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Original Research Article

Phototherapy-Induced Hypocalcemia in Icteric Term Neonates

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Abstract: *Neonatal jaundice requiring phototherapy is a common condition, but phototherapy has been associated with potential side effects, including hypocalcemia. Understanding the frequency and risk factors of phototherapy-induced hypocalcemia can aid in its prevention and management.* ***Objective:*** *This study aimed to determine the frequency of phototherapy-induced hypocalcemia in icteric term neonates and assess its association with demographic and clinical factors.* ***Methods:*** *A prospective cross-sectional study was conducted in the emergency department of a tertiary care hospital. After obtaining ethical board approval and informed parental consent, 150 term neonates with hyperbilirubinemia requiring phototherapy were enrolled from 26 July 2024 to 26th January 2025. Demographic data, including age, gender, birth weight, gestational age, and bilirubin levels at presentation, were recorded. Blood samples were collected before and after 48 hours of phototherapy to assess serum calcium levels. Hypocalcemia was defined as a serum calcium level <8.4 mg/dL. Data were analysed using SPSS version 25, with statistical significance set at $p \leq 0.05$.* ***Results:*** *The mean age of neonates was 2.41 ± 0.80 days, with a birth weight of 3.08 ± 0.80 kg and a gestational age of 37.77 ± 1.25 weeks. The mean bilirubin level at presentation was 22.62 ± 1.34 mg/dL, and the average duration of phototherapy was 31.97 ± 9.26 hours. Of the enrolled neonates, 54.7% were male, and 45.3% were female. Phototherapy-induced hypocalcemia occurred in 26.7% of cases. Stratification by age showed hypocalcemia rates of 17.5% in 1-day-old, 12.5% in 2-day-old, and 70% in 3-day-old neonates, though the differences were not statistically significant. Hypocalcemia was more frequent in neonates with bilirubin levels >21 mg/dL and those requiring prolonged phototherapy, though these findings also lacked statistical significance.* ***Conclusion:*** *Phototherapy-induced hypocalcemia is a notable concern in neonates undergoing treatment for hyperbilirubinemia. While no statistically significant associations were observed with age, gender, or gestational age, neonates with higher bilirubin levels and prolonged phototherapy appear to be at greater risk. Close monitoring of calcium levels in these neonates is recommended to prevent complications and improve patient outcomes.*

Keywords: Phototherapy-induced hypocalcemia, bilirubin, neonates

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Introduction

Neonatal jaundice is a common condition in newborns, particularly among term infants, and is often treated with phototherapy to reduce elevated bilirubin levels.(1) Elevated bilirubin levels can be harmful to the developing central nervous system and may lead to neurological damage in newborns.(2) Around 60% of full-term newborns exhibit visible jaundice during the first week of life, which is typically harmless and does not require treatment.(3) However, about 5-10% of these infants develop clinically significant jaundice, necessitating the use of phototherapy.(4) Phototherapy has proven to be an effective and safe method for managing hyperbilirubinemia, yet it is not without its potential risks.(5) One such risk is phototherapy-induced hypocalcemia, a condition characterised by abnormally low calcium levels in the blood.(6) The prevalence of hypocalcemia in neonates undergoing phototherapy was reported to be 8.7% in full-term newborns.(7) Another study showed only a slight variation in plasma calcium levels before and after phototherapy ($p<0.05$).(8) The mechanism behind phototherapy-induced hypocalcemia is not fully understood, but it has been suggested that exposure to light may interfere with calcium regulation by inhibiting the pineal gland, leading to decreased melatonin secretion. This, in turn, could disrupt the effect of cortisol on bone calcium metabolism. While studies have shown varying rates of hypocalcemia in neonates undergoing phototherapy, the incidence and its associated factors remain unclear in many populations.

This study aims to explore the prevalence of phototherapy-induced hypocalcemia in term neonates with jaundice and to examine factors that may contribute to its development. By understanding the relationship between phototherapy and calcium levels in term neonates, healthcare providers can implement more effective monitoring and management strategies to minimise the risk of hypocalcemia and its associated complications.

Objective: To determine the frequency of phototherapy-induced hypocalcemia in icteric term
Neonates.

