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Original Article

FIB 4 Score (Liver Fibrosis) and Attending Level of Vitamin D in Chronic Hepatitis C Patients

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ABSTRACT

Millions of people around the world are affected by chronic hepatitis C (HCV), which is a global health issue. It is a major contributor to chronic liver conditions such as cirrhosis, hepatocellular carcinoma, and liver fibrosis. For optimal therapy and intervention, prompt identification of liver fibrosis is essential. The rate of hepatic fibrosis progression in HCV-infected patients varies substantially. **Objective:** To evaluate the vitamin D level and liver fibrosis degree by non-invasive Fib 4 score among chronic hepatitis patients. **Methods:** This Cross-sectional study was conducted at a tertiary care hospital in Karachi, Pakistan, from August 2020 to September 2022. 65 participants were recruited through a non-probability sampling technique. **Results:** Study findings show that 21.9% of the patients have low risk for advanced fibrosis, whereas 9.2% have an Intermediate risk for advanced fibrosis, and 69.2% have a high risk for advanced fibrosis. Moreover, findings also revealed that among 65 patients, 66.2% have a deficient amount of Vitamin D, whereas 16.9% have an insufficient amount of Vitamin D level and 16.9% have a sufficient amount of vitamin D. Furthermore, the findings also showed significant association based on p-value (0.001) between Age and Fib4 score of the participant. **Conclusions:** In conclusion, the study revealed that a significant proportion of chronic hepatitis C patients were at high risk for advanced fibrosis, while vitamin D deficiency/ insufficiency were prevalent among the majority of the patients.

INTRODUCTION

Millions of people around the world are affected by chronic hepatitis C (HCV), which is a worldwide health issue. It is a major contributor to chronic liver conditions such as cirrhosis, hepatocellular carcinoma, and liver fibrosis. For optimal therapy and intervention, prompt identification of liver fibrosis is essential. The rate of liver fibrosis development in HCV-infected patients varies substantially [1]. Moreover, one of the main causes of morbidity and mortality is the chronic liver diseases, having a variety of etiologies. Hepatic fibrosis gets advancement through pathogenic stages of chronic liver disorders. Extracellular matrix builds up in the liver as a result of chronic liver

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disease or injury, including viral infection, alcoholic liver disease, and NAFLD. Cirrhosis, liver failure, and hepatocellular cancer can be consequently happened in this condition [2]. Furthermore, diagnosis of liver disease is essential for the treatment and after treatment [3]. Chronic liver disease is the most prevalent in the world right now, affecting 20% to 35% of individuals in the overall population. It is a significant public health concern on a global scale. Additionally, the number of infected patients is increasing, and the disease has now spread to epidemic levels. Chronic liver disease is thought to affect 20%–30% of people in Western nations and 15% or less of the people in Asian nations [4]. There are many non-invasive techniques which have been suggested for diagnosing liver fibrosis. According to reports, the FIB-4 index is extremely useful for calculating advanced liver fibrosis. The FIB-4 index is a straightforward formula that uses the conventional biochemical parameters (Age [years]_AST[U/L]/Platelets [109/L] / ALT[U/L]) to predict liver fibrosis [5]. The importance of vitamin D as a physiological regulator outside of its traditional function in maintaining skeletal homeostasis is being recognized more and more. The link between vitamin D and liver illness is becoming greater and clearer. Chronic liver illness frequently has vitamin D insufficiency; hence vitamin D analogues are beneficial for liver diseases [6]. It is becoming better acknowledged that vitamin D is as important as a physiological regulator in addition to its conventional role in preserving skeletal homeostasis. It is becoming increasingly evident that vitamin D and liver disease are related. Because chronic liver disease is commonly accompanied by vitamin D deficiency, vitamin D mimics are helpful for liver disease. Numerous investigations also revealed a direct link between low vitamin D levels and a raised risk of liver fibrosis. Vitamin D status may be utilized as a biochemical marker to track the development of hepatic fibrosis because patients with liver fibrosis also had a large prevalence of vitamin D deficit [7]. Regardless of the etiology, vitamin D insufficiency is quite common in people with chronic liver disease (CLD) and is linked to liver dysfunction and death [8]. In a recent investigation, human primary transforming growth factor stimulated hepatic stellate cells were shown to respond favorably to vitamin D's anti-fibrotic properties [9]. The role of vitamin D in immunomodulatory properties low serum 25 OH vitamin D are frequently found in chronic hepatitis C patients and seem to be linked to more advanced stages of liver fibrosis. As a result, the purpose of this study is to look into the FIB-4 score, which is a measure of liver fibrosis, and the vitamin D level in people with chronic hepatitis C.

