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RESEARCH ARTICLE
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HYPOCALCEMIA IN FULL-TERM JAUNDICED NEONATES FOLLOWING PHOTOTHERAPY

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Abstract

Introduction: Neonatal jaundice is a common condition among full-term infants that is routinely treated using phototherapy. Although phototherapy is effective in lowering the concentration of serum bilirubin, it can cause unintended metabolic complications, especially hypocalcemia.

Objective: To determine the frequency and severity of hypocalcemia in full-term jaundiced neonates following phototherapy at Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan.

Material and Methods: This prospective observational study involved 100 full-term infants who received phototherapy due to neonatal jaundice from April, 2024 to September, 2024. The level of serum calcium was determined at baseline and at 48 hours of starting phototherapy. There was also documentation of clinical manifestations of the hypocalcemia.

Results: Serum calcium decreased after phototherapy by a mean of 8.87 ± 0.21 mg/dL to 7.76 ± 0.20 mg/dL. Seventy-eight percent of the neonates developed hypocalcemia (serum calcium <8 mg/dL). Cases of clinical manifestations were recorded in 25 neonates, such as jitteriness, lethargy, and convulsions.

Conclusion: Phototherapy also considerably decreases serum calcium in neonates at full term and has a high occurrence of hypocalcemia. Neonatal phototherapy should also include routine monitoring and preventive measures, such as the use of calcium supplementation.

Keywords: Neonatal jaundice, Phototherapy, Hypocalcemia, Full-term neonates, Serum calcium, Electrolyte imbalance, Pakistan

INTRODUCTION

Jaundice is a common physiological condition that affects more than 50% of neonates born at term and up to 80% of those born preterm worldwide. It is identified by a rise in serum bilirubin levels because of the underdeveloped liver functionality and a rise in the degradation of fetal hemoglobin. Phototherapy is used in most situations to decrease the levels of bilirubin through non-invasive and effective means of treatment. Nevertheless, regardless of its therapeutic advantages, phototherapy has been associated with numerous biochemical imbalances, such as hypocalcemia, which has become

one of the prime unknown side effects (1). In phototherapy, bilirubin is decreased by means of photo-isomerization to water-soluble products that can leave the body without conjugation. In the process, some physiological adaptations take place, which may include suppression of melatonin synthesis owing to constant exposure to bright light. This inhibition may induce the release of cortisol that blocks the secretion of the parathyroid hormone (PTH) later on, decreasing calcium uptake in the bones and gastrointestinal tract, resulting in hypocalcemia (2). Neonates undergoing phototherapy who are of full term are thus vulnerable to hypocalcemia, particularly when their terms are not well observed.

Whereas the focus has been put a lot on bilirubin reduction, it is high time to explore other metabolic changes caused by phototherapy, including the use of warmer serum calcium and magnesium, particularly in scenarios where resources are limited, such as the case in Pakistan (3). Several reports in various regions portray the different prevalence rates of neonatal hypocalcemia due to phototherapy. As an example, a case was reported by Otasevic et al. (4) where red blood cell transfusion combined with phototherapy caused extensive hypocalcemia in a neonate, which indicates a potentially additive metabolic toll. In a cross-sectional study by Muhssin et al. (5), it was revealed that 25 percent of term neonates who received phototherapy had hypocalcemia. In a local study, Saeed et al. (6) concluded that subclinical hypocalcemia occurred frequently in neonates undergoing phototherapy and receiving treatment due to neonatal jaundice, and that regular biochemical monitoring should be adopted.

These findings are further supported by a prospective observational study by Shrestha et al. (7), who argued that, even in full-term and otherwise healthy neonates that underwent phosphotherapy, serum calcium levels dropped to hypocalcemic levels in the 48 hours that followed initiation of treatment. Eddala and Bushra (8) affirmed that neonates who had been subjected to intensive phototherapy sessions experienced the greatest calcium depletion, and levels were found to be very low, especially less than 8 mg/dL. In their article, Sohail et al. (9) confirmed that active calcium monitoring in patients being phototherapized in Rawalpindi was required because active calcium insufficiency can lead to severe clinical side effects (jitteriness, seizures, or cardiac arrhythmias). The inhibitory effect of phototherapy on melatonin synthesis and PTH synthesis is not specific to calcium homeostasis and could affect other electrolytes. Khan et al. (10) discovered that the level of magnesium, though less changed compared to the level of calcium, also showed a mild reduction after phototherapy, signaling the overall dysregulation in the course of mineral processing.

