

Electrolyte Changes in Neonates Receiving Phototherapy for Physiological Hyperbilirubinemia: A Prospective Observational Study from a Tertiary Care Centre in Bihar

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DOI: <https://doi.org/10.5281/zenodo.22902171>

Received: 25 August 2026, Revised: 10 September, Accepted: 20 September 2026, Online First: 03 October 2026

ABSTRACT

Background: Phototherapy is the first-line treatment for neonatal hyperbilirubinemia, but its influence on serum electrolyte homeostasis remains incompletely characterised, particularly in resource-limited settings. This study evaluated alterations in serum bilirubin and electrolytes in neonates receiving phototherapy for physiological hyperbilirubinemia. **Methods:** In this prospective observational study, 120 neonates with physiological or breastfeeding hyperbilirubinemia admitted to the Special Newborn Care Unit (SNCU), Darbhanga Medical College and Hospital, were enrolled. Baseline values (control group, n = 60) and post-phototherapy values obtained after 48 hours of treatment (study group, n = 60) were compared. Serum bilirubin, calcium, magnesium, sodium, potassium, and chloride were measured before and after therapy. Subgroup analyses were performed by gestational age and by phototherapy duration (24, 30, 36, and 48 hours). **Results:** The groups were comparable in age (5.47 ± 1.10 vs 5.57 ± 1.20 days; $p = 0.634$), sex distribution ($p = 1.00$), gestational age ($p = 0.315$), birth weight ($p = 0.203$), and jaundice type ($p = 0.465$). Phototherapy duration was significantly longer in the study group (39.23 ± 10.19 vs 28.63 ± 6.20 hours; $p = 0.0001$). Serum bilirubin was significantly higher after therapy (14.41 ± 2.49 vs 10.96 ± 1.67 mg/dL; $p = 0.0001$), whereas serum calcium declined significantly (8.34 ± 0.73 vs 9.22 ± 0.68 mg/dL; $p = 0.0001$). Hypocalcemia developed in 48% of treated neonates ($p = 0.0001$). Magnesium, sodium, potassium, and chloride remained largely unchanged. **Conclusions:** Phototherapy was associated with a significant fall in serum calcium, confirming hypocalcemia as the most consistent metabolic complication, while other electrolytes remained stable. Routine calcium monitoring during phototherapy is recommended to ensure early detection and timely correction, particularly in settings where laboratory surveillance is limited.

Keywords: Neonatal hyperbilirubinemia; Phototherapy; Hypocalcemia; Electrolytes; Calcium; Magnesium; Sodium; Potassium; Chloride; SNCU.

1. INTRODUCTION

Neonatal hyperbilirubinemia ranks among the most frequently encountered clinical conditions of the early postnatal period and continues to be a leading cause of neonatal morbidity worldwide. It arises from an

abnormal accumulation of bilirubin in the circulation, producing the characteristic yellow discoloration of the skin, sclera, and mucous membranes. Although most episodes are physiological and self-limiting, excessive concentrations of unconjugated bilirubin carry a well-

recognised risk of neurotoxicity. When serum levels exceed the binding capacity of albumin, free bilirubin crosses the immature blood-brain barrier and may precipitate acute bilirubin encephalopathy and, in its most severe form, kernicterus, with lasting consequences such as cerebral palsy, sensorineural hearing loss, and developmental delay [1, 2].

Bilirubin is generated as an end product of haemoglobin degradation. In the newborn, a relatively high red cell mass combined with a shortened erythrocyte lifespan accelerates bilirubin production, while hepatic conjugating enzyme systems and biliary excretory pathways remain functionally immature. The delayed maturation of uridine diphosphate glucuronosyltransferase, increased enterohepatic recycling secondary to an underdeveloped gut flora, and delayed establishment of feeding together perpetuate the circulation of unconjugated bilirubin during the first days of life [3, 4].

Phototherapy remains the cornerstone of treatment for moderate to severe neonatal jaundice. Exposure of the infant's skin to light in the blue spectrum, approximately 430 to 490 nanometres, converts lipid-soluble unconjugated bilirubin into water-soluble photoisomers that can be excreted in bile and urine without prior hepatic conjugation. The technique is non-invasive, inexpensive, and highly effective, and it has substantially reduced the need for exchange transfusion and the incidence of bilirubin-induced neurological injury [5, 6].

Nevertheless, phototherapy is not entirely without risk. Reported adverse effects include loose stools, cutaneous reactions, thermal instability, increased insensible water loss, dehydration, retinal exposure if eye protection is inadequate, and disruption of mother-infant bonding [7, 8]. Among the metabolic complications, disturbance of electrolyte homeostasis has attracted increasing attention. Neonates possess immature renal concentrating capacity, underdeveloped endocrine regulation, and limited physiological reserves, so even modest electrolyte perturbations may carry clinical significance [9].

Hypocalcemia is the electrolyte disturbance most consistently linked to phototherapy. The principal proposed mechanism involves light-mediated suppression of pineal melatonin secretion; reduced melatonin activity alters parathyroid hormone dynamics and promotes skeletal calcium uptake, thereby lowering circulating calcium. Increased urinary calcium loss and reduced intestinal absorption may contribute additionally [10]. Biochemical hypocalcemia is frequently asymptomatic, but when symptomatic it may manifest as jitteriness, irritability, poor feeding, apnea, seizures, or cardiac arrhythmia. Alterations in sodium, potassium,

chloride, and magnesium have also been described, although published findings remain inconsistent [11, 12]. In many tertiary centres of low- and middle-income regions, including Bihar, routine electrolyte surveillance during phototherapy is frequently constrained by limited laboratory access, financial considerations, and the absence of locally validated monitoring protocols. Systematic data generated from such settings are scarce, yet they are essential for adapting national and international guidance to regional realities. The present study was therefore undertaken to quantify changes in serum bilirubin and electrolytes, specifically calcium, magnesium, sodium, potassium, and chloride, in neonates receiving phototherapy for physiological hyperbilirubinemia, and to determine whether the duration of treatment or gestational maturity modifies these changes.

2. MATERIALS AND METHODS

2.1 Study design and setting

This prospective observational study was conducted in the Special Newborn Care Unit (SNCU) and the Department of Paediatrics at Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from the parents or legal guardians of all enrolled neonates, and all procedures were performed in accordance with the ethical standards for research involving human participants.

2.2 Participants

A total of 120 neonates diagnosed with physiological hyperbilirubinemia and requiring phototherapy were enrolled, comprising 60 males and 60 females. Neonates were assigned to two groups according to the timing of blood sampling: baseline measurements obtained before the initiation of phototherapy constituted the control group, whereas measurements obtained after 48 hours of therapy constituted the study group.

Eligibility criteria included term neonates weighing more than 2.5 kg, preterm neonates, neonates aged between 4 and 7 days, and neonates with physiological jaundice or breastfeeding jaundice. Neonates with Rh or ABO incompatibility, neonatal sepsis, birth asphyxia, infants of diabetic mothers, congenital hypothyroidism, or congenital anomalies affecting metabolism or renal function were excluded.

