

## STUDY TO KNOW THE EFFECT OF PHOTOTHERAPY ON SERUM CALCIUM LEVEL IN NEONATAL HYPERBILIRUBINEMIA

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### ABSTRACT

**Objective:** Phototherapy is the most common method to treat neonatal jaundice. The effect of phototherapy on serum calcium levels is a questionable issue.

To study to know the effect of phototherapy on serum calcium level in neonatal hyperbilirubinemia.

**Methods:** Cohort study compared total serum calcium level before and after phototherapy in neonates with hyperbilirubinemia. Study was conducted on 54 neonates with high total serum bilirubin levels, according to the Bhutani curve and was treated with phototherapy at neonatal intensive care unit in the Department of Pediatrics at Mayo Institute of Medical Sciences from November 2021 to April 2022.

**Results:** Hypocalcaemia was observed in 33.33% of neonates after phototherapy. The difference between pre- and post-phototherapy serum calcium levels was found to be statistically significant ( $p < 0.005$ ).

**Conclusion:** Hypocalcemia has a significant association with phototherapy.

**Keywords:** Hyperbilirubinemia, Hypocalcemia, Phototherapy.

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### INTRODUCTION

Hyperbilirubinemia (commonly termed as Jaundice) is a common and, in most cases, benign problem in neonates. Jaundice is observed during the 1<sup>st</sup> week of life in approximately 60% of term neonates and 80% of pre-term neonates. Jaundice from deposition of indirect bilirubin (non-obstructive jaundice) in the skin tends to appear bright yellow or orange, whereas obstructive jaundice (direct bilirubin) has a greenish or muddy yellow cast. Jaundice appears in cephalocaudal progression, starting from face to abdomen and then feet, as serum levels increases. Infants with severe hyperbilirubinemia may present with lethargy and poor feeding and, without proper management, can progress to acute bilirubin encephalopathy (Kernicterus) [1]. Clinical jaundice has been seen in more than two-thirds of newborn. It has also been studied that mostly in neonates, unconjugated hyperbilirubinemia reflects a normal or exaggerated physiological phenomenon [2]. Neonatal hyperbilirubinemia is a clinical manifestation of several factors, which cause the inability of the liver to produce, combine, absorb, and excrete bilirubin which manifests as neonatal jaundice [3].

Phototherapy changes the structure of bilirubin and thus increases its excretion: currently the standard treatment for neonatal jaundice [4]. Phototherapy is one of the routine methods for the management of neonatal hyperbilirubinemia. However, it is not a harmless intervention. It can produce various side effects such as skin rashes, temperature instability, feeding intolerance, loose stools, dehydration, retinal damage, redistribution of blood flow, hypocalcemia, bronze baby syndrome, and genotoxicity. In phototherapy, there is photo-oxidation of bilirubin into water soluble or less lipophilic colorless form of bilirubin which is readily excreted in bile, feces, and urine.

One of the less well-known side effects of phototherapy is hypocalcemia. It is defined as total serum calcium of  $< 7$  mg/dL

( $1.75$  mmol/L) or ionized calcium  $< 1$  mmol/L ( $4$  mg/dL) in pre-term infants and  $< 8$  mg/dL ( $2$  mmol/L) or ionized calcium  $< 1.2$  mmol/L ( $4.8$  mg/dL) in term neonates. It can cause serious complications such as neuromuscular irritability, jitteriness, convulsion, myoclonic jerks, apnea, cyanosis, and laryngospasm [5].

Cardiac manifestations of hypocalcemia are tachycardia, prolonged QT interval, decreased contractility, and heart failure [5].

### Aims and objectives

Aims and objectives were to study the calcium levels in neonates with physiological unconjugated hyperbilirubinemia after phototherapy.

### METHODS

Baby in neonatal intensive care unit in the Department of Pediatrics at Mayo Institute of Medical Sciences between November 2021 and April 2022 were used. Ethical approval for the study was obtained from the Institutional Ethical Review Committee.

### Sample size

54 neonates.

### Study design

It was a hospital-based prospective study.

### Study duration

The study duration was 6 months.

