

# Incidence of Hypocalcaemia in Term Jaundiced Infants after Phototherapy

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## ABSTRACT

Jaundice is one of the main problems in the neonates early in life having an impact on around 60% of full term and 80% of premature infants. Current worldwide date reports that annually, almost 1.1 million neonates go on to suffer from serious neonatal jaundice and large amount of those reside in sub-Saharan Africa and South Asia. The goal of our research is to quantify the incidence of hypocalcaemia in term infants with hyperbilirubinemia who have been treated with phototherapy for 48 hours.

**Objective And Methodology:** This research makes use of a descriptive case series study approach. Data collection was done in the Pediatrics unit 1 services hospital Lahore from six months from Jan, 2022 to July 2022. Patients' basic information (such as their names, ages, sexes, and addresses) was collected during the Study's case registration process. Newborns that met the study's eligibility criteria were given 48 hours of laser treatment. After 48 hours of laser treatment, the serum calcium level was checked and recorded.

**Results:** The average age of the neonates was 8.83±3.99 days. The average birth weights of the newborns were 2.28±0.39 kg. The mean Serum Calcium level at Baseline was 9.33±1.09 mg/dl. The mean Serum Calcium level after 48 hours of laser therapy was 7.64±1.36 mg/dl. There were 30(34.5%) neonates with hypocalcemia and 57(65.5%) neonates without hypocalcaemia in this study.

**Conclusion:** The frequency of hypocalcaemia was moderate 34.5% among neonates with hyperbilirubinemia who received laser therapy.

**Keywords:** Hypocalcaemia, Jaundice, Hyperbilirubinemia, Laser Therapy, Neonatal Jaundice

## INTRODUCTION

Jaundice is a major problem of early weeks in the life of a newborn, occurring in about 60% of infants born and 80% of preterm newborns. According to contemporary international assessments, approximately 1.1 million newborns suffer serious neonatal jaundice each year, with the overwhelming bulk residing in Sub-Saharan Africa and South Asia.<sup>2</sup>

Five to ten percent of infants with jaundice necessitate hyperbilirubinemia treatment.<sup>3</sup> Jaundice is caused by neonates' biological inability to deal with enhanced bilirubin manufacturing. The basic etiology of jaundice is the same in full-term and premature neonates, but premature infants are more likely to suffer from hyperbilirubinemia. Even within term infants, higher bilirubin levels can be injurious to the neural tissues especially brain, spinal cord and can cause long lasting cognitive deficits (Neurotoxicity or Kernicterus).<sup>4</sup>

Neonatal hyperbilirubinemia is a widespread condition. Serious indirect hyperbilirubinemia left unaddressed has the possibility to be extremely toxic for neural tissues. Numerous multi institutional clinical trials have shown that laser treatment is beneficial in the treatment of neonatal hyperbilirubinemia.<sup>5, 6</sup> To reduce the overall load of bilirubin in the body, light therapy is the most commonly utilized method of treatment for babies born with hyperbilirubinemia.<sup>7, 8</sup>

Diarrhea along with moderate to severe dehydrations, pyrexia, skin burns, retinitis, platelet count falls, enhanced red cell osmotic fragility, bronze baby disorder, riboflavin insufficiency, Oxidative damage to DNA, and hypocalcaemia are all frequent complications of laser treatment. Numerous metabolic activities, such as blood clotting, cell membrane structure and purpose, neuromuscular over activity, and cellular metabolic activity, are dependent on calcium levels, and calcium performs a very significant role in the maintenance of the aforementioned systems in the cell. This was the first time, Romagnoli et al. proposed a link between hypocalcaemia and laser treatment in premature newborns. Likewise, Hakanson and Bergstrom observed this in newly born rodents.<sup>8</sup>

The high rate of hypocalcaemia in laser therapy neonates was estimated to be 8.7% in full-term newborns. Laser therapy, according to Hakinson et al., and Hunter et al., hinders pineal release of melatonin, which stops the impact of cortisol on bone

calcium. Cortisol increases calcium absorption in the bones, resulting in lower levels of calcium.<sup>8,9</sup> So this bone absorption of calcium is enhanced by the cortisol and induces hypocalcaemia. Kim et al., proposed that hypocalcaemia was caused by reduced parathormone production, and urinary calcium discharge was considerably increased in the laser therapy group.<sup>10,3</sup>

It has been documented that 66% of full term and 80% of preterm suffered from hypocalcaemia laser therapy (Yadav).<sup>11</sup> It has been found that prevalence of hypocalcaemia was 30% in healthy neonates<sup>12</sup> and in Ehsanipoor's study it was 15%<sup>13</sup>. According to Karamifar's Study 56% newborn had hypocalcaemia. It has been recognized in Jain's study the documented rates of hypocalcaemia was considerably more in those cases with higher levels of serum bilirubin.

