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Electrolyte Changes Following Phototherapy in Neonatal Hyperbilirubinemia

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Abstract: ***Neonatal Hyperbilirubinemia (NH) is the commonest abnormal physical finding during the first week of life. Neonatal Hyperbilirubinemia (NH) is the most common cause for readmission during the early neonatal period and is a cause of concern for the parents as well as for the pediatricians. Hence appropriate management of Neonatal Hyperbilirubinemia is of paramount importance. Phototherapy plays a significant role in prevention and treatment of hyperbilirubinemia. However, this treatment modality may itself result in inherent complications. Objective: To evaluate the electrolyte changes in neonates receiving phototherapy for neonatal hyperbilirubinemia. Method: A prospective hospital based observational comparative study conducted on 252 eligible neonates admitted in the Neonatal Intensive Care Unit receiving phototherapy at a teaching Hospital from December 1st 2012 to May 31st 2014. A predesigned proforma has aided the enrollment of newborns into the study according to AAP guidelines. Serum bilirubin and electrolytes were determined before and after termination of phototherapy. The first samples were considered as controls. A comparative study was made between before and after phototherapy groups to determine the incidence of electrolyte changes. Results: The study group included 252 neonates that were managed with phototherapy. Male: Female ratio was 1.45:1. Incidence of low birth weight babies was 23% and preterm was 20.2%. Mean birth weight and gestational age was 2.84±0.51 kg and 38.44±1.98 weeks respectively. Mean duration of phototherapy was 37.65±11.06hrs. The incidence of hypocalcemia post phototherapy found to be 13.1% (p=0.013) which was more in LBW babies (36.2%, p<0.001) and preterm neonates (41.2%, p<0.001) than in normal weight babies (6.2%) and term neonates (6.2%) and 18.8% when duration of phototherapy was >48hrs (p<0.001). The incidence of hyponatremia post phototherapy found to be 6% which was more in LBW babies (17.2%, p<0.001) and preterm neonates (17.6%, p<0.001) than in normal weight babies (2.6%) and term neonates (3.1%) and 17.4% when duration of phototherapy was >48hrs (p<0.001). Even the decline in mean serum calcium and sodium values found to be statistically significant. None of the hypocalcemic neonates were symptomatic clinically. The incidence of potassium and chloride changes following phototherapy was found to be non-significant irrespective of gestational age, birth weight and duration of phototherapy. Conclusion: The study shows that neonates undergoing phototherapy are at a higher risk of electrolyte changes. This risk is greater in premature and LBW babies and hence this group of babies should be closely monitored for changes in electrolytes and should be managed accordingly.***

Keywords: Electrolyte changes, Neonatal Hyperbilirubinemia, Phototherapy

1. Introduction

Neonatal hyperbilirubinemia (NH) is the commonest abnormal physical finding during the first week of life. Over two third of newborn babies develop clinical jaundice. The physical finding like yellowish discoloration of the skin and sclera in newborns is due to accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal physiological phenomenon[1].

Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during first week of life. 6.1% of well term newborn have a serum bilirubin over 12.9 mg%. Serum bilirubin over 15 mg% is found in 3% of normal term newborns. Nevertheless untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic and conjugated hyperbilirubinemia is a harbinger of underlying serious illness. [2]

Neonatal hyperbilirubinemia is a reflection of liver's immature excretory pathway for bilirubin and is the most common reason for readmission of neonates in first week of life in current era of postnatal discharge from hospital[3]. Neonatal hyperbilirubinemia is a cause of concern for the parents as well as for the pediatricians. [4]

Premature babies have much higher incidence of neonatal jaundice requiring therapeutic intervention than term neonates. Hyperbilirubinemia was found to be the most common morbidity (65%) among 137 extremely low birth weight neonates born over a period of 7 years in AIIMS. [5]

Elevated levels of unconjugated bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating permanent neurodevelopment handicaps. [6] Conjugated hyperbilirubinemia indicates potentially serious hepatic disorders or systemic illnesses. Hence appropriate management of neonatal hyperbilirubinemia is of paramount importance.

