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Original Research Article

Evaluation of Serum Electrolyte Changes in Neonates with Neonatal Hyperbilirubinemia Receiving Phototherapy with Special Reference to Hypocalcemia in a Tertiary Care Hospital in Jhalawar

Nikhat Khan[1], Bansal Yogesh[2], Palsania Subhash[3], Haridas Chippy[4]

[1,4]Department of Paediatrics, Jhalawar Medical College, Jhalawar, Rajasthan
[2,3]Department of Paediatrics, Government Medical College, Kota, Rajasthan

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Corresponding Author: Dr. Haridas Chippy
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Abstract:

Background: Neonatal hyperbilirubinemia, or neonatal jaundice, results from elevated bilirubin due to immature liver function and rapid red blood cell breakdown. It affects 60% of full-term and 80% of preterm infants, manifesting as yellowish discoloration of skin and eyes. Classification includes physiologic, breastfeeding, breastmilk, and pathologic jaundice. High bilirubin levels risk kernicterus and brain damage. Diagnosis relies on bilirubin assessment, with phototherapy as the first-line treatment. Though effective, phototherapy may cause mild side effects, including rare cases of hypocalcemia, especially in preterm infants.

Objective: This study evaluates serum electrolyte and calcium changes, including hypocalcemia, in neonates with hyperbilirubinemia before and after phototherapy.

Design: A Hospital based observational study.

Setting: Department of Paediatrics, Jhalawar Medical College, Jhalawar

Participants: Neonates admitted in Neonatal Intensive Care Unit in SHKBM Hospital receiving phototherapy for neonatal hyperbilirubinemia without any comorbidities.

Results: In this study, 57.9% of neonates were male, with a male-to-female ratio of 1.375:1. Low birth weight was observed in 32.2% of neonates, and preterm births accounted for 24%. Phototherapy significantly reduced bilirubin, sodium, and calcium levels ($p<0.001$), with hyponatremia (15%) and hypocalcemia (38.3%) increasing after >48 hours of phototherapy. Potassium and chloride changes were non-significant.

Conclusions Neonatal hyperbilirubinemia requires prompt treatment to prevent complications. Phototherapy is effective for reducing bilirubin levels but should be used cautiously, considering its risks and benefits. Further research on its safety is needed.

Keywords: Neonatal hyperbilirubinemia, Phototherapy, Hypocalcemia, Kernicterus, Hyponatremia, Bilirubin, Preterm infants, Electrolyte changes, Jaundice, Low birth weight.

Introduction

Neonatal hyperbilirubinemia, or jaundice, is caused by elevated bilirubin levels, leading to yellowish discoloration in newborns. It affects 60% of full-term and 80% of preterm infants, often causing hospital readmission. [1,2]

In newborns, immature liver function and rapid RBC breakdown cause an imbalance in bilirubin production and conjugation, leading to elevated bilirubin levels, as it is not fully metabolized. [2,3]

Adults' gut bacteria help process conjugated bilirubin, but neonates lack sufficient bacteria, impairing bilirubin breakdown. This leads to hyperbilirubinemia through decreased hepatic uptake, impaired excretion, and increased enterohepatic circulation. [3]Conjugated hyperbilirubinemia occurs when direct bilirubin exceeds 1.0 mg/dl for a TSB up to 5 mg/dl or 20% of TSB when >5 mg/dl. It includes physiologic, breastfeeding, or pathologic jaundice. [3,4]

Physiologic hyperbilirubinemia is common, with increased bilirubin production and low conjugation due to UGT scarcity. It peaks at 17 mg/dL by days 3-4. Breastfeeding jaundice occurs in the first week due to low intake, while breastmilk jaundice develops after 5-7 days, peaking at 2 weeks. Pathologic hyperbilirubinemia includes early jaundice, illness signs, or high bilirubin levels. [3]

Jaundice in babies should be assessed visually by practitioners and parents. Kramer's rule helps assess severity, and a transcutaneous bilirubin meter can estimate levels. Serum bilirubin testing is the gold standard. [6,7]High bilirubin levels in neo-

nates can cause brain damage and kernicterus, with preterm infants at higher risk than term infants. [4]

