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Effect of Phototherapy On the Serum Calcium Level in Term Neonates with Indirect Hyperbilirubinemia

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ABSTRACT

Normal calcium levels in neonates are crucial for preventing hypocalcemia. Phototherapy disrupts melatonin secretion, enhancing cortisol-induced hypocalcemia and urinary calcium excretion. **Objectives:** To determine the effect of phototherapy on serum calcium levels and its association with the incidence of hypocalcemia in term neonates with indirect hyperbilirubinemia. **Methods:** A descriptive case series was carried out in the Department of Pediatrics, Islamic Teaching Hospital, Sialkot, between Nov 5, 2023, and April 4, 2024. A total of 134 newborns who met the study's inclusion and exclusion criteria were enrolled. Demographic information, including name, age, sex, weight, and address, was noted. Three milliliters of venous blood were drawn before the commencement of conventional phototherapy and following forty-eight hours of nonstop phototherapy. The sample was subsequently transferred to a laboratory for the measurement of calcium and serum indirect bilirubin levels. All data was collected through a well-designed proforma. **Results:** A Total of 134 patients, 77 (57.5%) belonged to the age category of 0-15 days, while 57 (42.5%) belonged to the age group of 16-28 days. The mean age of the patients was determined to be 14.32 ± 5.25 days. There were 66 (49.3%) female and 68 (50.7%) male. The percentage of hypocalcemia was 31 (23.1%) in term neonates receiving phototherapy for indirect hyperbilirubinemia. **Conclusions:** It was concluded that the percentage of hypocalcemia was 31 (23.1%) in term neonates receiving phototherapy for indirect hyperbilirubinemia. Phototherapy effectively reduces serum bilirubin levels but is associated with a significant decline in serum calcium, suggesting a potential risk of hypocalcemia in neonates.

INTRODUCTION

Normal levels of calcium in the body are very important in neonates not only to carry out normal physiological processes in body like maintaining the integrity of cell membrane, mineralization of bone, coagulation of blood and as a cofactor for the functioning of many enzymes, but also to prevent them from the adverse effects of hypocalcemia. Calcium's major reservoir in the body is bony tissue, and the rest is present in extracellular fluid. About 50% of the extracellular fluid contains ionized calcium, whereas forty percent is complexed with albumin, and about ten percent is bound to ions such as citrate, phosphate, sulphate and lactate [1]. Changes in serum levels of phosphate, magnesium, albumin, and bicarbonate all affect measured serum calcium levels. The body's total calcium levels are affected by changes in albumin concentration, but this does not affect ionized calcium levels. Overall serum calcium levels typically drop by 0.8 mg/dL for every 1.0 g/dL drop in serum albumin levels [2]. Cyanosis, apnea, reluctance to feed, focal or generalized convulsions, carpopedal spasm, irritability, jitteriness, vomiting, prolongation of QT interval with resultant torsade de pointes are all clinical manifestations of hypocalcemia. Early-onset of neonatal hypocalcemia is frequently clinically asymptomatic [3]. For the prevention and treatment of hyperbilirubinemia in neonates, phototherapy has a key role. It causes a decline in the level of serum bilirubin by converting it into isomers that are water soluble and thus can be easily removed from the body without