2.3 Sample size

The sample size was calculated to detect a significant difference in mean serum electrolyte levels before and after phototherapy, using the anticipated change in serum calcium as the reference parameter, given that hypocalcemia is the most frequently reported electrolyte

disturbance associated with phototherapy. The comparison of paired means was performed using the standard formula $n = (Z\alpha + Z\beta)^2 \times SD^2 \div d^2$, where $Z\alpha = 1.96$ at a 5% level of significance, $Z\beta = 0.84$ for 80% power, SD represents the standard deviation of the difference, and d represents the expected mean difference. The final enrolment of 120 neonates satisfied this requirement and was consistent with the recruitment feasibility of the centre during the study period.

2.4 Assessments and outcomes

After enrolment, a detailed antenatal, perinatal, and postnatal history was recorded, followed by thorough clinical examination encompassing gestational age, birth weight, vital parameters, and general health status. Baseline venous blood samples were collected under strict aseptic precautions to estimate serum bilirubin and electrolytes (calcium, magnesium, sodium, potassium, and chloride). Phototherapy was then commenced using standardised blue-light units in accordance with institutional protocol, with maximal skin exposure, protective eye patches, and genital shields. Body temperature, hydration status, urine output, and feeding patterns were monitored throughout treatment, and fluid intake was adjusted to preserve adequate hydration. A second blood sample was obtained after completion of 48 hours of continuous phototherapy using the identical collection procedure, and post-treatment serum bilirubin and electrolyte values were compared with baseline. All investigations were performed in the central laboratory using standardised methods and calibrated equipment to ensure accuracy and reproducibility.

3.1 Baseline characteristics

Table 1: Age distribution of study participants

Age (days)	Control (n=60), n (%)	Study (n=60), n (%)
4	14 (23)	14 (23)
5	18 (30)	19 (32)
6	14 (23)	6 (10)
7	14 (23)	21 (35)
Mean $\pm$ SD	5.47 $\pm$ 1.10	5.57 $\pm$ 1.20

Age distribution: $p = 0.201$; mean age comparison: $p = 0.634$. Values are mean $\pm$ SD where indicated.

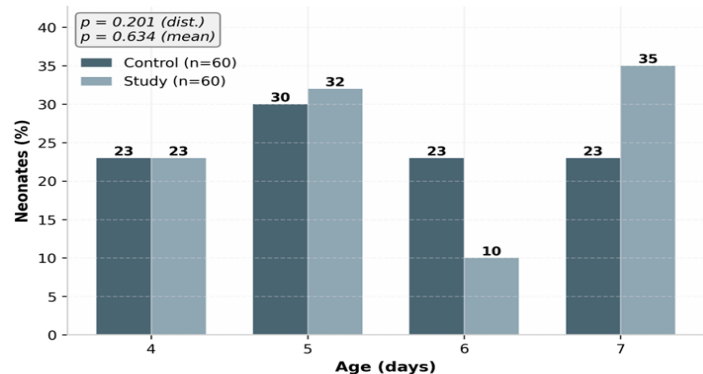


Figure 1: Age distribution of study participants. $p = 0.201$ (distribution); $p = 0.634$ (mean age)

2.5 Statistical analysis

Data were entered into Microsoft Excel and analysed using SPSS software. Continuous variables such as age, gestational age, birth weight, phototherapy duration, and biochemical parameters were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequency and percentage. Between-group comparisons of continuous variables used the independent-samples t-test, and categorical variables were compared using the chi-square test, with Fisher's exact test applied where appropriate. A two-sided p-value below 0.05 was considered statistically significant, and a p-value below 0.001 was considered highly significant.

2.6 Ethics approval and consent

The study protocol was reviewed and approved by the Institutional Ethics Committee of Darbhanga Medical College and Hospital, Laheriasarai. Written informed consent was obtained from the parents or legal guardians of all participants in a language they understood prior to enrolment.

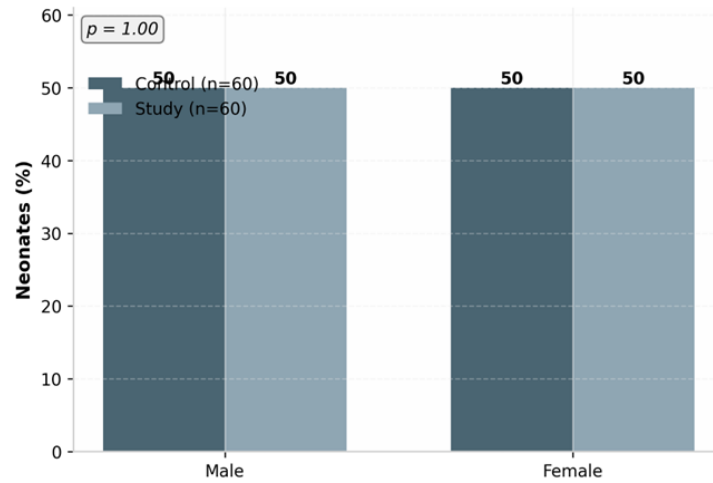
3. RESULTS

Of the 120 jaundiced neonates enrolled and analysed, baseline and post-therapy measurements were compared across demographic, clinical, and biochemical domains. Baseline characteristics were broadly comparable between the control (pre-phototherapy) and study (post-phototherapy) groups (Tables 1–7).

Table 2: Sex distribution of study participants

Sex	Control (n=60), n (%)	Study (n=60), n (%)
Male	30 (50)	30 (50)
Female	30 (50)	30 (50)

Chi-square: $p = 1.00$.

**Figure 2: Sex distribution of study participants. Chi-square $p = 1.00$** **Table 3: Gestational age distribution of study participants**

Gestational age (weeks)	Control (n=60), n (%)	Study (n=60), n (%)
34	11 (18)	5 (8)
35	9 (15)	8 (13)
36	10 (17)	11 (18)
37	7 (12)	11 (18)
38	7 (12)	9 (15)
39	7 (12)	6 (10)
40	9 (15)	10 (17)
Mean $\pm$ SD	36.78 $\pm$ 2.09	37.15 $\pm$ 1.89

Gestational age distribution: $p = 0.727$; mean gestational age comparison: $p = 0.315$.

