ORIGINAL ARTICLE

Effect of Phototherapy on Serum Calcium Level in Neonatal Jaundice

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ABSTRACT

Objective: The aim of this study was to determine the effect of phototherapy induced hypocalcemia in icteric newborns and to compare it between preterm and term neonates.

Study Design: Quasi experimental study.

Place and Duration of Study: Pakistan Air Force (PAF) hospital Islamabad, from 1st July 2021 to 31st January 2022.

Materials and Methods: A total of 62, full term and late preterm neonates, requiring phototherapy for indirect hyper-bilirubinemia were included. The serum calcium levels were checked, pre and post phototherapy or 48 hours after start of phototherapy whichever came earlier. The data of patients, regarding gender, gestational age, chronological age and mode of delivery was recorded. The data was analysed in SPSS version 22. The frequency and percentages were calculated for qualitative variables i.e gender and mode of delivery. The mean and standard deviation were calculated for quantitative variables i.e age, gestational age, duration of phototherapy, pre and post phototherapy serum calcium levels. The paired sample t test was applied to compare pre and post phototherapy serum calcium levels. The *p*-value < 0.05 was considered statistically significant.

Results: There were 39 (62.90%) males and 23 (37. 10%) females, with mean age of 4.52 ± 1.25 days. The mode of delivery was cesarean section in 41 (66.13%) cases while 21 (33.87%) were delivered as vaginal delivery. The mean gestational age was 38.11 ± 1.49 weeks. The mean duration of phototherapy was 3.17 ± 0.55 hrs. The mean value of pre and post therapy serum calcium level was 9.59 ± 0.52 mg/dl and 9.07 ± 0.44 mg/dl respectively (*p* value = 0.0001). The post phototherapy calcium levels did not have any significant association with gestational age, gender and chronological age of the newborns i.e. the *p* value was 0.174, 0.269, 0.134 respectively.

Conclusions: Phototherapy resulted in a significant reduction in serum calcium levels after 48 hours; however, none of the neonates developed hypocalcemia.

Key Words: *Calcium, Neonatal Jaundice,Phototherapy.*

Introduction

Neonatal jaundice is a significant contributor to morbidity and the primary cause for hospitalization within the initial week of life. The global occurrence of severe neonatal jaundice varies across regions, ranging from 3.34% in Africa to 2.58% in South-East Asian regions.[1] About 60% of term and 80% of preterm infants develop jaundice in the first seven days of their lives.[2] Majority of these cases are of physiologic jaundice. Various factors contribute towards physiologic jaundice including increased neonatal erythrocyte destruction, slow bilirubin elimination through hepatocytes and underdeveloped liver conjugating enzymes. In full term infants, physiologic jaundice tends to self resolve within a week while in preterm neonates, it is more severe and takes a longer time to resolve.[3]

Pathological hyperbilirubinemia always has some serious underlying pathology. It can be caused by genetic or familial factors, immune or non-immune hemolytic anemia, congenital infections, birth trauma or prematurity.[4]

In either scenario, it is imperative to maintain the total bilirubin (TB) concentration below the specified

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threshold as per AAP hour-specific phototherapy nomograms, to prevent the grave ramifications of kernicterus.[5] Various treatment modalities including phototherapy, exchange transfusion or immunoglobulins can be used, depending upon the cause.[3] Phototherapy is required in 5-10% of term neonates for preventing a steep rise of bilirubin to harmful level.[2]

The adverse effects associated with phototherapy include diarrhea, temperature instability, rashes, retinal damage, increased fragility of red blood cells, bronze baby syndrome, dehydration, and thrombocytopenia.[6] A less acknowledged side effect of phototherapy is its potential association with neonatal hypocalcemia.[7]

Calcium is an important micronutrient involved in normal homeostasis, neuromuscular excitability, proper membrane and cellular enzymatic activity. Hypocalcemia can lead to disturbance of all these functions leading to seizures in neonates.[8]

A decrease in serum calcium is observed in infants receiving phototherapy.[8,9] Blue light of phototherapy increases vitamin D breakdown in the skin, enhances urinary excretion of calcium and stimulates multiple hormonal and enzymatic pathways that result in transient drop of serum calcium.[9]

