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Original Research

Phototherapy-Induced Electrolyte Disturbances in Neonates with Hyperbilirubinemia: A Longitudinal Study on Calcium Depletion and Clinical Implications

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Abstract

Background: Neonatal hyperbilirubinemia is a common condition requiring phototherapy, which, despite its efficacy, is associated with electrolyte imbalances, particularly hypocalcemia. This study evaluates the impact of phototherapy on serum calcium levels in term and preterm neonates.

Methods: A longitudinal study was conducted on 150 neonates (term and preterm) with unconjugated hyperbilirubinemia receiving phototherapy at a tertiary care hospital. Serum calcium and bilirubin levels were measured pre- and post-phototherapy. Exclusion criteria included comorbidities like sepsis or pre-existing electrolyte abnormalities.

Results: Phototherapy significantly reduced bilirubin levels in both term (17.7 ± 2.04 mg/dL to 12.1 ± 1.75 mg/dL) and preterm neonates (16.7 ± 1.92 mg/dL to 11.2 ± 1.79 mg/dL; *p* < 0.05). Hypocalcemia was observed post-phototherapy, with a more pronounced decline in preterm neonates (9.2 ± 1.03 mg/dL to 7.84 ± 1.29 mg/dL) compared to term neonates (9.29 ± 1.00 mg/dL to 8.78 ± 1.16 mg/dL; *p* < 0.05). The mean phototherapy duration was longer in term neonates (40.3 hours) than preterm neonates (37.6 hours).

Conclusion: Phototherapy effectively reduces bilirubin but significantly lowers serum calcium, particularly in preterm neonates. Routine calcium monitoring and potential supplementation are recommended to mitigate hypocalcemia risks during phototherapy.

Keywords: Neonatal hyperbilirubinemia, Phototherapy, Hypocalcemia, Electrolyte imbalance, Serum calcium, Preterm neonates, Term neonates

Introduction

Neonatal hyperbilirubinemia is a common condition affecting newborns, characterized by elevated levels of bilirubin in the blood, leading to yellowish discoloration of the skin and sclera (1). The prevalence of neonatal jaundice varies globally and remains a significant concern in both developed and developing countries (2). Clinical features of neonatal jaundice range from mild symptoms like lethargy to severe complications such as kernicterus (3). Treatment options include phototherapy, exchange transfusion, and pharmacological interventions such as intravenous immunoglobulin for specific conditions (1, 4). Phototherapy, the most commonly used treatment, involves exposing the neonate to blue light. This light transforms bilirubin in the skin into lumirubin, a water-soluble form that is easily excreted via urine.While phototherapy is generally safe and effective, recent

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studies have raised concerns about potential side effects. These include dehydration, skin changes, and particularly, electrolyte imbalances (5). Electrolytes, especially calcium, play a critical role in maintaining cellular function, nerve conduction, and muscle contraction. Any external intervention during the neonatal period, such as phototherapy, may disrupt this delicate balance (6).

Hypocalcemia is one of the major side effects associated with phototherapy. It is believed to occur due to the inhibition of melatonin production by the pineal gland under exposure to light, which negatively impacts cortisol levels and reduces bone resorption (7).

Current research suggests that phototherapy can alter electrolyte levels in neonates, but the extent and severity of these changes remain underexplored. Documented imbalances such as hypocalcemia have been reported, yet comprehensive data on their correlation with the duration of phototherapy and other risk factors is limited. Despite the existing research, significant gaps remain in understanding the full impact of phototherapy on electrolyte balance in neonates. Given the vital role of electrolytes in neonatal physiology and the widespread use of phototherapy in treating hyperbilirubinemia, further investigation is essential. Therefore, this study aimed to bridge these gaps by examining electrolyte disturbances in neonates receiving phototherapy in a tertiary care hospital, with the goal of identifying prevalence, patterns, and risk factors to help optimize neonatal care and improve clinical outcomes.

Material and Methods

The present longitudinal study was conducted in the Department of Pediatrics at Rajshree Medical Research Institute from July 2023 to December 2024, involving a total of 150 neonates. The study population included both term and preterm inborn neonates with unconjugated hyperbilirubinemia requiring phototherapy for at least 24 hours. Written informed consent was obtained from parents or caregivers. Neonates with comorbidities such as septicemia, renal failure, birth asphyxia, pre-existing electrolyte abnormalities, history of exchange transfusion, persistent jaundice beyond 14 days, or mothers on anticonvulsants or infants fed with bovine milk were excluded. After institutional ethical approval, venous blood samples were collected before initiating phototherapy to assess baseline serum calcium and bilirubin levels (0-hour sample). Following phototherapy, the same electrolyte parameters were rechecked (post-therapy sample). Bilirubin was estimated using the Diazo method, and calcium was analyzed using the Arsenazo III method. All data were recorded using a structured, pre-approved proforma for analysis.