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conjugation in the liver [4]. Type of light source used i.e., fluorescent, LED or halogen, distance between neonate and the light source, treated surface area, etiology of jaundice, and total serum bilirubin level before phototherapy are among the notable factors which alter the efficacy of phototherapy. Nevertheless, phototherapy has its own side effects which include diarrhea, dehydration, erythematous skin rash, damage to DNA, retinitis, hyperthermia [5]. Phototherapy results in inhibition of pineal gland secretion of melatonin by transcranial illumination. Melatonin prevents cortisol from having its hypocalcemia-causing impact. As a result, low serum melatonin levels allow cortisol's actions to go unchecked, which leads to the development of hypocalcemia. Moreover, phototherapy is also associated with increase urinary calcium excretion. Although neonatal hypocalcemia is a potentially fatal condition, laboratory hypocalcemia is often inconsistent and asymptomatic. In addition, it varies depending on gestational age (GA) and perinatal disease [6]. According to a study done in 2016, following 48 hours of phototherapy, the incidence of hypocalcemia in full-term infants with hyperbilirubinemia was around 22.76% (28/123) [4]. A study carried out in Iran reported about 7% of full-term neonates subjected to phototherapy hypocalcemia [7]. According to another study, 20.3% of term newborns experienced hypocalcemia following phototherapy [8]. Another study suggested that the prevalence of hypocalcemia to be very low in term neonates, i.e. only 2.5% [9]. In India, a study suggested a significant decrease in the levels of serum calcium after receiving phototherapy at a p value of 0.014, in 18 out of 30 term neonates (60%) [10]. The study of Saeed *et al.,* showed that 34.5% developed Hypocalcemia after 48 hours of phototherapy in term neonates [4].Phototherapy, commonly utilized for treating neonatal jaundice, can interfere with calcium balance by inhibiting melatonin production. This leads to an unregulated hypocalcemia effect from cortisol. Furthermore, it has been linked to higher urinary calcium excretion, which further exacerbates calcium depletion. Although it was noted a significant decrease in serum calcium levels was noted after phototherapy, the results have been inconsistent, influenced by factors such as gestational age and perinatal conditions [12]. This study is driven by inconsistencies in existing literature regarding the impact of phototherapy on serum calcium levels. While some studies report a significant decline, others present variable findings, highlighting a gap in understanding its effects. Additionally, limited research exists on the long-term clinical consequences and the identification of high-risk subgroups. Addressing these gaps is crucial for optimizing neonatal care and minimizing potential risks associated with phototherapy.

This study aims to determine the effect of phototherapy on serum calcium levels and its association with the incidence of hypocalcemia in term neonates with indirect hyperbilirubinemia.

METHODS

The study was a descriptive case series conducted at the Department of Pediatrics, Islam Teaching Hospital, Sialkot, after getting the ethical approval (900/IMC/ERC/000103). The research spanned six months, from November, 2023, to April, 2024. With the use of the World Health Organization sample size calculator, 134 neonates made up the sample, which was considered a 95% confidence level, 8% absolute precision, and an expected incidence of hypocalcaemia at 66.6% [11]. Nonprobability consecutive sampling was used in this study. Parental or guardian written and informed consent was obtained after explaining the study's purpose, procedures, and risks. Ethical approval was secured, and healthcare providers addressed concerns about blood sampling by explaining the safety measures. The study's inclusion criteria included neonates of both sexes who had normal serum calcium levels between 8.5 and 12 mg/dl before the start of phototherapy, as well as those who presented with indirect hyperbilirubinemia (bilirubin levels >5 mg/dl) and needed phototherapy for at least one day. The exclusion criteria included neonates with indirect hyperbilirubinemia necessitating exchange transfusion as indicated by the phototherapy chart, as well as those with conditions such as ABO/RH incompatibility, Glucose-6-Phosphate Dehydrogenase deficiency, intrauterine growth restriction (IUGR), obvious congenital malformations, or a birth weight of less than 2.5 kg. Additionally, neonates suffering from asphyxia neonatorum, cardiopulmonary distress, sepsis, or those born to diabetic mothers were excluded. Any newborn who developed complications during the study, such as septicemia, or whose mother had a history of taking anticonvulsants during pregnancy or had other high-risk factors, was also excluded from the study. The study's operational definitions were as follows. An increase of 5 mg/dl of indirect bilirubin in the serum was considered indirect hyperbilirubinemia [13]. Less than 8.5 mg/dl of total calcium in the serum was deemed hypocalcaemia [14]. Term neonates were identified as those with a gestational age ranging from 37 to 42 completed weeks, determined from the 1st day of the last day of menstrual cycle, and who were aged between 0 to 28 days of life. Phototherapy was described as the application of blue light with a wavelength of 420-470 nm, administered at a distance of 15-20 cm, specifically used for the treatment of indirect hyperbilirubinemia [13]. For every newborn, a thorough history and pertinent examination were conducted. Gestational age was estimated, using the LMP, which was assessed from history. Three milliliters of