### Study technique

#### Inclusion criteria

1. Icteric stable neonates
2. Neonates who required management with phototherapy.

**Exclusion criteria**

- 1- Neonates with other life-threatening conditions/extreme preterm
- 2- Neonates not willing to join the study
- 3- Neonates with decreased serum calcium levels before phototherapy
- 4- Neonates requiring exchange transfusion
- 5- Neonates born with apparent major congenital anomalies.

Pre-test and post-test counseling was given to the parents. After written consent from the parents, those neonates who fulfilled the inclusion criteria were performed blood test such as serum calcium levels and serum bilirubin levels before and after phototherapy.

Complete maternal history was taken.

Complete history and physical examination were carried out of all neonates included in the study. Demographic and clinical variables were recorded. It included gestational age, sex, mode of delivery, birth weight and anthropometric measurements (weight, length, and head circumference), maternal blood group and Rh status, baby blood group and Rh status and time of appearance of icterus (in Days of life) of neonates at the time of admission and duration of phototherapy.

**Materials requirements**

Taking all aseptic precaution, peripheral vein was punctured and blood was taken immediately for serum bilirubin. In addition to CBC and blood group, serum bilirubin was estimated by Jendrassik and Groff's method.

Total serum bilirubin and serum calcium levels before and at the end of phototherapy were recorded. The first sample was considered as control. Hypocalcemia was considered as total serum calcium of <8 mg/dL or ionized calcium of <1 mmol/L (4 mg/dL). Neonates were clinically assessed for features of hypocalcemia.

**Steps of procedure**

A conventional phototherapy equipment, containing blue light fluorescent lamps with wavelengths of 420–470 nm, was placed at a distance of 25–35 cm and irradiance 15 μW/cm<sup>2</sup>/nm from the skin surface of neonates under standard protocol with eyes and genitals completely covered and taking precautions for hydration of the neonates.

Single- or double-surface phototherapy was given to the neonates, based on their serum bilirubin values.

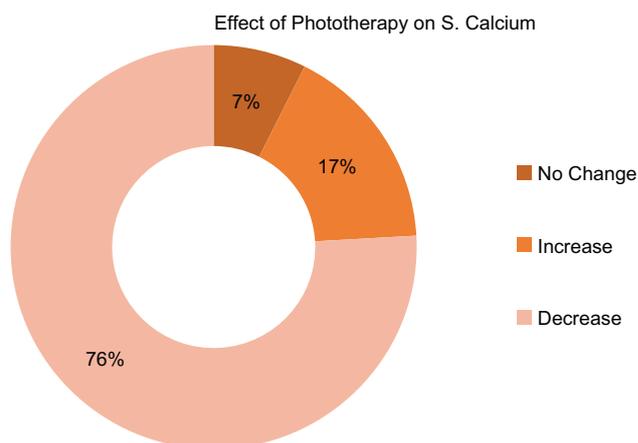
**Statistical software used**

1. Microsoft Excel sheet 2019
2. 17<sup>th</sup> version of SPSS software.

**RESULTS**

Study was done in 54 newborns. Out of these, 30 babies were male and 24 babies were female. 11 babies were born through vaginal delivery and 40 through cesarean section and 1 through assisted vaginal delivery. Majority of babies (around 69%) develop jaundice between the 3<sup>rd</sup> and 5<sup>th</sup> day of life.

Table 1 shows that after exposure to phototherapy, in pre-term neonates, there was a significant fall in ionized calcium level (p<0.0001). Similarly, in term neonates, there was a significant fall in ionized calcium level (p<0.0001).



Even though 75.9% (n=41) of babies had reduction in ionized calcium, only 33.3% (n=18) of babies developed hypocalcemia, which include all pre-term babies in the study sample.

Of the 10 term neonates that developed hypocalcemia, 2 became symptomatic, developed jitteriness, and none of the neonate developed convulsion. All the preterm neonates who developed hypocalcemia after exposure to phototherapy, became symptomatic developed jitteriness, and none of the neonate developed convulsion. All the symptomatic babies were started on oral calcium supplement with serum calcium level monitoring.