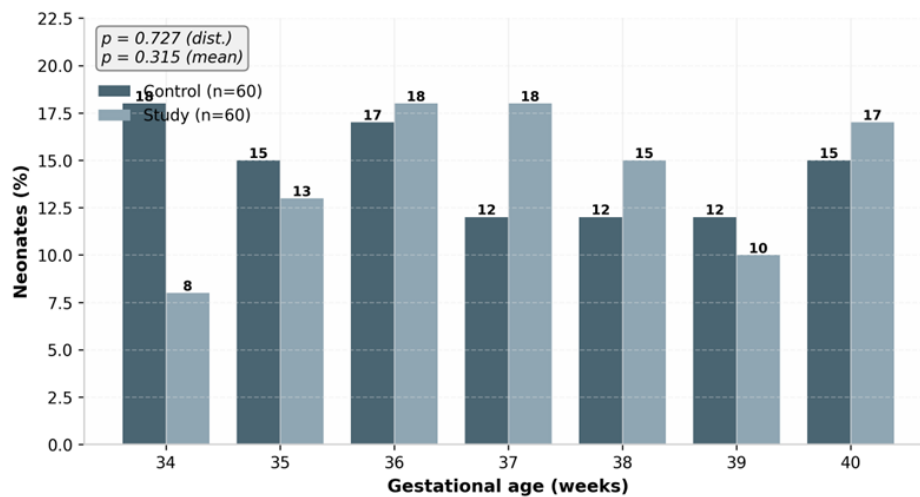
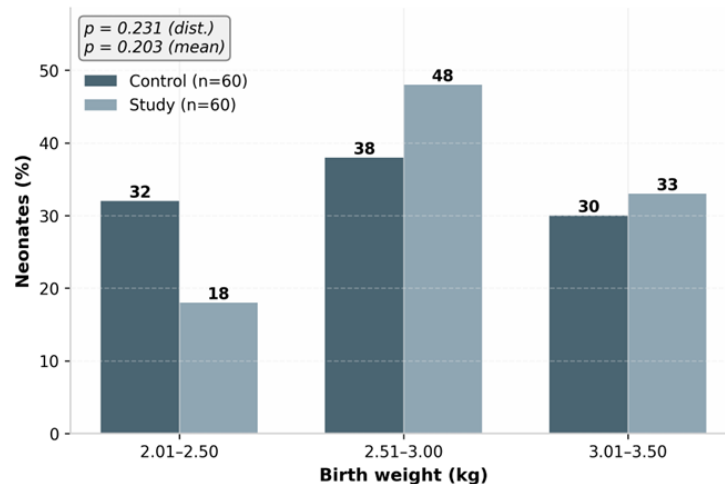
**Figure 3: Gestational age distribution of study participants. $p = 0.727$ (distribution); $p = 0.315$ (mean GA)**

Table 4: Birth weight distribution of study participants

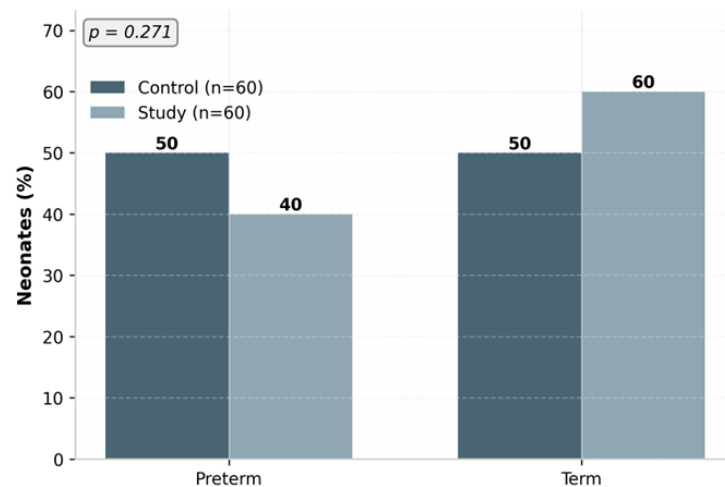
Birth weight (kg)	Control (n=60), n (%)	Study (n=60), n (%)
2.01–2.50	19 (32)	11 (18)
2.51–3.00	23 (38)	29 (48)
3.01–3.50	18 (30)	20 (33)
Mean $\pm$ SD	2.73 $\pm$ 0.41	2.82 $\pm$ 0.40

Birth weight distribution: $p = 0.231$; mean birth weight comparison: $p = 0.203$.

**Figure 4: Birth weight distribution of study participants. $p = 0.231$ (distribution); $p = 0.203$ (mean birth weight)****Table 5: Gestational category of study participants**

Neonate type	Control (n=60), n (%)	Study (n=60), n (%)
Preterm	30 (50)	24 (40)
Term	30 (50)	36 (60)

Chi-square: $p = 0.271$.

**Figure 5: Gestational category (preterm vs term) of study participant. Chi-square $p = 0.271$** **Table 6: Type of jaundice in study participants**

Type of jaundice	Control (n=60), n (%)	Study (n=60), n (%)
Breastfeeding jaundice	33 (55)	29 (48)
Physiological jaundice	27 (45)	31 (52)

Chi-square: $p = 0.465$.

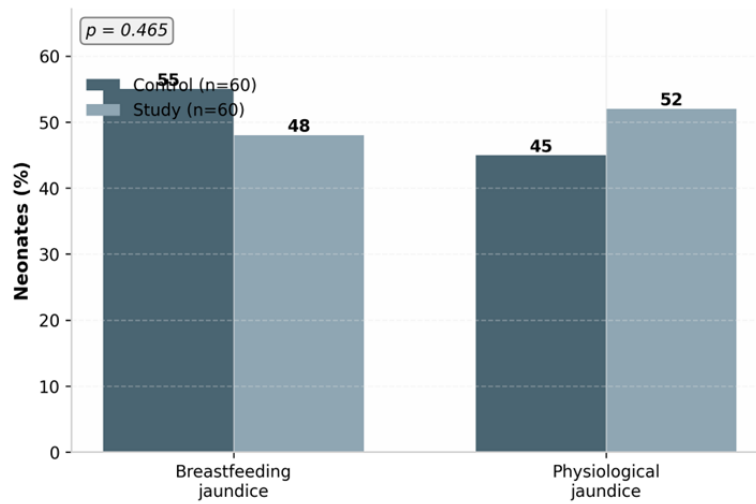


Figure 6: Type of jaundice in study participants. Chi-square $p = 0.465$

3.2 Treatment characteristics

Table 7: Phototherapy duration in study participants

Phototherapy duration (hours)	Control (n=60), n (%)	Study (n=60), n (%)
24	34 (57)	14 (23)
30	9 (15)	3 (5)
32	1 (2)	1 (2)
36	14 (23)	10 (17)
48	2 (3)	32 (53)
Mean $\pm$ SD	28.63 $\pm$ 6.20	39.23 $\pm$ 10.19

Chi-square for distribution: $p = 0.0001$; mean duration comparison: $p = 0.0001$.

