular Accident, Revascularization, Tirofiban

How to Cite:
Bukhari, S. H. R., Rana, M. A., Mirza, M. S., Kazmi,M. N., Ur Rehman, Z., & Sulah Ud Din, J. (2023). Comparison of Intracoronary Tirofiban And Intravenous Tirofiban for Major Adverse Cardiac Events and Cerebrovascular Accident : Comparison of Intracoronary Tirofiban and Intravenous Tirofiban .Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1149

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Received Date: 20th October, 2023
Acceptance Date: 9th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Major Adverse Cardiovascular Events (MACE) and and Cerebrovascular Accidents (CVA) have become primary areas of interest due to the ongoing focal research in cardiovascular diseases. **Objective:** To assess the frequency of major adverse cardiac events and cerebrovascular accidents for intracoronary tirofiban and intravenous tirofiban. **Methods:** It was a comparative study conducted at the Punjab Institute of Cardiology, Lahore from March 2019 to March 2020. A total of 250 patients of both genders, aged between 20 to 65 years were enrolled in this study who had STEMI and have high thrombus burden or TIMI flow grade < 3 during primary PCI. They were divided into two groups namely intracoronary tirofiban group and intravenous tirofiban. The impact of intracoronary tirofiban versus intravenous tirofiban outcomes were assessed. **Results:** Statistically insignificant difference in MACE (myocardial infarction, cerebrovascular accident & revascularization) between intracoronary & intravenous tirofiban groups was noted. The frequency distribution for cerebrovascular accidents (CVA) showed that haemorrhage was found similar in both groups. Ischemic stroke, in patients of the intracoronary tirofiban group compared with intravenous tirofiban group, was 1 (0.8%) vs 3 (2.4%) with p-value 0.348 respectively. Reversible ischemic neurological deficit (RIND) was found in 3 (2.4%) in the intracoronary and 4 (3.2%) in the intravenous group. Transient ischemic attack (TIA) found in the intracoronary was 8(6.4%) whereas in the intravenous group was 9 (7.2%). **Conclusions:** The results of our study make us conclude that tirofiban when given intracoronary or intravenous does not show any significant difference for major adverse cardiac events and cerebrovascular accidents.

INTRODUCTION

Since cardiovascular disease is the primary cause of death in the US, interventional research frequently focuses on it [1]. As a result, "major adverse cardiovascular events" (MACE) composite endpoint is becoming a more popular primary outcome of interest. Guidelines for the use of a three-point MACE outcome, comprising myocardial infarction (MI), stroke (cerebrovascular accident), and cardiovascular mortality, were issued by the US Food and Drug Administration (FDA) in 2008 and the European Medicines Agency (EMA) in 2012 for all trials assessing the cardiovascular safety of diabetic agents [2]. A four-point MACE has also been used in some trials [3], when hospitalization for unstable angina or revascularization treatments is included. This is further elaborated upon by five-point MACE, which includes heart failure (HF). The application of MACE is becoming a more well recognized and common endpoint among randomized controlled trials [4]. ST-elevation myocardial infarction (STEMI) is a pro-thrombotic state in which excessive platelets are activated. Complete cessation of platelet activity is the main goal of treatment. Aspirin and clopidogrel are considered as standard treatment to cease platelet

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

function [5]. Some patients may develop clopidogrel resistance that does not stop the platelet function properly during intervention [6]. When the platelet activity is ceased efficiently, the myocardial damage will be less and the prognosis will be better. Glycoprotein inhibitors (GPIs) are used during percutaneous coronary intervention (PCI) as class IIa recommendation since 2004 [7]. The term "heart attack" refers to myocardial infarction (MI), which is the result of reduced or stopped blood supply to a section of the myocardium. An MI could be "silent," going unnoticed, or it could be a catastrophic occurrence that results in hemodynamic decline and abrupt death. Myocardial infarction (MI) can cause huge clot in culprit artery. Immediate stenting after MI is best possible treatment that leads to better outcome of the patients [8]. With the delayed intervention after acute event the chances of clot burden increases and causes the clot to break into small pieces and blocks the distal artery [9]. The vasospasm and distal embolization can be prevented by some techniques used during intervention like thrombus aspiration and use of glycoprotein IIb/IIIa inhibitors [10]. GPIs along with other platelet inhibitors and drugs that decrease the inflammation during MI decrease the infarct expansion, small vessel damage and improve circulation. This improve blood circulation in culprit artery by all these means improves prognosis [11]. It was observed that glycoprotein IIb/IIIa inhibitors (GPIs) improve Major Adverse Cardiac Events (MACE) by lowering death rates and recurrent myocardial infarction and maintaining vessel patency post-PCI [10]. There are few GPI drugs available like abciximab, tirofiban and eptifibatide in the form of monoclonal antibodies and small molecules [12]. Several earlier studies claim that by combining other drugs with GPIs during primary percutaneous coronary intervention there is better coronary circulation, less deaths and recurrent myocardial infarctions reported [13]. Tirofiban is used to avoid any thrombotic consequence after Percutaneous Coronary Intervention (PCI) and helps treat Acute Coronary Syndrome (ACS) [14]. The usual routes for delivery are intravenous and intracoronary injections. A high dose tirofiban (loading dose of 25 mg/kg followed by maintenance of 0.15 mg/kg per min for 18 hours) can inhibit platelet activity up to 95 percent proving itself as effective as the competitive drug in the studies [12]. Using intracoronary tirofiban causes GP IIb/IIIa receptors to inhibit more efficiently in contrast to the intravenous pathway. When this drug is given intracoronary, it is believed to have a better prognosis due to its high amount in coronaries [15]. It is observed in several trials with small to an intermediate sample size that intracoronary abciximab demonstrates favourable outcome such as improved circulation, infarct area and reperfusion injury, whereas, those with a larger sample size reveals that there is no variation in long-term MACE with intracoronary abciximab in contrast to intravenous when given during primary PCI of STEMI patients [16]. Still, there is a shortage of clinical data on general prognosis [5]. Intravenous GPI gives a quick and full inhibition of platelet aggregation. They dissolve already present thrombus and decrease the complications linked with PCI [17]. GPI decreases death, MI and MACE but a major drawback are that it increases the chances of bleeding, long stays at the hospital, increased price and late mortality [18]. There are certain benefits of intracoronary GPI. It gives a greater local amount of antiplatelet drug at obstructing sites in the coronary capillary bed. This result in better receptor binding and destroys the platelet cross-linking [19]. It gives better results for blood flow restoration after treatment and does not give rise to bleeding problems. Benefits are due to increased local concentration but also diffuse to native vessels and the aorta [20].

In this study, we tried to find the answer to the question of whether there is any difference between intracoronary tirofiban and intravenous tirofiban for major adverse cardiac events and cerebrovascular accidents.

METHODS

A total of 250 patients of both gender, age between 20 to 65 years were enrolled in this comparative study conducted at the Punjab Institute of Cardiology, Lahore from March 2019 to March 2020. Only patient who had STEMI and has high thrombus burden thrombolysis in myocardial infarction (TIMI) flow grade <3 during Primary PCI were included. The patients were divided in two groups namely intracoronary tirofiban group (125 patients) and intravenous tirofiban group (125 patients). Informed consent was obtained from all patients. Laboratory findings of all the patients were assessed to obtain the data for clinical outcome and a comparison of frequency of major adverse cardiovascular events and cerebrovascular accidents among intracoronary tirofiban versus intravenous tirofiban was assessed. The Statistical Package for the Social Sciences (SPSS) software, version-25.0, was used to enter and analyze the data. For the qualitative research variables, percentages and frequencies were computed.

RESULTS

The mean age of participants was 41.64 ± 12.30 while the average age of the intracoronary tirofiban group was 40.40 ± 12.41 compared with the intravenous group 42.88 ± 12.90. There were 36% (90) participants of age 20-35 years, 34% (85) were of age 36-50 years, remaining patients 30% (75) were between 51-65 years, so the age range was 20-65 years in our study (Table -1).

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

Table 1: Descriptive Statistics of Age

Age Groups (Year)	Frequency (%)
20-35	90 (36)
36-50	85 (34)
51-65	75 (30)
Total	250 (100)
Mean ± SD	41.64 ± 12.30
Mean ± SD (Intracoronary tirofiban group)	40.40 ± 12.41
Mean ± SD (Intravenous group)	42.88 ± 12.90
Minimum-Max	20-65

The p-value of MACE (MI, Cerebrovascular accident & Revascularization) in intracoronary & intravenous tirofiban groups is statistically insignificant as the values are 0.351, 0.436 and 0.373 respectively which showed that variables of MACE were not independent as p-value > 0.05 (Table -2).