Neonatal jaundice is treated with phototherapy, exchange transfusion, and pharmacological options like phenobarbitone and IVIG. Phototherapy is the first-line treatment, effective for bilirubin >80 mmol/liter, with mild side effects like fluid loss and skin discoloration, now minimized with improved systems. [7]Phototherapy can lead to hypocalcemia, a side effect first reported by Romagnoli et al. in 1979. This condition is more common in preterm infants, with symptoms like apnea, seizures, and jitteriness appearing when calcium levels drop below 1mmol/L. Although rare, long-term complications may occur, though calcium levels typically normalize within 24 hours. [9]

Materials & Methods

Source of Data: Neonates admitted in the Neonatal Intensive Care Unit receiving phototherapy in the department of paediatrics in Shrimati Heera Kunwar Baa Mahila Hospital, Jhalawar during the study period.

Duration of the study: 1 Year from February 2022 to January 2023 (as approved by Ethical committee).

Type of the study: A Hospital based observational study.

Sample Size: n = t2 * p * (1-p) / e2 t = 95% confidence interval (t = 1.96) p = proportion of admitted neonates receiving phototherapy as per inclusion criteria (31) out of total admission (258) in a particular month. hence p = 31/258 = 0.12 e = allowed error 5% (e = 0.05) Putting these values, 162.20(or162) Now Effect of error N = n + 5% of n = 163 + 5% of 163 = 163+ 8.15 N = 171.15 [or 171]

Sampling technique: Simple Random Allocation/Sampling.

Inclusion criteria: Neonates admitted in Neonatal Intensive Care Unit in SHKBM Hospital receiving phototherapy for neonatal hyperbilirubinemia without any comorbidities.

Exclusion criteria: Neonates

1. With conjugated hyperbilirubinemia,
2. With co-morbidities like birth asphyxia, septicemia, renal failure,
3. With abnormal electrolyte status detected before start of phototherapy, Normal range of Serum Electrolytes : S. Na+ - 135-145 meq/l S. K+ - 3.5-5.5 meq/l S. Cl- - 96-109 meq/l S. Ca+2- 7-11 meq/l
4. Whose mother had history of taking anticonvulsants,
5. Fed with cow's milk, 6. Who had exchange transfusion,
6. With jaundice lasting more than 14 days of life,
7. With major congenital malformations.

Statistical analysis: All data were collected through pre-designed proforma and will be entered in MS-Excel. Statistical analysis was done by SPSS software (22.0) and appropriate statistical tests of significance were applied to analyse the results.

Results

Table 2: Birth weight distribution of neonates according sex Birth weight SEX F M Total N % N % N % 2.5 kg 45 62.5% 71 71.7% 116 67.8% Total 72 100.0% 99 100.0% 171 100.0% Incidence of low birth weight babies was 32.2%. Mean birth weight was 2.58±0.45 kg.

A total number of 128 newborns with birth weight less than 1500 gms were admitted in SNCU during the study period of one year. Out of these 128 VLBW newborns, 16 newborns were excluded based on exclusion criteria and only 112 cases were included in the study. 112 healthy newborns (with birth weight > 2.5 kg) which were born on same day as of case were randomly selected in ratio of 1:1 and were enrolled as controls.

Table no. 1 mentions the neonatal factors in relation to birth weight. Among the case group, out of 112 cases, 86 were preterm appropriate for gestational age, 11 were term small for gestational age and 15 were preterm small for gestational age. In control group all the newborns were full term normal birth weight babies. The gender of the baby had no significant effect on the birth weight.

Table 1:

Neonatal Factors	VLBW group n(%)	NBW group n (%)	Total n (%)	P Value
Gestational maturity				
Preterm AGA	86 (100)	0 (0)	86 (100)	
Term SGA	11 (100)	0 (0)	11 (100)	
Preterm SGA	15 (100)	0 (0)	15 (100)	
Term AGA	0 (0)	112 (100)	112 (100)	
Total	112	112	224	
Sex				
Male	51 (47)	57 (53)	108 (100)	P =0.4224
Female	61 (52)	55 (48)	116 (100)	
Total	112	112	224	

Case group subjects (mothers) were those who delivered VLBW babies (<1.5 kg) while the control group subjects (mothers) had delivered normal birth weight babies (>2.5 kg). Table No. 2 presents the maternal factors in relation to birth weight of the babies.