**DISCUSSION**

Neonatal jaundice or neonatal hyperbilirubinemia is the commonest cause of NICU admission. Phototherapy is widely accepted as a relatively safe and effective method for treatment of neonatal hyperbilirubinemia as described by Cremer *et al* in 1953 but there are very less number of studies showing the adverse effects of phototherapy [6]. One of the known side effects of phototherapy is hypocalcaemia.

Romagnoli was the first to suggest the association of hypocalcaemia and phototherapy in preterms [7]. Hakinson and Hunter hypothesized that phototherapy inhibits pineal secretion of melatonin which blocks the effect of cortisol on bone calcium [8,9]. So, cortisol increases bone uptake of calcium and induces hypocalcaemia.

In the present study, it was found that after phototherapy about 75.9% (n=41/54) babies had a decrease in ionised calcium level from the initial value. Out of these 33.3% (18/54) babies had hypocalcaemia, that include 14.8% (n=8/54) preterm and 18.5% (n=10/54) term neonates. All preterm in the study had hypocalcaemia post phototherapy, i.e. 100%. Even though 33.3% babies had hypocalcaemia only 13% babies (5 preterm and 2 term babies) were symptomatic and were having jitteriness.

In a study by Yadav RK *et al*, there was significant decrease in calcium levels, P Value <0.0001 after phototherapy which was similar to ours study, mean value of ionised calcium before phototherapy was 1.26 +/- 0.04 and after phototherapy, 1.20 +/- 0.09 in term babies ( P Value <0.0001) and mean value of ionised calcium before phototherapy in Preterm Babies, 1.10 +/- 0.06 and after phototherapy was 0.96 +/- 0.02 ( P Value <0.0001) [10].

**Table 1: Comparison of ionized calcium levels before and after phototherapy**

	Mean value of ionized calcium before phototherapy (mmol/L)	Mean value of ionized calcium after phototherapy (mmol/L)	p-value
Term	1.26±0.04	1.20±0.09	<0.0001
Preterm	1.10±0.06	0.96±0.02	<0.0001

**Table 2: Frequency distribution showing change in ionised calcium value after phototherapy**

Effect of phototherapy on serum calcium	Frequency (%)
No change	4 (7.4)
Increase	9 (16.7)
Decrease	41 (75.9)
Total	54 (100)

**Table 3: Descriptive data of ionised calcium levels postphototherapy**

Variable	n=54, n (%)
Hypocalcaemia in preterm (i ca<1 mmol/L)	8/54 (14.8)
Hypocalcaemia in term (i ca<1.2 mmol/L)	10/54 (18.5)
Normal serum calcium	36/54 (66.7)

**Table 4: Descriptive data of symptoms among hypocalcemic cases post phototherapy**

Variable	n=18/54
Asymptomatic	11/54
Symptomatic (jitteriness)	7/54

**Table 5: Incidence of hypocalcemia based on the duration of phototherapy**

Duration of phototherapy (h)	Hypocalcaemia	Percentage
24	1	5.6
36	8	44.4
48	9	50
Total	18	100

In a study by Rozario CI *et al*, they concluded that the mean serum calcium level before phototherapy and after phototherapy but the difference between our and their study was that they had measured the serum calcium levels rather than ionized calcium levels as in our study [11].

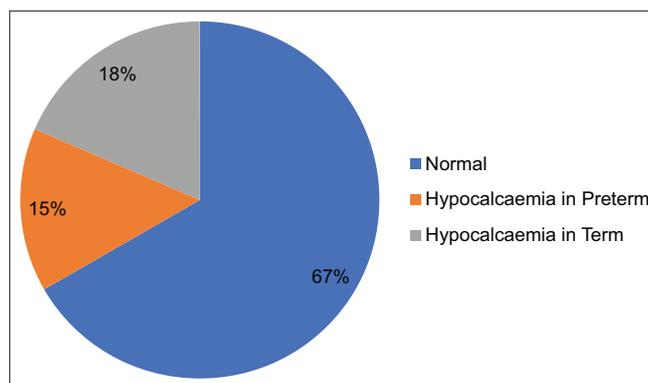
In effect of phototherapy on serum calcium level in neonatal Jaundice by Bahbah M H *et al*, it was concluded that there is significant difference between serum calcium level post phototherapy in neonatal hyperbilirubinemia. This study was a prospective case control study [12].