Table 2: Cross Tabulation for Major Adverse Cardiac Events (MACE)

Variables	Research Groups				p-value
	Intracoronary Tirofiban Group f (%)		Intravenous Tirofiban Group f (%)		
	Yes	No	Yes	No	
Myocardial Infarction (MI)	8(6.40%)	117(93.6%)	12(9.6%)	113(90.4%)	0.351
Cerebrovascular accident (CVA)	13(10.4%)	112(89.6%)	17(13.6%)	108 (86.4%)	0.436
Revascularization	16(12.8%)	109(87.2%)	21(16.8%)	104(83.2%)	0.373

"Yes" means MI, CVA and revascularization occurred in these patients

"No" means MI, CVA and revascularization did not occur in these patients

A stroke is a disruption in the blood supply to brain cells; it is also known as a brain assault or a cerebral vascular accident (CVA). Brain cells die when they are depleted of oxygen. The frequency distribution for cerebrovascular accident (CVA) showed that haemorrhage was found similar in both groups with a statistically insignificant p-value of 0.510. Ischemic stroke in patients of intracoronary tirofiban group compared with intravenous tirofiban group 1(0.8%) vs 3(2.4%) with p-value 0.348 respectively. A stroke lasting longer than twenty-four hours and recovering in a week is referred to as a reversible ischemic neurologic deficit (RIND). Reversible ischemic neurological deficit (RIND) was found in 3 (2.4%) in the intracoronary and 4 (3.2%) in the intravenous group. A stroke that lasts only a few minutes is known as a transient ischemic attack (TIA). Transient ischemic attack (TIA) found in the intracoronary is 8(6.4%) whereas in the intravenous group is 9 (7.2%) with a p-value of 0.431(Table-3). Table 3 showed that there was no difference in haemorrhage, ischemic stroke, reversible ischemic neurological deficit (RIND) and transient ischemic attack (TIA) in both groups with statistically insignificant p-values 0.510, 0.348, 0.513 and 0.431 respectively (Table 3).

Table 3: Cross Tabulation for Cerebrovascular Accident (CVA)

Variables	Research Groups				p-value
	Intracoronary Tirofiban Group f (%)		Intravenous Tirofiban Group f (%)		
	Yes	No	Yes	No	
Haemorrhage	1(0.8%)	30(24.0%)	1(0.8%)	32(25.6%)	0.510
Ischemic Stroke	1(0.8%)	18(14.4%)	3(2.4%)	28(22.4%)	0.348
Reversible Ischemic Neurological Deficit (RIND)	3(2.4%)	24(19.2%)	4(3.2%)	30(24.0%)	0.513
Transient Ischaemic Attack (TIA)	8(6.4%)	40(32.0%)	9(7.2%)	18(14.4%)	0.431

"Yes" means MI, CVA and revascularization occurred in these patients

"No" means MI, CVA and revascularization did not occur in these patients

DISCUSSION

Recanalization of the vessel in ST-elevation myocardial infarction (STEMI) patients can be achieved by either timely percutaneous coronary intervention (PCI) or via medical management to save the diseased myocardium and decrease mortality [21]. The improved treatment received by ST-elevation myocardial infarction (STEMI) patients is primary percutaneous coronary intervention in comparison to medical treatment [22]. Over the past ten years the best treatment for acute myocardial infarction is percutaneous coronary intervention (PCI) to achieve complete reperfusion and thus decrease the death rate [23]. The advantages of PCI are improvement in myocardial blood flow and normal TIMI flow grade thus fewer chances of cardiovascular events [24]. When percutaneous coronary intervention is performed vascular complication is more commonly encountered and as a result, leads to an increase in the number of deaths along with an economic burden on the patient. These complications also put the patients at risk of coronary artery disease and ultimately death [25]. Even after successful placement of stents no-reflow phenomena can occur which is considered to be the second most dangerous angiographic-related problem [26]. Therefore, additional medical treatments like GPI not only decrease platelet aggregation but also improve vessel patency, so clinical outcome is better [27, 28]. The usual routes for delivery of tirofiban are intravenous and intracoronary injections. When it is given via intra-arterial injection, it allows efficient drug absorption in the diseased area and improves platelet aggregation. Glycoprotein especially tirofiban can be given through venous and intra-arterial routes. It has been proposed that when tirofiban is given through the intra-arterial pathway, has better

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

efficacy in the infarct area and has better platelet inhibition function. Moreover, this route has a low bleeding risk [29]. This study was conducted to compare intracoronary tirofiban with intravenous tirofiban for major adverse cardiac events and cerebrovascular accidents during the percutaneous coronary intervention (PPCI). A total of 250 patients were enrolled, and the mean age of the participants was 41.64 ± 12.30. Total participants were divided into two groups (intracoronary and intravenous tirofiban group). The average age was 40.40 ± 12.41 and 42.88 ± 12.90 respectively. There were 184 (73.6%) males and 66 (26.4%) females. In our study, the results of MACE (MI, CVA & Revascularization) in intracoronary & intravenous tirofiban groups remained statistically insignificant. Erdim et al conducted a study and observed that major adverse cardiovascular event during the hospital stay is 2.7% and 2.1% in the intracoronary and intravenous group respectively with a p-value of 1.00. The separate parts of the MACE in intracoronary versus intravenous groups: deaths were 2.1% as compared to 2.7%, repeat revascularizations were 4.1% versus 8.3%, recurrent myocardial infarction 4.1% and 8.3% respectively [30, 31]. These MACE values support our study. The results of our study showed that there was no difference in haemorrhage, ischemic stroke, reversible ischemic neurological deficit (RIND) and transient ischemic attack (TIA) in both groups with statistically insignificant p-values.

CONCLUSIONS

The results of our study make us conclude that tirofiban when given intracoronary or intravenous does not show any significant difference for major adverse cardiac events and cerebrovascular accidents.

Acknowledgement

The authors would like to acknowledge the Medical Affairs Department of Getz Pharma for their technical support and assistance in the publication process.

Authors Contribution

Conceptualization: SHRB, MAR
Methodology: SHRB, MNK, ZUR
Formal analysis: SHRB, MAR, MSM, JSUD
Writing-review and editing: SHRB, MAR, MSM, MNK, ZUR, JSUD
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Gal D, Thijs B, Glänzel W, Sipido KR. Hot topics and trends in Cardiovascular Research. European Heart Journal. 2019 Jul; 40(28): 2363–74. doi:10.1093/eurheartj/ehz282.

[2] Sharma A, Pagidipati NJ, Califf RM, McGuire DK, Green JB, Demets D et al. Impact of regulatory guidance on evaluating cardiovascular risk of new glucose-lowering therapies to treat type 2 diabetes mellitus. Circulation. 2020 Mar; 141(10): 843–62. doi: 10.1161/circulationaha.119.041022.

[3] Marx N, McGuire DK, Perkovic V, Woerle HJ, Broedl UC, von Eynatten M et al. Composite primary end points in cardiovascular outcomes trials involving type 2 diabetes patients: Should unstable angina be included in the primary end point? Diabetes Care. 2017 Sep;40(9):1144–51. doi:10.2337/dc17-0068.

[4] Gavrielov-Yusim N and Friger M. Use of administrative medical databases in population-based research: Table 1. Journal of Epidemiology and Community Health. 2013 Mar; 68(3): 283–7. doi:10.1136/jech-2013-202744.

[5] Lieschke F, Zheng Y, Schaefer JH, van Leyen K, Foerch C. Measurement of platelet function in an experimental stroke model with aspirin and clopidogrel treatment. Frontiers in Neurology. 2020 Feb; 11. doi:10.3389/fneur.2020.00085.

[6] Lam L. Flow cytometric analysis of intra-platelet VASP for evaluation of clopidogrel resistance in ischemic heart disease patients undergoing percutaneous coronary intervention. HKU Theses Online (HKUTO). 2012. doi:10.5353/th_b4842120.

[7] Tang X and Li R. Comparison of intracoronary versus intravneous tirofiban in acute STEMI patients undergoing primary PCI. Research Square. 2021 Dec; doi:10.21203/rs.3.rs-1081547/v1.

[8] Kang DH and Park J. Endovascular stroke therapy focused on stent retriever thrombectomy and direct clot aspiration: Historical Review and modern application. Journal of Korean Neurosurgical Society. 2017 May; 60(3): 335–47. doi:10.3340/jkns.2016.0809.005.

[9] Bernsen ML, Goldhoorn RJ, Lingsma HF, Van Oostenbrugge RJ, Van Zwam WH, Uyttenboogaart M et al. Importance of occlusion site for thrombectomy technique in stroke: comparison between aspiration and stent retriever. Stroke. 2021 Jan;52(1):80-90.

[10] Neumann FJ. Glycoprotein iib/iiia receptor blockade in myocardial infarction: Adjunctive therapy to percutaneous coronary interventions. Platelet Glycoprotein IIb/IIIa Inhibitors in Cardiovascular Disease. Totowa, NJ: Humana Press. 2003: 275–87.

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

doi:10.1385/1-59259-376-3:275.

[11] Balghith M. High bolus tirofiban vs abciximab in acute STEMI patients undergoing primary PCI - the TAMIP study. Heart Views: The Official Journal of the Gulf Heart Association. 2012 Jul; 13(3): 85. doi:10.4103 /1995-705x.102145.

[12] Montalescot G, Öngen Z, Guindy R, Sousa A, Lu S-Z, Pahlajani D et al. Predictors of outcome in patients undergoing PCI. results of the riviera study. International Journal of Cardiology. 2008 Oct; 129(3): 379–87. doi:10.1016/j.ijcard.2007.07.127.

