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A Prospective Hospital Based Observational Study On Electrolyte Changes Following Phototherapy In Neonatal Hyperbilirubinemia

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ABSTRACT

Background: Neonatal hyperbilirubinemia (NH) is a common condition affecting a large proportion of term and preterm infants. Phototherapy is a widely used treatment modality; however, it may result in electrolyte disturbances such as hypocalcemia, hyponatremia, and hyperkalemia, which pose significant clinical concerns.

Objectives: This study aimed to evaluate changes in serum calcium, sodium, and potassium levels in neonates undergoing phototherapy for unconjugated hyperbilirubinemia.

Methods: A hospital-based prospective observational study was conducted at RL Jalappa Hospital, Kolar, from August 2023 to August 2024. A total of 193 neonates aged between 24 hours to 14 days receiving phototherapy were enrolled. Electrolyte levels were measured before and after phototherapy and analyzed using appropriate statistical methods.

Results: Hypocalcemia was observed in 24% of neonates post-phototherapy, significantly more common in preterm and low birth weight infants ($p<0.001$). Hyponatremia was found in 3.5% of cases, with a higher prevalence in preterm and LBW neonates. Hyperkalemia occurred in 4.2% of neonates post-phototherapy, although no significant hypokalemia was detected. The duration of phototherapy and gestational age showed a statistically significant correlation with electrolyte disturbances.

Conclusion: Phototherapy in neonates is associated with significant electrolyte imbalances, particularly hypocalcemia and hyponatremia, especially in preterm and low birth weight infants. Routine monitoring of electrolytes during phototherapy is recommended to prevent complications.

Keywords: *Neonatal hyperbilirubinemia, phototherapy, hypocalcemia, hyponatremia, electrolyte imbalance, neonate.*

1. INTRODUCTION

Neonatal hyperbilirubinemia (NH) is considered as a more widespread prevalent aberrant physical manifestations in neonates. Neonatal jaundice is a common clinical ailment during the initial 14 days of life and a significant reason for revisit to hospital post-delivery.[1]It affects around half of the neonates who were born at term. It also affects 80.0% of neonates born preterm through the first seven days of life [2]. Elevated levels of unconjugated bilirubin in the blood lead to a yellowish discoloration of the skin , sclera. NH may be healthy or pathological, indicating either hepatic immaturity in bilirubin excretion or excessive bilirubin synthesis. Unconjugated bilirubin has bad influence on the CNS more in preterm neonates and those with inherited enzyme abnormalities.[3,4]

Unconjugated hyperbilirubinemia in neonates left untreated leads to considerable morbidity due to its neurotoxic effects. Untreated, it leads to bilirubin encephalopathy and kernicterus as it has the capacity to traverse the blood-brain barrier [5]. Therefore, early detection and intervention are crucial. Phototherapy presents side effects such as diarrhoea, ocular damage, dehydration, bronze baby syndrome, hyperthermia, and gonadal toxicity. One of the side effects related to electrolyte disturbance is hypocalcaemia. Hypocalcaemia can lead to terrible consequences such as irritability, jitteriness, convulsions, and breathlessness [6].

Few studies have shown additional kinds of electrolyte imbalance in babies under phototherapy for NH treatment. Phototherapy could cause symptomatic hypocalcaemia and hyponatremia, which would need treatment. This study was conducted to investigate electrolyte imbalances in neonates undergoing phototherapy.

2. OBJECTIVES

1. To evaluate the alterations in electrolyte levels among neonates undergoing phototherapy for neonatal hyperbilirubinemia, at RL Jalappa Hospital,Kolar.
2. To determine the impact of phototherapy on Serum concentrations of Sodium, Potassium and Calcium

MATERIALS AND METHODS

Source of Data: Consecutive newborns with hyperbilirubinemia cases receiving phototherapy admitted in department of paediatrics, RL JALAPPA HOSPITAL, KOLAR

Study Design: Hospital based prospective observational clinical study.

Study Period: 1 year period from 2023 August to 2024 August

Inclusion Criteria:

- All the neonates with unconjugated hyperbilirubinemia from 24 hours of life to 14 days of life receiving phototherapy.
- Whose parents or caregivers are willing to give consent for the study.