METHODS

Cross-sectional study design was used on chronic hepatitis C patients using a non-probability sampling technique. The study was conducted at Baqai Medical University Hospital in Nazimabad, Karachi. The study spanned over two years, from August 2020 to September 2022. The total sample size for the study was 65 patients. Inclusion criteria for the study included Patients of both genders and various age groups, diagnosed with chronic hepatitis C infection, who visited the Outpatient Department (OPD) of Baqai Medical University Hospital in Nazimabad, Karachi. Exclusion criteria for the study included Patients with other liver diseases (e.g., hepatitis B, alcoholic liver disease), Patients with coexisting chronic medical conditions (e.g., diabetes, hypertension) that could potentially impact liver fibrosis or vitamin D metabolism, Patients on specific medications or therapies known to affect vitamin D levels or liver fibrosis. Data for the study were collected through data compilation in the outpatient department (OPD) of chronic hepatitis C patients. The 25 OH vitamin D3 levels of the attendees were measured and classified as deficient (20 ng/ml), insufficient (21-29 ng/ml), and sufficient (>30 ng/ml) based on their vitamin D content. Each patient's Fib 4 Index score was also determined, which is used to determine their likelihood of developing advanced fibrosis. The criteria for the Fib 4 Index are: 1.45 (low risk for advanced fibrosis), 1.45-3.25 (mid risk for advanced fibrosis), and >3.25 (high risk for advanced fibrosis). The relevant institutional review board (IRB) obtained ethical approval for conducting the study. This approval ensures that while conducting the study, ethical principles, protection of the rights and well-being of the participants is considered. The study ensured ethical considerations by obtaining signed consent from the willing participants and assuring the confidentiality of their information. The collected data were entered into statistical software for analysis, specifically SPSS version 25.0. Frequency and percentages were used to describe the vitamin D levels and the Fib 4 scores. Furthermore, the association between the Fib 4 score and age was assessed using the chi-square test.

RESULTS

Table 1 show that there are total of 65 patients. Out of these, 32 patients (49.2%) are male, and 33 patients (50.8%) are female. In the 24-34 age group, there were 4.6% participants. Moreover, the 35-44 age group comprises of 6 patients, accounting for 9.2% of the total. The majority of patients fall into the 45-54 age group, which is, 61.5%. In the 55-64 age group, there are 18.5% of the participants. Lastly, the 65+ age group there is 6.2% of the participants.

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Table 1: Sociodemographic characteristics n=65

Gender	Number of Patients
Male	32(49.2)
Female	33(50.8)
Age	
24-34	3(4.6)
35-44	6(9.2)
45-54	42(61.5)
55-64	12(18.5)
65+	4(6.2)

Table 2 shows that among 65 patients, 14 (21.9%) were have Fib4 Score equal to or less than 1.45, considered a low risk for advanced fibrosis, whereas 6 (9.2%) had Fib4 Score ranging from 1.46 to 3.25, considered as Intermediate risk for advanced fibrosis and 45 (69.2%) have fib4 Score equal or more than 3.26 considered as high risk for advanced fibrosis.

Table 2: Level of Fib 4 Score

Fib4 Score	Frequency (%)
≤1.45	14(21.9)
1.46-3.25	6(9.2)
≥3.26	45(69.2)

Table 3 shows that among 65 patients, 43(66.2%) have a deficient amount of Vitamin D level, which is equal to or less than 20, whereas 11(16.9%) have an Insufficient amount of Vitamin D level ranging from 20.1 to 29.99 and 11 (16.9%) have a sufficient amount of vitamin D equal or more than 30.

Table 3: Level of Vitamin D

Vitamin D	Frequency (%)
Deficient < 20	43(66.2)
Insufficient 20.1-29.99	11(16.9)
Sufficient > 30	11(16.9)

Table 4 shows a significant association based on the p-value between the Age and Fib4 score of the participant.

