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Effect of Phototherapy on Neonatal Electrolytes and Plasma Glucose: An Observational Study

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Abstract:
Background*: Neonatal hyperbilirubinemia or jaundice is a common medical comorbidity. It is one of the common causes of hospitalization during 1st two weeks of life. Untreated hyperbilirubinemia can lead to encephalopathy, mental retardation, cerebral palsy, and kernicterus. Treatment for this condition varies from just exposing the neonate to sunlight to phototherapy. But phototherapy can cause various electrolyte and plasma glucose variations. Hence the current study was undertaken to evaluate the impact of phototherapy on neonates.*
Materials and Methods*: In this observational study, 100 neonates (aged below 28 days), who were scheduled for receiving phototherapy for their hyperbilirubinemiawere included.The study was conducted for 6 months from July 2022 to December 2022 at a tertiary care centre named Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh.Bilirubin levels, plasma glucose and electrolytes like sodium potassium, and calcium wereassessedbefore and afterthe completion ofphototherapy.*
Results*:14% of babies were of low birth weight. The mean gestational age was 37.4±0.8 weeks. The mean duration of phototherapy was13.7±0.19 hours. The mean plasma glucose was 89±12 mg/dl. There was asignificantdifference in electrolyte levels and plasma glucose before and after phototherapy. The mortality rate was zero.*
Conclusion:*There is a high chance that phototherapy can cause electrolyte disturbances. Hencethe use of phototherapy must be restricted and should be suggested to neonates whoreallyneed it. Clinicians should always weigh the risk-benefit ratio before providing appropriate management for neonates with hyperbilirubinemia.*
Key Word*:Electrolytes chances, neonates, plasma glucose, phototherapy. hyperbilirubinemia*

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I. Introduction

Neonatal hyperbilirubinemia is a common comorbidity during the early neonatal period. It occurs due to the presence of excess inappropriate erythropoiesis, lack of adequate amounts of liver enzymes, more production of bilirubin, and deficient conjugation with enhanced enterohepatic circulation. It manifests as yellowish discoloration of sclera and skin(jaundice) and is evident clinically if total serum bilirubin was above 5 mg/dL[1]. Indirect hyperbilirubinemia develops occurs in approximately 60% of term babies and 80% of preterm babies during 1st week of life, and neonatal jaundice is one of the major causes of hospitalization during 1st 2 weeks of life.[2-4]Various risk factors were found for severe unconjugated hyperbilirubinemia. They include low birth weightand pretermbirth. Untreated hyperbilirubinemia can lead to encephalopathy, mental retardation and kernicterus.[5] Phototherapy has been used worldwide as the main therapy for this purpose.[6]The treatmentoptions includephototherapy, which can be divided toconventional,intensiveand exchange transfusion. Pharmacologicaltreatment includes phenobarbitone,prophyrins,and intravenous immunoglobulins (IVIG), apart from natural sunlight. Treatment for this condition varies from just exposing the neonate to sunlight to phototherapy.Phototherapy causes oxidative reactions and leads to the formation of urine-excretable mutant bilirubin molecules through intermolecular rearrangement.[7-8]Common adverse effects linked to phototherapy include skin rashes, dehydration, bronze baby syndrome, skin burns, diarrhoea, hemolysis, and retinal and genital damage. Less common side effects include hypocalcemia; lack of closure of patent ductus arteriosus, deficiency of vitamins, reduced levels of growth, luteinizing, and follicle-stimulating hormones, apart fromsuppressingimmunity.[9-13]

II. Material And Methods

This observational study was carried out on neonates admitted into the neonatal intensive care unit(NICU) at Fathima institute of medical sciences, Kadapa, Andhra Pradesh from July 2022 to December 2022.

Study Location: This was a tertiary care teaching hospital-based study done in the Department of Pediatrics, at Fathima institute of medical sciences, Kadapa.

Study Duration: July 2022 to December 2022

Sampling procedure: Simple random sampling

Sample size calculation: The sample size was estimated on the basis of a population proportion design.