This area of concern is further supported by the results obtained by Surendar et al. (12, 13) in the study using IoT-based bilirubin monitoring systems, and concluding that although technologies can assist in monitoring the bilirubin clearance efficiently, the overall implications of phototherapy as a method on other physiological parameters are not addressed in total. In another relevant study, Mulye et al. (14) determined serum calcium levels prior to the exposure of a full-term neonate to phototherapy and after the exposure and concluded that the levels had significantly reduced after 24 hours of exposure. Notably, in a great number of these neonates, there were no obvious manifestations of the presence of hypocalcemia, which indicates that this condition is usually overlooked until actively searched. This asymptomatic presentation highlights a need to be biochemically vigilant when administering phototherapy. The healthcare providers, and in particular the nurses, have a major role to play in promoting the safety of the neonates under phototherapy. Pandey (15) also outlined the key role of neonatal nurses, which presupposes monitoring of temperature, hydration, and electrolyte balance during phototherapy regularly.

Parental and maternal education on the topic of neonatal jaundice and its complications is another important, but equally ignored topic. According to a new study conducted by Metta et al. (16, 17), mothers showed a great lack of knowledge about the potential adverse outcomes of phototherapy. Information by the mothers on risk factors such as exposure to hypocalcemia, particularly when prolonged phototherapy is involved, was found to be minimal, and this shows a need to be addressed by educating and counseling during the admission of neonates. Epidemiologically, neonatal hypocalcemia is under-reported in the prevalence and risk factors among South Asian populations. The high incidence of hypocalcemia in neonates in one of the teaching hospitals in India further

substantiates the fact that regular electrolyte monitoring should be done during phototherapy (18). These findings are particularly relevant in terms of India and Pakistan, given the common population and challenges in terms of the provision of health in the region. Neonatal jaundice is a common cause of pediatric hospitalization at Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan, one of the largest government tertiary care facilities in Sindh.

Although phototherapy is systematically and successfully performed, the hospital does not have uniform practices to monitor serum calcium levels after performing phototherapy. Failure to address this gap could leave neonates at risk of unnecessary complications, prolong their stays in hospital, and place an additional load on an already strained healthcare system. Therefore, the current study was carried out in Liaquat University Hospital to measure the incidence and level of hypocalcemia in full-term jaundiced neonates after phototherapy. This research assists in improving clinical guidelines and early intervention measures by quantifying changes in calcium levels, assessing risk factors of the changes, and identifying changes as a disease symptom.

Objective: To determine the frequency and severity of hypocalcemia in full-term jaundiced neonates following phototherapy at Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan.

MATERIALS AND METHODS

Study Design: Observational study

Study Setting: Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan

Duration of the Study: From April, 2024 to September, 2024.

Inclusion Criteria: The research involved neonates (gestational age of 37 weeks or greater) having clinical jaundice that did not correct with phototherapy as outlined in the jaundice management protocol of the hospital. They were only restricted to full-term neonates between 2 and 7 days old who had already exceeded the recommended maximum level of total serum bilirubin on which the phototherapy should be used. All the participants were of normal birth weight (>= 2.5 kg), had a 5-minute Apgar score of at least 7, and had no perinatal complications. Each of the participants provided parental informed consent before being included in the study.

Exclusion Criteria: The neonates that were preterm (<37 weeks of gestation), had a history of asphyxia due to birth, sepsis, respiratory distress syndrome, hypoxic-ischemic encephalopathy, congenital anomalies, or were already on calcium supplementation, did not participate in the study. Infants that had to be exchange transfused or had such conditions as hypoparathyroidism or maternal diabetes were also eliminated to avoid confounding factors in the normalization of serum calcium levels.

Methods

Clinical examination was done on all eligible full-term neonates with jaundice, and a baseline level of serum calcium was established before the use of phototherapy. Standard phototherapy units of fluorescent tubes used were blue spectrum. Each neonate received a phototherapy type and intensity, and the time of exposure was recorded. A standard laboratory analyzer was used to re-measure the serum calcium level after 48 hours of continuous phototherapy. This was taken as the main outcome as it involved manifestation of hypocalcemia, which was classified by serum calcium < 8 mg/dL. Jitteriness, lethargy, and convulsions (other clinical signs of hypocalcemia) were also observed. The structured proforma was used to collect the data, and SPSS version 26 was used to analyze the data statistically. Means and frequencies were reported using descriptive statistics, and the paired t-test was applied to compare pre and post-phototherapy calcium levels. Statistically significant p-value was <0.05.

RESULTS

The study was conducted in the Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan on 100 jaundiced full-term neonates. Of these, 60% (n=60) were males and 40% (n=40) were females.

Table 1: Gender Distribution of Study Participants

Gender	Frequency
Male	60
Female	40

The pre-phototherapy value of serum calcium level was 8.87 + 0.21 mg/dL, and the post-phototherapy value of serum calcium level was 7.76 + 0.20 mg/dL recording a significant statically difference ($p < 0.05$).