[13] Fitts J, Ver Lee P, Hofmaster P, Malenka D. Fluoroscopy-guided femoral artery puncture reduces the risk of pci-related vascular complications. Journal of Interventional Cardiology. 2008 Jun; 21(3): 273–8. doi:10.1111/j.1540- 8183.2008 .00351.x.

[14] Upreti P, Saad M, Pandey N, Krim NR, Vittorio T. Diastolic Dysfunction Might Predict Outcomes in Acute Coronary Syndrome Patients Undergoing Primary Percutaneous Coronary Intervention. Circulation. 2023 Nov 6; 148(Suppl_1): A17921.

[15] Coller BS. Glycoprotein iib/iiia antagonists: Development of abciximab and pharmacology of abciximab, Tirofiban, and Eptifibatide. Platelet Glycoprotein IIb/IIIa Inhibitors in Cardiovascular Disease. Totowa, NJ: Humana Press. 203 :073–101. doi:10.1385/1-59259-376-3:073.

[16] Anandan PK, Tamilarasu K, Rajendran G, Sundaram S, Ramasamy P, Vidyakar RB. Thrombus aspiration plus intracoronary abciximab vs intracoronary abciximab alone in patients with STEMI undergoing primary PCI. Cardiology and Angiology: An International Journal. 2019 Nov; 8(4): 1–10. doi:10.9734/ca/2019/v8i430120.

[17] Andre P and Phillips DR. Glycoprotein iib/iiia in platelet aggregation and acute arterial thrombosis. Platelet Glycoprotein IIb/IIIa Inhibitors in Cardiovascular Disease. Totowa, NJ: Humana Press. 2003 :039–71. doi:10.1385/1-59259-376-3:039.

[18] Lago IM, Novaes GC, Badran AV, Pavão RB, Barbosa R, Figueiredo GL et al. In-lab upfront use of Tirofiban may reduce the occurrence of no-reflow during primary percutaneous coronary intervention. A pilot randomized study. Arquivos Brasileiros de Cardiologia. 2016 Nov; 403-10.107(5): 403-10. doi:10. 5935/abc.20160149.

[19] Savonitto S, De Luca G, Goldstein P, van t' Hof A, Zeymer U, Morici N et al. Antithrombotic therapy before, during and after emergency angioplasty for ST Elevation Myocardial Infarction. European Heart Journal: Acute Cardiovascular Care. 2016 Mar; 6(2): 173–90. doi:10.1177/2048872615590148.

[20] Sun B, Liu Z, Yin H, Wang T, Chen T, Yang S et al. Intralesional versus intracoronary administration of glycoprotein iib/iiia inhibitors during percutaneous coronary intervention in patients with acute coronary syndromes. Medicine. 2017 Oct; 96(40). doi:10.1097/md.0000000000008223.

[21] Elbadawi A, Elgendy IY, Megaly M, Ha LD, Mahmoud K, Alotaki E et al. Meta-analysis of randomized trials of intracoronary versus intravenous glycoprotein iib/iiia inhibitors in patients with st-elevation myocardial infarction undergoing primary percutaneous coronary intervention. The American Journal of Cardiology. 2017 Oct; 120(7): 1055–61. doi:10.1016/j. amjcard.2017.06.040.

[22] Shen J, Zhang Q, Zhang RY, Zhang JS, Hu J, Yang ZK et al. Clinical benefits of adjunctive tirofiban therapy in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Coronary Artery Disease. 2008 Jun; 19(4): 271-7. doi: 10.1097/ MCA.0b013e3282f487e0.

[23] Wilmer CI. Intracoronary high-dose bolus tirofiban administration during complex coronary interventions: A United States-based case series. Cardiovascular Revascularization Medicine. 2018 Jan; 19(1): 112–6. doi:10.1016/j.carrev.2017.06.009.

[24] Zaki TM, Gamal A, El Hamady WA, Mansour S, Abu Arab TM. Comparison between the effect of intracoronary bolus of tirofiban versus EPTIFIBATIDE as adjunctive antiplatelet therapy on the outcome of primary coronary intervention in patients with acute anterior ST segment elevation myocardial infarction. The Egyptian Heart Journal. 2011 Jun; 63(2): 109–15. doi:10.1016/j.ehj.2011.09.002.

[25] Ma Q, Ma Y, Wang X, Li S, Yu T, Duan W et al. Intracoronary compared with intravenous bolus tirofiban on the microvascular obstruction in patients with STEMI undergoing PCI: A cardiac MR study. The International Journal of Cardiovascular Imaging. 2020 Jun; 36(6): 1121–32. doi:10.1007/s 10554020018 00-0.

[26] Zhao XM, Gao CY, Chu YJ, Yang L, Yang XZ, Xu WK et al. Fondaparinux vs. enoxaparin in patients with non-ST elevation acute coronary syndromes (NSTE-ACS) treated with percutaneous coronary intervention and tirofiban: An exploratory study in China. Journal of Clinical Pharmacy and Therapeutics. 2015 Oct; 40(5): 584–9. doi:10.1111/jcpt.12315.

[27] Liu X, Dong P, Xing S, Wang H, Li Z, Zhang H et al. Clinical evaluation of thrombus aspiration combined with tirofiban in patients with acute myocardial infarction with elective percutaneous coronary intervention. Journal of International Medical

DOI: https://doi.org/10.54393/pjhs.v4i11.1149

Research. 2013 Oct; 41(5): 1532–40. doi:10.1177/03000605134809 15.

[28] Zhangjin D. GW25-E0788 the effect of thrombus-aspiration combined tirofiban in the patients with ST-segment elevation myocardial infraction (STEMI) after the direct percutaneous coronary intervention. Journal of the American College of Cardiology. 2014 Oct; 64(16). C144. doi:10.1016/j.jacc.2014.06.663.

[29] Watanabe H, Shiomi H, Nakatsuma K, Morimoto T, Taniguchi T, Furukawa Y et al. Clinical efficacy of thrombus aspiration on 5-year clinical outcomes in patients with ST-segment elevation acute myocardial infarction undergoing percutaneous coronary intervention. Journal of the American Heart Association. 2015 Jun; 4(11). e001962. doi:10.1161/jaha.115.001945.

[30] Hsin HT, Wu CF, Liao PC, Lin PC, Chen LY. Upstream tirofiban reduces reperfusion cardiac arrhythmias in patients of acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. International journal of cardiology. 2011 Jan; 146(2): 292-4. doi:10.1016/j.ijcard.2010.10.088.

[31] Wang H and Feng M. Influences of different dose of Tirofiban for acute ST elevation myocardial infarction patients underwent percutaneous coronary intervention. Medicine. 2020;99(23). doi:10.1097/md.0000000000020402.

DOI: https://doi.org/10.54393/pjhs.v4i11.781

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Randomized Trial of FOLFOX 4 and FOLFIRI in The Treatment of Advance Colorectal Cancer

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ARTICLE INFO

Key Words:
Colorectal Cancer, Colon, Chemotherapy Regimen, FOLFOX 4, FOLFIRI, Treatment Outcomes, Response Rate, Survival Time

How to Cite:
Kumari, R., Haider, G., Aalam, N., Shah, A., Sarim, T., & Abid, K. (2023). Randomized Trial of FOLFOX 4 and FOLFIRI in The Treatment of Advance Colorectal Cancer : Randomized Trial of FOLFOX 4 and FOLFIRI . Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.781

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Received Date: 10th May, 2023
Acceptance Date: 11th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Colorectal cancer is a major global health concern, ranking third in prevalence and second in mortality. Developed countries have high incidence rates, while Pakistan is considered a low-risk region. Metastatic colorectal cancer requires targeted therapies like FOLFIRI and FOLFOX 4, but their effectiveness in Pakistan is unknown. This study aims to provide insights, guide treatment decisions, and expand global understanding in the field. **Objective:** To compare therapeutic effects of FOLFOX 4 and FOLFIRI for advanced colorectal cancer patients. **Methods:** The Medical Oncology Department of Jinnah Postgraduate and Medical Centre conducted a randomized controlled trial research from May 2022 to February 2023. Hundred patients of advanced colorectal cancer with a confirmed diagnosis of age 18 to 80 years, of either gender, were included. Randomly, 50 of these patients were in FOLFIRI group, and 50 in FOLFOX4 group. Both groups were compared for the treatment outcomes. **Results:** In the FOLFIRI group, the total response rate was 66%, whereas in the FOLFOX 4 group, it was 78%. In the FOLFIRI group, the median time to progression was 8 months, but in the FOLFOX 4 group, it was 9 months (p=0.06). In the FOLFIRI group, the total median survival time was 13 months, whereas in the FOLFOX 4 group, it was 14 months (p=0.280). **Conclusions**: The response rates between the two groups were similar, while FOLFOX 4 had a little higher rate of tumor control. FOLFIRI had a lower incidence of neutropenia, whereas FOLFOX 4 had a lower incidence of nausea and vomiting.