The sample size formula $N=Z^2PQ/E^2$

Consideringthe confidence intervals at 96%, the prevalence of 55.2% as per the study of **Brits H**[14], error of 10% the minimum sample size came to be 96. So, we included 100 neonates in our study, considering a few losses to follow up.

Subjects & selection method: The study population was taken from neonates diagnosed with hyperbilirubinemia and scheduled for phototherapy at our tertiary care center.

Inclusion criteria:

1. Neonates of any gender
2. Neonates with breastmilk jaundice
3. Neonates with physiological jaundice
4. Parents of neonates who provided informed consent to participate in the study

Exclusion criteria:

1. Neonates with suspected asphyxia
2. Neonates born to diabetic mothers
3. Neonates undergoing exchange transfusion
4. Neonates with sepsis
5. Neonates with congenital malformations
6. Neonates with respiratory distress
7. Neonates with cephalhematoma
8. Neonates with incomplete data
9. Neonates with hemolytic anaemia or ABO incompatibility
10. Neonates with conjugated hyperbilirubinemia

Procedure or methodology: After written informed consent was obtained from the neonate's parents,a case record form or proforma was used to collect the data of admitted neonates. The proforma included data onsocio-demographic features like age, gender, birth weight, gestational age, term, levels of direct, total and indirect bilirubin, serum sodium, potassium, calcium, and glucose. The samples were collected before the initiation of phototherapy and 48 hours after the completion of phototherapy.A comparison between these parameters was done to assess electrolyte and glucose disturbances. Direct bilirubin was assessed to rule out conjugated hyperbilirubinemia.Indirect bilirubin was measured using Diazo method, Serum calcium was measured using Arsenazo III method, and serum electrolytes were measured by Ion selective electrodes analyzer. Plasma glucose was measured using the hexokinase/glucose-6-phosphate dehydrogenase method.We followed the guidelines of the American Academy of Pediatrics 2022 in providing phototherapy for neonates. Few guidelines include:[15]To provide intensive phototherapy as per the neonates' surface area. Intensive phototherapy needs narrow-spectrum LED blue light having an irradiance of a minimumof 30 $\mu W/cm^2$ per nm with a wavelength of around 475 nm. The lightoutside 460 to 490 nm range gives unnecessary heat. [16-17] Phototherapy thresholds are based on gestational age.

Normal values: Serum sodium: 135-145mg/dl, serum potassium:3.5-5.5mg/dl, serum calcium:8.5-10.2mg/dl and serum chloride: 96-106 mg/dl.

Statistical a**nalysis**

Data was analyzed using EPI INFO version 7.2.5. Student's paired*t*-test was used to know the significance of differences between mean values of numerical variables before and after phototherapy. *P value*< 0.05 was considered as the cutoff value or significance.

III. Results

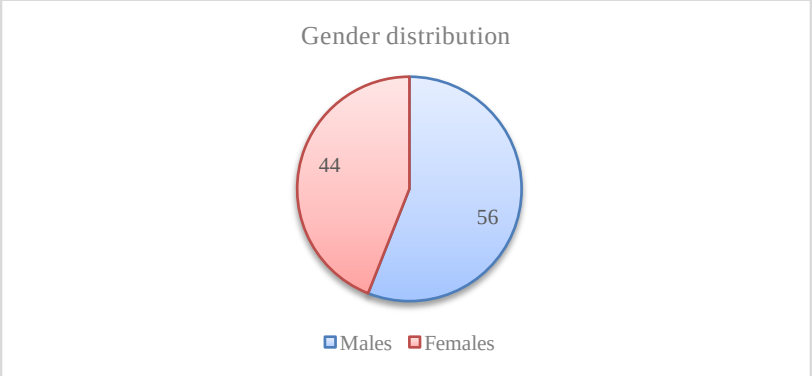
Age: Most of the neonates were aged 2-4 days in our study.