Results

Table 1: Distribution of study subjects according to birth weight (n=150)

Birth weight	Frequency	% of Total	P value
<2 (25%)	7	4.7 %	**χ^2=119, p=<0.001**
2-3(25%)	77	51.3 %	
3-4(25%)	64	42.7 %	
>4(25%)	2	1.3 %	
Total	**150**	**100.0%**	

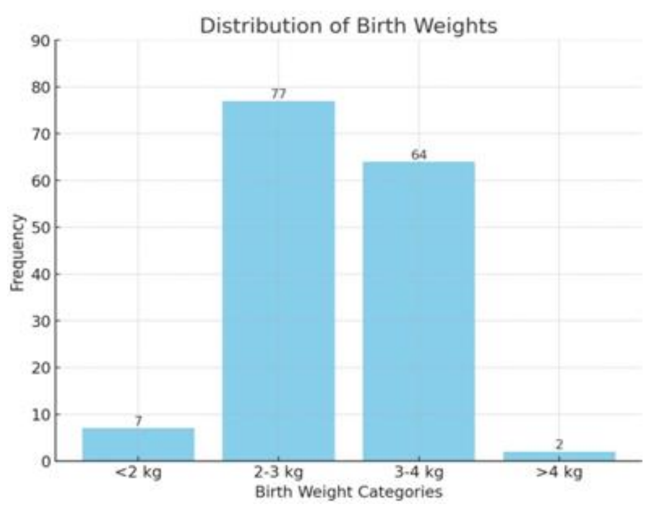

Figure 1: Distribution of study subjects according to birth weight

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Table 2:-Total bilirubin levels before and after phototherapy(n=150)

	GA	Mean
Pre PhototherapyTotal Bilirubin	**Term**	17.7+2.04
	Pre-Term	16.7+1.92
Post PhototherapyTotal Bilirubin	**Term**	12.1+1.75
	Pre-Term	11.2+1.79

