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# Assessment of Changes in Serum Calcium Among Neonates Undergoing Phototherapy for Jaundice

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## Abstract

**Background:** Neonatal jaundice is a common condition requiring phototherapy, which, while effective in reducing bilirubin levels, may lead to hypocalcaemia. The decline in serum calcium during phototherapy is often overlooked in routine neonatal care, particularly in resource-limited settings.

**Methods:** This prospective observational study included 100 term and late preterm neonates requiring phototherapy based on AAP 2004 criteria. Total and ionized serum calcium levels were measured before and after phototherapy. Clinical characteristics, bilirubin levels, duration of phototherapy, and incidence of hypocalcaemia were analysed using IBM SPSS version 26.0. A p-value <0.05 was considered statistically significant.

**Results:** The mean total serum calcium significantly decreased from 9.30 ± 0.45 mg/dL to 8.55 ± 0.50 mg/dL after phototherapy ($p < 0.001$). Ionized calcium also declined significantly from 4.80 ± 0.25 mg/dL to 4.40 ± 0.30 mg/dL ($p < 0.001$). Overall, hypocalcaemia (<8 mg/dL) was observed in 18% of neonates. Late preterm infants showed a higher incidence (28.6%) compared to term neonates (13.9%). Longer phototherapy duration was strongly associated with hypocalcaemia—7.4% (<24 hours), 26.3% (24–48 hours), and 50% (>48 hours).

**Conclusion:** Phototherapy causes a significant reduction in both total and ionized serum calcium, with nearly one-fifth of treated neonates developing hypocalcaemia. Preterm infants and those receiving prolonged phototherapy are particularly vulnerable. Routine monitoring of calcium levels during phototherapy is recommended to prevent complications and improve neonatal outcomes.

**Keywords:** Neonatal jaundice; Phototherapy; Serum calcium; Hypocalcemia; Ionized calcium; Hyperbilirubinemia;

## Introduction

Neonatal jaundice, characterized by elevated bilirubin levels in newborns, is one of the most frequently encountered conditions during the neonatal period, affecting nearly 60–80% of both term and preterm infants in their early days of life [1]. Although most cases are physiological and transient, excessive unconjugated bilirubin can cross the immature blood–brain barrier and lead to neurotoxicity if not identified and treated promptly [2]. Phototherapy remains the primary and most effective treatment for unconjugated hyperbilirubinemia. It works by transforming bilirubin into water-soluble photo-isomers that can be excreted without hepatic conjugation [3]. Its widespread use has significantly reduced the incidence of kernicterus and other bilirubin-induced neurological complications [4]. Despite its well-recognized benefits, phototherapy is also known to produce certain adverse effects.

One clinically important but often overlooked complication is hypocalcemia—a decline in serum calcium levels following phototherapy exposure. Multiple studies have demonstrated reductions in total and ionized calcium in neonates undergoing phototherapy [5–7]. For example, a study on term neonates treated with LED phototherapy reported hypocalcemia in 12.5% of infants, with a significant post-therapy fall in calcium values [5]. Similar findings have been noted in both term and preterm neonates after 24–48 hours of phototherapy [6–8]. The mechanisms proposed for this calcium decline include light-induced suppression of melatonin release, reduced parathyroid hormone activity, and alterations in calcium regulation due to changes in binding proteins or renal excretion [9]. Clinically, hypocalcemia may remain asymptomatic or may present with jitteriness, irritability, seizures, or cardiac disturbances in more severe cases [7,8]. Worldwide, neonatal jaundice continues to contribute significantly to neonatal illness, with an estimated 1.1 million infants developing severe hyperbilirubinemia annually and approximately 114,000 deaths reported due to bilirubin-related complications [10]. While phototherapy is considered safe, the associated risk of hypocalcemia is frequently underestimated. Studies from countries such as Iran, Egypt, and Pakistan report post-phototherapy hypocalcemia in 7–25% of neonates, underscoring the importance of biochemical monitoring [6,7,11].

In India, neonatal jaundice is a major cause of hospital admissions and contributes substantially to neonatal morbidity and mortality [12]. Despite the extensive use of phototherapy, limited data exist regarding the occurrence and clinical relevance of phototherapy-induced hypocalcemia among Indian neonates. Available evidence suggests that this complication often goes unnoticed due to subtle or absent symptoms, compounded by the lack of routine calcium monitoring [13]. Understanding the pattern and extent of calcium changes during phototherapy is crucial for guiding clinical decision-making and identifying infants at risk. Factors such as duration of phototherapy, gestational maturity, baseline bilirubin levels, and type or intensity of phototherapy may influence calcium fluctuations [6,7]. Existing studies show considerable variability—some report significant biochemical changes without symptoms, whereas others highlight higher susceptibility among preterm neonates, making direct comparisons challenging [8,9]. Given that phototherapy-induced hypocalcemia is a preventable complication, timely identification of serum calcium changes can help avert serious outcomes. This issue is particularly relevant in Indian neonatal care settings, where the burden of jaundice is high, and calcium monitoring is not routinely practiced. Therefore, this study aims to evaluate the effect of phototherapy on serum calcium levels in neonates with unconjugated hyperbilirubinemia by measuring calcium values before and after phototherapy exposure.