In Eghbalian's study, apnea was reported in hypokalemic neonates.<sup>14</sup> 80% of hypo-calcific term neonates were found in Yadav,s study symptomatic and the commonest feature being the jitteriness.<sup>11</sup> Mishal et al concludes that 22.6% neonates had developed hypocalcemia after phototherapy.<sup>15</sup> These studies raised our attention towards adverse effect of laser therapy like hypocalcaemia while improving the jaundice.

## OBJECTIVE AND METHODOLOGY

The goal of this study is to determine the incidence of hypocalcaemia in term infants with hyperbilirubinemia who have been treated with phototherapy for 48 hours. This research makes use of a descriptive case series study approach. Data collection was done in the Pediatrics unit 1 services hospital Lahore from six months from Jan, 2022 to July 2022.

Non-probability consecutive sampling was employed for this study. Choosing a Sample Criteria for inclusion Male and female neonates who are assured to have been delivered after 37 weeks of pregnancy based on antenatal history will be included, as will those who have had 48 hours of phototherapy for hyperbilirubinemia. Exclusionary sampling criteria Conjugated hyperbilirubinemia in newborns, Phototherapy-related complications in newborns, Neonates with any other co morbidities.

We performed this prospective research at Neonatal Intensive Care. Informed consent from parents/attendants was taken. An ethical approval letter was acquired before the data

collection. Cases were registered for the data collection and basic demographics of the cases (name, age, sex, address) were noted. Neonates were included in the study group who fulfilled inclusion criteria received phototherapy for 48 hrs. Serum calcium was assessed after 48 hours of phototherapy and was recorded.

All the data was entered and analyzed using computer software SPSS version 19. Mean and standard deviations was calculated for quantitative variable, age in days, birth weight, and serum calcium level at baseline. Frequency and percentage was calculated for gender and hypocalcaemia, post stratification chi square test was applied. A p-value

< 0.05 was considered statistically significant. Data was stratified for age in days, gender, birth weight, serum calcium level at baseline.

## RESULTS

The mean age of the neonates was 8.83±3.99 days the minimum age was 3 days and maximum was 15 days. The mean birth weight of the neonates was 2.28±0.39 kg the minimum birth weight was 1.70 kg and maximum was 3 kg. The mean Serum Calcium level at Baseline was 9.33±1.09 mg/dl. The mean Serum Calcium level after 48 hours of phototherapy was 7.64±1.36 mg/dl the minimum serum calcium level after 48 hours of phototherapy was 5 mg/dl and maximum level was 9 mg/dl. There were 30 (34.5%) neonates with hypocalcaemia and 57 (65.5%) neonates without hypocalcaemia in this study.

There was no significant difference observed regarding the frequency of hypocalcaemia in all age strata i.e. 42.1% in 3-7days age, 32.1% in 8-12days age and 23.8% in 13-14 days age group (p-value=0.34). There was insignificant difference observed regarding the frequency of hypocalcaemia in both genders i.e. 16(34.8%) in male neonates and 14(34.1%) in female neonates (p-value=0.34). There was insignificant difference observed regarding the frequency of hypocalcaemia in both weight strata i.e. 14(33.3%) in neonates weighed 1.5-2.25 kg and 16(35.6%) in neonates weighed 2.26-3.01 kg (p-value=0.82). There was significant difference observed regarding the frequency of hypocalcaemia in both baseline calcium level strata i.e. 24(51.1%) in neonates having 8-9 mg/dl calcium level at baseline and 6(15.0%) in neonates having 10-11 mg/dl calcium level at baseline (p-value=0.000).