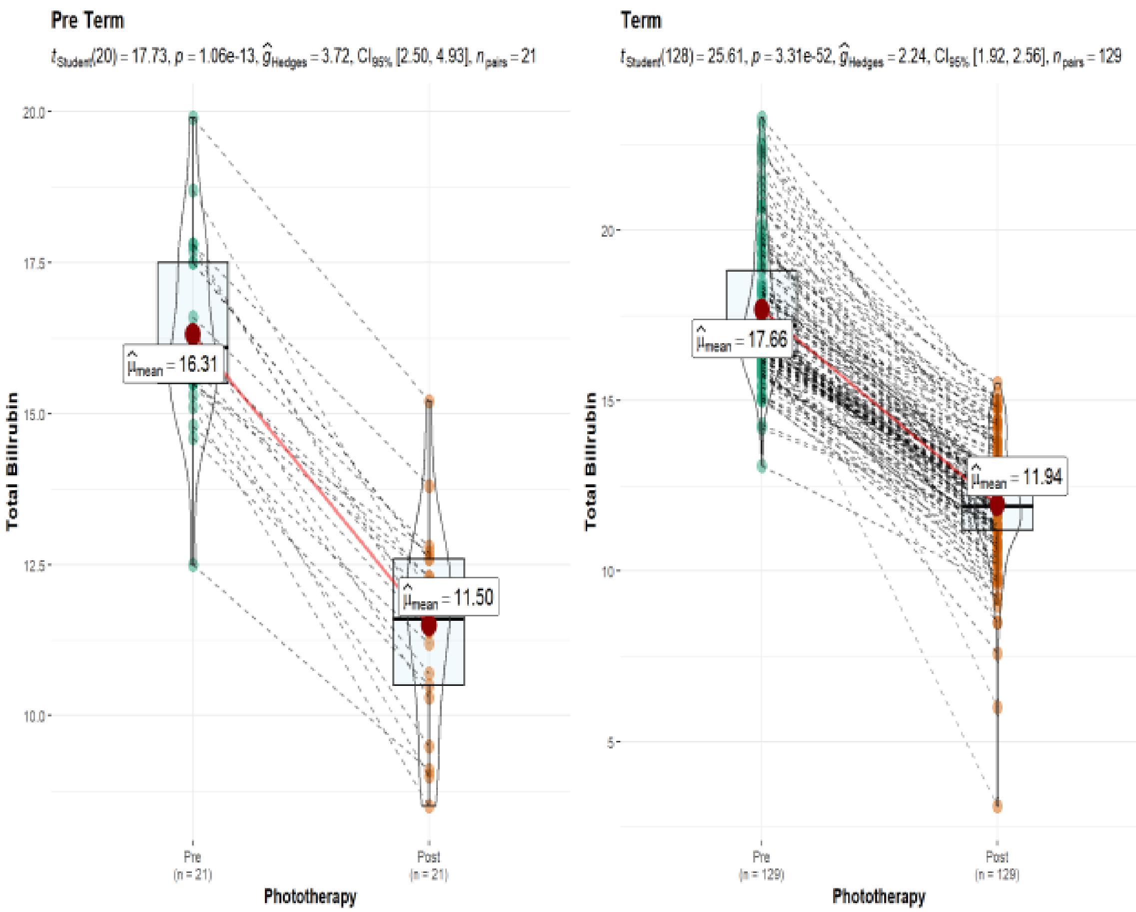

FIGURE 2:- Total Serum Bilirubin Levels Before and After Phototherapy

Table 3: Distribution of duration of phototherapy in Pre & term birth

				95% confidence Interval		
	Preterm/Term	**N**	**Mean**	**Lower**	**Upper**	**SD**
Duration of PT(in Hours)	Preterm	32	37.6	33.5	41.6	11.2
	Term	118	40.3	38.2	42.4	11.7

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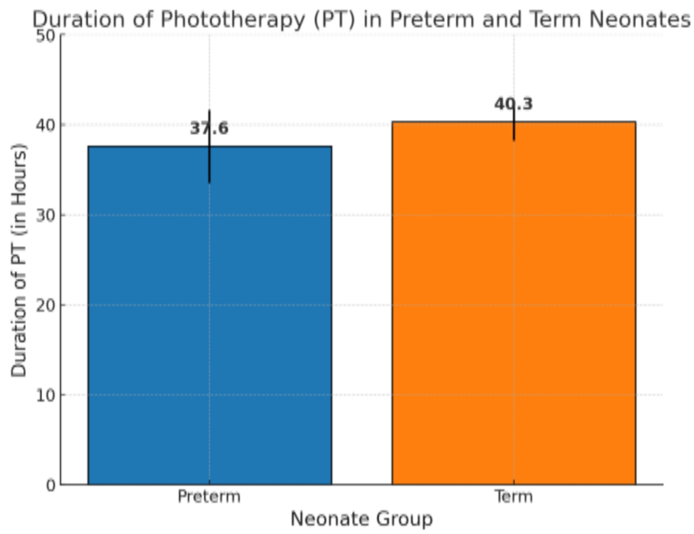

Figure 3. Distribution of duration of phototherapy in Pre & term birth

Table 4: Calcium changes before and after phototherapy

	GA	Mean	P value
Pre phototherapy Ca	**Term**	9.29+1.00	<0.05
	Pre-Term	9.2+1.03	
Post phototherapy Ca	**Term**	8.78+1.16	
	Pre-Term	7.84+1.29	