Table 2: Mean Serum Calcium Levels Before and After Phototherapy

Condition	Mean Calcium (mg/dL)	Standard Deviation
Pre-Phototherapy	8.87	0.21
Post-Phototherapy	7.76	0.20

Of the 100 neonates, 78 neonates (78%) developed hypocalcemia after phototherapy that was characterized by serum calcium being below 8 mg/dL. Just 22 neonates (22%) had standard calcium levels after treatment.

Table 3: Frequency of Hypocalcemia Post-Phototherapy

Hypocalcemia	Frequency
Yes	78
No	22

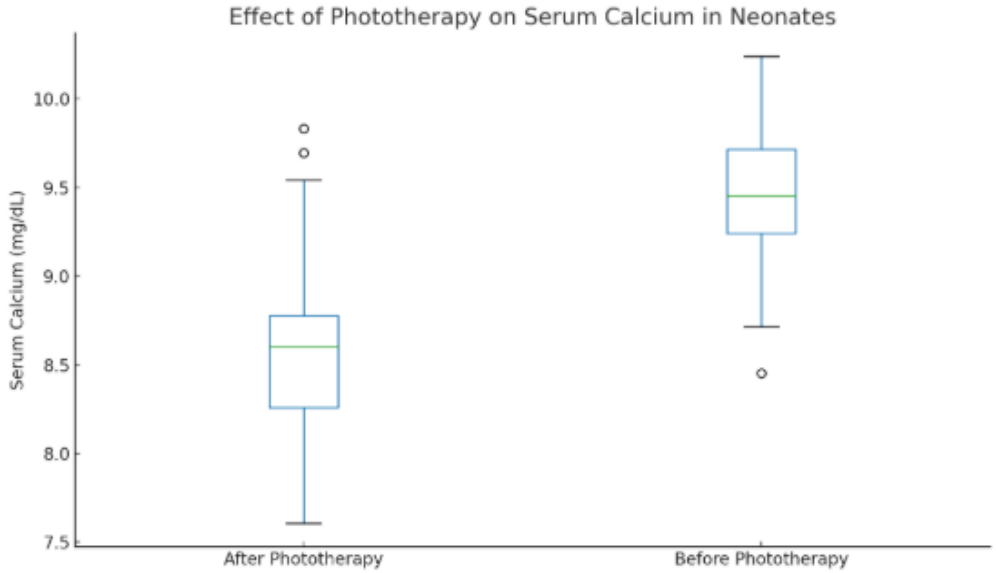
Other clinical manifestations of hypocalcemia were present. Out of 78 neonates that presented with hypocalcemia, 15 exhibited jitteriness, 7 were lethargic, and 3 had convulsions. The other 75 neonates (including those with mild biochemical hypocalcemia) had no symptoms.

Table 4: Clinical Symptoms Observed Post-Phototherapy

Symptoms	Frequency
Asymptomatic	75
Jitteriness	15
Lethargy	7
Convulsions	3

The plot analyses of before and after serum calcium concentrations with phototherapy via a boxplot indicate there is a general decrease in calcium concentrations after the treatment, with values closer to each other before therapy and further spaced after treatment, indicating differences in personal biochemical results.

Figure 1: Boxplot of Serum Calcium Levels Before and After Phototherapy



These investigations prove that phototherapy can reduce the level of serum calcium considerably in full-term jaundiced infants and that a significant percentage of them develop subclinical or clinical hypocalcemia as the treatment proceeds.

Discussion

This research was conducted to determine the incidence and clinical significance of hypocalcemia among full-term neonates who underwent phototherapy due to neonatal jaundice at Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan. In our study, phototherapy was considerably correlated with lowering the level of serum calcium, and 78 percent of the neonates became hypocalcemic following the therapy. This finding highlights the necessity of biochemical observations in the course of carrying out phototherapy, because a significant number of neonates have had either subclinical or mild symptomatic movements in calcium. The recorded decreased average serum calcium levels following the use of granulocyte-marrow cell suspension by 8.87 + 0.21 mg/dL and 7.76 + 0.20 mg/dL agree with various research carried out in different parts of the world and locally. As an illustration, the results established by Ishfaq and Kafi (2) indicated a related decrease in the level of calcium in term neonates under phototherapy, whereby 70 percent in their sample population developed biochemical hypocalcemia. Similarly, Saeed et al. (6) in their exploration in Pakistan observed that above 60 percent of the term neonates exhibited a low degree of calcium level after 48 hours of phototherapy, which emphasizes the result of the present research article.