Table 4: Association of Fib4 score and Age

Age	1(= <1.45)	2(1.46-3.25)	3 (= >3.26)	p-value
1(24-34)	3	0	0	
2 (35-44)	4	1	1	
3 (45-54)	7	4	29	**.001
4 (55-64)	0	0	12	
5(65& above)	0	1	3	

Chi square test was applied

**Significant at 1%; ~Cells proportion was <20%

DISCUSSION

Millions of people around the world are affected with chronic hepatitis C (CHC), a health issue. The increase of liver fibrosis, which can advance to cirrhosis and finally result in liver failure, is one of the serious side effects of CHC [10]. For patients with CHC, an accurate assessment of liver fibrosis is essential for evaluating the prognosis and directing therapy decisions [11]. Additionally, recent research indicates that vitamin D deficiency may contribute to the development and progression of liver illnesses [12]. Therefore, this study aims to investigate the FIB-4 score, a non-invasive marker of liver fibrosis, and the attending vitamin D level in CHC patients. Present findings show that the total number of patients was 65, in which males were 49.2% and females 50.8%. In contrast, another study shows 63% male and 37% female [13]. Moreover, another study by Luger *et al.*, also found different results and showed that 80 % were females, and only 20% were males [14]. The present finding shows that 66.2% have a deficient Vitamin D level, whereas 16.9% have Insufficient Vitamin D and 16.9% have sufficient vitamin D. Similarly, another study's findings parallel show some vitamin D insufficiency (92.4%). 16.3% (7/43) of those with hepatitis C cirrhosis had mild vitamin D deficiency, 48.8% (21/43) had moderate, and 30.2% (13/43) had severe [15]. In this regard, another study shows that 68 individuals had vitamin D deficiency (50 nmol/L), whereas 23 patients had vitamin D insufficiency (50-80 nmol/L) [13]. Vitamin D deficiency results in osteopenia, osteoporosis, osteomalacia, a painful condition, and increased muscle weakness, which enhances the risk of fractures and falls. In the seemingly healthy population, osteoporotic patients, and people who have previously fractured, vitamin D deficiency is widespread [16]. Present findings show a significant association based on the p-value (0.001) between the Age and Fib4 score of the participant. Likewise, another study also showed that age factors were independently linked with verified fibrosis (p 0.003)[17]. This age-related decline in immune function can reduce the ability to control viral infections such as HCV. Inadequate immune response to HCV may lead to persistent viral replication and increased liver damage, contributing to fibrosis progression. Consequently, older individuals may exhibit higher FIB-4 scores and a higher prevalence of verified fibrosis due to the age-related decline in immune function. Present findings indicated that among 65 patients, 21.9% had a low risk for advanced fibrosis, whereas 9.2% had an Intermediate risk for advanced fibrosis, and 69.2% had a high risk for advanced fibrosis. Another study by Caballería *et al.*, findings, similar to ours, show that increased LS prevalence estimates ranged from 9.0% to 5.8% to 3.6% (kPa = 6.8, 8.0, and 9.0). These results demonstrate an increased frequency of advanced fibrosis and silent liver disease [18]. Another study's findings revealed that 30% of the patients had significant fibrosis (F2), 9% had advanced fibrosis (F3), and 4% had cirrhosis (F4) [14]. In addition, another study found that 778 (9.5%) of the individuals had significant fibrosis (2.9 kPa), of which 214 (2.6%) had advanced fibrosis (3.6 kPa)[19]. The high prevalence of liver fibrosis in chronic hepatitis C (CHC) patients can

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significantly impact both the individual and the healthcare system like, disease progression and prognosis, impaired liver function and increased healthcare utilization [20].

CONCLUSIONS

A substantial amount of chronic hepatitis C patients had a high risk of developing advanced fibrosis, according to the study's findings, and the majority of patients had vitamin D shortage or insufficiency. Age and FIB-4 scores were discovered to be substantially correlated. These results highlight the significance of early fibrosis detection, suitable management techniques, and monitoring and maximizing vitamin D levels in the treatment of chronic hepatitis C patients.

Authors Contribution

Conceptualization: TS
Methodology: MA
Formal analysis: MA
Writing-review and editing: KK, MI, NR, SAW, JA, AB, AL, SM

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

Conflicts of Interest

The authors declare no conflict of interest.

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