Hyperbilirubinemia can be treated either by phototherapy or exchange transfusion or pharmacologic agents. Phototherapy plays a significant role in prevention and treatment of hyperbilirubinemia. The main demonstrated value of phototherapy is that it reduces the need for exchange transfusion. As any treatment has its side effects, phototherapy also has its adverse effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, hypocalcemia, redistribution of blood flow and genotoxicity. [4, 5, 7]

Unlike other side effects, a few studies are currently available that depicts the adverse effects of phototherapy on serum electrolytes. Hypocalcemia is one of the known adverse effects. 90% of preterm and 75% of fullterm neonates develop hypocalcemia after being subjected to phototherapy[7,8]. Hypocalcemia can cause serious complication like irritability, jitteriness, convulsion, apnea. Hence, phototherapy induced hypocalcemia is a significant problem. Therefore, it is suggested that in the newborn requiring phototherapy, administration of calcium may be considered in them. Hence emphasis is given in special reference to hypocalcemia.

Very few studies are available regarding the changes in the other electrolytes (sodium, potassium, chloride). Hereby we intended to study the electrolyte changes due to phototherapy: whether any significant changes in sodium, potassium occurs in addition to hypocalcemia.

2. Review of Literature: Effect on Electrolytes

Hakanson Do et al (1981) reported that when young rats were exposed to white fluorescent light, the serum concentration of calcium did decrease. He showed that this calcium drop was accompanied by a decrease in serum melatonin concentration. This effect can be prevented by shielding the occiput, by inhibiting corticosterone synthesis, and by administration of exogenous melatonin. Light induced hypocalcemia may result from increased calcium uptake by bone when the blocking effect of melatonin decreases after pineal inhibition by transcranial illumination.[9, 10, 11]

Zecca et al (1983) reported that administration of 25-hydroxy vitamin D3 was not able to lower the incidence of the phototherapy induced hypocalcemia in preterm infants. He concluded that vitamin D was unlikely to play an important role in the pathogenesis of phototherapy induced hypocalcemia. [12]

Curtis et al (1989) studied diarrhea in jaundiced neonates treated with phototherapy. Study showed that absorption of sodium, chloride and potassium was significantly impaired in the patients receiving phototherapy. [13]

Sethi et al (1993), in his study titled "Phototherapy induced hypocalcemia" at Lady Harding Medical College, New Delhi, have shown that 90% of preterm neonates and 75% of fullterm neonates with hyperbilirubinemia treated with phototherapy developed hypocalcemia. [14]

Jain et al (1998), in his study titled "Phototherapy induced hypocalcemia" at department of pediatrics, Dayanand Medical College, Ludhiana, have found that 55% of preterm neonates and 30% of fullterm neonates with hyperbilirubinemia developed hypocalcemia after 48 hours of phototherapy. Of the preterm neonates, 67.3% had jitteriness and 27.33% had irritability. Among fullterm neonates, 50% had jitteriness and 16.7% had irritability. Hence, they concluded that phototherapy induced hypocalcemia is a significant problem and calcium supplementation to these babies may be considered[15]

Sourabh dutta (2001), in his study titled "Phototherapy for neonatal jaundice, recent advances and controversies" at PGIMER, Chandigarh, concluded that 90% of preterm neonates and 75% of fullterm neonates with unconjugated hyperbilirubinemia developed hypocalcemia after phototherapy. [16]

Karamifar et al (2002), in his study titled "Prevalence of phototherapy induced hypocalcemia" at division of endocrinology and metabolism and division of neonatology, Shiraz university, Iran found that prevalance of hypocalcemia was 22.6% in preterm neonates and 8.7% (p=0.018) in fullterm neonates after 48 hours of phototherapy for hyperbilirubinemia. This study showed that neonates under phototherapy are at higher risk of hypocalcemia. This risk is greater in premature neonates. [17]