Table 1showsthe age distribution of neonates.The mean age was 2.5±0.4 days.

Age of neonates	Frequency	Percentage
2-4 days	54	54%
5 -9 days	28	28%
10-15 days	10	10%
16-18 days	2	2%

Gender: Most of the neonates were males.

Graph 1 shows the gender distribution of neonates.



Term and gestational age of neonates:88% of neonates were full term and 12% were preterm neonates. The mean gestational age was 37.4±0.8 weeks.

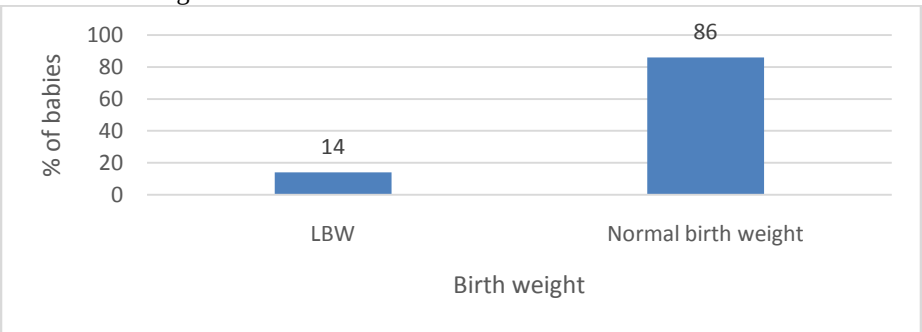
Table 2 shows term of neonates.

Term of neonates	Frequency	Percentage
Full term	88	88%
Pre term	12	12%
Post term	0	0%

Birth weight:

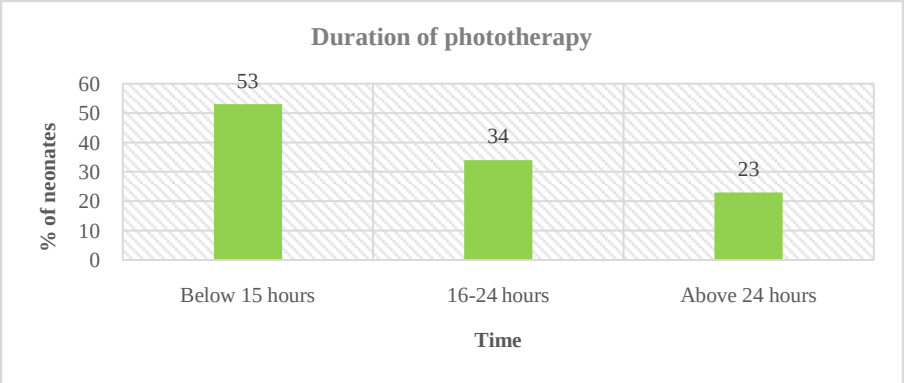
14% of babies were of low birth weight (LBW-weight below 2.5kgs at the time of birth). 86% had birth weight above 2.5 kgs and there were no very low birth weight babies. The mean birth weight was 3.1±1.09 kgs.

Graph 2 shows low birth weight babies



Duration of phototherapy: Most of the neonates were given phototherapy forbelow 15 hours**.**The mean duration of phototherapy was 13.7±0.19 hours.

Graph 3 shows duration of phototherapy given for neonates.