Methodology

Descriptive study Department of Pediatrics, Holy Family Hospital, Rawalpindi. The duration of the study was 6 months, from 26th July 2024 to 26th January 2025. Using the WHO sample size calculator, a sample size of 150 cases was determined based on a 95% confidence level, a population proportion of 20.67% (9), and an absolute precision of 6.5%. Non-probability Consecutive sampling was used for the recruitment of patients. Children of age 1-72 hours of age. Presenting with hyperbilirubinemia. Both genders. Patients undergoing phototherapy. Neonates with birth asphyxia, sepsis, respiratory distress, congenital malformation, and IDM. Neonates in need of exchange transfusion for hyperbilirubinemia. After obtaining approval from the ethical board, 150 neonates were enrolled in the emergency department. Informed consent was obtained from their parents. Demographic details, including name, age, gender, birth weight, gestational age at birth, and bilirubin levels at presentation, were recorded. A blood sample was collected and sent to the laboratory to assess calcium levels. The neonates then underwent phototherapy, and the duration of phototherapy was documented. After 48 hours of continuous phototherapy, another blood sample was collected

and sent to the laboratory for calcium level assessment. Reports were analysed, and phototherapy-induced hypocalcemia was labeled if calcium levels were found to be below 8.4 mg/dL (as per the operational definition). All data were recorded in a pre-designed proforma.

The data analysis was conducted using SPSS version 25. The Shapiro-Wilk test was applied to assess the normality of the data. Quantitative variables such as age, birth weight, duration of gestation, duration of phototherapy, bilirubin level, and calcium level were presented as mean and standard deviation (SD). Qualitative variables, including gender and phototherapy-induced hypocalcemia, were presented as frequency and percentage. Data were stratified by age, gender, birth weight, duration of gestation, bilirubin level at presentation, and duration of phototherapy. Post-stratification, the Chi-square test was used to compare phototherapy-induced hypocalcemia across the stratified groups. A p-value ≤ 0.05 was considered statistically significant.

Results

The mean values of the study variables were as follows: the neonates had an average age of 2.41 ± 0.80 days, a mean birth weight of 3.08 ± 0.80 kg, and a mean gestational age of 38.39±1.33 weeks. The mean bilirubin level was 22.62 ± 1.34 mg/dL, and the mean duration of phototherapy was 31.97 ± 9.26 hours. Among the study participants, 54.7% (82) were male, and 45.3% (68) were female. Phototherapy-induced hypocalcemia was observed in 26.7% (40) of the neonates, while 73.3% (110) did not develop hypocalcemia. The stratification of patients based on phototherapy-induced hypocalcemia about various variables is summarised as follows: Age-wise, hypocalcemia was observed in 17.5% of neonates aged 1 day, 12.5% of those aged 2 days, and 70% of those aged 3 days, with a p-value of 0.37. Gender-wise, hypocalcemia was present in 50% of both males and females, with a p-value of 0.48. Regarding gestational age, 37(92.5%) of neonates with gestational age 37-40 weeks and 3(7.5%) with gestational age 40-42 weeks experienced hypocalcemia (p-value: 0.33). Based on bilirubin levels, 15% of neonates with bilirubin levels of 19–21 mg/dL and 85% with levels >21 mg/dL had hypocalcemia, with a p-value of 0.74. In terms of phototherapy duration, 20% of neonates exposed for 14–30 hours, 77.5% for 31–40 hours, and 2.5% for >40 hours developed hypocalcemia, with a p-value of 0.07.

Table 1: Descriptive Statistics for Quantitative Variables of all enrolled patients (*n=150)*

Variables	Mean±SD
Age	2.41±0.80
Birth weight (kg)	3.080±.80
Duration of gestation (week)	38.39±1.33
Bilirubin mg/dl	22.62±1.34
Duration of phototherapy (Hours)	31.97± 9.26

Table 2: Characteristics of all enrolled patients (*n=150)*

Variables	Frequency (%)
Gender	
Male	82(54.7%)
Female	68(45.3%)
Phototherapy induces hypocalcemia	
Yes	40(26.7%)
No	110(73.3%)

Table 3: Stratification of patients based on phototherapy-induced Hypocalcemia concerning different variables