In a study by Arora *et al*, it was reported that 56% term babies developed hypocalcemia post phototherapy and Jain B K *et al*, also concluded hypocalcemic effects of phototherapy in 30% term babies and 55% preterm neonates [13,14]. The difference between this and our study was that Jain B K *et al*, considered serum calcium level <8 mg/dl as hypocalcemia so they have got a higher prevalence of hypocalcemia.

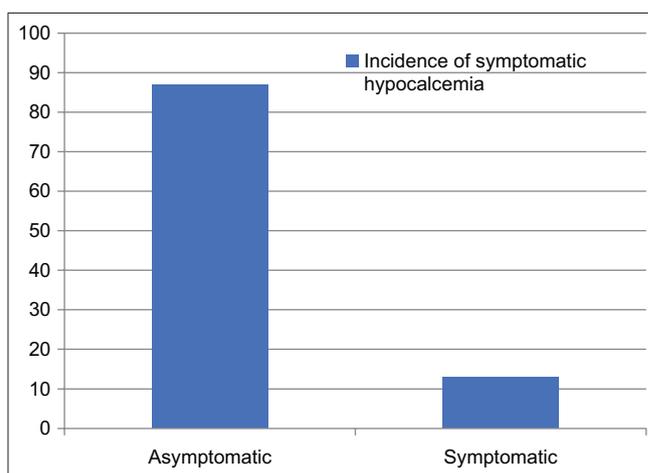
In a study by Yadav RK *et al* the comparison between mean serum calcium levels post phototherapy was significant between preterm n term neonates p<0.0001, similar result as of our study [10].

In our study, Out of 54 neonates, 30 (55.6%) were male and 24 (44.4%) were female. Similar gender ratio i.e. 59 babies males and 41 female babies was observed by Rozario IC *et al*, [11] Whereas Goyal S *et al*, reported 61.0% boys and 39.0% of girls [15].

Maximum 85.2%(n=46/54) were term and 14.8%(n=8/54) were pre-term neonates reported in the present study, in which all preterm post phototherapy were found hypocalcaemia and 10 term were found hypocalcaemia. Whereas Pankaj Singh K *et al* observed Preterm neonates were 33% and 67% cases were term neonates [16]. Al-ali MA *et al*, found that 50.0% were pre-term and term neonates [17].



**Fig. 1: Percentage of hypocalcemic neonates after phototherapy**



**Fig. 2: Incidence of symptomatic hypocalcemia**

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Out of 54, 22.2% (n=12/54) of neonates had normal vaginal delivery and 87.8% (n=40/54) delivered by cesarean section. Whereas study reported by Goyal S *et al*, 57.0% neonates were delivered by normal vaginal delivery and 43.0% by lower segment caesarean section [15]. In a study by Gupta A *et al*, it was concluded that there is increased incidence of hyperbilirubinemia in neonates born with caesarian section than in normal vaginal delivery which also was in correlation with our study [18].

**CONCLUSION**

Phototherapy-induced hypocalcemia is a significant problem. We need further more studies which exactly will prove their correlation post-phototherapy also comparison on the various factors such as gestational age, gender, and mode of delivery. Hence, authors could say that although phototherapy is widely accepted as a relatively safe and effective method for the treatment of neonatal hyperbilirubinemia, we recommend monitoring serum calcium concentrations during and after phototherapy in babies receiving phototherapy. Calcium supplementation can be considered as prophylaxis in neonates undergoing phototherapy.

**ETHICAL ISSUES**

No ethical issues have been found to be occurring in this study.

**CONFLICTS OF INTERESTS**

No conflicts of interests have been found to be occurring.

**FINANCIAL SUPPORT AND SPONSORSHIP**

No financial support. Sponsorship has been obtained.

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