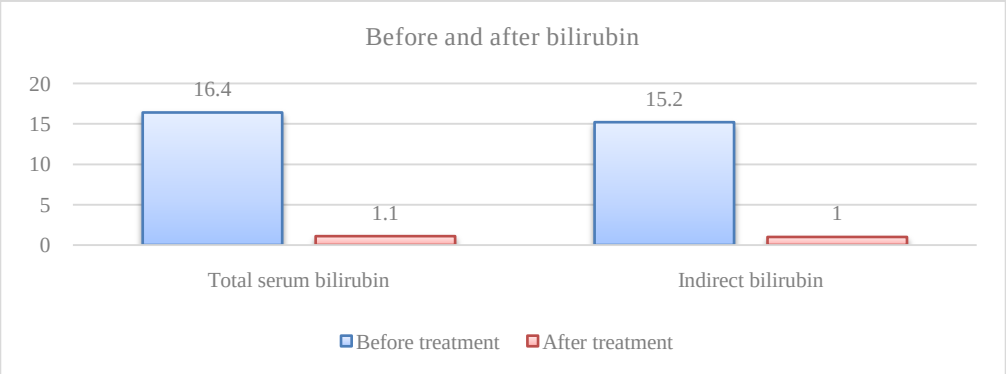


Mean serum bilirubin levels before and after treatment with phototherapy:

Table 3 shows mean serum bilirubin levels before and after treatment- Paired T test was done. There is significant difference in the mean total serum bilirubin and indirect bilirubin levels as evident from p values before and after treatment with phototherapy.

Mean levels	Before treatment	After treatment	P value	T value
Total serum bilirubin	16.4±3.2	1.1±0.2 mg/dl	0.0001	47.71
Indirect bilirubin	15.2±2.9	1.0±0.09mg/dl	0.0001	48.94

Graph 4 shows meanbilirubin levels before and after treatment

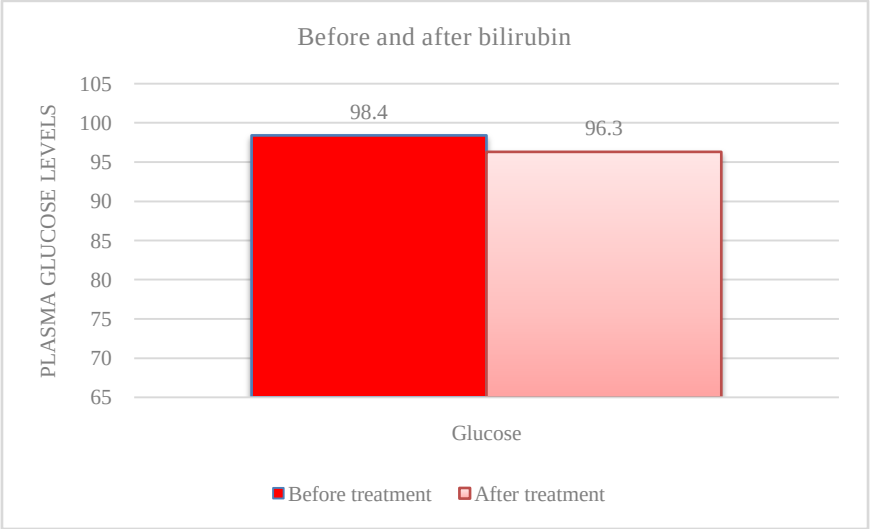


Mean plasma glucose levels before and after treatment with phototherapy:

Table 4 shows mean serum glucose levels before and after treatment- Paired T test was done. There is no significant difference in the mean plasma glucose levels before and after treatment with phototherapy.

Mean levels	Before treatment	After treatment	P value	T value
Plasma glucose	98.4±10.2 mg/dl	96.3±12.3 mg/dl	0.19	1.31