Neonatal hypocalcemia is defined as serum calcium level <8mg/dl in full-term infants and < 7mg/dl in preterm.[8] Early-onset hypocalcemia can be seen within 48-72 hours of life, in preterm and very low birth weight infants (VLBW), babies experiencing hypoxic ischemic encephalopathy (HIE), infant of diabetic mother (IDM) and intrauterine growth retardation (IUGR) babies.[8] Late-onset hypocalcemia is caused by excessive phosphate intake, low serum magnesium levels, hypoparathyroidism, and vitamin D deficiency.[10]

In 80% of neonates ,serum calcium level decreases after phototherapy.[9,10] Research conducted in Egypt reveals that calcium level, pre and post phototherapy was 9.63±0.79 and 9.04±0.78 respectively. Neonates (26%) developed hypocalcemia following phototherapy.[9] The effect of phototherapy on serum calcium level in neonates is not well perceived in Pakistan. This makes it imperative to assess and quantify phototherapy induced decrease in serum calcium level, in order to avoid life threatening complications of hypocalcemia in neonates. Current study aimed to determine the magnitude of decline in serum calcium level after 48 hours of therapy and to find the effect of gestation , chronological age of neonate or gender on this decline .

Materials and Methods

This Quasi experimental study was carried out in NICU of PAF hospital, Islamabad from 1st July 2021 to 31st January 2022, after approval from the hospital ethical committee (ERC#12).The sample size was calculated as 62, using world health organization (WHO) calculator.The confidence level was taken as 95%, precision of 1%, population mean was 0.43 and SD was 0.04 .[11] After taking informed written consent, full term and late preterm neonates of gestational age (34 0/7 - 41 6/7) having indirect hyper-bilirubinemia and requiring phototherapy according to American Academy of Pediatrics (AAP) guidelines, were enrolled in study.[5] Neonates <34 weeks of gestation, neonates with cardiopulmonary compromise, those having hypocalcemia or any maternal risk factor like gestational diabetes (GDM) and pregnancy induced hypertension (PIH) were excluded. The data was collected on a self-designed proforma. Under aseptic measures, 3ml blood was drawn from a peripheral vein of neonate by duty staff/duty resident and sent to labortary for serum bilirubin and serum calcium levelsS.

Serum calcium levels were repeated after discontinuation of phototherapy or 48 hours after start of phototherapy whichever came earlier. The labortary investigations were free for the study participants. Neonatal hypocalcemia was defined as total serum calcium concentration < 8 mg/dL (< 2 mmol/L) in term infants or < 7 mg/dL (< 1.75 mmol/L) in preterm infants.[11] The data was entered and analysed in statistical package for social sciences version (SPSS) 22. The qualitative variables like gender, mode of delivery were calculated in terms of frequency or percentage. The quantitative variables like age, gestational age, duration of phototherapy, pre phototherapy serum calcium levels, post phototherapy serum calcium levels were calculated as mean and standard deviation. The effect modifiers such as age, gender, and gestational age were accounted for by applying stratification techniques. A post stratification paired t-test was conducted to assess the significance of the findings. In order to

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compare the pre and post therapy serum calcium, t-test was appplied. A *p* value of < 0.05 was considered statistically significant.

Results

There were 62 neonates in total. The mean age was 4.52 ± 1.25 days. Males were 39 (62.90%) and 23 (37.10%) were females. The male to female ratio was 1.7:1. The mean gestational age was 38.11 ± 1.49 weeks (Table 1). The mean duration of phototherapy was 3.17 ± 0.55 hrs. The delivery via caesarean section was seen in 41 (66.13%) patients and 21 (33.87%) were delivered by vaginal delivery. The mean pre-therapy serum calcium levels were 9.59 ± 0.52 mg/dl and post-therapy levels were 9.07 ± 0.44 mg/dl (*p* value 0.0001) (Table 2). Stratification of post-therapy calcium levels with respect to age groups, gestational age and gender is shown in Table 3.