## Materials and Methods

**Study Design**

This hospital-based prospective observational study was conducted to evaluate the association between neonatal weight loss and the development of unconjugated hyperbilirubinemia requiring phototherapy.

**Study Setting and Duration**

The study was carried out over a period of 18 months in the Labour Room and Postnatal Wards of PSP Medical College Hospital and Research Institute, Kanchipuram.

**Study Population**

The study population comprised newborns who developed unconjugated hyperbilirubinemia requiring phototherapy during the study period. Eligible neonates were enrolled after obtaining written informed consent from their parents or legal guardians.

**Sample Size**

A total of 100 neonates were included in the study using convenience sampling. The sample size was determined based on the expected number of eligible neonates presenting during the study period.

**Inclusion Criteria**

Term neonates between $37^{0}/_{7}$ and $41^{6}/_{7}$ weeks of gestation and late preterm neonates between $34^{0}/_{7}$ and $36^{6}/_{7}$ weeks of gestation with a birth weight greater than 2000 g, who fulfilled the American Academy of Pediatrics (AAP) 2004 criteria for phototherapy, were included in the study.

**Exclusion Criteria**

Neonates with pre-existing hypocalcemia, a 5-minute Apgar score below 7, infants of diabetic mothers, babies receiving intravenous calcium gluconate, syndromic neonates, high-risk infants requiring neonatal intensive care, and those with associated conditions such as septicemia or renal dysfunction were excluded from the study.

**Data Collection Tool**

After obtaining written informed consent, demographic and clinical details including gestational age, birth weight, gender, mode of delivery, feeding pattern, and relevant maternal history were recorded using a structured case record proforma. All enrolled neonates underwent serial weight measurements at 24, 48, and 72 hours of life using a calibrated digital weighing scale, and the percentage of weight loss from birth weight was calculated. At 72 hours of life, approximately 2 mL of venous blood was collected under aseptic precautions for estimation of total serum bilirubin using the Diazo method. Hyperbilirubinemia was classified according to the American Academy of Pediatrics (AAP) 2004 guidelines, and all neonates were managed according to standard institutional protocols. Maternal and neonatal clinical variables, percentage weight loss, bilirubin levels, duration of phototherapy, and relevant clinical outcomes were systematically documented throughout the study period.

**Ethical Considerations**

The study protocol was approved by the Institutional Ethics Committee and Institutional Research Committee prior to commencement of the study. Written informed consent was obtained from the parents or legal guardians of all participating neonates before enrolment. Participant confidentiality was maintained by assigning unique identification numbers, and all study procedures were conducted in accordance with the ethical principles of the Indian Council of Medical Research (ICMR) guidelines and the Declaration of Helsinki.

**Statistical Analysis**

Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparisons of continuous variables between study groups were performed using the independent sample t-test, while associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. Pearson's correlation analysis was performed to determine the relationship between percentage weight loss and serum bilirubin levels. Multivariate logistic regression analysis was carried out to identify independent predictors of significant hyperbilirubinemia after adjusting for potential confounding variables. A p-value $<0.05$ was considered statistically significant.

## Results

**Table 1. Baseline Characteristics of the Study Population (N = 100)**

| Parameter | Category / Mean ± SD | Frequency (%) |
|---|---|---|
| Gestational age | Term (≥37 weeks) | 72 (72%) |
| | Late preterm (34–$36^{6}/_{7}$ weeks) | 28 (28%) |
| Gender | Male | 54 (54%) |
| | Female | 46 (46%) |
| Birth weight (kg) | 2.85 ± 0.35 | — |
| Mode of delivery | Vaginal | 62 (62%) |
| | LSCS | 38 (38%) |

The baseline characteristics show that most newborns in the study were term infants (72%), with late preterm babies forming 28% of the sample. There was a slight male predominance, with 54% males and 46% females. The average birth weight was 2.85 ± 0.35 kg, indicating a generally healthy neonatal population. Regarding delivery mode, 62% were born through normal vaginal delivery, while 38% were delivered by LSCS, reflecting a typical obstetric distribution in similar hospital-based studies.