Hunter et al (2004) hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium. Cortisol exerts a direct hypocalcemic effect and increases bone uptake of calcium as well. [18]

Eghbalian et al (2008), in his study titled "Phototherapy induced hypocalcemia in icteric newborns" at newborn ward of Ghaem and Ekbataen Hospitals of Hamadan, have found that serum calcium levels declined considerably after neonates with hyperbilirubinemia treated with phototherapy. The mean duration of phototherapy was three days. Decline in serum calcium level at times reached hypocalcemic threshold. There was direct relationship between duration of phototherapy and development of hypocalcemia. It was recommended that in order to prevent hypocalcemia in phototherapy treated newborns, calcium should be given as prophylaxis. [19]

Yadav RK et al (2011) in his study "The evaluation of effect of phototherapy on serum calcium level" have studied the effects of phototherapy in 20 term and 20 preterm hyperblirubinemic neonates. After 48 hours of phototherapy, a significant fall in calcium level in 66.6% of term and 80% of preterm neonates was observed. It is suggested that calcium level be assessed in neonates treated with phototherapy for more than 48 hours and managed accordingly.[20]

Taheri PA et al (2013) in his study titled " Prevalence of Phototherapy induced hypocalcemia in term neonate" at Tehran University of Medical Sciences, Iran in 147 term neonates and found decrease in serum calcium level in 56% babies, out of which 7% developed significant hypocalcemia (p=0.03) after 48 hours of phototherapy[21]

Arora S et al (2014) in her study "serum calcium levels in preterm and term neonates on phototherapy" at neonatal unit of Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar found statistically significant hypocalcemia in 43% of preterm neonates and 56% of term neonates after 48 hours of phototherapy and stated symptomatic hypocalcemia was more common in preterm

group than term group. [22]

Tan KL et al study was performed on 3 groups of healthy full term infants with hyperbilirubinemia exposed to continous phototherapy. This study showed raised potassium levels at 72 hrs in 2 of 3 phototherapy groups, but reverted to normal with cessation of phototherapy. [23]

Dee Beresford and Glenys Conolly stated that babies under phototherapy can have sodium imbalances due to insufficient fluid replacements. [24]

3. Materials and Methods

A prospective hospital based comparative observational study conducted on 252 eligible neonates admitted in the Neonatal Intensive Care Unit of a teaching hospital, south India from December 1st 2012 to May 31st after taking informed consent from parents which was approved by the hospital ethics committee.

All the neonates data who were receiving phototherapy for unconjugated hyperhyperbilirubinemia was recorded on a predesigned proforma. Those neonates with conjugated hyperbilirubinemia, associated co-morbidities like birth asphyxia, sepsis, renal failure, mothers taking anticonvulsant drugs, abnormal electrolyte findings before phototherapy, babies undergone exchange transfusion and in those babies with jaundice lasting for >14 days were excluded from the study.

Venous blood samples were collected from the neonates and sent for total bilirubin, direct bilirubin, electrolytes, and blood group. Total & direct bilirubin is measured by Diazo method: electrolytes (Na,K,Cl) by autoanalyser Erba EM 200 machine & calcium by Arsenazo method. Blood group of newborn was analyzed by antisera method.

Electrolytes were checked at 0 hour (first sample) and at 48 hours of phototherapy or at discontinuation of phototherapy (second sample) whichever is earlier. The first sample was considered as control. Comparative study was made between these two samples groups to determine the changes in electrolytes. All data of various groups was tabulated and statistically analyzed using suitable statistical tests (students tests) and the proportions were compared using chi-square test.

4. Results

The study was conducted on 252 neonates admitted to NICU for phototherapy. Data were analyzed using appropriate statistical software like SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1.
Study design: An observational prospective comparative clinical study.