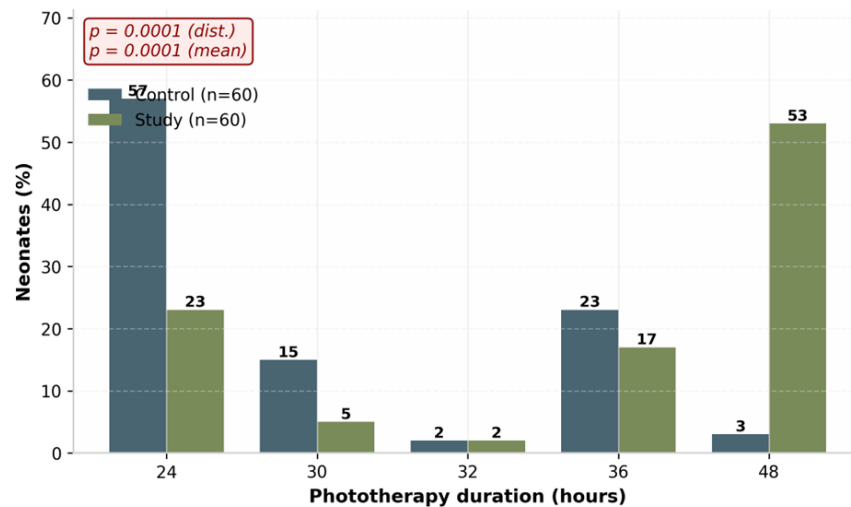


Figure 7: Phototherapy duration in study participant. $p = 0.0001$ (distribution and mean duration)

3.3 Biochemical outcomes

Table 8: Serum biochemical profile of study participants

Parameter	Control (n=60), Mean $\pm$ SD	Study (n=60), Mean $\pm$ SD	p-value
Serum bilirubin (mg/dL)	10.96 $\pm$ 1.67	14.41 $\pm$ 2.49	0.0001
Serum calcium (mg/dL)	9.22 $\pm$ 0.68	8.34 $\pm$ 0.73	0.0001
Serum magnesium	1.97 $\pm$ 0.22	2.05 $\pm$ 0.21	0.050

(mg/dL)			
Serum sodium (mEq/L)	138.59 ± 4.27	138.09 ± 4.48	0.534
Serum potassium (mEq/L)	4.54 ± 0.55	4.49 ± 0.58	0.627
Serum chloride (mEq/L)	102.81 ± 4.51	102.91 ± 4.24	0.906

Values are mean ± SD.

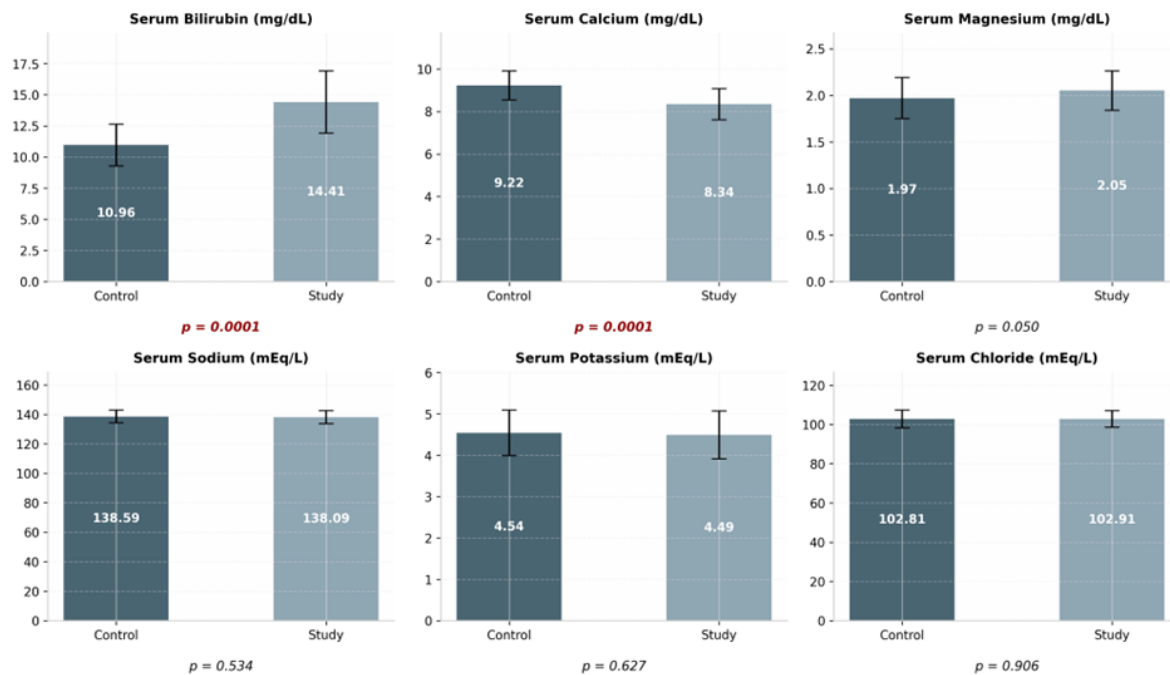


Figure 8: Serum biochemical profile of study participants. Bars show mean ± SD; p-values shown below each panel

Table 9: Adverse effects during follow-up

Adverse effect	Control (n=60), n (%)	Study (n=60), n (%)	p-value
Hypocalcemia	0 (0)	29 (48)	0.0001
None	60 (100)	31 (52)	

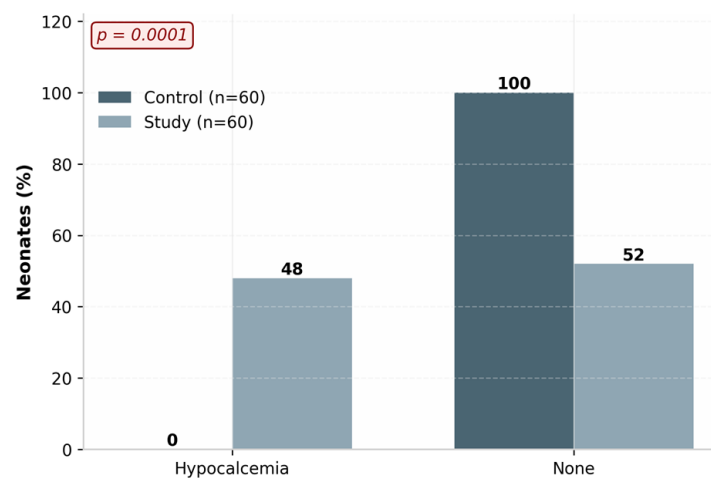


Figure 9: Adverse effects during follow-up. Chi-square p = 0.0001

3.4 Biochemical changes by gestational age

Table 10: Effect of therapy on serum electrolytes and bilirubin by gestational age

