



PHOTOTHERAPY-ASSOCIATED CHANGES IN BIOCHEMICAL MARKERS AMONG NEONATES WITH HYPERBILIRUBINEMIA

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ABSTRACT:

Introduction: Hyperbilirubinemia is one of the commonest clinical problems encountered in the neonatal period, especially during the first week of life which can be classified into unconjugated & conjugated hyperbilirubinemia. Phototherapy (PT) is the current modality of choice for treatment of neonatal hyperbilirubinemia. The study intended to evaluate changes in serum electrolyte levels in neonates undergoing phototherapy for exaggerated physiological hyperbilirubinemia.

Aim: This study aims to comprehensively assess the biochemical changes (Sodium & Potassium) associated with phototherapy in neonates with hyperbilirubinemia.

Materials and Methods: A total of 50 neonates were included in the study. Blood samples were taken at the start and end of phototherapy to measure serum Sodium & Potassium.

Results: The incidence of hypernatraemia and hyperkalaemia after phototherapy was found to be statistically significant (P values <0.001 and <0.001 respectively) before and after phototherapy.

Conclusion: Although phototherapy is well established as an effective treatment for neonatal hyperbilirubinemia, its influence on other biochemical parameters is also significant. Consequently, neonates receiving phototherapy should be carefully monitored for these changes throughout the course of treatment.

Keywords: Phototherapy, neonatal hyperbilirubinemia, biochemical parameters in neonates.

Introduction:

Neonatal hyperbilirubinemia (NH) is one of the most common medical conditions affecting newborns, particularly during their first week of life. It is characterized by yellowish discoloration of the skin and sclera due to elevated bilirubin levels in the blood. Approximately 60% of full-term infants and 80% of preterm infants are affected by Neonatal hyperbilirubinemia globally ⁽¹⁻³⁾. The condition arises from the accumulation of unconjugated bilirubin (UCB) in the bloodstream, resulting from factors such as immature hepatic enzymes, increased bilirubin production, ineffective conjugation, and delayed bilirubin excretion ⁽⁴⁻⁷⁾. Unconjugated bilirubin can cross the blood-brain barrier, leading to bilirubin-induced neurological damage, including kernicterus ⁽⁸⁾. Severe neonatal

hyperbilirubinemia (HB) is a prevalent etiology of “sensorineural hearing loss (SNHL) and auditory neuropathy (AN)”⁽⁹⁾. If left unmanaged, neonatal hyperbilirubinemia may result in hyperbilirubinemic encephalopathy or newborn mortality. Furthermore, surviving newborns have a significant chance of neurological impairment, which may present as cerebral palsy, epilepsy, sensorineural hearing loss, or cognitive deficiencies. Phototherapy is a commonly employed therapeutic intervention in newborn care, serving as the preferred treatment for jaundice. This non-invasive technique involves exposing the neonate to blue-green light (wavelengths 460–490 nm), which converts bilirubin into water-soluble isomers such as lumirubin that can be excreted through urine and stool^(10,11,12). The primary mechanisms include configurational isomerization, structural isomerization, and photo-oxidation, all of which facilitate bilirubin clearance^(13,14). Phototherapy can decrease bilirubin levels in all babies, irrespective of gestational age, hemolysis status, or skin pigmentation. Despite its efficacy in reducing bilirubin levels and minimizing the need for invasive procedures like exchange transfusion, phototherapy is not without side effects. These include dehydration, temperature instability, dermal rashes, diarrhea, retinal damage, bronze baby syndrome, altered blood flow distribution, genotoxicity and electrolyte imbalances such as hypocalcemia and hypomagnesemia^(15,16,17, 18, 19, 20).

Electrolytes are essential ions in the body that play pivotal roles in maintaining cellular function, fluid balance, and overall physiological stability. Understanding the intricate relationship between phototherapy and electrolyte changes is crucial for providing comprehensive care to neonates with unconjugated hyperbilirubinemia⁽²¹⁻²⁵⁾. Therefore, the present study was intended to determine the effect of phototherapy on various biochemical parameters including bilirubin, serum electrolytes in NH patients before and after phototherapy.

Materials and Methods:

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU), Department of Paediatrics of Chirayu Medical College & Hospital, Bhopal (M.P.), India over a period of 18 months (March 2023 to August 2024) after taking informed consent from parents and approval from the institutional ethics committee.

Sample Size: The study included 50 neonates (both term and preterm) with hyperbilirubinemia receiving phototherapy. Neonates were categorized as:

- Preterm Neonates: Gestational age 34 to less than 37 weeks.
- Term Neonates: Gestational age 37 to 40 weeks.