Exclusion criteria:

- Neonates with conjugated bilirubinemia.
- Newborn with perinatal asphyxia.
- Baby of mother who had history of taking anti convulsants.
- Newborn fed with cow milk.
- Baby born to diabetic mother.
- Babies born with apparent major congenital anomaly.
- Baby with parents who are not willing to give consent.

Sample Size:

Sample size was calculated by using the proportion of hypocalcaemia in subjects who underwent phototherapy was 13.1% from the study by Thriupathi reddy et al. using the formula

$$\text{Sample Size} = \frac{Z_{1-\alpha/2}^{\ 2}\ P\ (1-P)}{d2}$$

Considering 10% nonresponse rate 175 + 17.5 ≈ 193 subjects was included in the study.

3. METHODS OF COLLECTION OF DATA:

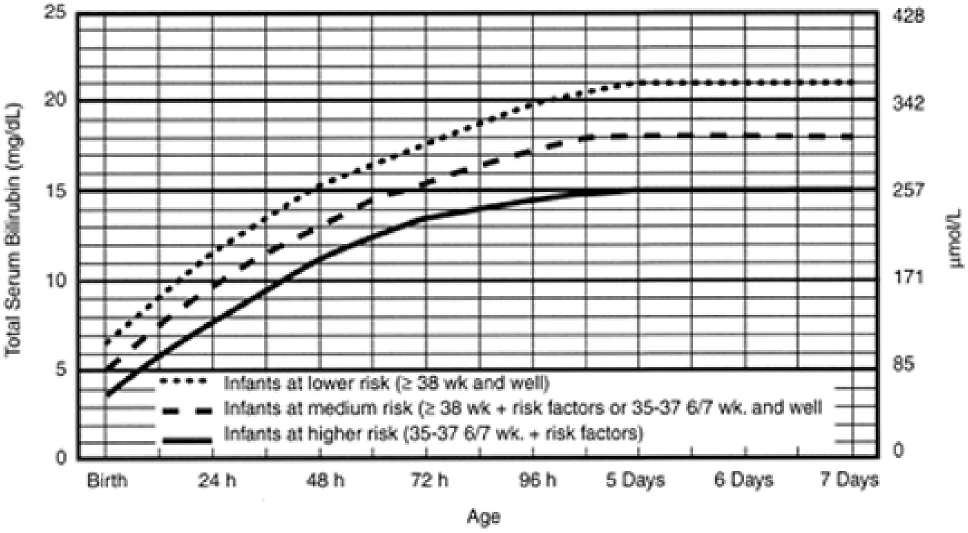
Prior written informed consent was taken for their cooperation to participate in the study. The patients were included in the study if they fulfilled the inclusion/exclusion criteria. Baseline data were stored from the patients along with pertinent clinical history and relevant lab investigations. We tested the newborns' venous blood for TB, DB,S/E , blood groups.

The Arsenazo technique was used to test calcium, the Diazo method to assess total and direct bilirubin, and an autoanalyzer (Erba EM 200 machine) to analyze electrolytes (Na, K). The antisera technique was used to evaluate the blood groups of neonates.

Both the first and second samples of electrolytes were taken at zero hours and forty- eight hours of PT, respectively, or upon termination of PT, whichever came first. As a control, the first sample was taken. In order to find out what happened to the electrolytes, researchers compared these two sample sets. We used appropriate statistical tests (Student's t-test) to tabulate and evaluate all of the data from the different groups. We compared the proportions using the chi-square test.

The American Academy of Pediatrics established guidelines for determining whether a child born at 35 weeks or more gestation required PT or an exchange transfusion. The American Academy of Pediatrics has developed two age-specific nomograms - one to guide the initiation of phototherapy and the other for determining the need for exchange transfusion. Three separate categories of newborn risk were marked on the nomograms. Three groups were established: one for babies at lower risk (defined as 38 weeks or more with no risk factors), one for babies at medium risk (defined as 38 weeks or more with risk factors or 35 to 37 weeks without risk factors), and one for babies at higher risk (defined as 35 to 37 weeks with risk concerns).