Parameter	Before therapy, Mean $\pm$ SD	After therapy, Mean $\pm$ SD	p-value
Gestational age < 37 weeks			
Serum bilirubin (mg/dL)	10.95 $\pm$ 1.64	14.38 $\pm$ 2.45	0.0001
Serum calcium (mg/dL)	9.18 $\pm$ 0.69	8.27 $\pm$ 0.82	0.0001
Serum magnesium (mg/dL)	1.95 $\pm$ 0.22	2.03 $\pm$ 0.22	0.091
Serum sodium (mEq/L)	138.94 $\pm$ 4.61	137.94 $\pm$ 4.90	0.378
Serum potassium (mEq/L)	4.45 $\pm$ 0.52	4.54 $\pm$ 0.63	0.530
Serum chloride (mEq/L)	103.11 $\pm$ 4.06	102.97 $\pm$ 4.21	0.891
Gestational age > 37 weeks			
Serum bilirubin (mg/dL)	10.99 $\pm$ 1.77	14.44 $\pm$ 2.60	0.0001
Serum calcium (mg/dL)	9.27 $\pm$ 0.69	8.43 $\pm$ 0.57	0.0001
Serum magnesium (mg/dL)	2.01 $\pm$ 0.22	2.07 $\pm$ 0.22	0.343
Serum sodium (mEq/L)	138.02 $\pm$ 3.69	138.29 $\pm$ 3.91	0.807
Serum potassium (mEq/L)	4.67 $\pm$ 0.57	4.41 $\pm$ 0.49	0.102
Serum chloride (mEq/L)	102.34 $\pm$ 5.22	102.82 $\pm$ 4.36	0.732

Values are mean $\pm$ SD as transcribed from the source dataset.

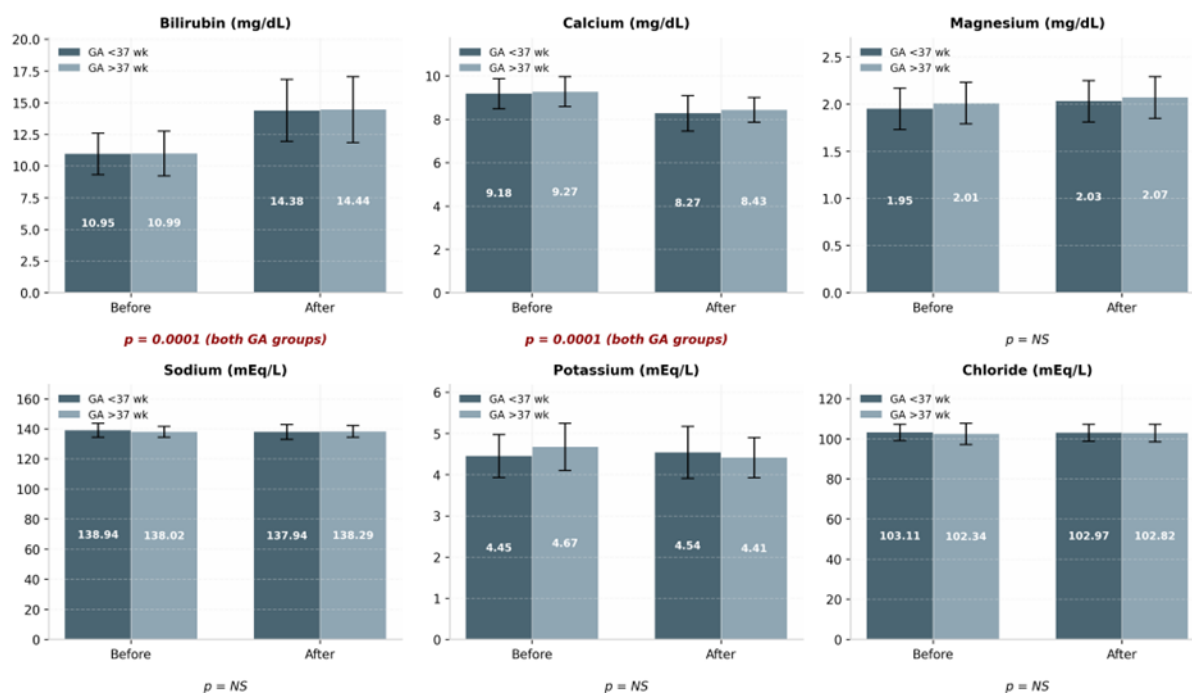


Figure 10: Effect of therapy on serum electrolytes and bilirubin by gestational age. Bars show mean $\pm$ SD; p-values shown below each panel

3.5 Biochemical profile by phototherapy duration

Table 11: Biochemical parameters after 24 hours of phototherapy

Parameter	Control (n=34), Mean $\pm$ SD	Study (n=14), Mean $\pm$ SD	p-value
Serum bilirubin (mg/dL)	11.15 $\pm$ 1.79	15.40 $\pm$ 2.40	0.0001
Serum calcium (mg/dL)	9.31 $\pm$ 0.64	8.48 $\pm$ 0.68	0.0001
Serum magnesium (mg/dL)	1.97 $\pm$ 0.22	2.10 $\pm$ 0.21	0.057
Serum sodium (mEq/L)	139.34 $\pm$ 4.43	138.19 $\pm$ 3.98	0.443
Serum potassium (mEq/L)	4.51 $\pm$ 0.50	4.61 $\pm$ 0.50	0.533
Serum chloride (mEq/L)	102.92 $\pm$ 4.78	103.56 $\pm$ 4.03	0.662

Values are mean $\pm$ SD.

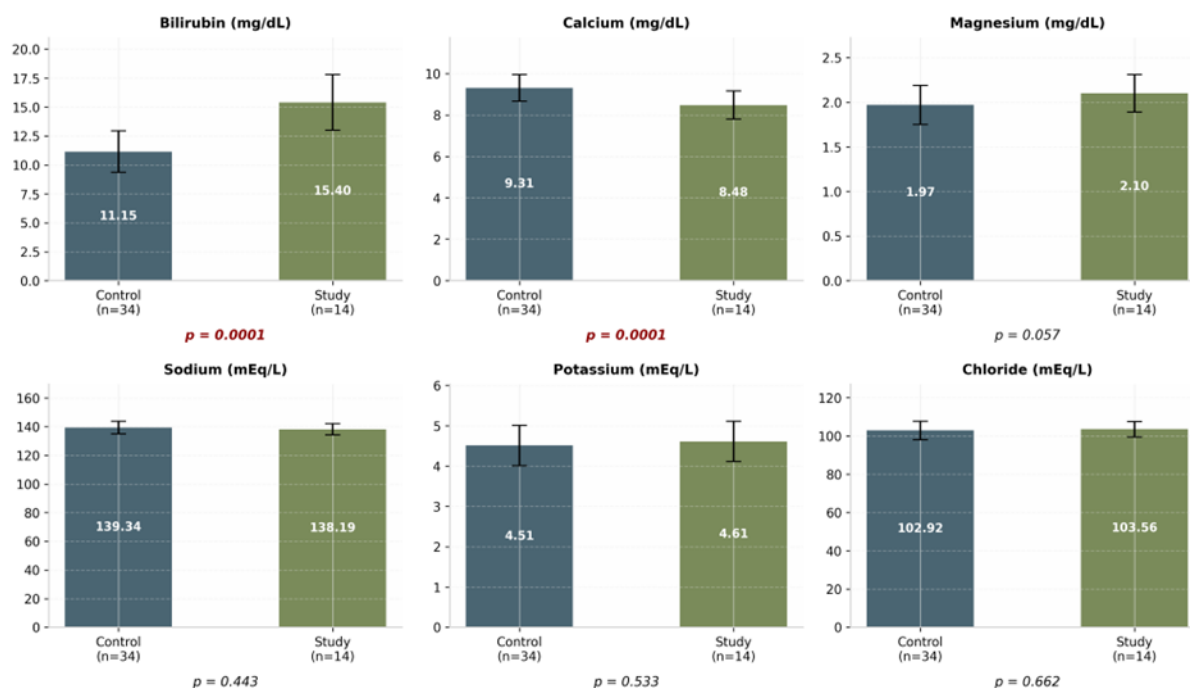


Figure 11: Biochemical parameters after 24 hours of phototherapy. Bars show mean $\pm$ SD; p-values shown below each panel

