



Original Article

## A Study on Electrolyte Changes in Newborns with Unconjugated Hyperbilirubinemia Treated with Phototherapy in A Tertiary Care Hospital

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### ABSTRACT

**Background:** Neonatal jaundice is a common problem seen in newborns, particularly in the first week of life. Phototherapy is a widely accepted modality of treatment for neonatal jaundice and is largely considered harmless. It does cause some minor side effects, but significant problems like electrolyte disturbances need to be looked for and managed appropriately. **Methodology:** This is a hospital-based prospective observational study conducted on 100 eligible neonates admitted in the Neonatal Intensive Care Unit of Government General Hospital, Kakinada from July 2023 to June 2024. **Results:** In the present study, 52 (52%) were males, and 48 (48%) were females, with the male-to-female ratio being 1.08:1. The incidence of hypocalcemia following phototherapy was 16%, and it was higher in LBW (28.58%) and preterm neonates (27.9%). The incidence of hypocalcemia was 10.6%, 15.78%, and 33.33% in babies who received phototherapy for 24-48 hours, 48-72 hours and 72-96 hours respectively. The mean total serum calcium before phototherapy was  $8.972 \pm 0.452$  and after phototherapy was  $8.155 \pm 0.617$ . The incidence of hyponatremia following phototherapy was 6%, noticed only in preterm (13.9%) and low birth weight neonates (14.2%). The incidence of hyponatremia was 4.25%, 5.26%, and 13.3% in patients receiving phototherapy for 24-48 hours, 48-72 hours, and 72-96 hours, respectively. The mean serum sodium before phototherapy was  $141.350 \pm 2.50$  and  $137.063 \pm 3.046$  after phototherapy. Only preterm neonates had hyponatremia (13.9%). **Conclusions:** As preterms and low birth weight babies are at higher risk, periodic monitoring of electrolytes after phototherapy in the neonates can prevent dyselectrolytemia, in turn prevent the related complications.

**Keywords:** Neonatal Jaundice, Phototherapy, Dyselectrolytemia, Hypocalcemia, Hyponatremia.

### INTRODUCTION

Phototherapy is the most common treatment modality for the management of neonatal jaundice in newborns. Neonatal jaundice is a common problem seen in babies in the first few days of life. About 80% of preterm babies and 60% of term babies can develop jaundice [1][2]. In most cases (30% to 66%), jaundice is physiological, harmless, transient, and does not require treatment. But in a few babies, it can be pathological and needs management in the form of phototherapy or exchange transfusion in severe cases. Hyperbilirubinemia with serum bilirubin levels more than 15mg/dl is considered pathological and is seen in around 5% to 25% of newborns, as per Indian studies [3]. Phototherapy is a safe method and is considered largely harmless, with a few minor and temporary problems like loose stools, dehydration, skin rashes, etc.

Some serious effects, such as electrolyte imbalances like hypocalcemia and hyponatremia, can occur, particularly in preterm babies, thereby warranting close monitoring of all babies receiving phototherapy.

## MATERIALS & METHODS:

This is a hospital-based prospective observational study conducted on 100 eligible neonates admitted to the Neonatal Intensive Care Unit of the Department of Neonatology, Government General Hospital, Kakinada, from July 2023 to June 2024, after taking informed consent from parents, and was approved by the Institutional Ethics Committee with registration number IEC/RMC/2023/1042.

Neonates who received phototherapy for unconjugated hyperbilirubinemia were included in this study. Those neonates with conjugated hyperbilirubinemia or associated with co-morbidities like birth asphyxia, sepsis, renal failure, mothers taking anticonvulsant drugs, abnormal electrolyte findings before phototherapy, babies treated with exchange transfusion, and those babies with jaundice lasting for >14 days were excluded from the study.

The details of included babies were recorded in a predesigned proforma. The details included were mode of delivery, gender, gestational age, birth weight, type of feeding, time of jaundice onset, cause of jaundice, and duration of phototherapy. Venous blood samples were collected from the neonates and sent for total bilirubin, direct bilirubin, electrolytes, and blood group. Total & direct bilirubin were measured by the Diazo method, electrolytes (sodium) by an Erba autoanalyzer, and calcium by the Arnezo method. Blood group of newborns was analyzed by the antisera method.