Total bilirubin (TB) values were used to guide clinical decisions without subtracting the direct (conjugated) fraction. In medium risk neonate , phototherapy was initiated at TSB levels of 10mg/dl at 24 hours, 13mg/dl, at 48 hours, 15mg/dl at 72 hours and 18mg/dl at 96 hours or later. The cutoffs for lower-risk and higher-risk babies were about 2 mg/dL higher and 2 mg/dL lower, respectively, compared to the medium-risk infants. Hypoalbuminemia, sepsis, significant lethargy, acidosis, hypoxia, temperature instability, G6PD deficiency, and immune hemolytic anemia were among the risk factors.



4. STATISTICAL ANALYSIS

Microsoft 365 Excel and SPSS v27.0 were used for data collection and analysis, respectively. Results with a P value less than 0.05 were deemed statistically significant, and all statistical analyses were conducted at a 5% level of significance.

5. RESULTS

Table 1: PRE-Phototherapy calcium values according to weight (n =193)

Calcium	LBW (n =88)	Normal wt (n=105)	Total (n=193)	P value
< 8	9 (10 %)	2 (2.4%)	11 (5.6%)	0.048*
8 - 11	79 (90 %)	103 (97.5%)	182 (94.4%)	

Table 2 : PRE-Phototherapy Sodium values according to weight (n =193)

Sodium	LBW	Normal wt	Total	P value
< 135	3 (3.3 %)	0	3 (1.4%)	0.245
135 -145	60 (66.6%)	92 (87.8 %)	152 (78.8%)	
> 145	25 (30 %)	13 (12.2 %)	38 (19.7%)	

Table 3: PRE-Phototherapy Potassium values according to weight (n =193)

Potassium	LBW	Normal wt	Total	P value
< 3.5	0	0	0	<0.001
3.5 – 5.5	88	105	193 (100%)	
> 5.5	0	0	0	

Table 4: Correlation of post phototherapy calcium with weight

Calcium	LBW (n=88)	Normal wt (n=105)	Total (n=193)	P value
< 8	32 (36.6%)	14 (14.6%)	46 (24%)	<0.001
8 - 11	56 (63.3%)	91 (85.4%)	147 (76%)	

Table 5: Association between post phototherapy sodium and weight

Sodium	LBW	Normal	Total	P value
< 135	6 (8.4%)	0	6 (3.5%)	<0.001
135 -145	50 (53.3 %)	96 (91.5%)	146 (75.4%)	
>145	32 (38.3 %)	9(8.5%)	41 (21.2%)	

Table 6: Association of post phototherapy potassium and weight

Potassium	LBW	Normal	Total	P value
< 3.5	0	0	0	<0.001*
3.5 – 5.5	85 (96.6 %)	100 (95.3%)	185 (95.8%)	
> 5.5	3 (3.4%)	5 (4.8%)	8 (4.2%)	

Table 7: Association of post phototherapy calcium with gestational age

Calcium	< 37 weeks (n=47)	37-40 weeks (n=114)	40 weeks (n =32)	Total (n=193)	P value
< 8	29 (61.2%)	16 (13.6%)	0	45 (24%)	<0.001

8 - 11	18 (38.8 %)	98 (86.4 %)	32(100%)	148 (76%)	

Table 8: Association of post phototherapy sodium and gestational age

Sodium	**< 37 weeks**	**37-40 weeks**	**> 40 weeks**	**Total**	**P value**
< 135	4 (8.4%)	3 (2.3%)	0	7 (3.5%)	<0.001
135 – 145	34 (72.3%)	104 (89.7 %)	4 (11.2%)	142 (75.4%)	
> 145	9 (19.4%)	7 (8%)	28 (88.8%)	44 (21.2%)	

Table 9: Correlation of post phototherapy potassium with gestational age

Potassium	**< 37 weeks**	**37-40 weeks**	**> 40 weeks**	**Total**	**P value**
< 3.5	0	0	0	0	<0.001
3.5 – 5.5	43(91.6%)	111(97.7%)	30 (94.4%)	184 (95.8%)	
> 5.5	4 (8.4%)	3 (2.3%)	2 (5.6%)	9 (4.3%)	