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venous blood were drawn before to commencement of phototherapy and following forty-eight hours of uninterrupted phototherapy. The sample was sent to a laboratory to measure the levels of calcium and indirect bilirubin in the serum. Serum bilirubin was measured to determine phototherapy eligibility, while serum calcium was assessed to establish a baseline due to the potential risk of hypocalcemia. The data of patients like age, gender, gestational age, incidence of hypocalcemia, serum calcium level and serum bilirubin levels were recorded on a predesigned Performa. Hypocalcemia was recorded as per operational definition. All the data were analyzed in SPSS version 20.0. Categorical variable such as gender, incidence of hypocalcemia was described as frequency and percentage. Continuous variables such as age, serum calcium level, serum bilirubin levels, gestational age were presented by a mean and standard deviation. To control effect modifiers, the data were stratified by age, gender, and gestational age. Following stratification, a Chi square test had been applied. The comparison of pre and post serum Bilirubin and calcium levels were assessed by paired sample t test. A significant p-value was defined as less than 0.05.

RESULTS

In order to ascertain the occurrence of hypocalcemia in term newborns receiving phototherapy for indirect hyperbilirubinemia, 134 individuals who met the conditions for inclusion and exclusion were enrolled in the study. The patients' ages were distributed as follows: of the 134 patients, 77 (57.5%) were in the 0–15-day age group, and 57 (42.5%) were in the 16–28-day age group. The mean age was found to be 14.32 ± 5.25 days. After the patients' genders were distributed, it was found that 68 (50.7%) of them were males and 66 (49.3%) of them were females. It was found that percentage of hypocalcemia was 31 (23.1%) in term neonates receiving phototherapy for indirect hyperbilirubinemia, (Table 1).

Table 1: Baseline Characteristics of Patients

Variables	n (%)
Age	
0–15 Days	77 (57.5%)
16–28 Days	57 (42.5%)
Gender	
Male	68 (50.7%)
Female	66 (49.3%)
Distribution of Hypocalcemia	
Yes	31 (23.1)
No	103 (76.9)

Results present the comparison of serum bilirubin and calcium levels before and after phototherapy.The mean serum bilirubin level significantly decreased from 14.0 ± 2.4 mg/dL pre-phototherapy to 8.49 ± 1.81 mg/dL post-phototherapy ($p<0.001$), confirming the effectiveness of phototherapy in reducing bilirubin levels. Similarly, the mean serum calcium level showed a significant decline from 7.96 ± 0.81 mg/dL before phototherapy to 7.51 ± 1.03 mg/dL after phototherapy ($p<0.001$), (Table 2).

Table 2: Pre and Post-Comparison of Serum Bilirubin and Calcium Levels Among Patients

Variables	Pre-Comparison	Post-Comparison	p-Value
Serum Bilirubin Levels	14.0 ± 2.4	8.49 ± 1.81	0.000
Serum Calcium Levels	7.96 ± 0.81	7.51 ± 1.03	0.000

Among neonates aged 0–15 days, 24 (31.2%) developed hypocalcemia, compared to only 7 (12.3%) in the 16–28-day age group. The majority of neonates in both age groups remained normo-calcemic, with 53 (68.8%) in the 0–15-day group and 50 (87.7%) in the 16–28-day group. Overall, hypocalcemia was observed in 31 (23.1%) of the total study population, indicating a higher vulnerability in younger neonates. The occurrence of hypocalcemia in term neonates receiving phototherapy for indirect hyperbilirubinemia was significantly associated with age group ($p=0.010$) (Table 3).