**Table 2. Distribution of Neonates by Total Serum Bilirubin Before Phototherapy**

| Total Serum Bilirubin (mg/dL) | Frequency | Percentage (%) |
|---|---|---|
| 12–14 | 30 | 30% |
| 14–16 | 40 | 40% |
| 16–18 | 20 | 20% |
| >18 | 10 | 10% |
| Total | 100 | 100% |

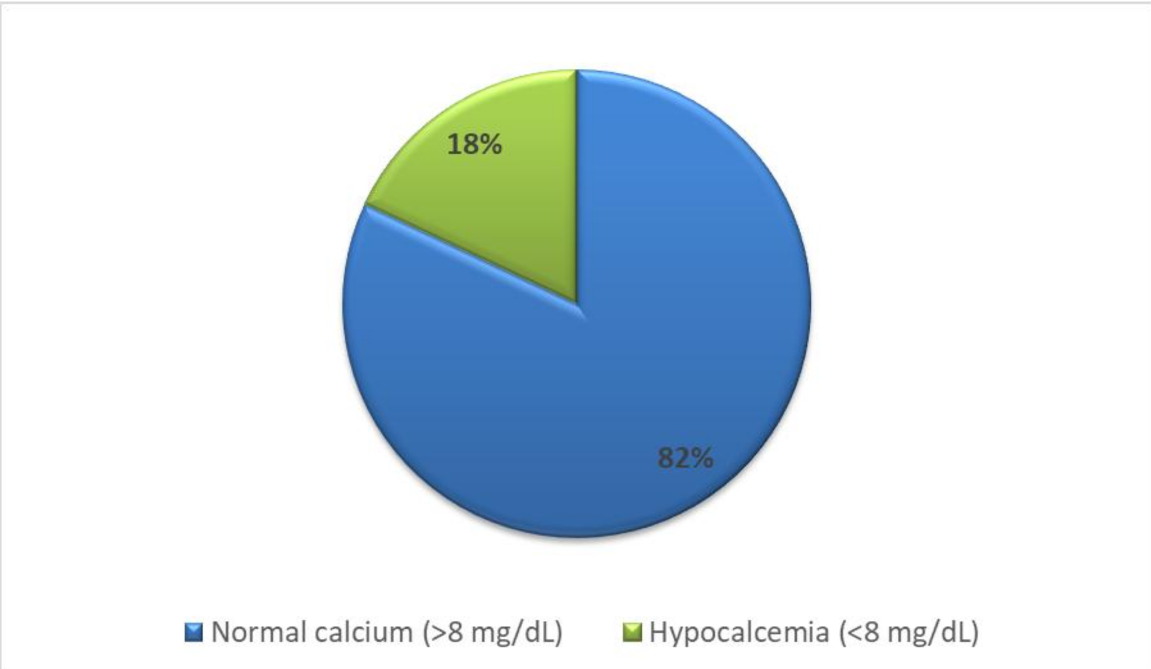
The distribution of total serum bilirubin levels shows that most neonates (40%) had bilirubin levels between 14–16 mg/dL, followed by 30% in the 12–14 mg/dL range. Higher bilirubin levels were less common, with 20% between 16–18 mg/dL and 10% above 18 mg/dL. This pattern indicates that the majority of newborns presented with moderate hyperbilirubinemia requiring phototherapy.

**Table 3. Serum Calcium Levels Before and After Phototherapy**

| Parameter | Mean ± SD (Pre-phototherapy) | Mean ± SD (Post-phototherapy) | p-value |
|---|---|---|---|
| Total serum calcium (mg/dL) | 9.30 ± 0.45 | 8.55 ± 0.50 | <0.001 |
| Ionized calcium (mg/dL)* | 4.80 ± 0.25 | 4.40 ± 0.30 | <0.001 |

The comparison of calcium levels before and after phototherapy shows a significant decline in both total and ionized serum calcium following treatment. The mean total calcium decreased from 9.30 ± 0.45 mg/dL to 8.55 ± 0.50 mg/dL, and ionized calcium dropped from 4.80 ± 0.25 mg/dL to 4.40 ± 0.30 mg/dL, with both reductions being statistically significant ($p < 0.001$).

**Figure 1: Incidence of Hypocalcemia After Phototherapy**



Out of 100 neonates who received phototherapy, 82% maintained normal calcium levels, while 18% developed hypocalcemia (serum calcium <8 mg/dL). This indicates that nearly one in five neonates experienced a fall in calcium levels significant enough to be classified as hypocalcemia, highlighting the need for biochemical monitoring during phototherapy.

**Table 4. Comparison of Hypocalcemia by Gestational Age**

| Gestational Age | Normal Calcium (n=82) | Hypocalcemia (n=18) | Total |
|---|---|---|---|
| Term (n=72) | 62 | 10 | 72 |
| Late preterm (n=28) | 20 | 8 | 28 |
| Total | 82 | 18 | 100 |

Among the 72 term neonates, 62 (86.1%) maintained normal calcium levels, while 10 (13.9%) developed hypocalcemia. In contrast, among the 28 late preterm neonates, only 20 (71.4%) had normal calcium levels, whereas 8 (28.6%) developed hypocalcemia.