INTRODUCTION

Colorectal cancer ranks as the third most prevalent cancer and the second leading cause of death worldwide. In 2020, globally, there were over 1.9 million new colorectal cases, resulting in more than 930,000 deaths [1]. Developed countries like Europe, New Zealand, Australia, and North America have a high incidence rate of colorectal cancer [2]. However, countries in Southern Asia have the lowest incidence rates and Pakistan is regarded as a low-risk region for colorectal cancer [2, 3]. Nearly one in five colorectal cancer patients already had distant metastases at the time of diagnosis. Targeted therapies and systemic chemotherapy are advised treatments for metastatic colorectal cancer (mCRC) [4]. In the past, folinic acid (CF) and fluorouracil (5-FU) were the primary first-line therapies for mCRC. However, in the twenty-first century, chemotherapy regimens such as FOLFIRI (CF, 5-FU, and irinotecan) and FOLFOX 4 (CF, 5-FU, and oxaliplatin) have shown success as 1st line treatments for advanced stage colon cancer, improving the prognosis and quality of life for patients [5-10]. A phase III study conducted by Colucci et al., compared the effectiveness of FOLFIRI and FOLFOX4 regimens for treating advanced colorectal cancer. The FOLFIRI regimen was linked to a greater death rate during the first 60 days of treatment, despite the fact that both

DOI: https://doi.org/10.54393/pjhs.v4i11.781

regimens had comparable overall response rates (31% for FOLFIRI and 34% for FOLFOX4) [11]. Another recent study by Neuget et al., found no discernible difference between FOLFOX 4 and FOLFIRI in terms of survival, however FOLFIRI demonstrated a progression-free survival of 7 months and an overall response rate of 39% [12].

These studies highlight the value of individualized treatment programme for individuals with advanced colorectal cancer and the continued pursuit of the most effective therapeutic approaches. Although both regimens have shown benefits for patients with advanced colorectal cancer, there is limited data on their use in Pakistan. This trial aims to provide valuable insights into the effectiveness of these treatments specifically in the Pakistani population and identify any differences in response and side effects. The results of this study will guide clinical decision-making, contribute to the development of standardized treatment guidelines for advanced colorectal cancer patients in Pakistan, and expand the global understanding of optimal treatment strategies. Furthermore, it may pave the way for further research in this field.

METHODS

It was an interventional study carried out at the department of Medical Oncology, Jinnah Postgraduate and Medical Center from May 2022 to Feb 2023. Sample size of 92≈100 (50 in each group) was estimated using Open epi sample size calculator by taking statistics of overall response rate of FOLFIRI as 39%, margin of error as 10% and 95% confidence level. The included patients of age 18 to 65 years of both sex with confirmed diagnosis of advanced colorectal carcinoma (stage III-IV). Patients with history of uncontrolled and active infections, previous chemotherapy including irinotecan or oxaliplatin, carcinomatous meningitis or known brain metastases, interstitial fibrosis or interstitial pneumonia, total colectomy, history of any cardiovascular event, lactating or pregnant females, and psychological or mental disorders were excluded from the study. Non-random consecutive sampling method was employed. All eligible patients provided informed consent, and the study taken approval from the ethical review committee. Subjects were divided into two groups using a 1:1 random ratio. Group A, consisting of 50 individuals, was administered the FOLFIRI regimen. This particular regimen involves administering leucovorin 100 mg/m2 (L-isomer form) as a two-hour infusion, followed by a bolus injection of 5-fluorouracil 400 mg/m2. On the initial day, patients in this group were additionally administered irinotecan 180 mg/m2 (150 mg/m2 for those aged over 70-75 years). Furthermore, leucovorin 100 mg/m2 (L-isomer form) was given as a two-hour infusion before a bolus injection of 5-fluorouracil 400 mg/m2, followed by a 22-hour infusion of 5-fluorouracil 600 mg/m2. Group B, also comprising of 50 individuals, received solely the FOLFOX4 regimen. This regimen includes oxaliplatin 85 mg/m2 on the first day, along with leucovorin and 5-fluorouracil on both days 1 and 2. Both treatments were administered at two-week intervals for a maximum of 12 cycles. The response rate of each patient was assessed, with complete response and partial response used as criteria. CT scans were conducted before and after the therapy at follow-up visits every eighth week to evaluate the response. The toxicity of each treatment cycle was also evaluated. The data analysis were performed using SPSS version 23.0. The median and interquartile range were used to report the age, time to progression, and survival time. Frequency and proportions were reported for gender, ECOG status, prior therapy, primary tumor site, site of metastasis, response, and toxicity. To conduct a comparative analysis of the response to treatment of the two groups, the Fisher's exact test was employed. Furthermore, the Mann-Whitney U test was utilized to compare the median time to progression and overall survival of the two groups. It was conventionally agreed that a p-value of equal to or less than 5% would be indicative of statistical significance.

RESULTS

The mean age was 37.5 years in FOLFIRI group and 44.5 years in FOLFOX 4 group. Most of the patients with advance colorectal cancer were males, had ECOG performance status as 1, previously received adjuvant chemotherapy and primary colon cancer in both groups. While, 42% patients had liver metastases in FOLFIRI group and 36% in FOLFOX 4 group, respectively (Table 1).

Table 1: Patients' characteristics in both groups

Characteristics	FOLFIRI (n=50)	FOLFOX 4 (n=50)
Age (years)	37.5 (28-53)	44.5 (35-50)
Gender		
Female	19 (38)	16 (32)
Male	31 (62)	34 (68)
ECOG performance status		
0	33 (66)	25 (50)
1	13 (26)	18 (36)
2	4 (8)	7 (14)
Prior therapy		
Adjuvant chemotherapy	33 (66)	30 (60)
Primary tumor resection	17 (34)	20 (40)
Primary tumor site		
Colon	32 (64)	33 (66)
Rectum	13 (26)	12 (24)
Colon and rectum	5 (10)	5 (10)
Site of metastasis		
Liver	21 (42)	18 (36)
Lungs	13 (26)	11 (22)

DOI: https://doi.org/10.54393/pjhs.v4i11.781

Lymph nodes	4 (8)	2 (4)
Brain	1 (2)	0
Bone	1 (2)	2 (4)
Peritoneum	2 (4)	4 (8)
Pelvis	0	6 (12)
Multiple sites	8 (16)	7 (14)
Data presented as Median (IQR) or n (%)		

In the FOLFIRI group, complete response was achieved in 30%, whereas, partial response was achieved in 46%. In FOLFOX 4 group, the complete response was achieved in 24% and partial response was achieved in 52%. The p-value for the Fisher Exact test is 0.145, which greater than 0.05. Hence, there is insignificant difference in response between the two groups, FOLFIRI and FOLFOX 4 (Table 2).

Table 2: Comparison of response rates between both groups

Response	FOLFIRI (n=50)	FOLFOX 4 (n=50)	p-value
Complete response	10 (30)	11 (24)	0.145
Partial response	23 (46)	28 (52)	
Stable disease	6 (12)	8 (16)	
Progressive disease	11 (22)	3 (6)	
Data presented as n (%)			

Additionally, the median time to progression in the FOLFIRI group was 8 months, compared to 9 months in the FOLFOX 4 group. The comparison for median time to progression was done using Mann-Whitney U test, which showed statistical insignificant difference between both groups (p=0.06). In the FOLFIRI group, the total median survival time was 13 months, whereas in the FOLFOX 4 group, it was 14 months. The comparison for total median survival time was done using Mann-Whitney U test, which showed statistical insignificant difference between both groups (p=0.280)(Table 3).

Table 3: Comparison of time to progression and time to survival between both groups

Parameter	FOLFIRI (n=50)	FOLFOX 4 (n=50)	p-value
Median Time to Progression (months)	8	9	0.060
Median Time to survival (months)	13	14	0.280
Data presented as median			

Table 4 displays the toxicity profiles of both therapies. The most prevalent side effects in the FOLFIRI group were anemia (44%), neutropenia (46%) and nausea and vomiting (60%) in that order. The most prevalent toxicity in the FOLFOX 4 group was neutropenia (48%), followed by anemia (36%) and diarrhea (30%).