Table 12: Biochemical parameters after 30 hours of phototherapy

Parameter	Control (n=9), Mean $\pm$ SD	Study (n=3), Mean $\pm$ SD	p-value
Serum bilirubin (mg/dL)	11.32 $\pm$ 1.58	14.58 $\pm$ 2.77	0.026
Serum calcium (mg/dL)	9.22 $\pm$ 0.82	8.02 $\pm$ 0.56	0.042
Serum magnesium (mg/dL)	1.91 $\pm$ 0.22	2.10 $\pm$ 0.31	0.259
Serum sodium (mEq/L)	138.10 $\pm$ 3.91	140.50 $\pm$ 5.68	0.425
Serum potassium (mEq/L)	4.39 $\pm$ 0.68	4.53 $\pm$ 0.58	0.749
Serum chloride (mEq/L)	101.92 $\pm$ 4.43	100.07 $\pm$ 5.74	0.569

Values are mean $\pm$ SD.

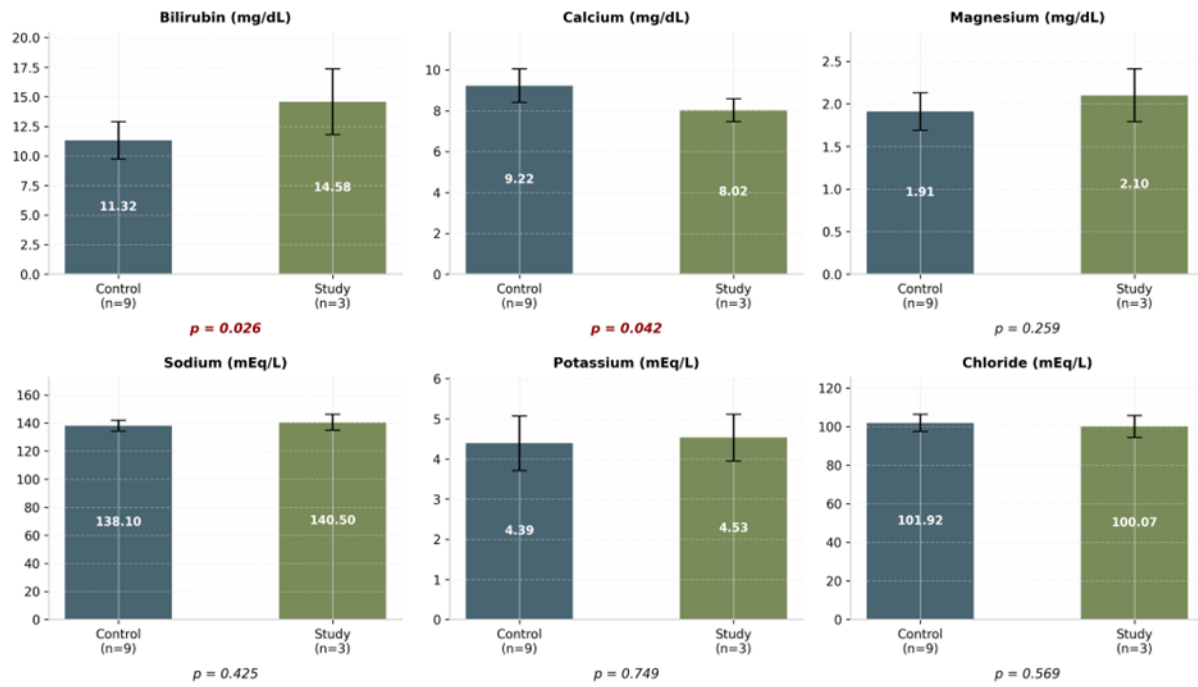


Figure 12: Biochemical parameters after 30 hours of phototherapy. Bars show mean $\pm$ SD; p-values shown below each panel

Table 13: Biochemical parameters after 36 hours of phototherapy

Parameter	Control (n=14), Mean $\pm$ SD	Study (n=10), Mean $\pm$ SD	p-value
Serum bilirubin (mg/dL)	10.41 $\pm$ 1.55	15.58 $\pm$ 2.69	0.0001
Serum calcium (mg/dL)	9.07 $\pm$ 0.72	8.33 $\pm$ 0.86	0.033
Serum magnesium (mg/dL)	2.02 $\pm$ 0.24	2.04 $\pm$ 0.20	0.853
Serum sodium (mEq/L)	137.95 $\pm$ 4.03	137.82 $\pm$ 4.73	0.943
Serum potassium (mEq/L)	4.61 $\pm$ 0.63	4.49 $\pm$ 0.62	0.656
Serum chloride (mEq/L)	103.93 $\pm$ 3.98	103.10 $\pm$ 4.11	0.625

Values are mean $\pm$ SD.