Table 1: Gender distribution of neonates

Gender	No. of neonates (n)	%
Male	149	59.1
Female	103	40.9
Total	252	100.0

In our study group, the incidence of males and females were 59.1% (149) and

40.9% (103) respectively. Male: Female ratio was 1.45:1

Table 2: Weight distribution of neonates

Weight (kg)	*Gender*		*Total n (%)*
	Male	*Female*	
LBW (<2.5kg)	27(18.1%)	31(30.1%)	58(23%)
Normal	122(81.9%)	72(69.9%)	194(77%)
Total	149(100%)	103(100%)	252(100%)

Incidence of low birth weight babies was 23% Mean birth weight was 2.84±0.51 kg.

Table 3: Gestational age distribution of neonates

Gestational	*Gender*		*Total n (%)*
	Male	*Female*	
<37 weeks	25(16.8%)	26(25.2%)	51(20.2%)
37-40 weeks	119(79.9%)	75(72.8%)	194(77%)
>40 weeks	5(3.4%)	2(1.9%)	7(2.8%)
Total	149(100%)	103(100%)	252(100%)

P=0.225, not significant, Fisher Exact test

In our study group, the incidence of preterm babies were 20.2% (51) compared to 77% (194) in 37-40 wks gestational age and 2.8% (7) in >40 wks gestational age group. Mean gestational age in the study group was 38.44±1.98 weeks.

Table 4: Correlation of post Phototherapy serum electrolytes with birth weight

	Weight (kg)		*Total (n=252)*	*p value*
	LBW (n=58)	*Normal (n=194)*		
Calcium				
• <7	21(36.2%)	12(6.2%)	33(13.1%)	<0.001**
• 7-11	37(63.8%)	182(93.8%)	219(86.9%)	
Sodium				
• <135	10(17.2%)	5(2.6%)	15(6%)	<0.001**
• 135-145	48(82.8%)	185(95.4%)	233(92.5%)	
• >145	0(0%)	4(2.1%)	4(1.6%)	
Potassium				
• <3.5	0(0%)	1(0.5%)	1(0.4%)	
• 3.5-5.5	57(98.3%)	191(98.5%)	248(98.4%)	
• >5.5	1(1.7%)	2(1%)	3(1.2%)	
Chloride				
• <95	1(1.7%)	2(1%)	3(1.2%)	
• 95-105	57(98.3%)	189(97.4%)	246(97.6%)	
• >105	0(0%)	3(1.5%)	3(1.2%)	

The Incidence of hypocalcemia following phototherapy was more in low birth weight babies (36.2%) than in normal babies (6.2%). Thus it infers that low birth weight babies were at more risk of hypocalcemia following phototherapy than normal babies. By chi-square test using test for paired sample means, the **p value obtained was <0.001,** which by conventional criteria is less than the alpha value (p-0.05). Thus, it is considered to be **statistically significant.**

The Incidence of hyponatremia following phototherapy was also more in low birth weight babies (17.2%) than in normal babies (2.6%). Thus it infers that low birth weight babies were at more risk of hyponatremia following phototherapy

than term babies. By chi-square test using test for paired sample means, the **p value obtained was <0.001,** which by conventional criteria is less than the alpha value (p-0.05). Thus, it is considered to be **statistically significant.** The incidence of potassium and chloride changes following phototherapy was found to be non-significant (p value of potassium vs chloride was 0.787 vs 0.583 respectively) in both low birth weight babies and normal babies.

Table 5: Correlation of post Phototherapy serum electrolytes with gestational age

	Gestational age			Total (n=252)	p value
	<37 weeks (n=51)	37-40 Weeks (n=194)	>40 weeks (n=7)		
Calcium					
• <7	21(41.2%)	12(6.2%)	0(0%)	33(13.1%)	<0.001**
• 7-11	30(58.8%)	182(93.8%)	7(100%)	219(86.9%)	$\chi^2 = 44.5$ d.f=2
Sodium					
• <135	9(17.6%)	6(3.1%)	0(0%)	15(6%)	<0.001*
• 135-145	42(82.4%)	185(95.4%)	6(85.7%)	233(92.5%)	*χ
• >145	0(0%)	3(1.5%)	1(14.3%)	4(1.6%)	$2=23.49$ d.f=4
Potassium					
• <3.5	0(0%)	1(0.5%)	0(0%)	1(0.4%)	0.876
• 3.5-5.5	51(100%)	190(97.9%)	7(100%)	248(98.4%)	$\chi 2 = 1.2$ d.f=4
• >5.5	0(0%)	3(1.5%)	0(0%)	3(1.2%)	
Chloride					
• <95	1(2%)	2(1%)	0(0%)	3(1.2%)	
• 95-105	50(98%)	189(97.4%)	7(100%)	246(97.6%)	
• >105	0(0%)	3(1.5%)	0(0%)	3(1.2%)	