Table 4: Toxicity profile of both groups

Toxicity	FOLFIRI (n=50)	FOLFOX 4 (n=50)
Neutropenia	23 (46)	24 (48)
Anemia	22 (44)	18 (36)
Thrombocytopenia	7 (14)	8 (16)
Leukopenia	9 (18)	7 (14)
Nausea and vomiting	30 (60)	10 (20)
Diarrhea	19 (38)	15 (30)
Fever	11 (22)	10 (20)
Data presented as n (%)		

DISCUSSION

This particular study was designed with the objective of comparing the efficacy and toxicity of two different chemotherapy regimens, namely FOLFIRI and FOLFOX 4, among patients who are suffering from advanced-stage colorectal cancer. Upon observing the baseline characteristics of the study population, it was observed that both treatment groups exhibited similarities with respect to age, gender, performance status, and previous chemotherapy history. Most of the patients had liver metastases and colon cancer. Elzouki et al., conducted a study on 152 CRC patients and found the median age was 57.4 ± 12.92 years, 55% of the patients were males, and 68% had colon cancer [13]. Similarly, one more study by Masi et al., reported the median age was 62 years and 63% of the patients were males (63%) and colon was the most common site (73%). Additionally, 81% patients had liver as the site of metastases and 68% had synchronous metastases. They observed that baseline characteristics were comparable between the FOLFIRI and FOLFOX 4 treatment groups [14]. Our study examined treatment outcomes and found that the FOLFOX 4 group had a higher overall response rate (78%) compared to the FOLFIRI group (66%). However, the FOLFOX 4 group demonstrated significantly better tumor control rates (94%) compared to the FOLFIRI group (78%). Although the median time to progression was slightly longer in the FOLFOX 4 group, this difference was not statistically significant. Likewise, the median overall survival time did not significantly differ between the two groups. However, the FOLFOX 4 group exhibited a higher 1-year survival rate (58%) compared to the FOLFIRI group (50%). Regarding toxicity profiles, the FOLFIRI group experienced a higher incidence of nausea and vomiting, while the FOLFOX 4 group had higher incidences of neutropenia and diarrhea. However, the overall occurrence of adverse events was similar in both groups. Wu et al., conducted a network meta-analysis to evaluate the effectiveness of various first-line chemotherapy regimens for advanced colorectal cancer. The study revealed that FOLFOX 4, FOLFIRI, and TOMOX demonstrated superior short-term and long-term efficacy compared to other regimens. Based on their findings, the authors recommended these three regimens as suitable options for the clinical treatment of advanced colorectal cancer [15]. Another study by Neuget et al. reported that

DOI: https://doi.org/10.54393/pjhs.v4i11.781

both FOLFOX 4 and FOLFIRI exhibited comparable response rates ranging from 54% to 56%, along with similar progression-free survival rates of approximately 8 months to 8.5 months, respectively. However, patients receiving FOLFOX 4 treatment had a higher probability of experiencing neuropathy, while those undergoing FOLFIRI treatment reported a greater incidence of adverse side effects such as nausea, diarrhea, and neutropenia. The study did not observe a significant disparity in survival outcomes between the two treatment approaches [12]. In another RCT by Ikoma et al., found that FOLFOX 4 and FOLFIRI are both effective combination therapies for treating advanced and metastatic colorectal carcinoma. Both FOLFOX 4 and FOLFIRI have shown similar response rates and overall survival rates. FOLFOX 4 has been associated with more neuropathy, while FOLFIRI has been associated with more diarrhea and neutropenia [16]. In a review article by Idress and Tejani regarding elder patients, it was disclosed that both the FOLFOX 4 and FOLFIRI chemotherapy regimens have demonstrated advantageous outcomes in terms of response and survival rates for elderly patients diagnosed with metastatic colon cancer. Nonetheless, it is important to note that these treatments also pose the risk of drug toxicities, which can potentially be more severe in the elderly population. Therefore, when selecting a treatment plan, it is imperative that the decision is made on a case-by-case basis, with consideration of the patient's overall health and the potential risks and benefits associated with the treatment [17]. Stintzing et al., discussed the findings of the FIRE-3 trial, which conducted a comparative analysis of two distinctive treatment regimens for patients with RAS wild-type metastatic colorectal cancer. It was determined that the response rates were similar for both FOLFOX 4 and FOLFIRI when combined with either cetuximab or bevacizumab. Furthermore, it was observed that the overall survival was comparatively longer for patients who received FOLFIRI plus cetuximab as opposed to those who were administered FOLFIRI plus bevacizumab or FOLFOX 4 plus either cetuximab or bevacizumab. It was also noted that both FOLFOX 4 and FOLFIRI exhibited a certain degree of toxicity, however, the specific side effects varied depending on the treatment regimen and the type of targeted therapy employed. It was concluded that FOLFIRI plus cetuximab was associated with the highest incidence of grade 3/4 adverse events [18]. In another safety analysis conducted by Watanabe et al., a comparison was made between FOLFOXIRI and FOLFIRI, in combination with either bevacizumab or panitumumab for the purpose of treating metastatic colorectal cancer. Their findings indicated that FOLFOXIRI, in combination with either bevacizumab or panitumumab, produced higher response rates, longer progression-free survival, overall survival, and greater rates of toxicity when compared to FOLFIRI with either drug. They suggested that FOLFOXIRI could potentially be a more efficacious treatment option for individuals with metastatic colorectal cancer, but it also carries an elevated risk of side effects [19]. In another clinical trial conducted by Colucci et al., it was determined that there was no statistically significant difference in the overall response rates between the two therapeutic regimens (31% for FOLFIRI and 34% for FOLFOX4, p=0.60). Additionally, the median progression time was found to be identical for both groups, lasting 7 months. However, the FOLFIRI treatment protocol was associated with a higher mortality rate within the initial 60 days of administration (2.8% vs 1.1% for FOLFOX4, p=0.24). The researchers reported that all patients were included in the analysis of treatment-related toxicities. Within arm A (FOLFIRI), there were two therapy-related deaths due to hematologic toxicity (febrile neutropenia), while another patient died of disseminated intravascular coagulation, which was not related to the treatment but occurred due to concomitant progressive disease [11]. Haong and colleagues discovered that FOLFOX 4 and FOLFIRI/FOLFOX 4 + cetuximab significantly extended both overall survival and progression free survival. Furthermore, the adverse events (grade≥3) and serious adverse events were comparable between treatments [20]. Ultimately, these results indicate that treatment selection must be based on individual circumstances, including the patient's overall health and the potential risks and benefits of the treatment. The present study exhibits a few limitations. Specifically, the small sample size poses a potential threat to the generalizability of the findings. Additionally, the follow-up period may not have been extensive enough to capture long-term outcomes, such as overall survival. Moreover, the study's inclusion criteria were restricted to patients with advanced colorectal cancer, thereby limiting the applicability of the findings to patients with early-stage disease. It is also noteworthy that the study solely compares FOLFOX 4 and FOLFIRI, without investigating other treatment options or combinations. Nevertheless, the present study's strength lies in its utilization of a randomized controlled trial design, which is a rigorous method to minimize bias and augment the validity of the findings. In future, further research studies should be conducted to investigate other treatment options and combinations and compare the long-term outcomes of different treatments.

CONCLUSIONS

There was no discernible disparity in the response rates observed between the two groups, albeit FOLFOX 4 demonstrated a marginally superior tumor control rate.

DOI: https://doi.org/10.54393/pjhs.v4i11.781

However, FOLFIRI had a lower incidence of neutropenia, while FOLFOX 4 had a lower incidence of nausea and vomiting. These findings suggest that both regimens have similar efficacy but differ in their toxicity profiles.

Authors Contribution

Conceptualization: RK
Methodology: GH
Formal analysis: NA, AS
Writing-review and editing: TS, KA
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, et al. Global burden of colorectal cancer in 2020 and 2040: Incidence and mortality estimates from GLOBOCAN. Gut. 2023 Feb; 72(2): 338-44. doi: 10.1136/gutjnl-2022-327736.

[2] Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Gastroenterology Review/Przegląd Gastroenterologiczny. 2019 Jan; 14(2): 89-103. doi: 10.5114/pg.2018.81072.

[3] Shaikh Z and Haider G. Clinical spectrum of colorectal cancer: Experience of 186 patients from Jinnah Postgraduate Medical Centre Karachi. Journal of Fatima Jinnah Medical University. 2019 Apr; 13(1): 12-7.

[4] Zhang X, Duan R, Wang Y, Liu X, Zhang W, Zhu X, et al. FOLFIRI (folinic acid, fluorouracil, and irinotecan) increases not efficacy but toxicity compared with single-agent irinotecan as a second-line treatment in metastatic colorectal cancer patients: a randomized clinical trial. Therapeutic Advances in Medical Oncology. 2022 Jan; 14: 17588359211068737. doi: 10.1177/17588359211068737.

[5] Grothey A, Sargent D, Goldberg RM, Schmoll HJ. Survival of patients with advanced colorectal cancer improves with the availability of fluorouracil-leucovorin, irinotecan, and oxaliplatin in the course of treatment. Journal of Clinical Oncology. 2004 Apr; 22(7): 1209-14. doi: 10.1200/JCO.2004.11.037.

[6] Gustavsson B, Carlsson G, Machover D, Petrelli N, Roth A, Schmoll HJ, et al. A review of the evolution of systemic chemotherapy in the management of colorectal cancer. Clinical Colorectal Cancer. 2015 Mar; 14(1): 1-0. doi: 10.1016/j.clcc.2014.11.002.

[7] Xu RH, Muro K, Morita S, Iwasa S, Han SW, Wang W, et al. Modified XELIRI (capecitabine plus irinotecan) versus FOLFIRI (leucovorin, fluorouracil, and irinotecan), both either with or without bevacizumab, as second-line therapy for metastatic colorectal cancer (AXEPT): a multicentre, open-label, randomised, non-inferiority, phase 3 trial. The Lancet Oncology. 2018 May; 19(5): 660-71. doi: 10.1016/S1470-2045(18)30140-2.