Both the groups were found to statistically comparable (p>0.05) as per maternal age distribution, parity, mother's height, family structure, mother's occupation and maternal diseases meaning that there is no significant effect of these factors on birth weight.

A significant difference was observed among the two groups when compared for birth interval. Among the cases, most of them were primi mothers with <2 yrs birth intervals (85/112). Only 27 mothers in case group had birth interval >2 yrs suggesting that if the birth interval is less, there are more chances of VLBW deliveries (p=0.0012).

It was found that the incidence of very low birth weight babies was higher in mothers with lower weight and poor nutritional status and the differences were found to be statistically significant. Among controls, only 8 subjects had <40 kg weight while among cases, 37 subjects had <40 kg of weight, proving to be contributing to VLBW condition (p=0.001). A significant difference was also observed among the two groups when compared for mothers mid arm circumference (representing nutritional status). Among controls, most subjects had >21 cm of MAC whereas 26 subjects among cases had MAC of <21 cm representing malnutrition, proving to be contributing to VLBW condition (p=0.0065).Among control group, majority of the subjects had >5 antenatal visits, only 4 out of 112 subjects had <3 antenatal visits. Whereas in the case group, 14 had <3 antenatal visits, 41 had 3-5 visits and 57 had >5 visits. There was a statistically significant difference as per antenatal visits among both the groups. Thus, less antenatal visits also contribute to VLBW deliveries (p=0.0149).

Furthermore, significant differences were also observed among the two groups when compared for mother's literacy status and per capita income. 36 mothers among the cases were found to be illiterate as compared to only 15 illiterate mothers in control group (p=0.0034) proving the importance of education in preventing low birth weight in newborns. Also only 23 subjects out of 112 in control group had <1000/- of per capita income whereas 45 subjects in cases had <1000/- of per capita income, proving it to be contributing to VLBW condition (p=0.0039).Bad Obstetric History (BOH) was observed more among the mothers of case group. 35 cases had mothers with bad obstetric history while only 14 controls had the same. This difference was found to be statistically highly significant (p=0.007) meaning that, bad obstetric history contributes to VLBW deliveries.

Table 2:

Maternal Factors	VLBW group n(%)	NBW group n (%)	Total n (%)	P Value
Age (in years)				
<20 years	25 (66)	13 (34)	38 (100)	P =0.1021
21-30 years	80 (47)	80 (47)	171 (100)	
21-30 years	7 (47)	8 (53)	15 (100)	
Total	112	112	224	
Gravida				
Primi	43 (57)	33 (43)	76 (100)	P =0.3695
2 and 3	62 (47)	71 (53)	133 (100)	
>3	7 (47)	8 (53)	8 (53)	
Total	112	112	224	
Birth interval				
<2 years	42 (62)	26 (38)	68 (100)	P =0.0012
>2 years	27 (34)	53 (66)	80 (100)	
Total	69	79	148	
Mother's height				
≤140 cm	10 (59)	7 (41)	17 (100)	P =0.7129
141-149 cm	29 (47)	32 (53)	61 (100)	
≥150 cm	73 (50)	73 (50)	146 (100)	
Total	112	112	224	
Mother's weight				
≤40 kg	37 (82)	8 (18)	45 (100)	P =0.7129
41-49 kg	41 (45)	51 (55)	92 (100)	
≥50 kg	34 (35)	53 (65)	87 (100)	
Total	112	112	224	