Graph 5shows mean plasma glucose levels before and after treatment

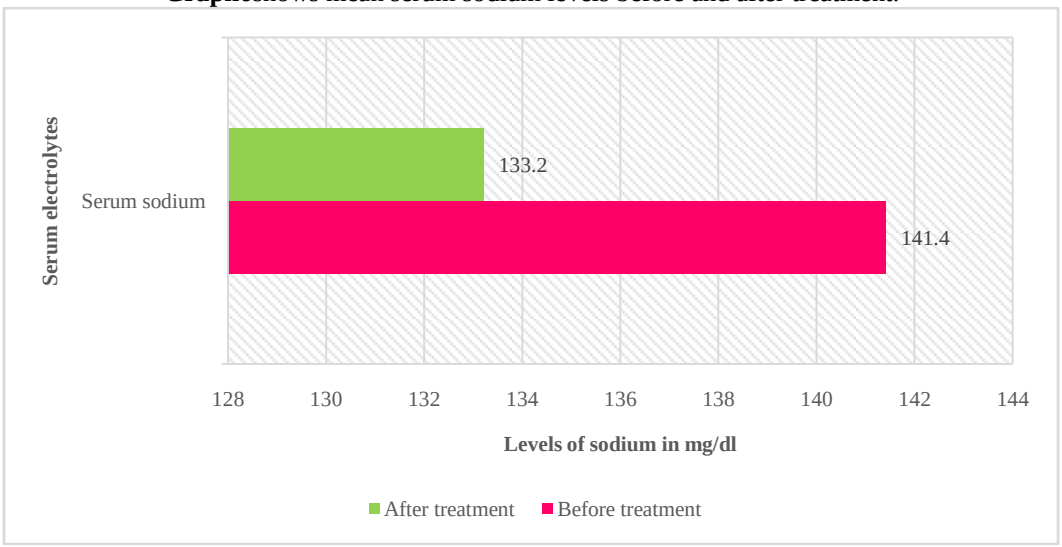


Mean serum electrolyteslevels before and after treatment with phototherapy:

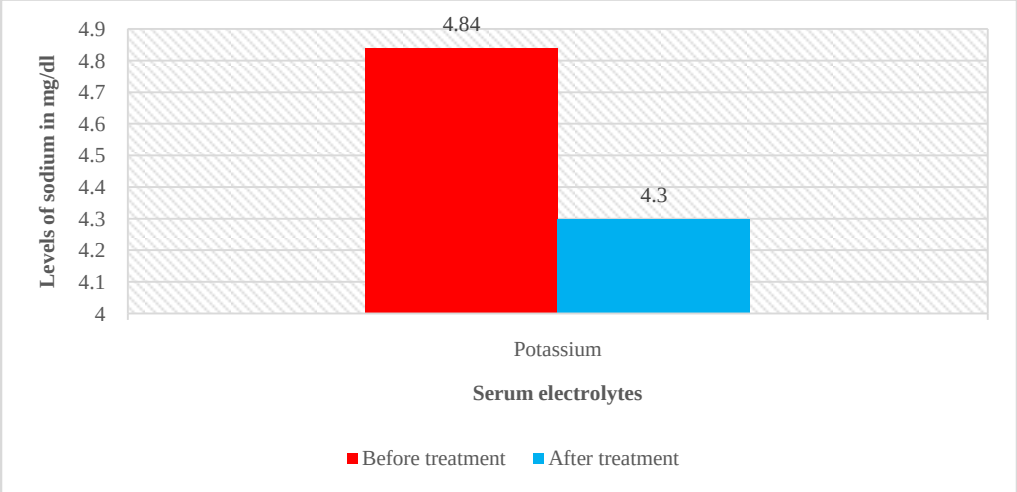
Table 5 shows mean serum electrolyte levels before and after treatment- Paired T-test was done. There is a significant difference in the mean serum electrolyte levels before and after treatment with phototherapy.

Mean levels	Before treatment	After treatment	P value	T value
Serum sodium	141.4±1.2 mg/dl	133.2±11.4 mg/dl	0.0001	5.13
Serum potassium	4.84±1.2 mg/dl	4.3±0.9 mg/dl	0.0004	3.6
Serum calcium	9.8±2.3 mg/dl	9.0±2.8 mg/dl	0.02	2.2
Serum chloride	105.4±10.4 mg/dl	103.2±12.1 mg/dl	0.0009	2.63