[8] Xu J, Kim TW, Shen L, Sriuranpong V, Pan H, Xu R, et al. Results of a randomized, double-blind, placebo-controlled, phase III trial of trifluridine/tipiracil (TAS-102) monotherapy in Asian patients with previously treated metastatic colorectal cancer: the TERRA study. Journal of Clinical Oncology. 2018 Feb; 36(4): 350-8. doi: 10.1200/JCO.2017.74.3245.

[9] Li J, Qin S, Xu RH, Shen L, Xu J, Bai Y, et al. Effect of fruquintinib vs placebo on overall survival in patients with previously treated metastatic colorectal cancer: the FRESCO randomized clinical trial. Jama. 2018 Jun; 319(24): 2486-96. doi: 10.1001/jama.2018.7855.

[10] Li J, Qin S, Xu R, Yau TC, Ma B, Pan H, et al. Regorafenib plus best supportive care versus placebo plus best supportive care in Asian patients with previously treated metastatic colorectal cancer (CONCUR): a randomised, double-blind, placebo-controlled, phase 3 trial. The lancet oncology. 2015 Jun; 16(6): 619-29. doi: 10.1016/S1470-2045(15)70156-7.

[11] Colucci G, Gebbia V, Paoletti G, Giuliani F, Caruso M, Gebbia N, et al. Phase III randomized trial of FOLFIRI versus FOLFOX4 in the treatment of advanced colorectal cancer: a multicenter study of the Gruppo Oncologico Dell'Italia Meridionale. Journal of Clinical Oncology. 2005 Aug; 23(22): 4866-75. doi: 10.1200/JCO.2005.07.113.

[12] Neugut AI, Lin A, Raab GT, Hillyer GC, Keller D, O'Neil DS, et al. FOLFOX 4 and FOLFIRI use in stage IV colon cancer: analysis of SEER-medicare data. Clinical Colorectal Cancer. 2019 Jun; 18(2): 133-40. doi: 10.1016/j.clcc.2019.01.005.

[13] Elzouki AN, Habel S, Alsoaeiti S, Abosedra A, Khan F. Epidemiology and clinical findings of colorectal carcinoma in two tertiary care hospitals in Benghazi, Libya. Avicenna Journal of Medicine. 2014 Oct; 4(04): 94-8. doi: 10.4103/2231-0770.140659.

[14] Masi G, Vasile E, Loupakis F, Cupini S, Fornaro L, Baldi G, et al. Randomized trial of two induction chemotherapy regimens in metastatic colorectal cancer: an updated analysis. Journal of the National Cancer Institute. 2011 Jan; 103(1): 21-30. doi: 10.10

DOI: https://doi.org/10.54393/pjhs.v4i11.781

93/jnci/djq456.

[15] Wu DM, Wang YJ, Fan SH, Zhuang J, Zhang ZF, Shan Q, et al. Network meta-analysis of the efficacy of first-line chemotherapy regimens in patients with advanced colorectal cancer. Oncotarget. 2017 Oct; 8(59): 100668-100677. doi: 10.18632/oncotarget.22177.

[16] Ikoma N, Raghav K, Chang G. An update on randomized clinical trials in metastatic colorectal carcinoma. Surgical Oncology Clinics. 2017 Oct; 26(4): 667-87. doi: 10.1016/j.soc.2017.05.007.

[17] Idrees M and Tejani M. Current treatment strategies for elderly patients with metastatic colon cancer. Cureus. 2019May; 11(5): 1-5. doi: 10.7759/cureus.4713.

[18] Stintzing S, van Oostrum I, Pescott CP, Ronga P, Heeg B, Heinemann V. Cost-effectiveness of FOLFIRI+ cetuximab vs FOLFIRI+ bevacizumab in the first-line treatment of RAS wild-type metastatic colorectal cancer in Germany: data from the FIRE-3 (AIO KRK-0306) study. Journal of Medical Economics. 2020 May; 23(5): 448-55. doi: 10.1080/13696998.2019.1709848.

[19] Watanabe T, Tsuji A, Shiozawa M, Ota H, Satake H, Yabuno T, et al. Safety analysis of the randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with RAS wild-type tumors: The DEEPER trial (JACCRO CC-13). Journal of Clinical Oncology. 2021 Jan; 39(3): 86-. doi: 10.1200/JCO.2021.39.3_suppl.86.

[20] Hoang T, Sohn DK, Kim BC, Cha Y, Kim J. Efficacy and safety of systemic treatments among colorectal cancer patients: A network meta-analysis of randomized controlled trials. Frontiers in Oncology. 2022 Feb; 11: 756214. doi: 10.3389/fonc.2021.756214.

DOI: https://doi.org/10.54393/pjhs.v4i11.1151

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 4, Issue 11 (November 2023)

Original Article

Per-Operative Predictors of Conversion of Laparoscopic Cholecystectomy into Open Procedure

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ARTICLE INFO

Key Words:
Laparoscopic Cholecystectomy, Open Procedure, Cholecystitis

How to Cite:
Khan, R., Javed, U., & Rehman, A. ur. (2023). Per-Operative Predictors of Conversion of Laparoscopic Cholecystectomy into Open Procedure : Conversion of Laparoscopic Cholecystectomy. Pakistan Journal of Health Sciences, 4(11). https://doi.org/10.54393/pjhs.v4i11.1151

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Received Date: 27th October, 2023
Acceptance Date: 16th November, 2023
Published Date: 30th November, 2023

ABSTRACT

Laparoscopic cholecystectomy, a minimally invasive procedure for gallbladder removal, is widely preferred due to its advantages like reduced postoperative pain and quicker recovery. However, in certain cases, this procedure may need to be converted to an open cholecystectomy. The ability to predict such conversions preoperatively is crucial for better surgical planning and patient counseling. **Objective:** To identify and analyze the per-operative predictors that may necessitate the conversion of laparoscopic to open cholecystectomy. **Methods:** This study was conducted in Surgical Unit 3 at Bahawal Victoria Hospital, Bahawalpur as a prospective observational study spanning over 6 months from September 2022 to February 2023. All patients who were booked for Laparoscopic cholecystectomy were included. The data of preoperative and perioperative factors were collected on a standard proforma. Operative findings which were analyzed and documented by the surgeon were then, compared to look for the factors that contribute to conversion of Laparoscopic cholecystectomy into open procedure**. Results:** Mean ± SD of age was 42.59 ± 13.14. Regarding frequency of per-operative findings. It reveals that adhesions were found in 20 (22.7%) of the 88 procedures, difficult anatomy at Callot's triangle was present in 12 (13.6%) cases, unmanageable bleeding occurred in 4 (4.5%) cases, and damage to nearby structures was observed in 6 (6.8%) procedures. The remaining procedures did not exhibit these issues. **Conclusions:** Our study has conclusively identified critical per-operative predictors for the conversion of laparoscopic cholecystectomy to an open procedure. These insights are instrumental for preoperative assessment and planning, potentially guiding clinical decisions to optimize patient care and surgical outcomes.

INTRODUCTION

When it comes to minimal invasive surgeries, laparoscopic cholecystectomy brought a revolutionary change. A closer analysis reveals that gall stones are present in about 15 percent of the whole US population and are a major cause of abdominal pain [1]. One of the best management options for such patients is Cholecystectomy [2]. Since, its widespread use in surgery, Laparoscopic surgical management of gall stones has widely replaced the conventional open surgery and is considered a Gold Standard now [3]. For patients undergoing cholecystectomy, some risk factors have been well established with the disease incidence being more in the elderly and in the female gender. Surgical incidence in Pakistan is about 4.2% for males and 14.2% for females [4]. However, despite the increase in surgical expertise and the availability of latest surgical techniques; according to Hu *et al.*, the rate of conversion of Laparoscopic cholecystectomy to open procedure is 1-15% [5]. For a developing country like Pakistan, very little data-based evidence is available that can essentially predict the

DOI: https://doi.org/10.54393/pjhs.v4i11.1151

conversion of laparoscopic cholecystectomy to open procedures. It is even more important in our region because of limited resources as conversion increases the perioperative complications, perioperative time and hospital stay and expenses [6]. The most common reasons that are seen as a basis of conversion include difficult anatomy, presence of adhesions, life threatening bleeding and damage to nearby structures including inflammation [7]. In the context of this study, 'Adhesions' refer to the fibrous bands of tissue that abnormally connect the gallbladder or surrounding structures to other internal organs. These are identified intraoperatively through visual inspection and palpation by the surgeon. The presence of adhesions is noted if they impede access to the gallbladder or interfere with the safe dissection of tissues. The term "Difficult Anatomy at Calot's Triangle" refers to any anatomical variations or complications within Calot's Triangle that hinder standard laparoscopic procedures. This includes anomalies like aberrant ducts, unusual vascular structures, or excessive fatty tissue. Identification is based on the surgeon's intraoperative assessment and the need for additional maneuvers to safely expose and dissect within Calot's Triangle. Unmanageable Bleeding is defined as any intraoperative bleeding that cannot be controlled by standard laparoscopic hemostatic techniques and thus poses a risk to patient safety. The threshold for 'unmanageable' is determined by the volume of blood loss that necessitates additional interventions beyond the usual laparoscopic procedures, such as conversion to open surgery or the use of advanced hemostatic tools. Damage to Nearby Structures refers to any inadvertent injury or harm caused to adjacent organs or tissues (e.g., bowel, liver, bile ducts) during the laparoscopic procedure. Such damage is characterized by the type of structure affected, the extent of the injury, and the intervention required to repair it. This is determined through intraoperative findings and postoperative diagnostic assessments when applicable. Furthermore, patients who undergo conversion are seen to have major complications like bile duct injury, biliary leak or unmanageable bleeding all of whom are associated with high morbidity and mortality [8]. It is therefore emphasized that a greater understanding of the per operative factors that lead to conversion of laparoscopic cholecystectomy is very important for ensuring safe surgical practices. Patients are also made more aware of the associated risks before undergoing surgery and are psychologically ready should any such situation arise. Lists can also be more effectively scheduled with the availability of such information.

