

"Study of Serum Calcium Levels in Neonates Undergoing Phototherapy for Hyperbilirubinemia in a NICU at a Tertiary Care Centre Serving a Suburban Population"

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Abstract:

Neonatal jaundice is a common clinical condition that affects a significant proportion of newborns, particularly during the first week of life. It presents as a yellowish discoloration of the skin and sclera due to an elevated level of bilirubin in the blood. The primary cause of neonatal jaundice is the immaturity of the liver, which leads to inefficient bilirubin conjugation and excretion. While most cases of neonatal jaundice are benign and resolve spontaneously, in some instances, elevated bilirubin levels may indicate an underlying pathological condition such as hemolysis, metabolic disorders, infection, or genetic abnormalities affecting bilirubin metabolism. If untreated, excessively high bilirubin levels can result in bilirubin encephalopathy, wherein unconjugated bilirubin crosses the blood-brain barrier and deposits in brain tissues, particularly the basal ganglia. This condition can progress to kernicterus, a severe and irreversible neurological disorder that can lead to long-term cognitive and motor impairments. Phototherapy is the most commonly used and effective treatment for neonatal hyperbilirubinemia. It works by converting unconjugated bilirubin into water-soluble photoisomers that can be easily excreted through urine and bile without requiring hepatic conjugation. Although phototherapy is generally considered safe, studies have reported that it may be associated with certain complications, including dehydration, hyperthermia, increased insensible water loss, loose stools, and electrolyte disturbances such as hypocalcemia. Hypocalcemia, or low serum calcium levels, is a recognized yet often overlooked side effect of phototherapy in neonates. The mechanism behind phototherapy-induced hypocalcemia is not entirely understood, but it is hypothesized that phototherapy suppresses melatonin secretion by the pineal gland, which in turn reduces calcium absorption by decreasing parathyroid hormone activity. Additionally, phototherapy-induced skin vasodilation may enhance calcium deposition in bones, further contributing to transient hypocalcemia. In neonates, calcium homeostasis is essential for maintaining neuromuscular excitability, cardiac function, and cellular metabolism. A decrease in serum calcium levels can manifest clinically as jitteriness, irritability, poor feeding, apnea, lethargy, and in severe cases, seizures. The present study aimed to assess the impact of phototherapy

on serum calcium levels in neonates with hyperbilirubinemia and evaluate the relationship between pre- and post-phototherapy calcium levels. This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics at Rama Medical College, Hospital and Research Center, Kanpur, Uttar Pradesh. The study population consisted of neonates diagnosed with hyperbilirubinemia requiring phototherapy. The participants were selected from various regions of Kanpur and nearby districts, ensuring a diverse representation of the local population. Inclusion criteria included neonates with clinically significant jaundice requiring phototherapy, while those with congenital anomalies, metabolic disorders, sepsis, or pre-existing hypocalcemia were excluded. Relevant laboratory investigations, including total serum bilirubin and serum calcium levels, were performed before initiating phototherapy and repeated 48 hours after treatment. Statistical analysis was conducted using SPSS24 software to compare pre- and post-phototherapy calcium levels and determine their significance. The results of the study demonstrated a significant reduction in serum calcium levels following phototherapy, with a notable proportion of neonates developing hypocalcemia. The findings suggest that hypocalcemia is a frequent yet often underdiagnosed complication of phototherapy, particularly in preterm and low birth weight neonates, who are already vulnerable to metabolic disturbances due to their immature organ systems. The study also revealed that neonates who developed hypocalcemia post-phototherapy exhibited mild to moderate clinical symptoms, such as jitteriness and irritability, though severe complications like seizures were rare. The study findings underscore the need for routine monitoring of serum calcium levels in neonates undergoing phototherapy, particularly in those with known risk factors such as prematurity, low birth weight, or maternal conditions affecting calcium metabolism. Given the potential consequences of hypocalcemia on neonatal health, prophylactic calcium supplementation could be considered for high-risk neonates to prevent symptomatic hypocalcemia and its associated complications. Additionally, further research with larger sample sizes and longer follow-up periods is warranted to establish definitive guidelines for calcium monitoring and supplementation in neonates receiving phototherapy. This study highlights the importance of a comprehensive approach to neonatal jaundice management that goes beyond bilirubin monitoring and incorporates the assessment of electrolyte balance to ensure holistic neonatal care. Integrating routine serum calcium measurement in neonates undergoing phototherapy could help in early identification and timely management of hypocalcemia, thereby reducing morbidity associated with this common but preventable complication. Future research should focus on elucidating the exact pathophysiological mechanisms underlying phototherapy-induced hypocalcemia and exploring potential preventive strategies, including the role of melatonin and calcium supplementation in mitigating this condition.