The Incidence of hypocalcemia following phototherapy was more in preterm neonates (41.2%) than in term neonates (6.2%). Thus it infers that preterm babies were at more risk of hypocalcemia following phototherapy than term babies. By chi-square test, using test for paired sample means, the **p value obtained was <0.001,** which by conventional criteria is less than the alpha value (p-0.05). Thus, it is considered to be **statistically significant.**

The Incidence of hyponatremia following phototherapy was more in preterm neonates (17.6%) than in term neonates (3.1%). Thus it infers that preterm babies were at more risk of hyponatremia following phototherapy than term babies. By chi-square test, using test for paired sample means, the **p value obtained was <0.001,** which was considered to be **statistically significant.**

The incidence of potassium and chloride changes following phototherapy was found to be non-significant (p value of potassium vs chloride was 0.876 vs 0.864 respectively) in both pre terms and term neonates.

Table 6: Correlation of post PT serum electrolytes with duration of phototherapy

	Duration of PT			Total (n=252)	p value
	<24 hrs (n=7)	24-48 hrs (n=176)	>48 hrs (n=69)		
Calcium					
• <7	0(0%)	20(11.4%)	13(18.8%)	33(13.1%)	
• 7-11	7(100%)	156(88.6%)	56(81.2%)	219(86.9%)	<0.001
Sodium					
• <135	0(0%)	3(1.7%)	12(17.4%)	15(6%)	
• 135-145	7(100%)	171(97.2%)	55(79.7%)	233(92.5%)	
• >145	0(0%)	2(1.1%)	2(2.9%)	4(1.6%)	
Potassium					
• <3.5	0(0%)	1(0.6%)	0(0%)	1(0.4%)	
• 3.5-5.5	7(100%)	173(98.3%)	68(98.6%)	248(98.4%)	
• >5.5	0(0%)	2(1.1%)	1(1.4%)	3(1.2%)	
Chloride					
• <95	0(0%)	0(0%)	3(4.3%)	3(1.2%)	
• 95-105	7(100%)	174(98.9%)	65(94.2%)	246(97.6%)	
• >105	0(0%)	2(1.1%)	1(1.4%)	3(1.2%)	

➢ Mean duration of phototherapy was 37.65±11.06hrs

The Incidence of hypocalcemia was 18.8% when duration of phototherapy was >48hrs as compared to duration <48hrs (10.9%). Thus it infers that babies were at higher risk of hypocalcemia if kept under phototherapy for more than 48hrs. By chi-square test, using test for paired sample means, the **p value obtained was <0.001.** Thus, it is considered to be **statistically significant.**

The Incidence of hyponatremia was 17.4% when duration of phototherapy was >48hrs as compared to duration <48hrs (1.6%). Thus it infers that babies were at higher risk of hyponatremia if kept under phototherapy for more than 48hrs. By chi-square test, using test for paired sample means, the **p value obtained was <0.001,** which was considered to be **statistically significant.**

The incidence of potassium and chloride imbalances was found to be non- significant (p value of potassium vs chloride was 0.967 vs 0.085 respectively) with duration of phototherapy.