## DISCUSSION

Neonatal jaundice is the one of the most common and frontline reasons of mortality as well as illness in newborns globally, as well as the most common reason for hospitalization and hospitalization during the first week of life.<sup>16</sup> According to current worldwide researches, approximately 1.1 million infants suffer from serious neonatal jaundice annually, with the great bulk residing in Sub-Saharan Africa and South Asia.<sup>2</sup> Laser therapy is an efficient and secure way to treat jaundice in neonates. Romagnoli et al. were the pioneers who proposed the link between newborn hypocalcaemia and light therapy.<sup>17</sup>

Calcium equilibrium control in the neonatal phase of life is of keen importance. The serum calcium levels in umbilical cord blood samples at birth surpass that of mother's circulation. The ionized calcium level in normal newborns declines in the initial days of life, so that by the second or third day of life, the amount is much lower than that discovered in infants above the neonatal age group. In full term neonates, the serum calcium levels return to baseline levels by the tenth day.<sup>18</sup>

The process of light therapy's hypocalcaemia impact has been noted to be suppression of the pineal gland via Trans cranial illumination, causing a reduction in melatonin production, which further hinders the impact of cortisol on bony calcium levels. Cortisol exerts its direct calcium lowering impact, increasing bony calcium absorption and causing hypocalcemia.<sup>8</sup> Hunter et al. hypothesized this pathway as well.<sup>19</sup> Eghbalian F formulated this concept in his research, demonstrating a direct relationship

between period of laser treatment and the progression to hypocalcemia.<sup>20</sup>

According to the findings of Khan 2016<sup>15</sup> the mean age of the neonates and was 8.35±6.74 days while in our study the mean age of the neonates was 8.83±3.99 days which is almost similar to the mean age of the neonates in the above mentioned study.

Another study by Khan et al., 2016<sup>15</sup> shows 22.76% of term neonates exhibited phototherapy induced hypocalcaemia while in our study there were 34.5% neonates with phototherapy induced hypocalcaemia which is little higher as compared to the above mentioned study. Around 7% of full term neonates suffered from the hypocalcaemia post laser therapy according to a research conducted in Iran.<sup>22</sup> A recent study conducted in Egyptian study performed by Bahbah et al., in 2014 included just 50 full-term infants treated with light therapy while 25 neonates who were having physiological jaundice but did not require light therapy. They found that after around 48 hours of laser therapy, 26% of patients had hypocalcemia.<sup>24</sup>

According to Bahbah 2015<sup>24</sup> in their study after 48 h of treatment of cases with phototherapy, serum calcium level decreased to 8.5 mg/dl, and they found highly statistically significant difference between serum calcium level before and after exposure to phototherapy where P value was less than 0.01 while in our study the calcium serum levels decreased to 7.64 mg/dl after 48 hours of phototherapy as there was significant association between hypocalcaemia and baseline serum calcium levels (p-value=0.000).

This was in agreement with several previous studies. In studies by Karamifar et al.<sup>21</sup> and Ehsanipour et al.<sup>13</sup> the incidence of hypocalcaemia after 48 h of phototherapy was 15 and 14.4%, respectively. In addition, Jain et al.<sup>12</sup> noticed that 55% of preterm neonates and 30% of full-term neonates suffered from low serum calcium after being subjected to laser treatment.

In addition, Sethi et al.<sup>17</sup> noticed hypocalcaemia after 48 h of phototherapy. Sixty neonates with hyperbilirubinemia were included in their research. The etiology of low serum calcium in infants treated with phototherapy is believed to be caused by a decrease in melatonin level and corticosterone secretion<sup>21</sup>. In addition, urinary calcium excretion is increased after exposure to phototherapy<sup>25</sup>. This decrease in calcium can be explained by melatonin secretion<sup>26</sup>. Melatonin induces corticosteroid release that also reduces calcium efflux by the bones. Laser treatment causes the pineal gland to be inhibited by Tran's cranial illumination, causing a reduction in melatonin levels and, as a consequence, lower levels of calcium.<sup>26</sup>

## CONCLUSION

Our study concludes that the frequency of hypocalcaemia was moderate 34.5% among neonates with hyperbilirubinemia who received phototherapy. The above, in essence, could have clinical implications and increase health burden. Calcium levels in infants handled with laser treatment for 48 hours or above this period should be evaluated and treated accordingly.

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