Serum total calcium and sodium were estimated serially at 0 hours (first sample), 24 hours, 48 hours of phototherapy, and at discontinuation of phototherapy, whichever is appropriate, and any changes in serum calcium and sodium after phototherapy were recorded. Hypocalcemia was considered when total serum calcium levels were less than 8 mg/dl and Hyponatremia if the total serum sodium levels were less than 135 Meq/l.

## STATISTICAL ANALYSIS:

The data were tabulated and statistically analyzed using SPSS version 24. The descriptive data were expressed as means and proportions. The difference in the parameters before and after phototherapy was analyzed by a paired t-test. The results with p-values less than 0.05 were considered statistically significant.

## RESULTS

A total of 100 neonates with unconjugated hyperbilirubinemia receiving phototherapy were enrolled. Male babies constituted 52%, whereas female babies constituted 48% of the study population. 57% of the babies were born at a gestational age of >37 weeks. 32% and 11% were born at gestational age of 34-36 weeks and 32-33 weeks, respectively. Over half of the babies (58%) weighed more than 2.5 kg. 37% weighed between 1.5-2.5 kg and 5% weighed less than 1.5 kg. 54% of babies were exclusively breastfed, and 46% of babies were formula-fed.

**Table 1: Shows general characteristics of the study population.**

| S No | Parameter                       | Number(%) |
|------|---------------------------------|-----------|
| 1    | <b>Gender</b>                   |           |
|      | Male                            | 52(52%)   |
|      | Female                          | 48(48%)   |
| 2    | <b>Gestational Age in weeks</b> |           |
|      | 32-33                           | 11(11%)   |
|      | 34-36                           | 32(32%)   |
|      | 37+                             | 57(57%)   |
| 3    | <b>Birth weight in Kgs</b>      |           |
|      | <1.5                            | 5(5%)     |
|      | 1.5-2.5                         | 37(37%)   |
|      | >2.5                            | 58(58%)   |
| 4    | <b>Type of feeding</b>          |           |
|      | Exclusive breastfeeding         | 54(54%)   |
|      | Formula feeds                   | 46(46%)   |

53% of the babies had jaundice after 48 hours, 36% had jaundice between 24 and 48 hours, and 11% had jaundice within 24 hours. The cause of jaundice was hemolytic in 54% of cases and non-hemolytic in 46% of cases. 47% of babies received phototherapy for 24-48 hours, 38% for 48-72 hours, and 15% for 72-96 hours. Electrolyte abnormalities were detected in 22% of the babies in the study. Hypocalcemia was noted in 16%, whereas hyponatremia was noted in 6% of the babies.

The majority of the babies (62.5%) did not have any symptoms of hypocalcemia. Jitteriness was noted in 25%, and seizures were noted in 12.5% of cases. None of the six babies showed any symptoms of hyponatremia. All six babies were asymptomatic.

**Table 2: Shows clinical parameters of the study population.**

| S No | Parameter                           | NUMBER(%) |
|------|-------------------------------------|-----------|
| 1    | <b>Time of Onset of Jaundice</b>    |           |
|      | Within 24 hours                     | 11(11%)   |
|      | 24-48 hours                         | 36(36%)   |
|      | After 48 hours                      | 53(53%)   |
| 2    | <b>Cause of Jaundice</b>            |           |
|      | Hemolytic                           | 54        |
|      | Non-hemolytic                       | 46        |
| 3    | <b>Duration of Phototherapy</b>     |           |
|      | 24-48 hours                         | 47(47%)   |
|      | 48-72 hours                         | 38(38%)   |
|      | 72-96 hours                         | 15(15%)   |
| 4    | <b>Electrolyte abnormalities</b>    |           |
|      | Hypocalcemia                        | 16(16%)   |
|      | Hyponatremia                        | 6(6%)     |
| 5    | <b>Symptoms due to Hypocalcemia</b> |           |
|      | Seizures                            | 2(12.5%)  |
|      | Jitteriness                         | 4(25%)    |
|      | Asymptomatic                        | 10(62.5%) |
| 6    | <b>Symptoms due to Hyponatremia</b> |           |
|      | Asymptomatic                        | 6         |
|      | Symptomatic                         | 0         |