INTRODUCTION

Neonatal jaundice is one of the most frequently observed conditions in newborns, particularly during the first week of life. It presents as a yellowish discoloration of the skin and sclerae due to elevated bilirubin levels in the blood. Bilirubin is a byproduct of the breakdown of red blood cells, and while the liver is responsible for its metabolism and excretion, the immature liver of a newborn often struggles to efficiently process bilirubin, leading to its accumulation. In most cases, neonatal jaundice is a benign and self-limiting condition, resolving as the liver matures. However, in some cases, it may indicate an underlying pathological condition such as hemolytic disease, metabolic disorders, or infections, requiring further investigation and management. If left untreated, severe hyperbilirubinemia can lead to bilirubin encephalopathy, a condition where unconjugated bilirubin crosses the blood-brain barrier and

deposits in the basal ganglia, causing neurotoxicity. This can progress to kernicterus, a permanent and debilitating condition associated with cerebral palsy, hearing impairment, and developmental delays. Since kernicterus is largely preventable with early intervention, monitoring and managing neonatal jaundice effectively is crucial to ensuring favorable outcomes in affected neonates. Phototherapy is the primary and most effective treatment for neonatal hyperbilirubinemia. It works by converting unconjugated bilirubin into water-soluble forms that can be excreted without hepatic conjugation. While phototherapy is considered a safe and non-invasive intervention, studies have reported potential complications, including dehydration, increased insensible water loss, retinal damage (if eyes are not properly shielded), and electrolyte imbalances such as hypocalcemia. Hypocalcemia, or low serum calcium levels, is an important yet often overlooked complication of phototherapy. The exact mechanism behind phototherapy-induced hypocalcemia remains unclear, but it is believed that phototherapy suppresses melatonin secretion from the pineal gland, thereby reducing calcium absorption by inhibiting parathyroid hormone activity. Additionally, skin vasodilation caused by phototherapy may enhance calcium deposition in bones, further lowering serum calcium levels. Calcium plays a vital role in several physiological processes, including neuromuscular function, cellular metabolism, and cardiac stability. In neonates, hypocalcemia can present with symptoms such as jitteriness, irritability, apnea, poor feeding, lethargy, and in severe cases, seizures. Preterm and low birth weight neonates are particularly susceptible to metabolic disturbances, making them more vulnerable to hypocalcemia. Given these potential risks, it is essential to monitor serum calcium levels in neonates undergoing phototherapy and assess whether proactive interventions, such as calcium supplementation, are necessary to prevent complications. This study aims to evaluate the effect of phototherapy on serum calcium levels in neonates with hyperbilirubinemia and to determine whether significant hypocalcemia occurs following treatment. By analyzing pre- and post-phototherapy calcium levels, this research will contribute to a better understanding of the metabolic effects of phototherapy and help refine neonatal care protocols to ensure the safe and effective management of neonatal jaundice.

Neonatal jaundice is a prevalent condition seen in newborns, particularly during the first week of life. It manifests as a yellowish discoloration of the skin and the sclerae, resulting from an elevated level of bilirubin in the blood[1]. Bilirubin is a byproduct of the normal breakdown of red blood cells, and while it is typically processed and eliminated by the liver, the immature liver of a newborn often lacks the full capacity to efficiently manage this process[2]. While neonatal jaundice is usually benign, it can sometimes indicate more serious underlying conditions[3]. Bilirubin encephalopathy occurs when unconjugated bilirubin crosses the blood-brain barrier and deposits in the brain tissues, particularly in the basal ganglia[4]. Kernicterus, the chronic and permanent outcome of bilirubin encephalopathy, is a preventable condition if hyperbilirubinemia is recognized and treated promptly[5].

Need for the study

To determine whether neonates receiving phototherapy are at risk of developing hypocalcemia and whether intervention is required to prevent potential complications.

Aims and Objectives of the study

- To study the clinical spectrum of Hyperbilirubinemia in Neonates
- To determine the value of serum calcium in neonates with hyperbilirubinemia on phototherapy and its relation between serum calcium levels 48 hrs prior and after phototherapy in neonates with hyperbilirubinemia.