Table 3: Stratification for Hypocalcemia Concerning Age

Age Group	Hypocalcemia		Total	p-Value
	Yes	No		
0-15 Days	24 (31.2%)	53 (68.8%)	77	0.010
16-28 Days	7 (12.3%)	50 (87.7%)	57	
Total	31 (23.1%)	103 (76.9%)	134	

Results present the stratification of hypocalcemia concerning gestational age among term neonates receiving phototherapy for indirect hyperbilirubinemia. Hypocalcemia was observed in 19 (21.1%) of neonates born at 37–39 weeks of gestation and in 12 (27.3%) of those born at 40–42 weeks. Although the prevalence of hypocalcemia appeared slightly higher in the 40–42-week group, the difference was not statistically significant ($p=0.427$). Overall, hypocalcemia was present in 31 (23.1%) of the total study population, indicating no significant association between gestational age and the occurrence of hypocalcemia in this cohort (Table 4).

Table 4: Stratification for Hypocalcemia Concerning Gestational Age

Gestational Age Group	Hypocalcemia		Total	p-Value
	Yes	No		
37-39 Weeks	19 (21.1%)	71 (78.9%)	90 (100.0%)	0.427
40-42 Weeks	12 (27.3%)	32 (72.7%)	44 (100.0%)	
Total	31 (23.1%)	103 (76.9%)	134 (100.0%)	

The stratification of hypocalcemia by gender among term neonates receiving phototherapy for indirect hyperbilirubinemia revealed that 12 (17.6%) of male and 19 (28.8%) of female developed hypocalcemia. While the prevalence was higher in female compared to male, this

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difference was not statistically significant (p=0.126). Overall, hypocalcemia was observed in 31 (23.1%) of the total study population, suggesting that gender does not have a significant impact on the occurrence of hypocalcemia in this cohort (Table 5).

Table 5: Stratification for Hypocalcemia Concerning Gender

Gender	Hypocalcemia		Total	p-Value
	Yes	No		
Male	12 (17.6%)	56 (82.4%)	56 (82.4%)	0.126
Female	19 (28.8%)	47 (71.2%)	47 (71.2%)	
Total	31 (23.1%)	103 (76.9%)	103 (76.9%)	

DISCUSSION

During the first week of life, the most common aberrant physical finding is neonatal hyperbilirubinemia (NH). Clinical jaundice affects roughly 60 percent term newborns and eighty percent premature neonates [15]. If left untreated, severe hyperbilirubinemia can produce bilirubin-induced brain damage [16]. Phototherapy, exchange transfusions, and pharmaceutical treatments can all be used to treat hyperbilirubinemia. In the prevention and treatment of hyperbilirubinemia, phototherapy is very important. Few studies demonstrate how phototherapy adversely affects serum electrolytes, in contrast to other side effects. One of the known side effects is hypocalcemia [17]. Transcranial illumination inhibits melatonin release from the pineal gland during phototherapy. Melatonin counteracts cortisol's hypocalcemia effects. As a result, low melatonin levels in the blood allow cortisol to act unchecked, resulting in hypocalcemia [18]. Additionally, phototherapy has been linked to an increase in urine calcium excretion. Even though neonatal hypocalcemia can be lethal, laboratory hypocalcemia is typically mild and asymptomatic. Furthermore, it changes with gestational age (GA) and perinatal illness [19]. Phototherapy, commonly used for neonatal hyperbilirubinemia, can affect blood calcium levels. Studies by Reddy *et al.*, and Elfiky *et al.*, both reported significant reductions in calcium levels post-phototherapy [20, 21]. Lidia *et al.* observed a statistically substantial drop in blood calcium in full-term newborns, but no cases of symptomatic hypocalcemia were noted [22].In contrast, another study highlighted significant electrolyte imbalances, including drops in calcium levels, with potential clinical implications [23]. Pereira *et al.*, found a decrease in total serum calcium levels in many neonates, but the prevalence of hypocalcemia was lower compared to earlier studies, suggesting it is not a common outcome in their population [24]. Due to discrepancies in the findings of earlier studies, this study aimed to ascertain the incidence of hypocalcemia in newborns born full term with indirect hyperbilirubinemia post-phototherapy in current selected local neonatal community. Worldwide endeavors acknowledge hypocalcemia as a plausible side effect of phototherapy, albeit with varying outcomes.These variations stem from the length of phototherapy exposure, the degree of hyperbilirubinemia at the onset of phototherapy and the term or preterm status of the newborns. Each of these elements influences the degree of hypocalcemia brought on by phototherapy. Current study demonstrates how phototherapy impacts calcium homeostasis in a term newborn being treated for indirect hyperbilirubinemia. To clarify the matter and determine if calcium supplements should be administered to neonates undergoing phototherapy for neonatal jaundice, more research is required.