**Table 3: Shows Duration of phototherapy vs Serum Sodium and Calcium**

| S No | ELECTROLYTE          | 0 Hrs | 24-48 Hours | 48-72 Hours | 72-96 Hours |
|------|----------------------|-------|-------------|-------------|-------------|
| 1    | <b>Serum Calcium</b> |       |             |             |             |
|      | <7mg/dl              | 0     | 1           | 1           | 0           |
|      | 7-8mg/dl             | 0     | 4           | 5           | 5           |
|      | >8mg/dl              | 100   | 95          | 47          | 10          |
|      | Total                | 100   | 100         | 53          | 15          |
| 2    | <b>Serum Sodium</b>  |       |             |             |             |
|      | <135 Meq/l           | 0     | 2           | 2           | 2           |
|      | 135-145 Meq/l        | 100   | 98          | 51          | 13          |
|      | Total                | 100   | 100         | 53          | 15          |

Hypocalcemia was seen in 5 babies after 24-48 hours of phototherapy, in 6 babies after 48-72 hours of phototherapy, and in 5 babies after 72 hours of phototherapy. The mean serum total calcium at 0 hours, 24-48 hours, 48-72 hours, and 72-96 hours were  $8.972 \pm 0.412$ ,  $8.543 \pm 0.493$ ,  $8.254 \pm 0.618$ , and  $7.872 \pm 0.561$  respectively.

Hyponatremia was seen in 2 babies after 24-48 hours of phototherapy, in 2 babies after 48-72 hours of phototherapy, and in another 2 babies after 72 hours of phototherapy. The mean serum sodium levels at 0 hours, 24-48 hours, 48-72 hours and 72-96 hours were  $141.35 \pm 2.50$ ,  $139.4 \pm 2.42$ ,  $137.55 \pm 3.080$ , and  $137.313 \pm 2.632$  respectively.

**Table 4: Shows Association of Hypocalcemia and hyponatremia with various clinical parameters of the study population.**

|                     | Hypocalcemia | P value          | Hyponatremia | P value      |
|---------------------|--------------|------------------|--------------|--------------|
| <b>Birth Weight</b> |              | <b>&lt;0.001</b> |              | <b>0.001</b> |

|                                 |           |        |           |       |
|---------------------------------|-----------|--------|-----------|-------|
| <1.5 kgs(5)                     | 5(100%)   | <0.001 | 3(60%)    | 0.001 |
| 1.5-2.5 kgs (37)                | 7(8.9%)   | <0.001 | 3(8%)     | 0.001 |
| >2.5 (58)                       | 4(6.89%)  | <0.001 | 0(0%)     | 0.001 |
| <b>Gestational Age in weeks</b> |           |        |           |       |
| 32-34 (11)                      | 5(45.45%) | 0.004  | 4(36.36%) | 0-.02 |
| 34-36 (32)                      | 7(21.87%) | 0.004  | 2(6.35%)  | 0-.02 |
| >37 (57)                        | 4(7.02%)  | 0.004  | 0(0%)     | 0-.02 |
| <b>Feeding</b>                  |           |        |           |       |
| Breastfeeding(54)               | 5(9.25%)  | 0.004  | 6(11.1%)  | 0.12  |
| FORMULA FEEDS(46)               | 11(23.9%) | 0.004  | 0(0%)     | 0.12  |
| <b>Duration of phototherapy</b> |           |        |           |       |
| 24-48hr(47)                     | 5(10.6%)  | 0.48   | 2(4.25%)  | 0.19  |
| 48-72hr(38)                     | 6(15.78%) | 0.48   | 2(5.26%)  | 0.19  |
| 72-96hr(15)                     | 5(33.33%) | 0.48   | 2(13.3%)  | 0.19  |

All the babies weighing less than 1.5 kg had hypocalcemia. Among babies weighing 1.5 kg to 2.5 kg and more than 2.5 kg, 18.9% and 6.89% showed hypocalcemia, respectively. This association was statistically significant. 60% of babies with a birth weight less than 1.5 kg and 8% of babies with a birth weight between 1.5- 2.5 kg had hyponatremia. Babies above 2.5 kg didn't develop hyponatremia. The difference was statistically significant.

The incidence of both hypocalcemia and hyponatremia was higher in newborns of 32-34 weeks gestational age compared to newborns of 34-36 weeks and more than 37 weeks gestation. The difference was statistically significant. Hypocalcemia was reported in 9.25% of breastfed babies and 23.9% of formula-fed babies. Hyponatremia was seen in breastfed babies only. The association was found to be statistically significant.