Inclusion Criteria: Neonates with hyperbilirubinemia requiring phototherapy.

Exclusion Criteria:

- Neonates with jaundice requiring exchange transfusion.
- Neonates with birth asphyxia, sepsis, respiratory distress, ABO/Rh incompatibility, convulsions, or IUGR.
- Major or life-threatening congenital malformations.
- Neonates with conjugated hyperbilirubinemia or prolonged jaundice.
- Neonates requiring phototherapy for less than 24 hours

Sample Collection and Processing: A comprehensive clinical history was recorded for each neonate, including gestational age, mode of delivery, birth weight, Apgar scores, maternal medical history, antenatal and perinatal risk factors, and feeding status. 2ml of venous blood samples was collected with due antiseptic method from the neonates before initiating phototherapy and after its completion and sent in biochemistry lab for the analysis of total bilirubin, indirect bilirubin and serum electrolytes (sodium & potassium). Comparative study was done between these two groups to evaluate the changes in electrolytes. During phototherapy, neonate's genitalia and eyes were shielded for safety. Following data collection, statistical analyses were performed on the compiled results.

Results:

A total of 50 neonates (both term and preterm) with hyperbilirubinemia were included in the study. Amongst study participants, 25 (52%) were females and 24 (48%) were males (Table: 1). Of all neonates, majority were Early term: 23 followed by late preterm: 15, full term: 9 and moderately preterm: 3 (Table: 2).

Table 1: Gender distribution of the study sample

GENDER	FREQUENCY (N=50)	PERCENTAGE (%)
Female	26	52.0
Male	24	48.0

Table 2: Distribution based on Gestational age of the study participants

GESTATIONAL AGE	FREQUENCY (n=50)	PERCENTAGE (%)
Moderately Preterm (32 to < 34 weeks)	3	6%
Late Preterm (34 to <37 weeks)	15	30%
Early Term (37 to <39 weeks)	23	46%
Full-term (39 to <41 weeks)	9	18%
Post-term (41 to <42 weeks)	0	0

Table 3: Comparative evaluation of Bilirubin, Serum Electrolytes- Sodium and Potassium before & after Phototherapy

PARAMETERS	PRE PHOTOTHERAPY	POST PHOTOTHERAPY	p VALUE
Bilirubin	14.42 ± 1.5	8.16 ± 2.04	< 0.001
Sodium	134.06±6.16	137.97±2.41	< 0.001
Potassium	3.2650 ± 0.50	5.94 ± 0.54	< 0.001

Table 4: Side effects of Phototherapy

PARAMETERS	FREQUENCY	PERCENTAGE
Rashes	20	40.8%
Dehydration	8	16.3%
Overheating	9	18.4%
Loose stools	9	18.4%
Bronze baby syndrome	0	0.0%

The most common side effect was rashes, reported in 20 neonates (40.8%), followed by overheating and loose stools, both seen in 9 neonates (18.4%). Dehydration was noted in 8 cases (16.3%), whereas bronze baby syndrome was not observed in any case (0.0%).

These findings indicate that while phototherapy is generally safe, a considerable number of neonates may experience dermatological or thermoregulatory side effects, underscoring the importance of vigilant monitoring during treatment.

Discussion:

Neonatal hyperbilirubinemia affects both term and preterm neonates within their first few weeks of life^(26, 27). Treatment of choice for unconjugated hyperbilirubinemia is phototherapy. The guidelines for using phototherapy that were published in 2004 by the American Academy of Pediatrics are based primarily on the Total Serum Bilirubin (TSB) levels⁽²⁸⁾. Therefore, the commonly used criteria for treatment of NH are based on TSB measurements. Jaundice appears in the newborn infants as their livers do not make sufficient bilirubin glucuronyl transferase enzyme because of which high levels of unconjugated bilirubin appear in blood. Phototherapy converts bilirubin into water soluble isomers lumibilirubin that are easily eliminated through the gastrointestinal tract or lost in urine.

In the present study, among the 50 neonates included, 26 (52%) were female and 24 (48%) were male, showing an almost equal distribution. Similar trends have been reported in studies such as by Beniwal et al.⁽²⁹⁾, where a nearly equal male-to-female ratio (1.1:1) was observed among jaundiced neonates requiring phototherapy, reinforcing the idea that gender may not significantly influence the incidence of neonatal hyperbilirubinemia. In contrast, observations of Kale et al.⁽³⁰⁾, reported male predominance among neonates with hyperbilirubinemia. The predominance of male neonates could be attributed to either biological susceptibility or societal factors favouring the admission and treatment of male children.