Materials and Methods

The study was conducted among the neonates admitted in the paediatric NICU, department of Paediatrics, coming from different parts of Kanpur and adjacent districts of Uttar Pradesh. Relevant laboratory investigations were done in all patients. Total 96 newly diagnosed cases of pneumonia were included in the study. SPSS24 was used for statistical analysis of results

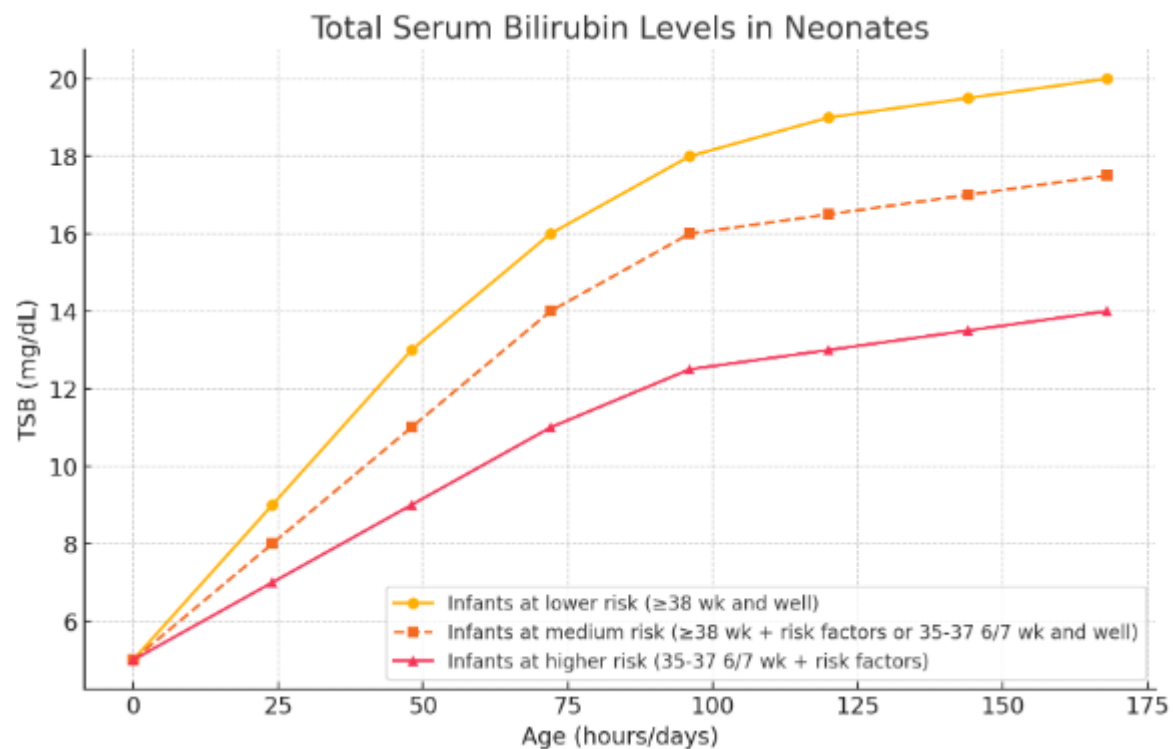


Fig. 1: AAP nomogram for phototherapy in neonats of 35 or more weeks' gestation.

Gestation (wk)	Phototherapy (mg/dL)	Exchange Transfusion (mg/dL)
	12h	24h
23	3.2	4
24	3.2	4.4
25	3.5	4.7
26	3.5	4.7
27	3.6	5
28	3.8	5
29	3.8	5.3
30	4	5.3
31	4.1	5.6
32	4.1	5.9
33	4.2	6.1

34	4.2	6.1
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Selection of the patient for study

The neonate presenting with H/O hyperbilirubinemia in Paediatric NICU department will be screened for selection for our study. Detailed history taking and clinical examination will be done as per prescribed proforma or protocol. Initial selection will be done as per the following criteria —

All neonates falling under the age specific nomograms provided by American Academy of Pediatrics in term neonates and pre-term babies falling under NICE guidelines, admitted in NICU, Department of Pediatrics, RAMA MEDICAL COLLEGE, KANPUR.

Phototherapy and exchange cut-offs of total serum bilirubin (mg/dL) for babies 34 weeks gestation or lower (NICE guidelines).

Children presenting with generalised edema but not fulfilling the above criteria or showing some additional symptoms/ signs for which these cases were kept outside our study i.e. criteria for exclusion are –

1. Any neonate who had or developed a complication during the course of study i.e. birth asphyxia, respiratory distress, septicemia, infants of diabetic mother or any other high risk factors will be excluded from the study.
2. Neonates whose parents did not give consent for them to be included in the study.
3. Age > 28 days of life will be excluded .
4. All neonates (term and per-term) not fulfilling the criteria provided by AAP criteria or NICE guidelines

Study tools

Routine / Baseline Investigations

After initial selection from history taking and clinical examination, some following routine baseline investigations were performed. —

1. Blood for serum bilirubin level (total and direct).
2. Blood for serum calcium level.

Results

Table 1: Demographic Characteristics of Neonates

A slight majority of the neonates were male (58%) and additionally, 63% of the neonates were full-term.