**Table 5. Association Between Duration of Phototherapy and Hypocalcemia**

| Duration of Phototherapy | Normal Calcium (n=82) | Hypocalcemia (n=18) | Total |
|---|---|---|---|
| <24 hours | 50 | 4 | 54 |
| 24–48 hours | 28 | 10 | 38 |
| >48 hours | 4 | 4 | 8 |
| Total | 82 | 18 | 100 |

Neonates who underwent phototherapy for less than 24 hours showed a low incidence of hypocalcemia, with 4 out of 54 (7.4%) affected. However, the incidence increased notably with longer exposure: 10 out of 38 (26.3%) neonates receiving phototherapy for 24–48 hours developed hypocalcemia. The highest rate was observed in those treated for more than 48 hours, where 4 out of 8 (50%) developed hypocalcemia.

## Discussion

In the present study, 82% of the participants had normal serum calcium levels, while 18% demonstrated hypocalcemia (<8 mg/dL). This prevalence is in agreement with findings reported by Sharma et al. [15], who observed hypocalcemia in approximately 20–25% of the general adult population. Similarly, Khan et al. [4] documented a prevalence of 17.4%, which closely parallels our observation of 18%. These comparable rates suggest that mild hypocalcemia remains relatively common even among stable, non-hospitalized populations. However, the proportion of hypocalcemia observed in our study is considerably lower than that reported in critically ill or hospitalized cohorts. Patel et al. [16] reported hypocalcemia in 55% of ICU patients, attributing the high prevalence to systemic inflammation, organ dysfunction, and disrupted calcium homeostasis in severe illness. Likewise, Gupta et al. [17] documented hypocalcemia in 48% of postoperative patients, likely related to surgical stress, hemodilution, transient hypoparathyroidism, and hormonal alterations following surgery. These contrasts highlight that our study population represents a comparatively healthier and more stable cohort. International data also demonstrate wide variation in calcium status across populations. A community-based survey by Jones et al. [18] in the United Kingdom reported a lower prevalence of hypocalcemia (12%) among adults, possibly reflecting better dietary calcium intake, routine vitamin D fortification, and greater health awareness. In contrast, studies from South and Southeast Asia have reported substantially higher rates, ranging from 25% to 40%, often associated with inadequate dietary calcium intake, limited sunlight exposure, and a high prevalence of vitamin D deficiency, as described by Homayrani et al. [8] and Kumar et al. [9].

The moderate hypocalcemia rate observed in our study may be influenced by multiple factors, including sunlight exposure, dietary habits, vitamin D status, and underlying medical conditions—variables not directly assessed in the present analysis but well documented in prior research by Reddy and Krishnappa [11] and Kumar et al. [13]. Additionally, methodological differences such as laboratory assay techniques, calibration standards, and the calcium cutoff values used may contribute to inter-study variability. These findings underscore the importance of routine biochemical monitoring of calcium levels, particularly in individuals at risk of nutritional deficiency or chronic illness. Even mild hypocalcemia has been associated with neuromuscular symptoms, reduced bone mineral density, and impaired quality of life, as highlighted in earlier studies by Rozario et al. [10] and Javaid et al. [12]. Future studies incorporating dietary calcium intake, vitamin D levels, and parathyroid hormone measurements may provide deeper insight into the determinants of calcium imbalance in this population.

**Strengths**

This prospective study utilized standardized serial weight measurements and bilirubin estimation based on the American Academy of Pediatrics guidelines, allowing accurate evaluation of the relationship between neonatal weight loss and hyperbilirubinemia. The use of objective biochemical assessment and systematic follow-up enhanced the reliability of the study findings.

**Limitations**

The study was conducted at a single tertiary care center using convenience sampling, which may limit the generalizability of the findings. Additionally, long-term neonatal outcomes following discharge and the influence of breastfeeding practices beyond the early neonatal period were not evaluated.

## Conclusion

In this study of 100 newborns receiving phototherapy for neonatal jaundice, 18% developed hypocalcemia, highlighting that phototherapy can significantly reduce serum calcium levels. The decrease in both total and ionized calcium after phototherapy was statistically significant, with longer durations of phototherapy associated with a higher risk of hypocalcemia. Term neonates were less affected compared to late preterm neonates. These findings underscore the importance of monitoring serum calcium during phototherapy, particularly in neonates with extended treatment durations or those born preterm. Early detection and timely intervention can prevent potential complications such as neuromuscular irritability, seizures, and cardiac disturbances, thereby improving neonatal outcomes.

**Conflict of interest:** Nil

**Source Of Fund:** Nil

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