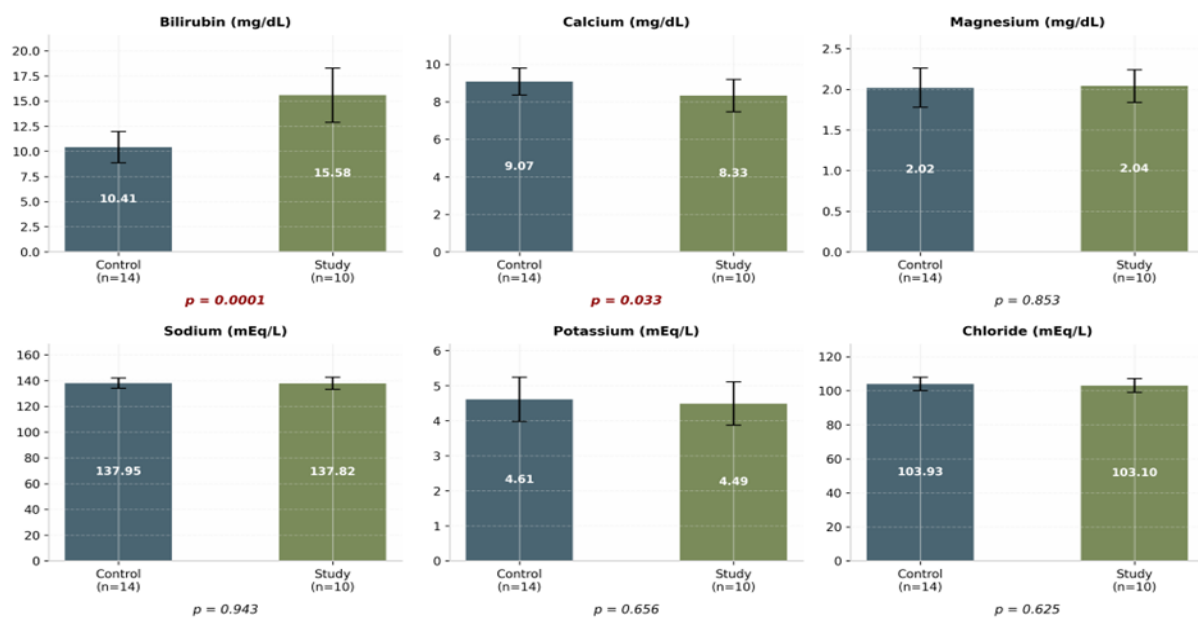


Figure 13: Biochemical parameters after 36 hours of phototherapy. Bars show mean $\pm$ SD; p-values shown below each panel

Table 14: Biochemical parameters after 48 hours of phototherapy

Parameter	Control (n=2), Mean $\pm$ SD	Study (n=32), Mean $\pm$ SD	p-value
Serum bilirubin (mg/dL)	10.66 $\pm$ 0.21	13.49 $\pm$ 2.17	0.021
Serum calcium (mg/dL)	8.46 $\pm$ 0.54	8.31 $\pm$ 0.75	0.780
Serum magnesium (mg/dL)	1.96 $\pm$ 0.12	2.04 $\pm$ 0.22	0.610
Serum sodium (mEq/L)	136.65 $\pm$ 5.87	138.15 $\pm$ 4.52	0.655
Serum potassium (mEq/L)	5.00 $\pm$ 0.00	4.45 $\pm$ 0.59	0.208
Serum chloride (mEq/L)	100.60 $\pm$ 0.14	102.84 $\pm$ 4.40	0.482

Values are mean $\pm$ SD.

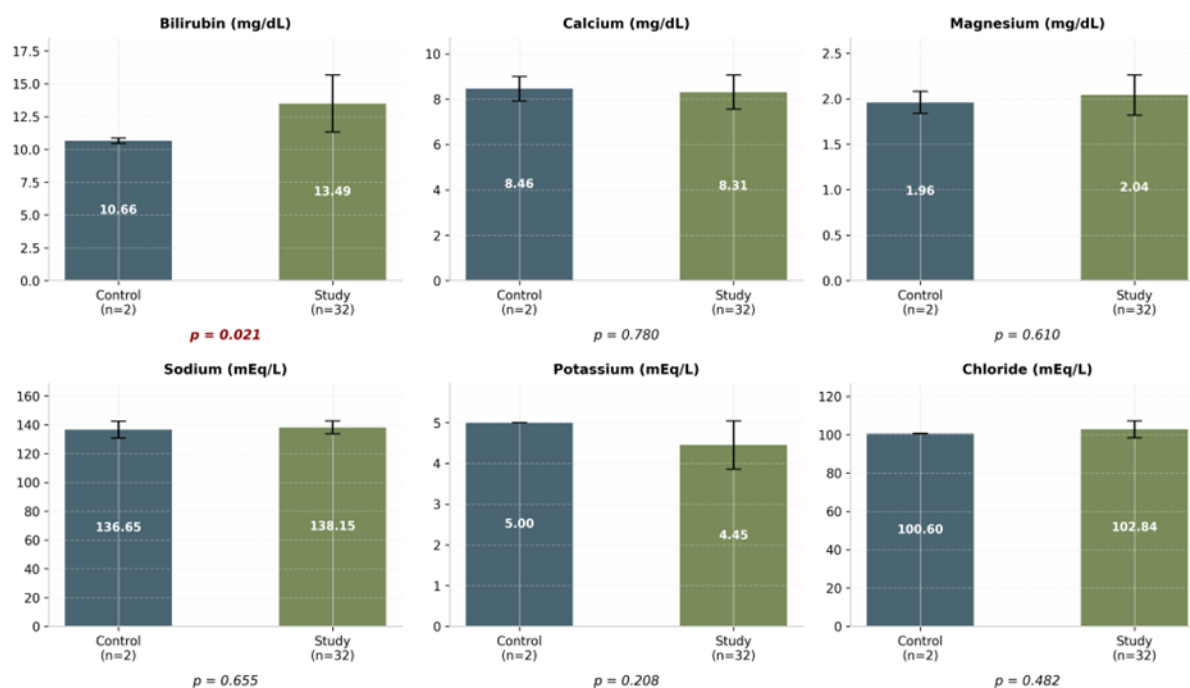


Figure 14: Biochemical parameters after 48 hours of phototherapy. Bars show mean $\pm$ SD; p-values shown below each panel

4. DISCUSSION

In this prospective observational study of 120 neonates with physiological hyperbilirubinemia treated at a tertiary care centre in Bihar, phototherapy was associated with a marked alteration in the calcium axis, while the remaining electrolytes remained comparatively stable. The two measurement cohorts were well matched with respect to age, sex, gestational age, birth weight, gestational category, and jaundice type, indicating that the biochemical differences detected after treatment are unlikely to be attributable to baseline demographic imbalance.

The cohort's demographic profile mirrors the natural history of neonatal jaundice. The mean age at assessment of approximately five to six days in both groups corresponds to the period when physiological bilirubin concentrations peak, as documented by Maisels and McDonagh [13] and by Bhutani et al. [14], who described the typical peak of physiological jaundice between the third and fifth days of life. Tosson et al.

similarly reported a mean age of around five days at the initiation of phototherapy, confirming that the age pattern observed here reflects routine clinical practice rather than selection bias [15]. The equal sex distribution observed in the present study is consistent with reports from Shlash Mohammad et al. and Jiang et al., who found that neonatal sex is not a strong independent determinant of hyperbilirubinemia and that balanced sex representation can be expected in unselected clinical samples [16, 17].

Gestational age is an established modifier of bilirubin handling because conjugating enzymes mature more slowly in preterm infants. Salman et al. and Radha Lavanya et al. demonstrated a higher incidence of significant jaundice among late preterm infants [18, 19], while Lin et al., in a systematic review, confirmed prematurity as a recognised risk factor [20]. In the present cohort, however, the proportion of preterm and term neonates did not differ significantly between the measurement groups, suggesting that gestational

maturity neither confounded the comparisons nor altered the direction of the biochemical response to phototherapy. Similarly, birth weight showed no significant between-group difference, echoing the observations of Norman et al. and Flaherman et al. that birth weight within the normal range does not independently predict jaundice severity, even though low birth weight infants remain a recognised high-risk group [21, 22].