CONCLUSIONS

It was concluded that the percentage of hypocalcemia was 31 (23.1%) in term neonates receiving phototherapy for indirect hyperbilirubinemia. Phototherapy effectively reduces serum bilirubin levels but is associated with a significant decline in serum calcium, suggesting a potential risk of hypocalcemia in neonates. Thus, to avoid complications, blood calcium levels and serum bilirubin levels should be routinely checked in infants receiving phototherapy.

Authors Contribution

Conceptualization: GP
Methodology: GP, MAA, ZA, MIM, MA, WA
Formal analysis: MAA, WA
Writing review and editing: ZA, MIM, MA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Matikainen N, Pekkarinen T, Ryhänen EM, Schalin-Jäntti C. Physiology of Calcium Homeostasis: An Overview. Endocrinology and Metabolism Clinics. 2021 Dec; 50(4): 575-90. doi: 10.1016/j.ecl.2021.07.005.
[2] Eddala K and Bushra RK. Effect of Phototherapy on Serum Calcium Levels in Physiological Neonatal Jaundice. Journal of Contemporary Clinical Practice. 2025 Jan; 11: 164-9.
[3] Dabas A, Dabas V, Dabla PK, Marwaha RK, Yadav S, Bharadwaj M *et al.* Daily v. Weekly Oral Vitamin D3 Therapy for Nutritional Rickets in Indian Children: A Randomized Controlled Open-Label Trial. British Journal of Nutrition.2023May;129(9):1473-80.doi: 10.1017/S0007114522001477.