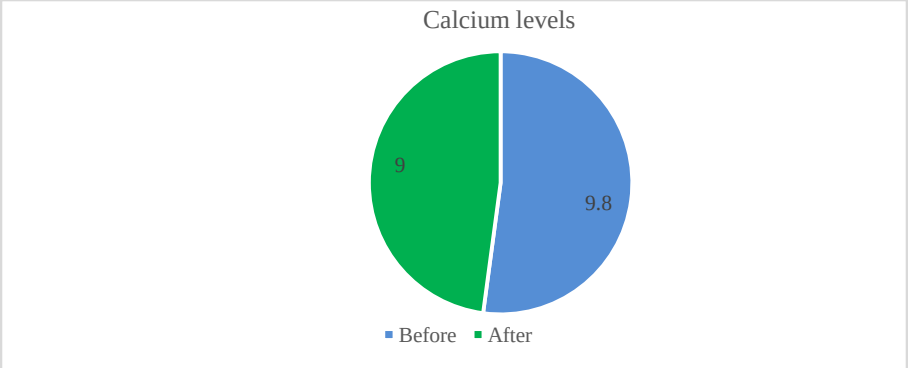
Graph6shows mean serum sodium levels before and after treatment.



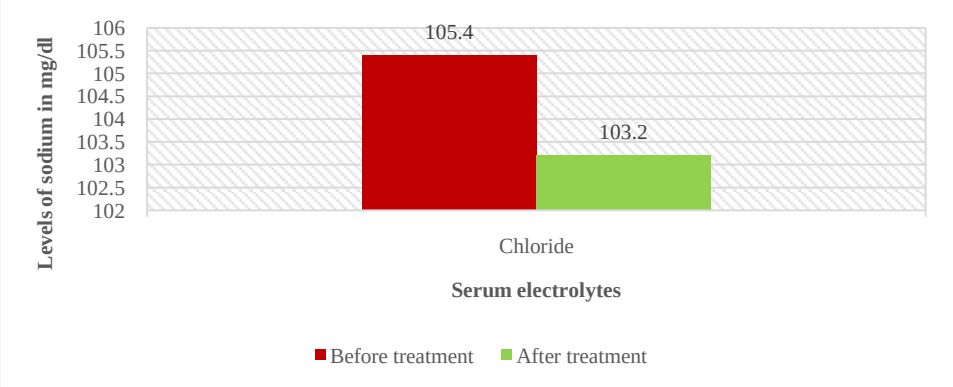
Graph7shows mean serum potassium levels before and after treatment.



Graph8shows mean serum calcium levels before and after treatment.



Graph9shows mean serum chloride levels before and after treatment.



Relation between various factors and reduction in serum electrolytes:
Overall serum electrolytes were reduced in 78% of neonates(Group A)28% had no reduction in electrolytes(Group B). Neonates in group A had less mean gestational age and more duration of phototherapy. There is no significant difference in mean birth weight, gender and mode of delivery among the two groups(A and B).

Table 6 shows risk factors for reduction in serum electrolytes

Parameter	**Group A**	**Group B**	**P value**
Gestational age	36.5±4.2 weeks	38.3±3.1 weeks	0.0007
Duration of phototherapy	14.9±1.2 hours	12.6±2.3 hours	0.0001
Birth weight	2.8±1.2 kgs	3.2±1.8 kgs	0.21
Gender	Males-52%	Males-48%	0.23

Mode of delivery-Lower segment cesarean section(LSCS)	53%	47%	0.39

IV. Discussion

Neonatal hyperbilirubinemiais a routine unusual physical finding seen by pediatricians during 1st week of life in around 70-80% of live births. The current study included 100 neonates with hyperbilirubinemia admitted into NICU, and scheduled for phototherapy. We identified the changes in plasma glucose and serum levels of electrolytes among them. Most of the neonates were aged 2-4 days.This implies that unconjugated hyperbilirubinemia commonly presents within 4 days. It is more commonly seen among male neonates, but the difference in gender proposition was slight.Most of the babies were of term babies and only 14% were born with low birth weight. This implies that birth weight and term of babies are not risk factors for unconjugated hyperbilirubinemia as per our study results.