Table I: Demographics of Study Population

Characteristics		Number (n=62)	Percentage (%)	Mean
Age (in days)	0-3 4-7	15 47	24.19 75.81	4.52 ± 1.25 days
Gender	male female	39 23	62.90 37.10	
Gestational Age (weeks)	34-36 37-41	7 55	11.29 88.71	38.11 ± 1.49 weeks

Table II: Effect of Phototherapy on Serum Calcium Level

Serum Calcium level (mg/dl)	Mean±SD (mg/dl)	*P* value
Pre therapy	9.59 ± 0.52	<0.001*
Post therapy	9.07 ± 0.44	

*The *p* value ≤ 0.05 was considered statistically significant

Table III: Stratification of Post Therapy Serum Calcium Level with Various Parameters

Post therapy Ca level (mg/dl)		Mean±SD (mg/dl)	*P* Value
Age in days	0-3	9.22 ± 0.33	0.134
	4-7	9.02 ± 0.46	
Gestational age (weeks)	34-36	8.86 ± 0.62	0.174
	37-41	9.09 ± 0.41	
Gender	Male	9.02 ± 0.45	0.269
	Female	9.14 ± 0.40	

*The *p* value ≤ 0.05 was considered statistically significant

Discussion

The initial proposition of an association between hypocalcemia in a neonate and phototherapy was made by Romagnoli *et al*.,[12] Phototherapy has inhibitory effect on pineal gland, reducing melatonin levels. Melatonin is known to influence calcium metabolism, and its reduction can lead to decreased calcium absorption and increased risk of hypocalcemia.[13]

Our study found a total of 22 neonates (35.4%) to exhibit a decrease in serum calcium level after 48 hours of phototherapy.This percentage is quiet high as compared to Rajesh *et al*.,[14] who documented a decline in serum calcium in 26% of full-term neonates.The difference is due to the fact that we have included both full and pre term neonates while Rajesh *et al*.,[14] have included only full term neonates. Preterm babies are already at risk of hypocalcemia due to their immature metabolisms.[9] Amna *et al*.,[15]reported a comparable value of 40% babies showing low serum calcium with phototherapy. They have checked the levels at 24 hours of therapy yet they have reported the similar value like ours. According to literature, early onset hypocalcemia can be seen anytime between day 1 to 3 of phototherapy, although low calcium is seen mostly after 48 hours of phototherapy. [16] Our study reinforces the same association with a significant decrease (*p* value <0.001) in serum calcium level of neonates after 48 hours of phototherapy.

As per our results, decrease in serum calcium level after 48 hours of phototherapy, was significant (*p* < 0.001). Rajesh *et al*.,[14] have reported comparable finding with a *p* value of <0.01. Literature reports a significant reduction in calcium level following phototherapy (9.14±0.78mg/dl to 8.53±0.77mg/dl) *p* value 0.001.[7] In a recent research conducted in Pakistan , the average serum calcium level of neonates before and after phototherapy was measured as 9.28 mg/dl ± 0.23 and 8.54 mg/dl ± 0.68 respectively.[15] Others report that duration of phototherapy does not affect the magnitude of hypocalcemia in term neonates.[16] In another research encompassing term neonates in Faisalabad, it was determined that the decrease in pre and post phototherapy serum calcium levels was statistically significant (*p* <0.005).[17]

In our study, we did not find any case of phototherapy induced hypocalcemia. (Mean post phototherapy calcium 9.07 ± 0.44). The neonates have compensatory mechanisms that can prevent a major decline in serum calcium. Once serum calcium

level falls below 6 mmol/L, hypocalcemia becomes symptomatic in the form of agitation, apnea, lethargy, stridor, irritability and seizures.[18] While the decrease in calcium level is significant, it often does not lead to symptomatic hypocalcemia. One study noted that although there was a decrease in calcium levels, none of the neonates developed symptomatic hypocalcemia.[19] However, some studies reported a small percentage of neonates developing asymptomatic hypocalcemia.[20,21] Muhammad *et al*.,[20] have reported symptomatic hypocalcemia of 1.2% in their research with restlessness as only clinical finding. Feeding pattern, concommittent illnesses and birth weight of babies can affect the serum calcium levels in neonates.[15] Subash *et al.*, [22] reported that there is a reduction in the serum calcium with increased duration of phototherapy, however, it does not fall to the level where treatment is required. Similar findings are reported by other researchers.[23,24] The reason for symptomatic hypocalcemia could be associated sepsis but as our study excluded septic neonates so, this could be the reason that we have not observed hypocalcemia.