Table 7: Conclusive comparative evaluation of study variables pre and post phototherapy in neonates

	Pre	Post	difference	t value	P value
Total Bilirubin	17.39±1.88	11.93±1.71	5.469	39.972	<0.001**
Calcium	9.16±1.00	8.53±1.17	0.622	9.201	<0.001**
Sodium	139.02±3.12	138.16±3.36	0.861	4.087	<0.001**
Potassium	4.59±0.51	4.69±0.53	-0.094	-2.286	0.23
Chloride	101.18±3.18	101.02±3.95	0.162	0.590	0.556

Overall, there was significant decline in serum calcium and sodium along with total bilirubin following phototherapy.

5. Discussion

Neonatal Hyperbilirubinemia (NH) is the commonest abnormal physical finding during the first week of life. Early discharge of healthy term newborns from the hospital

after delivery has recently become a common practice for medical, social and economic reasons. However, it has been shown that newborns whose post- delivery hospital stay < 72 hours are at a significantly greater risk for readmission than those whose stay is >72 hours. Phototherapy has emerged as the most widely used form of treatment and is the current therapy of choice to reduce severity of neonatal unconjugated hyperbilirubinemia. As any treatment has its side effects, phototherapy also has. Few studies are currently available that depicts the adverse effects of phototherapy on serum electrolytes. A few studies in the recent past, have stressed on the incidence of hypocalcemia following phototherapy and very few studies till date regarding the effect of phototherapy on all electrolytes. Hence our study was designed to determine the electrolyte changes in neonates receiving phototherapy for neonatal jaundice.

A. Phototherapy induced hypocalcemia has been reported in several studies.

Table 8: Comparison of gestational age groups with other studies

Study	*Year*	*Study group*	*Preterm*	*Term*
Sethi et al[14]	1993	40	20	20
Jain et al[15]	1998	40	20	20
Karamifar et al[17]	2002	153	62	91
Yadav RK et al[20]	2012	30	15	15
Arora et al[22]	2014	100	46	54
Our study		252	51	201

The present study included a total of 252 neonates which comprised of 51 preterms and 201 term neonates. Sethi et al[14] (1993) and Karamifar et al[17] (2002) selected preterms more than 31 weeks whereas Eghbalian et al[19] (2002) included only term neonates. Arora et al (2014) [22] included 46 preterm and 54 term neonates.

All the term and preterm neonates in the present study were appropriate for gestational age. Same was the case in the studies done by Romagnoli et al (1979), Sethi el al[14] (1993), Jain BK et al[15] (1998) and Arora et al[22] (2014).

Our study group included more number of neonates compared to other above mentioned studies.

Table 9: Comparison of mean gestational age with other study

Study	**Preterms**	**Terms**
Jain et al[15]	34.30 ±1.16 weeks	37.55 ± 0.69 weeks
Our study	34.94± 1.24 weeks	39.26±0.68 weeks

Mean Gestational age of our study group preterms vs term were 34.94±1.24weeks vs 39.26±0.68 weeks respectively which was in correlation to Jain et al[15] study 34.30±1.16 weeks vs 37.55 ± 0.69 weeks respectively.

Table 10: Comparison of mean birth weight with other studies

Study	Preterms	Terms
Jain et al[15]	2150 ± 150 grams	2800 ± 220 grams
Karamifar et al[17]	2077±316 grams	2889±474 grams
Our Study	2240±340 grams	2980±410 grams

Mean birth weight of our study group preterms vs term were 2240±340 grams vs 2980±410 grams respectively which were in consonance to Jain et al[15] study in which mean birth weight in preterm vs term were 2150 ± 150 grams vs 2800 ± 220 grams and Karamifar et al[17] 2077±316 grams Vs 2889±474 grams respectively. In study done by Taheri et al[21], mean birth weight in term neonates was 3182±430 grams.

Table 11: Comparison of mean total serum bilirubin (TSB)

Study	Preterms	Terms
Karamifar et al[17]	16.2±3.0 mg/dl	18.0±2.4 mg/dl
Taheri et al[21]	-	20.1±3.3 mg/dl
Our Study	16.98±1.78mg/dl	17.52±1.91mg/dl

Mean total serum bilirubin (TSB) in our study group were 16.98±1.78mg/dl and 17.52±1.91mg/dl in preterms and term neonates respectively compared to a similar study by Karamifar et al[17] which showed 16.2±3.0 mg/dl and 18.0±2.4 mg/dl. In the study by Taheri et al[21], mean TSB in term neonates was 20.1±3.3 mg/dl.