METHODS

This study was conducted in Surgical Unit 3, Bahawal Victoria Hospital, Bahawalpur as a prospective observational study spanning over 6 months from September 2022 to February 2023. This study was approved by the CPSP on August 02, 2022 Ref. # CPSP/REU/SGR-2018-032-10124. Sample size was calculated using Yamene's formula. Total 88 patients who were booked for Laparoscopic cholecystectomy either male or female having age 20-80 years were included using non-probability sampling technique. All patients gave written and informed consents. Immunocompromised patients, patients with malignancy or those having any other infectious etiology were excluded from this study. The data of preoperative and perioperative factors were collected on a standard proforma. These included age, gender, co-morbidity (diabetes, hypertension, hepatitis B and C status as well as history of any previous surgery). History of previous abdominal surgery was also considered. The underlying diagnosis was also divided into patients having Cholelithiasis, Empyema GB or Cholecystitis. Operative findings which were analyzed and documented by the surgeon were then, compared to look for the factors that contribute to conversion of Laparoscopic cholecystectomy into open procedure. Difficult anatomy, Adhesions, Unmanageable bleeding and damage to nearby structures were all classified into presence or absence of these findings. The data were statistically analyzed using Statistical Package for Social Sciences SPSS v.24.0.1. The mean and SD were calculated for age. Frequencies were calculated for per-operative findings (Adhesions, Difficult anatomy at Callot's triangle, Unmanageable bleeding, Damage to nearby structures). Association of per operative conversion with per-operative findings (Adhesions, Difficult anatomy at Callot's triangle, Unmanageable bleeding, Damage to nearby structures) and different variables (gender, co-morbidity, ASA Grade, Experience of surgeon, diagnosis) was detected by using chi-square test/ Fisher's Exact Test. A p-value of <0.05 was considered significant statistically.

RESULTS

The purpose of your our is to identify the frequency of per-operative predictors that result in the conversion of laparoscopic cholecystectomy into an open procedure. Mean ± SD of age was 42.59 ± 13.14. Regarding frequency of per-operative findings. It reveals that adhesions were found in 20 (22.7%) of the 88 procedures, difficult anatomy at Callot's triangle was present in 12 (13.6%) cases, unmanageable bleeding occurred in 4 (4.5%) cases, and damage to nearby structures was observed in 6 (6.8%) procedures. The remaining procedures did not exhibit these issues (Table 1).

DOI: https://doi.org/10.54393/pjhs.v4i11.1151

Table 1: Frequency of per-operative findings

Per Operative Findings	Yes (%)	No (%)
Adhesions	20 (22.7%)	68 (77.3%)
Difficult Anatomy at Callot's Triangle	12 (13.6%)	76 (86.4%)
Unmanageable Bleeding	4(4.5%)	84 (95.5%)
Damage to Nearby Structures	6 (6.8%)	82 (93.2%)

Regarding the association of per-operating with conversion, the results show that all 20 cases with adhesions were converted into an open procedure, whereas only 4 (5.88%) out of 68 cases without adhesions were converted. This indicates a significant correlation between the presence of adhesions and conversion of the procedure (p=0.000). All 12 cases with difficult anatomy at Callot's triangle resulted in a conversion, compared to 12 (15.79%) of the 76 cases where the anatomy was not problematic. This suggests a significant relationship between the complexity of anatomy at Callot's triangle and the conversion of the surgery (p=0.000). Association of damage to nearby structures with the conversion of the procedure was assessed. All six cases with damage to nearby structures were converted to an open procedure, while only 18 (21.95%) of the 82 cases without damage were converted. This provides a statistically significant correlation between the damage to nearby structures and conversion of the procedure (p=0.000). Association between unmanageable bleeding and conversion to an open procedure evaluate. Of the four cases with unmanageable bleeding, all were converted, while only 20 (23.81%) of the 84 cases without unmanageable bleeding were converted. This signifies a statistically significant association between unmanageable bleeding and the conversion of the procedure (p=0.005) (Table 2).

Table 2: Association of per-operative conversion with per-operative findings

Per-Operative Findings	Per-operative Conversion		Total (%)	p-value
	Not converted (%)	Converted (%)		
Adhesions				
No	64 (94.12%)	4 (5.88%)	68 (77.27%)	0.00
Yes	0	20 (100%)	20 (22.73%)	
Difficult Anatomy at Callot's Triangle				
No	64 (84.21%)	12 (15.79%)	76 (86.36%)	0.00
Yes	0	12 (100%)	12 (13.64%)	
Damage to Nearby Structures				
No	64 (78.05%)	18 (21.95%)	82 (93.2%)	0.00
Yes	0	6 (100%)	6 (6.8%)	
Unmanageable Bleeding				
No	64 (76.19%)	20 (23.81%)	84 (95.45%)	0.005
Yes	0	4 (100%)	4 (4.55%)	

Table 3 shows the association between gender and the conversion of the procedure. For males (16 cases), 10 (62.5%) required conversion to an open procedure. However, among females (72 cases), only 14 (19.4%) required conversion. This significant difference (p=0.000) suggests gender could be a potential predictor. Regarding association of co-morbidity with the conversion of the procedure, of the 72 cases without co-morbidities, 16 (22.2%) required conversion. Meanwhile, 50% of patients with co-morbidities (16 cases) required conversion. This indicates a significant association (p=0.024) between the presence of co-morbidities and procedure conversion. Relationship between the American Society of Anesthesiologists (ASA) Grade and conversion was also assed, for ASA Grade-I (44 cases) and Grade-II (38 cases), the conversions were 22.7% and 26.3% respectively. However, in the case of ASA Grade-III (6 cases), 66.7% required conversion, although this relationship was not statistically significant (p=0.075). in this table evaluates the link between the surgeon's experience and the conversion of the procedure. For surgeons with less than three years of experience, all two surgeries they performed were converted. For those with more than five years of experience, 18 out of 66 surgeries (27.3%) were converted. However, this association was not statistically significant (p=0.055). Regarding association of the initial diagnosis with the conversion of the procedure was evaluated. For patients diagnosed with cholelithiasis (74 cases), 16.21% required conversion. However, for those diagnosed with empyema (10 cases) and cholecystitis (4 cases), the conversion rates were 80% and 100% respectively, indicating a significant association (p=0.000).

Table 3: Association of per-operative conversion with different variables

Different Variables	Per-operative Conversion		Total (%)	p-value
	Not converted (%)	Converted (%)		
Gender				
Male	6 (37.5%)	10 (62.5%)	16 (18.18%)	0.00
Female	58 (80.6%)	14 (19.4%)	72 (81.82%)	
Co-Morbidity				
No	56 (77.8%)	16 (22.2%)	72 (81.82%)	0.024
Yes	8 (50.0%)	8 (50.0%)	16 (18.18%)	
ASA Grade				
Grade-I	34 (77.3%)	10 (22.7%)	44 (50%)	0.075
Grade-II	28 (73.7%)	10 (26.3%)	38 (43.18%)	
Grade-III	2 (33.3%)	4 (66.7%)	6 (6.82%)	
Experience of Surgeon				
<3 years	0	2 (100%)	2 (2.73%)	0.055
3-4 years	6 (100%)	0	6 (6.18%)	
4-5 years	10 (15.6%)	4 (16.7%)	14 (15.91%)	
>5 years	48 (75.0%)	18 (75.0%)	66 (75%)	
Diagnosis				
Cholelithiasis	62 (83.78%)	12 (16.21%)	74 (84.09%)	0.000
Empyema	2 (20%)	8 (80%)	10 (11.36%)	
Cholecystitis	0	4 (100%)	4 (4.55%)	