Table 10: Association of post phototherapy calcium in relation to duration of phototherapy

Calcium	**< 24 hours (n=44)**	**24-48 hours (n=137)**	**> 48 hours (n=12)**	**Total (n=193)**	**P value**
< 8	4 (9.3%)	38 (27.8 %)	4 (33.4 %)	46 (24%)	0.104
8 - 11	40 (90.7%)	99 (72.2 %)	8 (66.6 %)	147 (76%)	

Table 11: Association of post phototherapy sodium and duration of phototherapy

Sodium	**< 24 hours**	**24-48 hours**	**> 48 hours**	**Total**	**P value**
< 135	0	5 (4.9%)	0	5 (3.5%)	<0.001
135 – 145	38 (87.5%)	106 (77.3%)	2 (11.2%)	146 (75.4%)	
> 145	6 (12.5%)	26 (17.8%)	10 (88.8%)	42 (21.2%)	

Table 12: Association of post phototherapy potassium and duration of phototherapy

Potassium	< 24 hours	24-48 hours	> 48 hours	Total	P value
< 3.5	0	0	0	0	<0.001
3.5 – 5.5	44 (100 %)	129 (94 %)	12(100 %)	185 (95.8%)	
> 5.5	0	8 (6 %)	0	8 (4.3%)	

6. DISCUSSION

This study was conducted among 193 newborns who underwent phototherapy for unconjugated hyperbilirubinemia from 24 hours of life to 14 days of life. The electrolyte changes were studied before and after phototherapy

This study found that males made up the majority of the participants who underwent phototherapy, accounting for 54.9% of the total, in comparison to females. Males made up 59.1% of the participants in the research carried out by Reddy et al., 50.1% of the participants in the research carried out by Alizadeh-Taheri et al., and 62.9% of the participants in the research carried out by Karamifar et al.

In this particular study, the bulk of the participants were full-term babies, which accounted for 59.1% of the total. When compared to the percentage that was found in the Karamifar et al trial, which was 59.4%, the percentage that was found in the Reddy et al study was 77.0%. In the study conducted by Arora et al., full-term babies made up 54.0% of the individuals. 60.0% of the babies in the Yadav et al. trial were born at full term.

In our study, 42.2% of infants were born with a low birth weight, compared to 23% reported in the study by Reddy et al.,

Table 13: Calcium – post phototherapy distribution in various studies

		This study	Reddy et al.(10)	Yadav et al(7)	Alizadeh-Taheri et al(8)	Arora et al.(9)	Karamifar et al(11)
Calcium – post phototherapy	<8 g/dl	24.0%	<7g/dl - 13.1%	73.3%	56.0%	50.0%	14.4%

It was shown that 5.6% of the participants in this study had hypocalcemia prior to receiving phototherapy, but after receiving PT, the incidence of low calcium levels jumped to 24.0%. The incidence of post-PT hypocalcemia was 13.0% in the study that was carried out by Reddy et al., but the incidence of low calcium level was on the higher side in the study that was carried out by Yadav et al., with 73.3% of the participants having the same condition. The incidence of hypocalcaemia was found to be 56.0% in the study conducted by Alizadeh-Taheri and colleagues, while the incidence of hypocalcaemia was found to be 50.0% in the study conducted by Arora and colleagues. According to the findings of the study conducted by Karamifar et al., the incidence of hypocalcemia following phototherapy was reduced by 14.4%.

Table 14: Sodium – post phototherapy distribution in various studies

		This study	Reddy et al.(10)
Sodium – post phototherapy	<135	3.5%	6.0%

According to the findings of this research, 78.8 percent of the babies had normal sodium levels, and just 1.4% of them had hyponatremia prior to the phototherapy session. Following the completion of phototherapy, the rate of hyponatremia stood at 3.5%. Nearly twice as many cases were reported prior to the implementation of phototherapy. In the research carried out by Reddy and colleagues, the percentage of patients who experienced hyponatremia after phototherapy was 6.0%.