Characteristic	Number of Neonates (%)
Gender	
Male	56 (58%)
Female	40 (42%)
Gestational Age	

Term (≥ 37 weeks)	60 (63%)
Preterm (< 37 weeks)	36 (37%)
Birth Weight	
Low Birth Weight (LBW)	38 (40%)
Normal Birth Weight (NBW)	58 (60%)

Table 2: Pre-Phototherapy Bilirubin Levels in Neonates and Comparison Between Term and Preterm Groups

All neonates had bilirubin levels that met the threshold for phototherapy according to the American Academy of Pediatrics (AAP) guidelines.

Parameter	Value
Mean Pre-Phototherapy Bilirubin Level	14.2 mg/dL (SD = 1.6)
Threshold for Phototherapy (AAP)	All neonates met the threshold
Difference in Bilirubin Levels	No significant difference between term and preterm neonates

Table 3: Serum Calcium Levels 48 Hours Before Phototherapy

All neonates had normal serum calcium levels (between 8-10 mg/dL) before undergoing phototherapy. The mean pre-phototherapy serum calcium level was **9.3 mg/dL** (SD = 0.5).

Parameter	48 Hours Before Phototherapy
Serum Calcium Level	9.3 mg/dL
Standard Deviation (SD)	0.5 mg/dL

Table 4: Post-Phototherapy Serum Calcium Levels

Post-phototherapy blood samples were collected 48 hours after the initiation of treatment. The mean post-phototherapy serum calcium level was **8.5 mg/dL** (SD = 0.7).

Serum Calcium Levels (mg/dL)	Number of Neonates (%)
≥ 8.0 (Normal)	59 (61%)
< 8.0 (Hypocalcemic)	37 (39%)
Total	96 (100%)

Table 5: Comparison of Hypocalcemia Between Term and Preterm Neonates

Preterm neonates were more susceptible to phototherapy-induced hypocalcemia.

Group	Number of Neonates (%)	Hypocalcemia Incidence (%)
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Term	60 (63%)	32%
Preterm	36 (37%)	48%

Table 6: Hypocalcemia Incidence by Birth Weight

Neonates with low birth weight were more likely to develop hypocalcemia after phototherapy (45%)

Birth Weight Category	Number of Neonates (%)	Hypocalcemia Incidence (%)
Low Birth Weight	38 (40%)	45%
Normal Birth Weight	58 (60%)	33%

Table 7: Comparison of Symptomatic and Asymptomatic Hypocalcemic Neonates

Symptomatic neonates had a lower mean post-phototherapy serum calcium level (7.9 mg/dL) compared to asymptomatic neonates (8.2 mg/dL).

Group	Number of Neonates (%)	Mean Post-Phototherapy Calcium Level (mg/dL)
Symptomatic	21 (55%)	7.9 ± 0.3
Asymptomatic	16 (45%)	8.2 ± 0.2

Table 8: Clinical Symptoms of Hypocalcemia in Neonates

Jitteriness was the most common clinical symptom, affecting 32% of hypocalcemic neonates.

Symptom	Number of Neonates (%)
Jitteriness	12 (32%)
Tetany	6 (16%)
Feeding issues	7 (18%)
Irritability	10 (26%)
Seizures	0 (0%)

Table 9: Adverse Events Observed During Phototherapy

Hyperthermia was the most common adverse event, occurring in 16% of the neonates.

Adverse Event	Number of Neonates (%)
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Hyperthermia	15 (16%)
Dehydration	12 (12.5%)
Skin rashes	5 (5.2%)

Table 10: Summary of Key Findingsd

Outcome	Finding
Incidence of Hypocalcemia	38% of neonates
Term vs. Preterm Hypocalcemia	48% of preterm neonates, 32% of term neonates
Symptoms of Hypocalcemia	55% of hypocalcemic neonates
Phototherapy Effectiveness	Mean bilirubin reduction of 4.6 mg/dL
Birth Weight Influence	45% of low birth weight neonates developed hypocalcemia

Discussion

The findings revealed that 38% of the neonates developed hypocalcemia following phototherapy, with preterm and low birth weight neonates exhibiting higher susceptibility. . In this study, 55% of the hypocalcemic neonates exhibited clinical symptoms, indicating that nearly half of the cases of hypocalcemia remained asymptomatic. In addition to hypocalcemia, this study observed other minor adverse events associated with phototherapy, including hyperthermia, dehydration, and skin rashes.

Conclusion

This study highlights the significant risk of hypocalcemia in neonates undergoing phototherapy for hyperbilirubinemia, with an incidence of 38% with preterm and low birth weight neonates being particularly vulnerable. The study emphasizes that with proper monitoring and timely intervention, including calcium supplementation, phototherapy-induced hypocalcemia can be effectively managed, ensuring better clinical outcomes for neonates.

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