Incidence of hypocalcemia was 10.6%, 15.78% and 33.33% after 24-48hours, 48-72 hours and 72-96 hours of phototherapy. Incidence of hyponatremia was 4.25%, 5.26%, and 13.3% after 24-48 hours, 48-72 hours. and 72-96 hours of phototherapy, respectively. There was increased incidence of hypocalcemia and hyponatremia with increasing duration of phototherapy.

**However, this association was not found to be statistically significant.**

## DISCUSSION

Neonatal jaundice is an important problem in the first week of life. Jaundice is attributable to physiological immaturity of neonates to handle increased bilirubin production. The use of phototherapy has decreased the need for exchange transfusion.

This study was carried out in 100 neonates with unconjugated hyperbilirubinemia to determine the impact of phototherapy on serum sodium and serum calcium. The observed changes in serum electrolytes hold significance in managing hyperbilirubinemia. The correlation analysis between electrolyte changes and duration of phototherapy is a crucial aspect of this study. It aligns with existing literature that underscores the importance of monitoring electrolyte levels during phototherapy.

In the present study, 52 (52%) were males, and 48 (48%) were females, with a male: female ratio of 1.08:1. This is similar to other studies done by Deepak Kumar Garg et al (56% males)[4] and Varsha Reddy et al. (54.9% males)[5]. In the present study, out of 100 neonates, 47 were preterm, and 57 were term neonates, which is similar to Arora et al.'s study[6]. 59.1%, 59.4%, and 60% of babies were term in the studies conducted by Varsha Reddy et al[5], Karamifar et al [7] and Yadav et al[8].

In the present study, out of 100 neonates, low birth weight babies (<2.5 kg) were 42 and normal birth weight babies (>2.5 kg) were 58. The mean birth weight of the study subjects was 2.532kgs±0.6128. Most of the babies included in the study were appropriate for gestational age. Normal birth weight babies outnumbered low birth weight babies. Studies by Reddy et al.(77%)[9] and Jena et al. (77%)[10] showed a higher number of babies with birth weight more than 2.5 kg, similar to the present study.

The mean total serum bilirubin (TSB) in the present study group was 16.89±0.68mg/dl and 18.52±1.91mg/dl in preterm and term neonates, respectively. Similarly, studies done by Karamifar et al[7] and Reddy et al.[9] showed serum bilirubin of 16.2±3.0 mg/dl and 16.98±1.78mg/dl in preterm, 18.0±2.4mg/dl and 17.52mg/dl in term babies. In the study by Taheri et al., mean total serum bilirubin in term neonates were 20.1±3.3mg/dl[11]. The mean duration of phototherapy in the present study was 54.240±15.86 hours, which was comparable to other studies by Akande et al. (3days )and Reddy et al. (37.65±11.06hours)[12][9].

In the present study, out of 100 neonates, after treatment with phototherapy for unconjugated hyperbilirubinemia, 16 neonates had hypocalcaemia (serum total calcium less than 8 mg/dl). The incidence of hypocalcaemia was 13.1% and 22% in studies done by Reddy et al.[9] and Jena et al.,[10] respectively. Hypocalcemia was the most commonly reported electrolyte abnormality in studies by Garg et al [12] and P.Indira et al.[13]. In the current cohort, 16% of neonates developed hypocalcemia following phototherapy. When stratified by gestational age, the incidence rose markedly to 27.9% among preterm infants, while only 7.1% of term infants were affected—a difference that reached statistical significance (P = 0.004). Karamifar et al. found hypocalcemia in 22.6% of preterm and 8.7% of term infants, and aligning with the pattern identified in this study[7]. Sethi and colleagues reported even higher rates, with hypocalcemia occurring in 90% of preterm and 75% of full-term babies after phototherapy underscoring a consistently greater vulnerability among the premature group[14]. However, in contrast, Arora et al. described a reversal of this trend, with term infants exhibiting a higher frequency of hypocalcemia than their preterm counterparts[6].

In the present study, hypocalcemia was more common in low-birth-weight babies (<2.5 kg) (28.58%) compared to normal birth weight babies (6.89%), which is statistically significant. Reddy et al. reported hypocalcemia in 36.2% low birth weight neonates and 6.2% of normal birth weight neonates, respectively[5]. In this cohort, hypocalcemia developed in 23.9% (11/46) of infants fed with formula, whereas only 9.3% (5/54) of exclusively breast-fed neonates were affected. This disparity likely reflects the superior bioavailability of calcium in human milk, where approximately 60–76% of ingested calcium is absorbed, compared with about 40% from most formula preparations.