Table 12: Comparison of mean phototherapy duration with other study

Study	Mean PT duration
Eghbalian et al[19]	3.0 days(1 to 7 days)
Our Study	37.65±11.06 hrs

Mean duration of phototherapy in our study was 37.65±11.06 hour which is in contrast to Eghbalianet al[19] study where it was 3 days.

Table 13: Correlation of hypocalcemia with other studies

Study	*Year*	*No. of cases*	Hypocalcemia after PT		P value
			Preterms(n)	*Terms (n)*	
Sethi et al[14]	1993	40	90% (18)	75% (15)	$p<0.05$
Jain et al[15]	1998	40	55% (11)	30% (6)	$p<0.05$
Karamifar et al[17]	2002	153	22.6% (14)	8.7% (8)	$p<0.018$
			14.4% (22)		
Yadav RK et al[20]	2012	30	80% (12)	66.6% (10)	$p<0.05$
Arora et al[22]	2014	100	43% (20)	56% (30)	*P<0.05*
Our study		252	41.2% (21)	6.2% (12)	$p<0.001$**
			13.1% (33)		

In our study, we found that **13.1% (33)** cases to be hypocalcemic after phototherapy. The relationship found to be statistically significant **(p<0.001)**. The Significant fall in serum calcium level in preterms and term babies after phototherapy observed was in correlation to Karamifar et al study. [17]

Romagnoli and colleagues in 1979 were the first to suggest an association between hypocalcaemia and phototherapy in preterm neonates and observed hypocalcemia in 52.3% babies[12] This study was in consonance with our study.

Sethi et al (1993) study has shown that 90% of preterm neonates and 75% of full term neonates treated with phototherapy developed hypocalcemia. [14]

Jain et al (1998) have found that 55% of preterm neonates and 30% of full- term neonates developed hypocalcemia after phototherapy. There was a statistically significant ($p < 0.05$) difference in the serum calcium level. This study was in correlation with our study where the incidence in preterm found to be 41.2%.[15]

Sourabh Dutta (2001) concluded that 90% of preterm neonates and 75% of fullterm neonates developed hypocalcemia after being subjected to phototherapy. [16]

Karamifar et al (2002) found that prevalance of hypocalcemia was 22.6% in preterm neonates and 8.7% ($p=0.018$) in full term neonates after phototherapy. This risk was greater in premature neonates. This study was in correlation with our study where the incidence in term found to be 6.2%.[17]

Eghbalian study found statistically significant difference ($p<0.05$) between pre- and post-phototherapy plasma calcium levels in term neonates. [19]

Yadav RK et al (2011) found a significant fall ($p<0.05$) in calcium level in 66.6% of term and 80% of preterm neonates after 48 hours of phototherapy. [20] Taheri et al (2013) studied the prevalence of phototherapy induced hypocalcemia in 147 term neonates and found decrease in serum calcium level in 56% babies out of which 7% developed significant hypocalcemia ($p=0.03$) after 48 hours of phototherapy. [21]

Arora et al (2014) study concluded that hypocalcemia was more frequently observed in term neonates as compared to preterm neonates which was in contrast to our study. Higher incidence of hypocalcemia in term group in Arora et al study was probably attributed to higher cut off value of serum calcium level of 8mg/dl as compared to 7mg/dl in preterm babies. [22] The incidence of hypocalcemia in the above study was 43% in preterm neonates which was in consonance with our study.

Much higher incidence of hypocalcemia was observed by Sethi et al and lowest incidence was reported by Karamifar H et al. The reason for this difference is not very clear but can be explained by the lower number of study groups taken in the other studies.