The gender did not have any significant effect on serum calcium level in our study (*p* value 0.269). We had 39 (62.90%) male and 23 (37.10%) female infants. In a study by Khan *et al.*, [1] there were (n=77 ,62.6%) males and (n= 46,37.4%) females. Similar findings are reported by others. Gender does not significantly influence the outcome of hypocalcemia or other complications associated with phototherapy in neonates. According to literature, the primary factors affecting phototherapy outcomes are related to other clinical characteristics rather than gender.[24]

Most of our patients were term neonates of > 4 days old with the mean age of 4.52 ± 1.25 days. The possible reason is that physiologic jaundice starts at 2nd day of life (DOL) and reaches its peak at around 5th DOL. So phototherapy is mostly required during first week of life. Although literature describes a physiologic decline in neonatal serum calcium level within same time period which returns to normal by the tenth DOL but this is almost never symptomatic.[10] Chandra *et al.,*[22] also report majority of neonates in the age group of 1-5 days (n =156; 77.6%), with the mean age of 4.50± 3.39 days, in their study. Similar demographics are reported by Amna *et al.*, [15] with mean age of 7.0 ±2.62 days. Literature has reported an increased risk of phototherapy induced hypocalcemia with decreasing gestational age. [25] We did not find a significant relationship between the two (*p value* = 0.172) .This might be because we had less number of preterm babies in our cohort (n =7,11.29%) . Others also report that there is no association of birth weight and serum bilirubin levels with decrease in serum calcium level [24,] which was not scope of our study.

The main strength of our study was that it reports phototherapy induced decrese in calcium levels. Our study was subject to few constraints. The comprehensive prenatal profile of mothers, such as weight, toxemias of pregnancy, and serum calcium levels, was not documented. Additionally, crucial data such as the feeding history of neonates, their birth weight, and Ballard scoring could have been included. These variables hold the potential to act as confounding factors and should be taken into account in future investigations with a larger sampe size. It is imperative that future research incorporates the aforementioned information into its analysis.

Conclusion

Phototherapy resulted in a significant reduction in serum calcium levels after 48 hours; however, none of the neonates developed hypocalcemia.

REFERENCES

1. Panneerselvam K, Mani S, Vasudevan N, S P, Krishnamoorthy N, Rk P et al. Effect of Light- Emitting Diode Phototherapy on Serum Calcium Levels in Neonates with Jaundice. Cureus. 2022 Apr 7;14(4): e23938. doi: 10.7759/cureus.23938.
2. Zhou S, Wu X, Ma A, Zhang M and Liu Y. Analysis of therapeutic effect of intermittent and continuous phototherapy on neonatal hemolytic jaundice. Exp Ther Med. 2019 ;17(5):4007-4012. doi: 10.3892/etm. 2019.7432.
3. Ayalew T, Molla A, Kefale B, Alene TD, Abebe GK, Ngusie HS et al. Factors associated with neonatal jaundice among neonates admitted at referral hospitals in northeast Ethiopia: a facility-based unmatched case-control study. BMC Pregnancy Childbirth. 2024 Feb 21;24(1):150. doi: 10.1186/s12884-024-06352-y.
4. Bajwan D, Thakur N, Bhardwaj R and Chaorsiya A . Neonatal Jaundice: An Overview. *Int. J. of Adv. Res.* 2024 ; 110-113 . doi:10.21474/ijar01/18855.
5. Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watcho JF, Downs SM et al. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant

 https://doi.org/10.57234/jiimc.march25.1972

35 or More Weeks of Gestation. American Academy Of Pediatrics. Clinical Practice Guideline. Pediatrics 2022;150 (3): doi:10.1542/peds.2022-058859.
6. Wang J, Guo G, Li A, Cai WQ and Wang X. Challenges of phototherapy for neonatal hyperbilirubinemia (Review). Exp Ther Med. 2021; 21(3): 231.
7. Goyal M, Sharma R and Dabi DR. Phototherapy induced hypocalcemia in neonates: A case–control prospective study. Indian J Child Health. 2018; 5(3): 208-212.
8. ThomasT, Smith J, White P and Adhikari S . Transient Neonatal Hypocalcemia: Presentation and Outcomes. Pediatrics.2012; 129: e1461 - e1467. doi:10.1542/peds. 2011-2659.
9. Gaafar MM, Rasheed EM, Abdel Halim SM, Abdullah MM and El Gendi M. Effect of Phototherapy on serum Level of Calcium and Magnesium in Term and Preterm Neonates with Hyperbilirubinemia. Egyptian J Hosp Med. 2020; 80(1): 743-7.
10. Vuralli D. Clinical Approach to Hypocalcemia in Newborn Period and Infancy: Who Should Be Treated? Hindawi Int J Pediatr. 2019;(3):1-7. doi:10.1155/2019/4318075.
11. Abram SA. Section editor, Garcia-prates JA Tehrani N. Neonatal hypocalcemia Jun 2024. Up to date. Updated on Sep 19; 2022. Cited on July 2024.
12. Romagnoli C, Polidore G and Cataldi L. Phototherapy induced hypocalcaemia. J Pediatr., 1979;94(5):815-16.
13. Shahriarpanah S, Haji Ebrahim Tehrani F, Davati A, Ansari I. Effect of Phototherapy on Serum Level of Calcium, Magnesium and Vitamin D in Infants with Hyperbilirubinemia. Iran J Pathol. 2018;13(3):357-362.
14. Rajesh KC and Kanodia P. Phototherapy Induced Hypocalcaemia in Neonates with Jaundice. Journal of Nepalgunj Medical college, 2020; 18 (2) :1-3.
15. Khan A, Farhat A, Anwar H, Shamim S, Rehman M U and Khan I. Phototherapy Induced Hypocalcemia in Neonates with Unconjugated Hyperbilirubinemia. J Bahria Uni Med Dental Coll. 2021; 11(1) 4–8. doi:10.51985/GUBK9588.
16. Basnet S, Gauchan E, Bhatta M, Thapa R. Phototherapy induced hypocalcemia in neonatal hyperbilirubinemia and correlation of hypocalcemia with the duration of phototherapy. Int J Contemp Pediatr. 2022;9(4):324-328. doi:10.18203/2349-3291.ijcp20220756.
17. Javaid S, Sultana S, Omer MT, Murtaza A, Ahsan Ul Haq M. Effect of Phototherapy on Serum Calcium Levels in Neonates in A Tertiary Care Hospital. Ann Punjab Med Coll .2021; 15(3) 185-187. doi:10.29054/apmc/2021.1251.
18. Shoris I, Gover A, Toropine A, Iofe A, Zoabi-Safadi R, Tsuprun S et al. Light on Phototherapy-Complications and Strategies for Shortening Its Duration, A Review of the Literature. Children (Basel). 2023;10(10):1699. doi: 10.3390/children 10101699.
19. Pereira R, Avasthi B, Saste S, Bavdekar S . Prevalence of hypocalcemia in term newborns requiring phototherapy. Int. J. Contemp. Pediatr. 2023; 10(6):793-797 . doi:10. 18203/2349-3291.ijcp20231480.
20. Padippura MY, Mammen DS, Parameswaran J and Vadakedom S. Hypocalcaemia due to phototherapy in term neonates with neonatal hyperbilirubinemia. *J. Evolution Med. Dent. Sci. 2018;7(48):6007*-6011. doi:10.14260/ jemds/*2018*/1155.
21. Shrestha S, Budhathoki S, Sanjel S, Sindan N, Kayastha N, Shrestha A. Effect of phototherapy on serum calcium level in neonatal hyperbilirubinemia. JKAHS. [Internet]. 2021 Aug.31 [cited 2024Dec.6];4(2).
22. Jha CB, Rimal HS and Subedi RB. Phototherapy induced hypocalcemia in icteric newborns attending Birat medical College teaching hospital ,Morang,Nepal. JCMC [Internet]. 2022 Aug. 28 [cited 2024 Nov. 13];12(2):10-3. Available from: https://www.nepjol.info/index.php/JCMC/ article/view/47858.
23. Rozario CI, Pillai PS and Ranamol T. Effect of phototherapy on serum calcium level in term newborns. Int J Contemp Pediatr. 2017;4(6):1975-9.
24. Kumar G. A Study to Evaluate Phototherapy Induced Hypocalcemia and Its Correlation Of With the Duration of Phototherapy in Neonatal Hyperbilirubinemia. IJTPR .2023; 13(10); 395-399.
25. Refaee SAH. 821 Risk factors for short-term side effects of phototherapy in neonatal jaundice. Arch Dis Child. 2021;106 (1):A124-A125. doi:10.1136/archdischild-2021-rcpch.216.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.