Age Groups	Phototherapy induces Hypocalcemia		p-value
	YES	NO	
1 day	7(17.5%)	23(20.9%)	0.37
2 days	5(12.5%)	23(20.9%)	
3 days	28(70.0%)	64(58.2%)	
Gender			
Male	20(50.0%)	62(56.4%)	0.48
Female	20(50.0%)	48(43.6%)	
Duration of gestation (week)			
37-40	37(92.5%)	96(87.3%)	0.37
40-42	3(7.5%)	14(12.7%)	
Bilirubin			
19-21 mg/dl	6(15.0%)	19(17.3%)	0.74
>21 mg/dl	34(85.0%)	91(82.7%)	
Duration of phototherapy			
14-30 hours	8(20.0%)	32(29.1%)	0.07
31-40 hours	31(77.5%)	65(59.1%)	
>40 hours	1(2.5%)	13(11.8%)	

Discussion

Hypocalcemia, characterised by low serum calcium levels in the body, is a common biochemical abnormality. The present study aimed to determine the frequency of phototherapy-induced hypocalcemia in icteric term neonates, considering treatment-related factors. Phototherapy, a standard treatment for neonatal jaundice, has been associated with several complications, including hypocalcemia, which can exacerbate the neonate's condition if not identified and managed promptly. Phototherapy is an effective and safe method for reducing jaundice in newborns. Romagnoli et al. (10) were the first to propose a link between phototherapy and the development of hypocalcemia in neonates. In the present study, it was found that 26.7% (40) of the neonates had phototherapy-induced hypocalcemia. Our study was supported by a Pakistani study (11), which found that the frequency of phototherapy-induced hypocalcemia in icteric term neonates was 22.76%. Another Pakistani study (9) also stated that the frequency of phototherapy-induced hypocalcemia was 20.67% in icteric term neonates. An Indian study conducted in 2012 reported that 66.6% of term neonates developed hypocalcemia, while a 2013 Iranian study found a 10% prevalence of

phototherapy-induced hypocalcemia. (12, 13) The varying results observed in different populations emphasise the importance of conducting a study in our population. Our findings contrast with those of the Indian study, which reported a significantly higher incidence of hypocalcemia. Ehsanipoor et al.. (14) and Karamifar et al.. (15) reported the incidence of hypocalcemia as 15% and 8.7%, respectively. Jain BK et al.., after 48 hours of continuous phototherapy, observed hypocalcemia in 30% of term neonates. The regulation of calcium homeostasis during the newborn period is of significant interest. At birth, the plasma calcium level in cord blood is higher than that in maternal blood. In the early days of life, plasma calcium levels gradually decrease in normal infants, so by the second or third day, the level is lower than that found in older infants. In full-term infants, plasma calcium levels typically return to normal by the 10th day of life. The mechanism behind phototherapy-induced hypocalcemia has been linked to the inhibition of the pineal gland through transcranial light exposure, which reduces melatonin secretion and subsequently interferes with cortisol's effect on bone calcium. (16) A study by Bahbah et al., conducted in Egypt, examined 50 term neonates who received phototherapy for jaundice, with 25 neonates serving as controls who had physiological jaundice and did not require phototherapy. After 48 hours of phototherapy, hypocalcemia was observed in 26% of the treated neonates.

This study highlights the importance of closely monitoring calcium levels in neonates undergoing phototherapy, particularly in those with higher bilirubin levels and those requiring extended durations of phototherapy. Early detection of hypocalcemia and prompt intervention, such as calcium supplementation, may help prevent complications such as seizures or neurological damage. Additionally, further research is needed to explore the exact mechanisms by which phototherapy induces hypocalcemia and to identify predictive factors that could help healthcare providers better anticipate and manage this complication.

Conclusion

It was concluded that phototherapy-induced hypocalcemia remains a significant concern in the management of neonatal jaundice. The findings from this study underscore the need for vigilant monitoring and timely intervention to reduce the risk of complications in icteric-term neonates, particularly those with prolonged phototherapy duration and elevated bilirubin levels.

Declarations

Data Availability Statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-FHISB-0341FF-24)

Consent for publication
Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

N (Postgraduate resident**),**
Manuscript drafting, Study Design,
IL (Associate Professor**)**
Review of Literature, Data entry, Data analysis, and drafting article.
H (Postgraduate resident**)**
Conception of Study, Development of Research Methodology Design,
T (Postgraduate resident**)**
Study Design, manuscript review, critical input.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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