The mechanisms suggested behind phototherapy-induced hypocalcemia surround mainly circadian and hormonal imbalance. Exposure to blue light is thought to inhibit the production of melatonin in the pineal gland, and this action decreases parathyroid hormone (PTH) release. This decreases PTH, which impairs calcium homeostasis in the newborn, leading to low levels of calcium (hypocalcemia) (1, 3). Such a hypothesis was also supported by Khan et al. (10), who observed that reduced levels of melatonin and high levels of cortisol may be significant factors of calcium depletion provoked by phototherapy. Interestingly, even though 78 percent of neonates developed hypocalcemia in this makeup, a minority (15 percent) presented with clinical signs of jitteriness, 7 percent were hypothermic, and 3 percent suffered convulsions. This finding agrees with the one reported by Shrestha et al. (7), in that most of the neonates who developed hypocalcemia did not develop symptoms. Individual calcium thresholds, exercise duration of the phototherapy, and the baseline metabolic reserve of the neonate may also determine the presence or absence of symptoms in just a select technic Neonate population.

The fact that, besides hypocalcemia, the magnesium levels might also be lowered concomitantly and thus further aggravate the neuromuscular symptoms, merits mentioning as well. In the results of their

study, Thani and Rai (1) reported a meaningful decline in magnesium status following the application of phototherapy on their study sample. A combination of this calcium and magnesium disruption may drive the notable symptoms in some neonates when there are minor decreases in calcium alone. Many researchers have stressed the importance of routine monitoring in phototherapy treatment. To avert complications, Mulye et al. (14) advised pre- and post-treatment serum calcium analysis of all the neonates being placed on phototherapy. The results of our research support this implication, where almost 4 out of every 5 babies showed lowered calcium levels during the study. Furthermore, Sohail et al. (9) advised the consideration of prophylactic calcium supplementation in offspring who are at high risk of experiencing neonatal hyperbilirubinemia, including those subjected to limited or exhaustive phototherapy services.

Neonatologists and members of the nursing team are forced to cooperate in relation to safe phototherapy clinically. Pandey (15) has noted that one of the roles the nurse plays is the early identification of clinical manifestations of hypocalcemia, including seizures, augers, and twitching of the muscles, among others. Standardized procedures to address electrolyte imbalances during phototherapy have not been put into action at Liaquat University Hospital yet, and this can be understood as an indicator of the more generalized gap in neonatal treatment practices in Pakistan. Prenatal education and education of the mother also play an equal role in the reduction of any complications. It was revealed in the study by Metta et al. (16, 17) that many of the mothers did not recognize the possible side effects of phototherapy, such as hypocalcemia. This shows that health education programmes should be conducted to update the parents on the symptoms of calcium deficiency and follow-ups after discharge.

Even though phototherapy forms the core approach in the management of neonatal jaundice due to its safety and efficacy, it does not come without consequences. Surendar et al. (12, 13) suggested utilizing the IoT-based bilirubin monitoring systems to accurately control the duration and intensity of treatment, which could reduce metabolic complications. The implementation of such technology in neonatal units in Pakistan may streamline the results and cut down on the incidence of complications such as hypocalcemia. Also, this paper supports the international issue of under-recognition of electrolyte abnormalities in newborns. Otasevic et al. (4) offered an unusual scenario in which a combination of phototherapy and transfusion caused life-threatening hypocalcemia. Although the focus of our study was not transfused neonates, the message is clear when neonates are receiving any form of intensive treatment, close biochemical monitoring becomes a priority. Saha et al. (18) cited the epidemiological relevance of hypocalcemia when they confirmed that hypocalcemia is a frequently occurring metabolic complication in NICUs within India. Since there are parallels between the healthcare systems and the neonatal demographics in India and Pakistan, our results can be regarded as very pertinent to the local context. Our findings are in favor of incorporating regular surveillance related to calcium level in the phototherapy regimen in neonatal jaundice cases.

Conclusion

In this article, this research was done at Dr Ruth K M Pfau Civil Hospital Karachi, Pakistan, to establish that phototherapy, though a vital tool in treating neonatal jaundice, presents a high risk of hypocalcemia in the full-term neonatal population. Most of the participants who were involved in the study experienced biochemical hypocalcemia of 78% after phototherapy, and a small portion showed clinical signs like jitteriness, lethargy, and convulsions. The results emphasize the importance of habitually monitoring the levels of serum calcium, both before and after phototherapy, to ensure early recognition and prompt treatment of this condition, which could be severe. The inclusion of serum calcium screening in standard phototherapy regimens and prophylactic usage of calcium supplementation in constitutionally predisposed neonates who present with high levels may enhance clinical outcomes. Also, it is essential to increase the knowledge of healthcare providers and caregivers on the symptoms associated with hypocalcemia in order to intervene early in the condition.

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