DOI: https://doi.org/10.54393/pjhs.v4i11.1151

DISCUSSION

In this study, we aimed to identify the per-operative predictors of conversion from laparoscopic cholecystectomy to an open procedure. We analyzed a total of 88 patients who underwent laparoscopic cholecystectomy over a period of 6 months in our unit, and found that 27.3% (n=24) of them required conversion to an open procedure. Identifying risk factors associated with conversion can significantly improve patient outcomes and post-operative recovery. Comparing our findings with previous studies, we observed that the conversion rates varied. Gabriel *et al.*, reported a conversion rate of 26.1%, while Amin *et al.*, reported a rate of 7.78% [11, 15]. In our study, we found that male patients had a higher likelihood of conversion compared to female patients, with a conversion rate of 62.5% in men and 19.4% in women. This finding is consistent with studies by Kama *et al.*, and Gharaibeh *et al.*, which also indicated a higher predisposition towards conversion in males [16, 17]. Regarding comorbidities such as diabetes, hypertension, and hepatitis B and C, as well as the American Society of Anesthesiologists (ASA) status and the expertise of the operating surgeon, we found no significant associations with the conversion rate. This suggests that these factors may not play a significant role in predicting the need for conversion. When analyzing the per-operative diagnoses associated with conversion, we found that all three diagnoses - Empyema GB, Cholelithiasis, and Cholecystitis - showed significance. The conversion rate for patients with cholelithiasis was 16.2%, while it was 80% for patients with empyema and 100% for patients with acute cholecystitis. However, statistically, all three diagnoses had a significant p-value, indicating that any of them could lead to conversion. It is important to note that the presence of empyema GB and acute cholecystitis presents technical difficulties due to inflammation, as supported by a study by Chahin *et al* [18]. Regarding the intraoperative findings, we categorized them into four groups: presence or absence of adhesions, unmanageable bleeding, difficult anatomy at Callot's triangle, and damage to nearby structures. Adhesions were found in 20 out of 88 patients, and all 20 underwent conversion. This finding is consistent with a study by *Amin et al.*, which showed similar results [7]. Adhesions make dissection and identification of structures difficult due to tissue friability. Difficult anatomy at Callot's triangle also showed a significant p-value of 0.000, indicating that when the anatomy in this region is challenging, surgeons may find it difficult to identify the correct ducts and arteries, leading to conversion. Shamim *et al.*, also reported similar results, with 54.32% of patients with difficult anatomy undergoing conversion [19]. In cases where damage to nearby structures occurred during the laparoscopic cholecystectomy, only 6 out of 88 patients had such damage, further supporting the safety of laparoscopic surgery. However, all 6 patients required conversion. Damage to nearby structures, particularly the bowel or common bile duct, can make it challenging to proceed with the laparoscopic approach, leading surgeons to prefer conversion for better visualization and repair. Unmanageable bleeding, although rare (6 out of 88 patients), also resulted in conversion due to the obscured vision it causes. This finding is consistent with a study by Shea *et al.*, which emphasized the significance of both damage to nearby structures and bleeding in predicting conversion[20].

CONCLUSIONS

In conclusion, our study identified several pre-operative predictors of conversion from laparoscopic cholecystectomy to an open procedure. Male gender, specific diagnoses such as empyema GB and acute cholecystitis, the presence of adhesions, difficult anatomy at Callot's triangle, and damage to nearby structures or unmanageable bleeding were significant factors associated with conversion. These findings contribute to a better understanding of the decision-making process in converting laparoscopic procedures to open procedures and can help guide surgical planning and patient counseling. Further research is warranted to validate and expand upon these findings in larger cohorts and diverse populations.

Authors Contribution

Conceptualization: RK
Methodology: RK
Formal analysis: UJ
Writing-review and editing: RK, AUR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

All authors have read and agreed to the published version of the manuscript.

REFERENCES

[1] Kelley Jr WE. The evolution of laparoscopy and the revolution in surgery in the decade of the 1990s. JSLS: Journal of the Society of Laparoendoscopic Surgeons. 2008 Oct; 12(4): 351.

[2] Hasbahceci M. Laparoscopic cholecystectomy: what has changed over the last three decades. Clinics in Surgery. 2016 Oct; 1(1): 1166. doi: 10.25107/2474-

DOI: https://doi.org/10.54393/pjhs.v4i11.1151

1647.1166.

[3] Everhart JE and Ruhl CE. Burden of digestive diseases in the United States Part III: Liver, biliary tract, and pancreas. Gastroenterology. 2009 Apr; 136(4): 1134-44. doi: 10.1053/j.gastro.2009.02.038.

[4] Sultan AM, El Nakeeb A, Elshehawy T, Elhemmaly M, Elhanafy E, Atef E. Risk factors for conversion during laparoscopic cholecystectomy: retrospective analysis of ten years' experience at a single tertiary referral centre. Digestive Surgery. 2013 Apr; 30(1) :51-5. doi: 10.1159/000347164.

[5] Kaafarani HM, Smith TS, Neumayer L, Berger DH, Depalma RG, Itani KM. Trends, outcomes, and predictors of open and conversion to open cholecystectomy in Veterans Health Administration hospitals. The American Journal of Surgery. 2010 Jul; 200(1): 32-40. doi: 10.1016/j.amjsurg.2009.08.020.

[6] Cawich SO, Mitchell DI, Newnham MS, Arthurs M. A comparison of open and laparoscopic cholecystectomy done by a surgeon in training. West Indian Medical Journal. 2006 Mar; 55(2): 103-9. doi: 10.1590/S0043-31442006000200008.

[7] Musbahi A, Abdulhannan P, Bhatti J, Dhar R, Rao M, Gopinath B. Outcomes and risk factors of cholecystectomy in high-risk patients: A case series. Annals of Medicine and Surgery. 2020 Feb; 50: 35-40. doi: 10.1016/j.amsu.2019.12.003.

[8] Channa NA, Khand F, Bhanger MI, Leghari MH. Surgical incidence of Cholelithiasis in Hyderabad and adjoining areas (Pakistan). Pakistan Journal of Medical Sciences. 2004 Jan-Mar; 20(1): 13-17.

[9] Hu ASY, Menon R, Gunnarsson R, de Costa A. Risk factors for conversion of laparoscopic cholecystectomy to open surgery - A systematic literature review of 30 studies. The American Journal of Surgery. 2017 Nov; 214(5): 920-930. doi: 10.1016/j.amjsurg.2017.07.029.

[10] Lengyel BI, Panizales MT, Steinberg J, Ashley SW, Tavakkoli A. Laparoscopic cholecystectomy: What is the price of conversion? Surgery. 2012 Aug; 152(2): 173-8. doi: 10.1016/j.surg.2012.02.016.

[11] Amin A, Haider MI, Aamir IS, Khan MS, Khalid Choudry U, Amir M *et al.* Preoperative and Operative Risk Factors for Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy in Pakistan. Cureus. 2019 Aug; 11(8): e5446. doi: 10.7759/cureus.5446.

[12] Warchałowski Ł, Łuszczki E, Bartosiewicz A, Dereń K, Warchałowska M, Oleksy Ł *et al.* The analysis of risk factors in the conversion from laparoscopic to open cholecystectomy. International Journal of Environmental Research and Public Health. 2020 Oct; 17(20): 7571. doi: 10.3390/ijerph17207571.

[13] Wolf AS, Nijsse BA, Sokal SM, Chang Y, Berger DL. Surgical outcomes of open cholecystectomy in the laparoscopic era. The American Journal of Surgery. 2009 Jun; 197(6): 781-4. doi: 10.1016/j.amjsurg.2008.05.010.

[14] Machado NO. Biliary complications postlaparoscopic cholecystectomy: mechanism, preventive measures, and approach to management: a review. Diagnostic and Therapeutic Endoscopy. 2011; 2011: 967017. doi: 10.1155/2011/967017.

[15] Gabriel R, Kumar S, Shrestha A. Evaluation of predictive factors for conversion of laparoscopic cholecystectomy. Kathmandu University Medical Journal. 2009; 7(25): 26-30. doi: 10.3126/kumj.v7i1.1761.

[16] Kama NA, Doganay M, Dolapci M, Reis E, Atli M, Kologlu M. Risk factors resulting in conversion of laparoscopic cholecystectomy to open surgery. Surgical Endoscopy. 2001 Sep; 15(9): 965-8. doi: 10.1007/s00464-001-0008-4.

[17] Gharaibeh KI, Qasaimeh GR, Al-Heiss H, Ammari F, Bani-Hani K, Al-Jaberi TM *et al.* Effect of timing of surgery, type of inflammation, and sex on outcome of laparoscopic cholecystectomy for acute cholecystitis. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2002 Jun; 12(3): 193-8. doi: 10.1089/10926420260188092.

[18] Chahin F, Elias N, Paramesh A, Saba A, Godziachvili V, Silva YJ. The efficacy of laparoscopy in acute cholecystitis. JSLS: Journal of the Society of Laparoendoscopic Surgeons. 1999 Apr-Jun; 3(2): 121-5.

[19] Shamim M, Memon AS, Bhutto AA, Dahri MM. Reasons of conversion of laparoscopic to open cholecystectomy in a tertiary care institution. JPMA. The Journal of the Pakistan Medical Association. 2009 Jul; 59(7): 456-60.

[20] Shea JA, Healey MJ, Berlin JA, Clarke JR, Malet PF, Staroscik RN *et al.* Mortality and complications associated with laparoscopic cholecystectomy. A meta-analysis. Annals of Surgery. 1996 Nov; 224(5): 609-20. doi: 10.1097/00000658-199611000-00005.