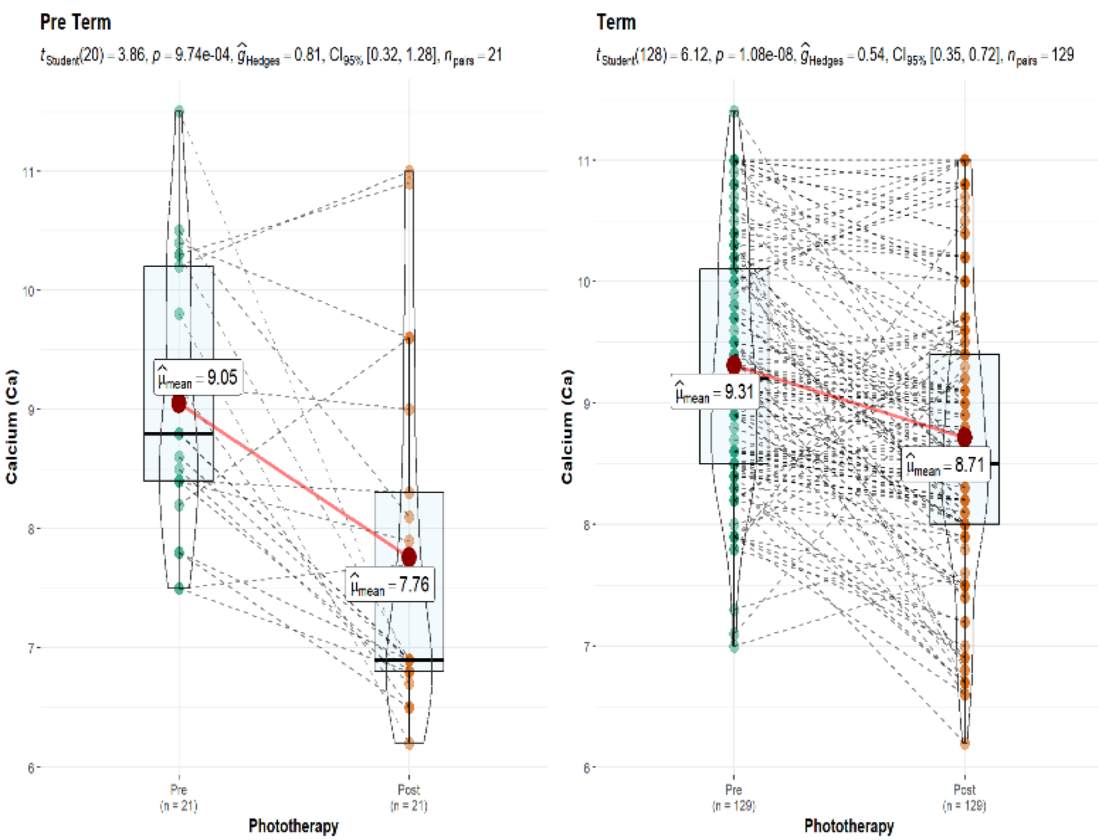

Figure 4:- calcium changes before and after phototherapy

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Discussion

In our study, most neonates receiving phototherapy for neonatal hyperbilirubinemia had birth weights between 2-3 kg (51.3%) and 3-4 kg (42.7%). Only 4.7% of the neonates weighed less than 2 kg, and 1.3% had a birth weight above 4 kg, indicating that neonates within the 2-4 kg range are most commonly treated with phototherapy (Table 1, $\chi^2 = 119$, $p < 0.001$). This is in line with the study by **PhaniKrishna et al. (2017)(8)** , who reported a mean birth weight of 3.01 kg for term neonates and 2.21 kg for preterm neonates, highlighting a similar weight disparity. **Goyal et al.** (2018)(9) also documented comparable findings, with term neonates having a mean birth weight of 3.04 kg and preterm neonates averaging 2.25 kg. **Jena et al**. (2019)(10) found a significant difference in birth weight between term (2.95 kg) and preterm (2.20 kg) neonates, reinforcing the inverse relationship between gestational age and birth weight. **Purohit et al. (2020)(11)** noted a mean birth weight of 3.02 kg in term neonates, closely matching our results**. Ranjit Kumar et al. (2021)**(12)reported a mean birth weight of 3.08 kg for term neonates and 2.28 kg for preterm neonates, similar to our study. **Patel et al.** (2023)(13) observed a mean birth weight of 3.00 kg for term neonates and 2.23 kg for preterm neonates, further corroborating our findings. **Nivetha et al. (2024)**(14) found that birth weight differences were statistically significant, with term neonates averaging 3.05 kg and preterm neonates averaging 2.20 kg, aligning closely with our results.**Taheri et al. (2013)(**15)also studied phototherapy-induced hypocalcemia and found that neonates weighing less than 2 kg had a significantly higher prevalence of hypocalcemia (23%). This aligns with the pattern observed in our study, suggesting that neonates at the lower end of the birth weight spectrum are particularly vulnerable to complications during phototherapy.These studies show that although phototherapy is essential for managing hyperbilirubinemia, it disproportionately affects neonates with lower birth weights, necessitating individualized care. Our findings complement existing literature by confirming that neonates in the mid-weight range are more frequently subjected to phototherapy, while those at lower birth weights require extra caution to prevent adverse outcomes.