Table 15: Potassium – post phototherapy distribution in various studies

		This study	Reddy et al.(10)
Potassium – post phototherapy	<3.5 and > 5.5	0.0 and 4.2%	<3.5 - 0.4%

Before beginning the phototherapy sessions, none of the neonates who participated in this trial had hypokalemia or hyperkalemia conditions. After phototherapy, around 4.2% of neonates were found to have hyperkalemia. The results of our analysis did not reveal any instances of hypokalemia. Following phototherapy, there were 0.4% of cases of hypokalemia that were documented in the study that was conducted by Reddy and colleagues.

Phototherapy was associated with a significant overall increase in the incidence of hypocalcemia. Notably, low birth weight infants exhibited a significantly higher incidence of hypocalcemia compared to those with normal birth weight ($p<0.001$), with the difference in calcium levels between the two groups also reaching statistical significance ($p = 0.048$). This study demonstrated that calcium levels varied significantly based on birth weight, with LBW infants tending to have lower calcium levels. Similarly , in the study by Reddy et al., hypocalcemia following phototherapy was more prevalent among LBW infants (36.2%) compared to normal birth weight infants (6.2%). Therefore, it may be deduced that newborns with a LBW were at a greater risk of hypocalcemia after receiving phototherapy than babies with a normal birth weight

The levels of calcium in neonates who were born prematurely, those born at term, and those born after term were shown to be significantly different after phototherapy ($p<0.001$). Neonatal patients who were born prematurely were more likely to have hypocalcemia than those who were born at term. According to the research conducted by Reddy and colleagues, there was a statistically significant difference in the incidence of hypocalcemia following phototherapy intervention between preterm and late infants. Following phototherapy, the occurrence of hypocalcemia was found to be significantly higher in before term newborns (41.2%) compared to term newborns (6.2%) on average. As a result, it may be deduced that preterm infants suffered from a higher probability of hypocalcemia after receiving phototherapy than term infants. The study by Yadav et al. found no significant difference in serum calcium levels between the study and control groups prior to phototherapy. After 48 hours of phototherapy , a significant reduction in serum calcium levels was observed among preterm infants in the study group ($p<0.0001$)

Term neonates also exhibited a statistically significant decline in calcium levels following phototherapy ($p<0.005$). In the study by Arora et al., hypocalcemia was detected in almost half of the preterm infants (43%) and 30 of 54 term newborns (56%) after 2 days of continuous PT.

Following phototherapy, serum sodium levels changed, and our research revealed that there were substantial changes between preterm, term, and post-term newborns in terms of sodium production. The statistical significance of the difference was also found to be less than 0.001.0. The investigation that was conducted by Reddy and colleagues also revealed results that were substantially comparable. Preterm neonates had a higher incidence of hyponatremia following phototherapy (17.6%) compared to term neonates (3.1%), who had a comparatively lower incidence. Based on this, it can be deduced that preterm newborns were more likely to experience hyponatremia after receiving phototherapy than term babies.

In our study the variation in potassium levels with respect to gestational age was not statistically significant . Reddy et al, study also couldn't find any significant difference in the potassium levels based on gestational age.

7. CONCLUSION

Among the 193 samples of neonates who received phototherapy, incidence of hyponatremia was 3.5% . This was notably higher in preterm (8.4%) and LBW (8.4%) compared to term newborns (2.3%) and those with normal birth weight.

Incidence of hypocalcemia is also significantly varied between gestational age of the newborns and weight of the newborns. The incidence of hypocalcemia was 24.0% in this study. Preterm neonates and low birth weight babies tend to have higher incidence of hypocalcemia.

After phototherapy, around 4.2% of neonates were found to have hyperkalemia. The results of our analysis did not reveal any instances of hypokalemia.

LIMITATIONS

- Further follow ups were not done for the neonates post discharge from hospital.
- It is a single centre study and a multicentre study can reveal more information on the same topic

Time limitations restricted the further follow up and collecting more samples for the study.

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