In our study, hypocalcemia occurred more frequently after 48 hrs of continuous phototherapy which was similar to Arora et al study. Symptomatic hypocalcemia was observed in Sethi et al[14], Jain et al[15] and Arora et al[22]

In the present study, it was observed that phototherapy induces considerable decline in serum calcium level in icteric newborn therapy and this decline may continue down to the threshold of hypocalcemia but was not accompanied by signs and symptoms found in hypocalcemia such as jitteriness, apnea, cyanosis and or convulsion which was in comparison to Karamifar et al study.

Table 14: Comparison of mean serum calcium levels before and after phototherapy in preterm neonates with other study

Study	Mean±SD serum calcium level		p value
	Before phototherapy (in mg/dl)	*After phototherapy (in mg/dl)*	
Karamifar et al[17]	8.73±1.38	8.40±1.71	0.039
Our Study	9.10±1.13	7.96±1.34	<0.001**

In our study mean serum calcium level before and after phototherapy in preterm neonates was 9.10±1.13mg/dl and 7.96±1.34 mg/dl respectively. There was a significant decline in the mean calcium level following phototherapy ($p<0.001$). This was similar to the study done by Karamifar et al with significant p value 0.039.

Table 15: Comparison of mean serum calcium levels before and after phototherapy in term neonates with other studies

Study	Mean±SD serum calcium level		*p* value
	Before phototherapy (in mg/dl)	After phototherapy (in mg/dl)	
Eghbalian et al[19]	9.85±1.23	9.09±0.93	<0.001
Karamifar et al[17]	9.53±0.92	9.30±1.11	0.043
Taheri et al[21]	9.8±0.80	9.5±0.90	<0.05
Our Study	9.32±0.97	8.82±1.04	<0.001**

In our study there was a significant decline in mean serum calcium level following phototherapy in term neonates also ($p<0.001$) which was similar to the other studies done by Eghbalian et al[19], Karamifar et al[17] and Taheri et al[21]

B. Phototherapy induced other electrolyte changes

There are very few studies regarding phototherapy induced other electrolyte changes. The differential effect of other electrolytes with phototherapy has not been studied by other workers except that for Curtis MD et al (1981) study which stated that absorption of water, sodium chloride, and potassium was significantly impaired in the patients receiving phototherapy. [13]

Incidence of hyponatremia in our study group was 6% and found to be higher in <37 wks group (17.6%) and LBW babies (17.2%) than in >37 wks group (3.1%) and normal weight babies (2.6%). Mean serum sodium levels were significantly decreased after phototherapy. As the P value <0.001, this difference is considered to be statistically significant.

There were no significant potassium or chloride changes in our study. Tan KL et al[23] (1981) study in healthy full term neonates demonstrated a transient raise in potassium levels after phototherapy which was in contrast to our study.

It is evident that in the present study phototherapy induced hypocalcemia and hyponatremia was more in preterm and LBW babies but the actual relationship in these babies with phototherapy has to be evaluated with larger sample studies for estimation of the incidence as the metabolic side effects are more common in preterm and LBW babies.

6. Conclusions

Incidence of hypocalcemia in our study group is 13.1% and is higher in preterm (41.2%) and low birth weight babies (36.2%) than in >37weeks gestational age group (6.2%) and normal weight babies (6.2%). Incidence of hypocalcemia following phototherapy is higher when the duration of phototherapy is more than 48 hours when compared to less than 48 hours. Mean Serum calcium levels were significantly decreased after phototherapy. Incidence of hyponatremia in our study group is 6% and is higher in preterm (17.6%) and low birth weight babies (17.2%) than in >37 weeks group (3.1%) and normal weight babies (2.6%). Incidence of hyponatremia following phototherapy is higher when the duration of phototherapy is more than 48 hours when compared to less than 48 hours. Mean Serum sodium levels were significantly decreased after phototherapy. There are no significant changes in potassium and chloride levels following phototherapy. Preterm neonates and low birth babies are at higher risk and hence this group of babies should be closely monitored. Proper monitoring of electrolytes after phototherapy in the neonates can prevent dyselectrolytemia, in turn prevent the related complications.

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