Mid arm circumference				
≤20 cm	26 (74)	9 (26)	35 (100)	P =0.0065
21-22 cm	40 (48)	44 (52)	84 (100)	
>22 cm	46 (44)	59 (56)	105 (100)	
Total	112	112	224	
Mothers literacy				
Illiterate	36 (71)	15 (29)	51 (100)	P =0.0034
Prim. and middle school	51 (43)	68 (57)	119 (100)	
High school &above	25 (46)	29 (54)	54 (100)	
Total	112	112	224	
Per capita income				
< 1000	45 (44)	58 (56)	103 (100)	P =0.0039
1000-1499	41 (28)	108(72)	149 (100)	
≥1500	26 (31)	58 (69)	84 (100)	
Total	112	112	224	
Family structure				
Nuclear	48 (44)	61 (56)	109 (100)	P =0.0822
Joint	64 (56)	51 (44)	115 (100)	
Total	112	112	224	
Maternal occupation				
Housewife	79 (51)	75 (49)	154 (100)	P =0.6364
Light work	25 (50)	25 (50)	50 (100)	
Heavy work	8 (40)	12 (60)	20 (100)	
Total	112	112	224	
Antenatal visits				
<3 visits	14 (78)	4 (22)	18 (100)	P =0.0149
3-5 visits	41 (55)	34 (45)	75 (100)	
>5 visits	57 (43)	74 (57)	131 (100)	
Total	112 (100)	112 (100)	224	
Maternal disease				
No disease	39 (45)	48 (55)	87 (100)	P =0.738
PIH	33 (51)	32 (49)	65 (100)	
Anemia	16 (31)	36 (69)	52 (100)	
APH	9 (47)	10 (53)	19 (100)	
Others	15 (33)	30 (67)	45 (100)	
Total	112	112	224	
Bad obstetric history				
Present	35 (71)	14 (29)	49 (100)	P=0.0007
Absent	77 (44)	98 (56)	175 (100)	
Total	112	112	224	

Discussion

This study was a hospital based prospective case control study, conducted over a period of 15 months at a tertiary care centre with well-equipped facilities, which included 112 newborns in each group as cases (birth weight <1500 gms) and controls (normal birth weight) with their mothers as subjects. Both groups were evaluated and compared based on the various neonatal and maternal factors.In our study, BOH (Bad obstetric history) was observed more among the subjects of case group. 31.2% cases had bad obstetric history while only 12.5% controls had the same. This difference was found to be statistically highly significant (p=0.007). This infers that BOH contributes to VLBW deliveries. This is supported by the studies like, Meresa et al [6] in which 18.8% had BOH, Singh et al [7] which observed that gestational diabetes, hypothyroid, malpresentations, hypertension, fetal distress, premature deliveries were the common causes of bad obstetric history in pregnant mothers and Anu MS et al [8] which also observed that an association existed between bad obstetric history and birth weight of the newborn (p<0.001).

A significant difference was observed among the two groups when compared for per capita incomes proving it to be contributing to VLBW condition in the present study. This is in akin to the study done by Anu MS et al [8]where an association existed between the maternal income and birth weight of the new born (p<0.001).But in our study, maternal occupation was not found to be significantly associated with birth weight of the babies which is

in contradiction to the study done by Anu MS et al[8] where an association also existed between the maternal occupation and birth weight of the newborn ($p<0.001$). The mean Height and weight of pregnant women included in the study by Anu MS et al[8]was observed to be 62.94±10.09 kg and 160.1±7.15 cm respectively and it was observed that a significant association existed between the maternal height and weight with birth weight of the new born($p<0.001$). Whereas in our study a significant difference was observed among the two groups when compared for mother's weight but mother's height was found to be statistically similar in both the groups. These observations were in accordance with the study by Arati Deka et al[9] where a significant association existed between the maternal weight with birth weight of the new born ($p<0.0016$) and no association between maternal height and birth weight of the baby was observed ($p>0.05$). Maternal Age and Birth weight of the new born were not found to be significantly associated with each other in the present study. This is in contradiction to the study done by Arati Deka et al [9] and Anu MS et al[8] where a significant association between maternal age and birth weight of the baby was observed. We also observed a significant difference ($p=0.0012$) among the two groups when compared for birth interval meaning that, if the birth interval is less, there are more chances of VLBW deliveries. Mother's mid arm circumference (representing nutritional status) and mother's literacy status were also found to have a significant association with birth weight of newborns.

Conclusion

Our study concludes that maternal factors like less birth intervals, low maternal weight, less mid arm circumference, illiteracy, low per capita income, less antenatal checkup visits and bad obstetric history are significantly related to Very Low Birth Weight in the newborns. Thus health education, antenatal counselling and nutritional care during pregnancy along with proper implementation of health programmes are essential to prevent low birth weight among newborns.

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