DOI: https://doi.org/10.54393/pjhs.v6i3.2824

[4] Saeed F, Ashraf I, Hayat S, Rukh M. Incidence of Hypocalcaemia in Term Jaundiced Infants after Phototherapy. Pakistan Journal of Medical and Health Sciences.2022Nov;16(09):718-.doi:10.53350/pjmhs 22169718.
[5] Abdel-Raouf Khattab R, Khalil Nawar F, SHafik Nada A, Mohamed Ahmad H. Evaluation of Blood Levels of Copper, Zinc, Magnesium and Calcium in Full Term Neonatal Unconjugated Hyperbilirubinemia.Al-Azhar Journal of Pediatrics. 2020 Jan; 23(1): 713-31.
[6] Beser E, Cakir U, Karacaglar NB, Kucukoglu Keser M, Ceran B, Tugcu AU *et al.* Phototherapy-Induced Hypocalcemia and Hypoparathyroidism in Icteric Term Newborns.Journal of Pediatric Endocrinology and Metabolism.2023Jan;36(1):43-52.doi:10.1515/jpem-2022-0284.
[7] Alizadeh-Taheri P, Sajjadian N, Eivazzadeh B. Prevalence of Phototherapy-Induced. Hypocalcemia in Term Neonate. Iranian Journal of Pediatrics.2013 Dec;23(6): 710.
[8] Shrestha S, Dhungana S, Shrestha SK, Shrestha GS, Kakshapati P. Hypocalcemia in Jaundiced Neonates Receiving Phototherapy.2021;19(2):284-7.doi:10.3331 4/jnhrc.v19i2.3423.
[9] Gupta L, Mandot S, Goyal D. An Observational Study: Correlation of Serum Calcium Levels in Relation to Phototherapy in Term Newborns. Indian Journal of Child Health.2020Feb;7(2):60-2.doi:10.32677/IJCH .2020.v07.i02.005.
[10] Rani MU. Comparison of Electrolyte Changes in Term Neonates Before and After Phototherapy. International Journal of Physiology.2019;7(2):179-84. doi:10.5958/2320-608X.2019.00069.6.
[11] Sohail H, Halim A, Aaraj S, Mushtaq N. Effect of Phototherapy on Serum Calcium Level in Neonatal Jaundice.Journal of Islamic International Medical College.2025Mar;20(1):49-53.
[12] Hussein SA, Flayyih FY, Adil SM. Effect of Phototherapy on Serum Calcium in Neonatal Jaundice in Baghdad: Single Center Experience. Iraqi Postgraduate Medical Journal.2023;22(3).doi:10.52573/ipmj.2023.141440 .1084.
[13] Kliegman RM. Geme J St.Nelson Textbook of Pediatrics. 21st Edition. 2019.
[14] Kleinman K, McDaniel L, Molloy M. The Harriet Lane Handbook E-Book: The Harriet Lane Handbook E-Book. Elsevier Health Sciences. 2020 Apr.
[15] Kadavakollu N and Gopal KV.To Evaluate the Effect of Phototherapy On Serum Calcium Levels in Newborns Requiring Phototherapy According to AAP Guidelines. International Journal of Pediatrics and Neonatology. 2023;5(1):15-18.doi:10.33545/26648350.2023.v5.i1a.31
[16] Par EJ, Hughes CA, DeRico P.Neonatal Hyperbilirubinemia:Evaluation and Treatment. American Family Physician.2023 May;107(5):525-34.
[17] Panneerselvam K, Mani S, Vasudevan N, Krishnamoorthy N, RK. P, Sundar S. Effect of Light-Emitting Diode Phototherapy On Serum Calcium Levels in Neonates with Jaundice.Cureus.2022Apr;14 (4).doi:10.7759/cureus.23938.
[18] Bibi A, Alam W, Asghar I, Ali R. Effect of Head Covering On Hypocalcaemia Resulting from Phototherapy in Full-Term Neonates with Hyperbilirubinemia.Pakistan Armed Forces Medical Journal. 2020 Aug; 70(4).
[19] Javaid S, Sultana S, Omer MT, Murtaza A, Haq MA. Effect of Phototherapy On Serum Calcium Levels in Neonates in A Tertiary Care Hospital. Annals of Punjab Medical College. 2021 Sep; 15(3): 185-7.
[20] Reddy AT, Bai KV, Shankar SU. Electrolyte Changes Following Phototherapy in Neonatal Hyperbilirubinemia.International Journal of Science and Research.2015;4(7):752-58.
[21] Elfiky O, Abd-elhaie O, Abdellatif W, Mohamed A. Electrolyte Changes Following Phototherapy in Neonatal Unconjugated Hyperbilirubinemia.Benha Journal of Applied Sciences.2023Sep;8(9):91-5.doi: 10.21608/bjas.2023.237263.1252.
[22] Lidia C, Kardana IM, Nilawati GA, Subanada IB, Adnyana IG, Mayangsari AS. Phototherapy and Serum Calcium Levels in Full-Term Neonates with Hyperbilirubinemia. Paediatrica Indonesiana.2021Jan;61(1):8-11.doi:10.14 238/pi61.1.2021.8-11.
[23] Purohit A and Verma SK. Electrolyte Changes in the Neonates Receiving Phototherapy.International Journal of Contemporary Pediatrics.2020Aug;7(8): 1753–1757. doi: 10.18203/2349-3291.ijcp20203170.
[24] Pereira RA, Avasthi B, Saste S, Bavdekar SB. Prevalence of Hypocalcemia in Term Newborns Requiring Phototherapy. International Journal of Contemporary Pediatrics.2023Jun;10(6):793.doi: 10.18203/2349-3291.ijcp20231480.