The total bilirubin analysis demonstrates a significant reduction in bilirubin levels post-phototherapy, confirming its effectiveness in both term and preterm neonates. Among term neonates, bilirubin levels decreased from 17.7 ± 2.04 mg/dL to 12.1 ± 1.75 mg/dL, whereas in preterm neonates, the reduction was from 16.7 ± 1.92 mg/dL to 11.2 ± 1.79 mg/dL. The computed p-value ($p < 0.05$) indicates a statistically significant difference, confirming that phototherapy effectively lowers bilirubin levels in both groups (Table 2). The slightly lower pre-phototherapy bilirubin in preterm neonates may be attributed to increased monitoring and earlier intervention due to their higher risk of complications. However, the magnitude of bilirubin reduction is comparable between groups, suggesting phototherapy is equally effective irrespective of gestational age. This aligns with the study's aim by quantitatively validating the clinical impact of phototherapy on neonatal jaundice management. Furthermore, since preterm neonates have immature hepatic function, they may require longer phototherapy durations, increasing their risk for electrolyte disturbances, reinforcing the study's focus on monitoring calcium levels to prevent phototherapy-induced imbalances (1).

In our study, we found that the mean duration of phototherapy was 40.3 hours for term neonates and 37.6 hours for preterm neonates. The confidence interval for preterm neonates ranged between 33.5 to 41.6 hours, with a standard deviation (SD) of 11.2 hours. For term neonates, the duration varied from 38.2 to 42.4 hours, with an SD of 11.7 hours (Table 3). These findings suggest that while term neonates generally required longer phototherapy, both groups showed overlapping treatment durations, indicating the individualized nature of phototherapy. In their study, **Purohit and Verma *(2020)*** (16)investigated electrolyte changes in neonates undergoing phototherapy but did not directly report specific comparisons of phototherapy duration based on gestational age. Their study focused on biochemical variations but acknowledged that preterm neonates are more closely monitored, which could explain shorter treatment durations observed in our study. Additionally, **Bhutani et al. (2016) (17)** highlighted that preterm neonates are monitored more frequently, resulting in faster treatment adjustments, while term neonates may undergo longer phototherapy to achieve bilirubin stabilization. Though the study did not provide exact treatment durations, it aligns with our finding that term neonates tend to require longer phototherapy due to different metabolic responses to bilirubin.

The calcium analysis highlights a significant decline in serum calcium levels post-phototherapy, confirming a risk of hypocalcemia, especially in preterm neonates. In term neonates, calcium levels dropped from 9.29 ± 1.00 mg/dL to 8.78 ± 1.16 mg/dL, whereas in preterm neonates, the reduction was more pronounced, from 9.2 ± 1.03 mg/dL to 7.84 ± 1.29 mg/dL. The computed p-value ($p < 0.05$) confirms that these changes are statistically significant, establishing phototherapy as a contributing factor to neonatal hypocalcemia (Table 4). This effect is likely due to phototherapy-induced suppression of melatonin, which in turn affects corticosterone levels, leading to reduced calcium mobilization from bone stores. The study **by Goyal et al. (2018)** similarly reported a significant decline in

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serum calcium levels post-phototherapy, with 35% of neonates experiencing hypocalcemia, some of whom exhibited clinical symptoms such as jitteriness and irritability (9). These findings reinforce the present study's observations regarding the risk of phototherapy-induced hypocalcemia. **Purohit et al. (2020)** also documented a significant decline in serum calcium levels, underscoring the necessity for calcium monitoring during phototherapy (11). Similarly, Ranjit**Kumar et al. (2021)** found a substantial reduction in calcium levels, particularly in term neonates, reinforcing the notion that phototherapy contributes to neonatal hypocalcemia (12). The study **by Phani Krishna et al. (2017)** further supports this conclusion, as they observed a significant decline in calcium levels post-phototherapy, particularly in neonates undergoing prolonged treatment (8). The study **by Patel et al. (2022) (**13) also highlighted a negative correlation between phototherapy duration and serum calcium levels, emphasizing the need for electrolyte monitoring. Moreover, the findings of **Nazim et al. (2023) (**18)align with the present study, as they reported a significant reduction in calcium levels post-phototherapy, reinforcing the importance of preemptive calcium supplementation strategies

The greater calcium depletion in preterm neonates reflects their immature parathyroid function and lower calcium reserves, making them more vulnerable to hypocalcemia-induced complications such as jitteriness, apnea, and seizures. These findings directly support the study's objective of evaluating electrolyte disturbances associated with phototherapy and reinforce the need for routine calcium monitoring and possible supplementation in neonates receiving prolonged phototherapy to prevent severe calcium imbalance-related complications.

Conclusion

This study underscores the dual role of phototherapy in neonatal hyperbilirubinemia management: while it effectively lowers bilirubin levels, it also induces significant electrolyte disturbances, notably hypocalcemia. Preterm neonates are particularly vulnerable, exhibiting greater calcium depletion due to immature metabolic pathways and lower reserves. The findings reinforcing the need for vigilant electrolyte monitoring during phototherapy.

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