Of the 100 infants treated, 47 received phototherapy for 24–48 hours, 38 for 48–72 hours, and 15 for 72–96 hours. Hypocalcemia was observed in 10.6% of those under treatment for 24–48 hours, rising to 15.8% in the 48–72-hour group, and 33.3% among infants exposed for 72–96 hours. Although these figures suggest a trend toward increased risk with longer phototherapy, the differences were not statistically significant.

Clinically, 62.5% of hypocalcemic infants did not have overt symptoms. Among those who did manifest signs, jitteriness occurred in 25%, and seizures in 12.5%. These findings underscore that most cases are subclinical, detectable only through routine serum monitoring rather than physical examination alone.

Premature and low-birth-weight infants were disproportionately represented among those who developed low calcium levels after phototherapy, despite the unit's protocol of administering calcium supplements (150–200 mg/kg/day) to all preterm neonates. This suggests that even with prophylactic supplementation, prolonged phototherapy can still precipitate hypocalcaemia in this vulnerable population. Mechanistically, fluorescent phototherapy may suppress melatonin by inhibiting pineal gland activity. Since melatonin normally restrains cortisol-driven calcium uptake into bone, its reduction could unleash an acute surge in bone calcium deposition, thereby lowering circulating calcium concentrations. Taken together, these data advocate for daily serum calcium assessments during phototherapy—especially beyond 48 hours—in preterm and low-birth-weight infants to promptly identify and manage hypocalcemia. In the present study, there is a significant decrease in mean serum calcium after phototherapy, and it is statistically significant (p < 0.05); several other studies also showed the same.

In the present study, the incidence of hyponatremia after phototherapy was 6 % (6). In Reddy et al Study the incidence of hyponatremia was 5.95%, which is similar to this study [5]. The incidence of hyponatremia was 4.25 %, 5.26% and 13.3% after 24-48 hours, 48-72 hours, and 72-96 hours of phototherapy, respectively. There was increased incidence of hyponatremia with increasing duration of phototherapy. However, this association was not found to be statistically significant.

All hyponatremic cases were asymptomatic. The mean value of serum sodium before and after phototherapy was 141.350±2.50 and 137.063±3.046. In the present study, there was a decrease in serum sodium levels with an increase in duration of phototherapy, but it was not statistically significant; in other studies, it was seen that there is a statistically significant decrease in serum sodium after phototherapy.

In the present study, it was found that hyponatremia was noted in 13.9% of preterm babies receiving phototherapy. Hyponatremia following phototherapy was not seen in term babies. The decrease in serum sodium levels in preterm neonates was statistically significant. Other studies showed that the incidence of hyponatremia was higher in preterm compared to term neonates. So, it is inferred that preterm neonates are at higher risk of hyponatremia. The present study showed that 14.2% of LBW neonates developed hyponatremia following phototherapy, and no normal birth weight neonates developed hyponatremia. This was statistically significant and similar to other studies like Yeturi et al [16]. So, it suggests that LBW neonates are at risk for electrolyte abnormalities and therefore continuous monitoring is necessary for them.

In the present study, only breast-fed babies developed hyponatremia when compared to formula-fed babies. As breast milk has a low sodium content compared to formula feeds, breastfed babies are more prone to hyponatremia. Several studies reported that hyponatremia is common after phototherapy and is multifactorial.

Phototherapy leads to insensible water loss through the skin, which is greater in preterm babies due to more surface area. In some cases, SIADH can be associated with phototherapy, which can lead to hyponatremia, a much more serious complication. Premature babies, because of the immaturity of kidneys to handle electrolyte imbalance and decreased reabsorption of sodium from the proximal convoluted tubule, are more prone to hyponatremia.

Hyponatremia may be associated with symptoms like nausea, vomiting, lethargy, weakness, seizures, and altered sensorium, which are indistinguishable from symptoms of other complications in newborns, like sepsis.

Hence, regular monitoring of serum sodium is essential, particularly in vulnerable newborns undergoing phototherapy to prevent serious complications.

## CONCLUSION

Phototherapy is the most common modality of treatment for neonatal jaundice and largely considered to be a safe procedure with some but significant problems like dyselectrolytemia. As preterm and low birth weight babies are at a higher risk, periodic monitoring of electrolytes after phototherapy in the neonates can prevent dyselectrolytemia, in turn prevent the related complications.

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