The distribution of breastfeeding and physiological jaundice was likewise comparable between groups. This finding aligns with the descriptions of the American Academy of Pediatrics and the systematic review by Ip et al., which characterise breastfeeding-associated hyperbilirubinemia and physiological jaundice as overlapping expressions of normal neonatal adaptation rather than distinct pathological entities [23, 24].

The most striking treatment-related finding was the significantly longer duration of phototherapy in the post-therapy cohort. Because phototherapy duration functions as a marker of disease burden, this pattern is consistent with the guidance of the American Academy of Pediatrics Subcommittee on Hyperbilirubinemia and the observations of Maisels et al., who noted that neonates presenting with higher bilirubin burdens or additional risk factors require prolonged irradiation to achieve adequate clearance [25, 26]. Nuntnarumit et al. similarly correlated longer treatment sessions with higher peak bilirubin values [27].

The central biochemical observation was a significant decline in serum calcium after phototherapy, with a 48% incidence of hypocalcemia in the treated cohort and a highly significant between-group difference. This finding reproduces, in a regional Indian population, a phenomenon first described by Romagnoli et al. and subsequently confirmed by Jain et al. and Sethi et al. [10, 28, 29]. The prevailing mechanistic explanation implicates light-mediated suppression of pineal melatonin secretion, which disrupts the parathyroid hormone axis and favours skeletal calcium sequestration. Karamifar et al. and Eghbalian and Monsef documented significant calcium reductions in neonates undergoing prolonged phototherapy [30, 31], and Vigneshwar et al. provided supporting evidence of reduced melatonin concentrations during treatment [32]. Importantly, many affected neonates remain asymptomatic, so reliance on clinical observation alone would miss a substantial proportion of cases, reinforcing the argument for routine biochemical surveillance.

Calcium decline was demonstrable across treatment durations. After 24 and 30 hours of phototherapy, the between-group difference in calcium was highly significant, consistent with the observations of Sohail et al. and Gaafar et al. for short treatment courses [33, 34]. After 36 hours, the difference remained significant, in

keeping with the findings of Goyal et al. [35]. Interestingly, after 48 hours the calcium difference lost statistical significance, a pattern compatible with the reports of Gheshmi et al. and Pereira et al., who noted that calcium reduction does not always reach significance, particularly when treatment is moderate in duration and infants remain clinically stable with adequate hydration [36, 37]. This apparent attenuation at the longest duration should be interpreted cautiously given the small size of the 48-hour control subgroup.

In contrast to calcium, serum magnesium showed only borderline or non-significant variation across all treatment durations, in agreement with the prospective cohort data of Eghbalian et al., who concluded that magnesium homeostasis is generally preserved during phototherapy [38]. Sodium, potassium, and chloride likewise remained stable throughout, corroborating reports by Chinnappa and Rudrappa and Gözetici et al., who found no meaningful electrolyte disturbance beyond calcium during routine phototherapy when hydration and monitoring are maintained [39, 40]. The subgroup analysis by gestational age demonstrated that the pattern of a rising bilirubin and falling calcium after therapy was reproduced in both preterm and term neonates, indicating that gestational maturity did not materially modify the calcium response; this accords with the observations of Khan et al. and Jha et al., who identified hypocalcemia risk across gestational categories while noting greater vulnerability among preterm infants [41, 42].

Taken together, the findings indicate that the metabolic footprint of phototherapy is selective rather than generalised: calcium metabolism is the principal target, while sodium, potassium, chloride, and magnesium homeostasis is largely preserved. This selectivity has practical implications for resource-limited settings, where targeted monitoring of serum calcium may offer the greatest yield for a given laboratory expenditure, although broader electrolyte assessment remains advisable in preterm infants, those with prolonged treatment, and those with clinical deterioration.

Strengths of the Study

The present study has several strengths. First, it prospectively evaluated a clinically relevant question under real-world conditions in a population that is under-represented in the published literature. Second, the baseline comparability of the measurement cohorts across age, sex, gestational age, birth weight, and jaundice type minimises the risk that demographic imbalance explains the biochemical findings. Third, the study assessed a comprehensive electrolyte panel alongside serum bilirubin, allowing evaluation of treatment effects beyond a single analyte. Fourth, analyses stratified by gestational age and by

phototherapy duration provided insight into effect modification. Finally, the findings are directly translatable to routine practice in similar tertiary centres, where targeted calcium monitoring during phototherapy can be implemented at modest cost.

Future Recommendations

Future research should enrol larger, multicentre cohorts with serial rather than single post-treatment sampling to define the time course of calcium decline and its nadir with greater precision. Randomised or quasi-experimental designs comparing monitoring strategies would clarify whether routine calcium surveillance improves clinical outcomes. Studies should also incorporate ionised calcium, urinary calcium excretion, parathyroid hormone, and melatonin measurements to refine the mechanistic understanding of phototherapy-induced hypocalcemia. Preterm and low birth weight infants, who are biologically most vulnerable, warrant dedicated study. Finally, cost-effectiveness analyses conducted in resource-limited settings would help determine the optimal frequency of biochemical monitoring and inform locally applicable guidelines.

Limitations

This was a single-centre observational study with a modest sample size, and the subgroup analyses by treatment duration were limited by small cell counts, particularly in the 48-hour control subgroup. Treatment duration was not experimentally assigned, so confounding by indication cannot be excluded. Ionised calcium, parathyroid hormone, melatonin, and urinary calcium excretion were not measured. Maternal factors, feeding volumes, ambient temperature, and device irradiance were not standardised or analysed as covariates. Neonates with haemolytic disease, sepsis, and significant comorbidity were excluded, which improves internal validity but limits generalisability to sicker populations in whom electrolyte disturbance may be more pronounced.

6. CONCLUSION

Phototherapy for physiological neonatal hyperbilirubinemia was associated with a significant reduction in serum calcium and a 48% incidence of hypocalcemia, while serum magnesium, sodium, potassium, and chloride remained broadly stable across gestational ages and treatment durations. These findings confirm hypocalcemia as the most consistent metabolic complication of phototherapy and support the routine monitoring of serum calcium during treatment, particularly in resource-limited settings where laboratory surveillance must be prioritised. Larger controlled studies with mechanistic endpoints are needed to define optimal monitoring schedules and to establish whether

surveillance translates into measurable improvements in neonatal outcomes.

7. DECLARATIONS

Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of Darbhanga Medical College and Hospital, Laheriasarai. Written informed consent was obtained from the parents or legal guardians of all participants prior to enrolment.

Funding

No external funding was received for this study.

Competing interests

The authors declare no competing interests.

Authors' contributions

All authors contributed to the conception and design of the study, data collection, analysis and interpretation of the results, and preparation of the manuscript. All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

Acknowledgement

The authors thank the staff of the Special Newborn Care Unit, Department of Paediatrics, Darbhanga Medical College and Hospital, and the parents who consented to their infants' participation.

AI Use Disclosure

The authors declare that no generative artificial intelligence tools were used to generate or substantially modify the scientific content of this manuscript.

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