Comparison with other studies:

In the study of **Shrdha Sharma et al**[18]**.,** 115 neonates with hyperbilirubinemia were included. The median age of neonates was 48 hours or 2 days, almost similar to our study. Males were 63 and females were 52 in number. There is slight male preponderance similar to our study. Age of our study population if comparable with the study done by **Taheri P et al. Purohit et al**[19-20]**.** also found slight male preponderance for hyperbilirubinemia.

There was a significant difference in serum sodium, potassium, calcium, and chloride before and 48 hours after phototherapy. They were less after phototherapy in our study. In contrast in the study done by **KL Tan et al.**[21] serum osmolality and electrolyte values found no significant variations from pre-phototherapy levels. Their study concluded that phototherapy even for 3 days or 72 hours does not significantly impact fluid and electrolyte status. The variation of our study results with this study could be due to the fact that their study included only infants who were fed with only formula milk. But our study included infants who were both breastfed and formula fed.

Anthropometric measurements showed that 14% were of low birth weight and the mean birth weight was 3.1±1.09 kgs. **Karamifer et al**.[22] study found that the mean birth weight of neonates was 2.8±047 kgs, which is slightly less compared to our study among neonates with hyperbilirubinemia.

Overall serum electrolytes were reduced in 78% of neonates(Group A) 28% had no reduction in electrolytes(Group B). Neonates in group A had less mean gestational age and more duration of phototherapy. This implies that gestational age and duration of phototherapy as significant risk factors for developing dyselectrolemia.

There is no significant difference in mean birth weight, gender and mode of delivery among the two groups(A and B). This implies that gender, mode of delivery, and birth weight as not risk factors for developing dyselectrolemia among neonates with hyperbilirubinemia.

Overall, more neonates were born through LSCS in our study, similar to the study done by **Vigneshwar NKV et al**.[23] among neonates with hyperbilirubinemia.This could be due to the fact that our institution, being a tertiary care centre, morehigh-risk deliveries being conducted through LSCS, as risky patients from primary health care centers get referred to our centre.

Before giving phototherapy, the mean serum sodium was 141.4±1.2 mg/dl and after phototherapy, the mean serum sodium was 133.5 ± 11.2 mg/dl. Reduction in sodium levels was proposed to be due to diarrhea causing decreased gastrointestinal absorption of sodium. These results were similar to studies done by **Jena et al** and **Suneja et al.**[24-25]

Similarly, there was a significant reduction in mean serum calcium and chloride levels.

Before phototherapy, the mean serum potassium was 4.84±1.3 mg/dl and after phototherapy, it was 4.3±0.9mg.dl in our study. Though there is a significant reduction in potassium levels, the levels still stay within the normal range.(normal range of potassium: 3.5-5.5mg/dl). The results are similar to the study done by**Krishna P et al.**[26]

In our study, overall serum electrolytes were reduced in 78% of neonates. According to **Sethi et al**.[27] after phototherapy, 75% of term newborns will have hypocalcemia.

After phototherapy, 66.6% of neonates showed a significant decline in calcium levels as per studies done by**Yadav RK.**[28]

Mechanism behind the reduction in serum calcium could be attributed to the fact that phototherapy inhibits melatonin production by the pineal gland. So, corticosterone's, effect on calcium is decreased. There is reduced bone restoration, leading to hypocalcemia.

In our study, there is no significant decline in plasma glucose levels after phototherapy.**Tosson et al.**[29]found asignificant correlation between plasma glucose and theduration of phototherapy.

V. Conclusion

There is a high chance that phototherapy can cause electrolyte disturbances. Hence the use of phototherapy must be restricted and should be suggested to neonates who really need it. Clinicians should always weigh the risk-benefit ratio before providing appropriate management for neonates with hyperbilirubinemia.

We recommend future studies on the correlation between the duration of phototherapy and electrolyte levels as per Pearson's correlation.

The study is self-sponsored.

There were no conflicts of interest.

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