In the present study, in terms of gestational age, 46% (n=23) of the neonates were early term (37 to <39 weeks), 30% (n=15) were late preterm (34 to <37 weeks), 18% (n=9) were full-term, and 6% (n=3) were moderately preterm (32 to <34 weeks). No post-term neonates were observed (Table 2). This distribution highlights the vulnerability of early term and late preterm infants to hyperbilirubinemia. Early term neonates, despite being close to full term, have underdeveloped hepatic glucuronosyltransferase activity, increasing their risk for significant hyperbilirubinemia. As shown by Maisels and Kring⁽¹⁸⁾, late preterm infants are three times more likely to be readmitted for jaundice compared to term infants.

A statistically significant reduction was seen in bilirubin levels, from 14.42 ± 1.52 mg/dL to 8.16 ± 2.04 mg/dL ($p < 0.001$). This clearly validates the efficacy of phototherapy as the primary therapeutic intervention for neonatal hyperbilirubinemia. The results align closely with the outcomes reported by Bhutani et al.⁽³¹⁾, who demonstrated similar reductions post-48 hours of therapy. The findings are also in accordance with Suneja et al.⁽³²⁾ and Shashavari et al.⁽³³⁾

In the present study Sodium levels showed a significant rise post-phototherapy, from a mean of 134.06 ± 6.17 mmol/L to a mean of 137.97 ± 2.41 mmol/L ($p < 0.001$). This finding contrasts with the study by Plavskii et al., who reported a slight but statistically insignificant drop in serum sodium post-phototherapy, attributing it to insensible water loss due to increased transepidermal evaporation under phototherapy units⁽³⁴⁾. However, our results align with those of Majumder et al.⁽³⁵⁾, who observed a similar elevation in sodium levels, possibly due to improved renal perfusion after bilirubin reduction. Gozetic AM et al.⁽³⁶⁾ observed slight decline in sodium levels while no change in potassium levels. A significant reduction of mean serum potassium and magnesium levels were found after phototherapy in study done by Bezboruah G et al.⁽³⁷⁾

Potassium levels in this study rose significantly from a mean of 3.27 ± 0.50 mmol/L to a mean of 5.94 ± 0.54 mmol/L after phototherapy ($p < 0.001$). Elevated potassium levels post-phototherapy has also been noted by Purohit A., who suggested this might result from phototherapy-induced hemolysis or intracellular potassium release⁽³⁸⁾. Although transient, such changes may pose a clinical risk in premature or critically ill neonates. Uddin MB et al.⁽³⁹⁾ suggested neonates undergoing phototherapy are at risk of developing hyponatraemia, hypokalaemia and hypocalcaemia. The incidence of hypocalcaemia and hypokalaemia was more in neonates with LBWs as compared to neonates with normal birth weight observed in study of Husain A et al.⁽⁴⁰⁾

Phototherapy alters fluid and electrolyte balance due to increased insensible water loss and enhanced renal perfusion, leading to fluctuations in biochemical parameters. The rise in potassium and calcium levels in both sexes could be a result of cellular shifts or increased bone resorption under phototherapy-induced stress⁽⁴¹⁾. The significant rise in sodium in females—but not in males—may reflect gender-based differences in water balance regulation or hormonal modulation in neonates.

Conclusion:

Phototherapy is highly effective in reducing serum bilirubin levels in neonates with hyperbilirubinemia, regardless of birth weight, gestational age, sex, or feeding type. However, it significantly alters several biochemical parameters. Electrolyte shifts—particularly rises in potassium and sodium levels suggest metabolic and renal stress, especially in preterm and low birth weight neonates. Single surface phototherapy (SSPT) had a more pronounced effect on these parameters than double surface phototherapy (DSPT). While most neonates tolerated therapy well, side effects like rashes, overheating, and dehydration were common. The study highlights the importance of regular

monitoring during phototherapy to detect and manage potential complications, ensuring safe and effective treatment outcomes.

Phototherapy significantly altered potassium levels across all gestational categories. Sodium levels were most significantly affected in late preterm and early term neonates.

Phototherapy effectively reduces serum bilirubin in neonates but also results in significant alterations in haematological and biochemical parameters. Monitoring of electrolytes, renal function, and haematological indices is essential, especially in preterm, low birth weight, and IUGR infants. Despite some minor side effects, phototherapy remains a safe and effective treatment for neonatal hyperbilirubinemia.

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