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The Impact of Phototherapy on a Term Newborn's Blood Calcium Level at Al-Bayda Medical Center, Libya

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Abstract

During the first week of birth, the most prevalent abnormal physical finding is Neonatal Hyperbilirubinemia (NH). Phototherapy is important in both the prevention and treatment of hyperbilirubinemia. However, there's a chance that this therapeutic approach may have unintended consequences. The purpose of this study was to ascertain how phototherapy affected the serum calcium levels of term neonates with unconjugated hyperbilirubinemia. 50 newborns undergoing phototherapy who were admitted to the Neonatal Intensive Care Unit were the subjects of a prospective hospital-based observational study. Serum levels of calcium and bilirubin were measured both before and after phototherapy ended. The initial samples served as the reference points. The mean gestational age was 37.02 ± 0.25 weeks, and the mean birth weight was 3.21 ± 0.45 kg. The average phototherapy session lasted 39.36 ± 11.64 hours. Phototherapy significantly lowered serum calcium levels with the mean before phototherapy being 8.89± 0.99 SD and after 8.14±1.22 SD, $p<0.001$. Hypocalcemia developed in 32 (64%) babies, among them 16 (32%) had a calcium deficiency before phototherapy. The study concluded that phototherapy had a considerable impact on calcium levels in a term neonate with hyperbilirubinemia.

Keywords: Hyperbilirubinemia, Jaundice, Phototherapy, Full-term, Neonate, Hypocalcaemia**.**

INTRODUCTION

Jaundice is a yellow coloring of the skin, sclera, and other body tissues caused by the deposition of bilirubin in cases of hyperbilirubinemia when the bilirubin level exceeds 2 mg/dl or 34.2 µmol/l (Abbas et al., 2016). Jaundice is observed during the 1st week of life in approximately 60% of term neonates and 80% of pre-term neonates. Jaundice from the deposition of indirect bilirubin (non-obstructive jaundice) in the skin tends to appear bright yellow or orange. Infants with severe hyperbilirubinemia may present with lethargy and poor feeding and, without proper management, can progress to acute bilirubin encephalopathy (Kernicterus) (Carter & Feigelman, 2020). It has also been studied that unconjugated hyperbilirubinemia reflects normal or exaggerated physiological phenomena, mostly in neonates (Singh, 2017).Phototherapy changes the structure of bilirubin and thus increases its excretion, which is the standard treatment for neonatal jaundice (Faulhaber et al., 2019).

One of the findings observed in some studies during phototherapy is hypocalcemia, defined as a total blood calcium level of less than 8 mg/dl (2 mmol/l) in term neonates. However, the results of these studies were not conclusive. Hypocalcemia during phototherapy might be caused by transcranial light inhibiting the pineal gland, leading to decreased melatonin levels.. So, when melatonin level is decreased hypocalcemia develops (Alizadeh-Taheri et al., 2013). The purpose of this study was to assess the prevalence of and contributing variables to hypocalcemia in full-term neonates receiving phototherapy.

PATIENTS AND METHODS

Study population and setting: A total of 50 full-term neonates were delivered in Al-Bayda Medical Center**,** Al-Bayda**,** Libya, from June 2021 to January 2022.

Data collection: A special data collection sheet was designed for this study which includes family name, age, sex, mode of delivery, gestational age, perinatal and natal history, family history, maternal illness, onset of jaundice, duration of phototherapy, weight, length. Systemic examination for signs of hypocalcemia after phototherapy, like Jitteriness, apnea, and convulsion, as well as investigations which include: TSB, S. Ca before and after phototherapy.

Inclusion criteria: All term, normal jaundiced infants undergoing phototherapy were included in this study with S .bilirubin above 15 mg/dl.

Exclusion criteria: Pathological jaundice, preterm, asphyxia, infant of a diabetic mother, hypothyroidism, sepsis, IUGR, congenital malformation. Mothers received drugs: such as phenobarbital, Mg sulfate, and oxytocin, and infants received blood exchange.

Study design: prospective study.

Study setting: The Neonatal Unit in Al-Bayda Medical Center, which is a part of the Pediatric Department. It contains 18 incubators connected to a central oxygen supply and 15 baby cots, 3 mechanical ventilators, 5 CPAP machines, 6 phototherapy machines, 6 monitor machines for monitoring vital signs, one cylindrical phototherapy, and 2 radiant warmers. The unit is staffed by one resident doctor on duty and two nurses.

Study period: from June 2021 to January 2022.

Sample: the study sample included (50) neonates.

Statistical analysis: The statistical package for social science software (SPSS) was used to analyze the acquired data statistically. Variables that adhered to a normal distribution were summed up as mean and standard deviation. The independent sample t-test and the chi-square test were employed to compare the two groups. Numbers and percentages were used to present qualitative data. It was thought to be statistically significant at $p < 0.05$.

Limitations: The level of ionized calcium was not included in the study because it was unavailable.

RESULTS

A total of fifty cases meeting the inclusion/exclusion criteria were enrolled in this study. Their

ages ranged from 2 - 12 days with a mean of 5.48 ± 2.74 SD. 22 (44%) were male whereas 28 (56%) were females. Their weights ranged from 2.5-4.2 kg with a mean of 3.21±0.45 SD. Gestational age was between 37-38 weeks with a mean of 37.02 ± 0.25 SD, and the mean of the babies' height was 47.44± 0.54 SD (Tabe1).

Table (1). Distribution of babies according to demographic characteristics

Demographic Characteristic	Age/days	Weight/kg	Height/cm	# GA/weeks
Min	2	2.5	47	37
Max	12	4.2	49	38
Mean±SD	5.48±2.74	3.21±0.45	47.44±0.5447.0	37.02±0.25
Median	5	3	47.5	37

GA = gestational age

29 (58 %) of them were delivered vaginally (Figure 1). The onset of jaundice was between 2-5 days with a mean of 2.62± 0.75 SD, and no cases were recorded in the first 24 hours. The duration of phototherapy was 24-48 hours, mean of 39.36±11.64 SD (Table 2).

Table (2). Distribution of babies according to onset and duration of phototherapy

Variable	Onset of jaundice/days	Duration of photo/hrs.
Min	2	24
Max	5	48
Mean±SD	2.62±0.75	39.36±11.64
Median	2.5	36

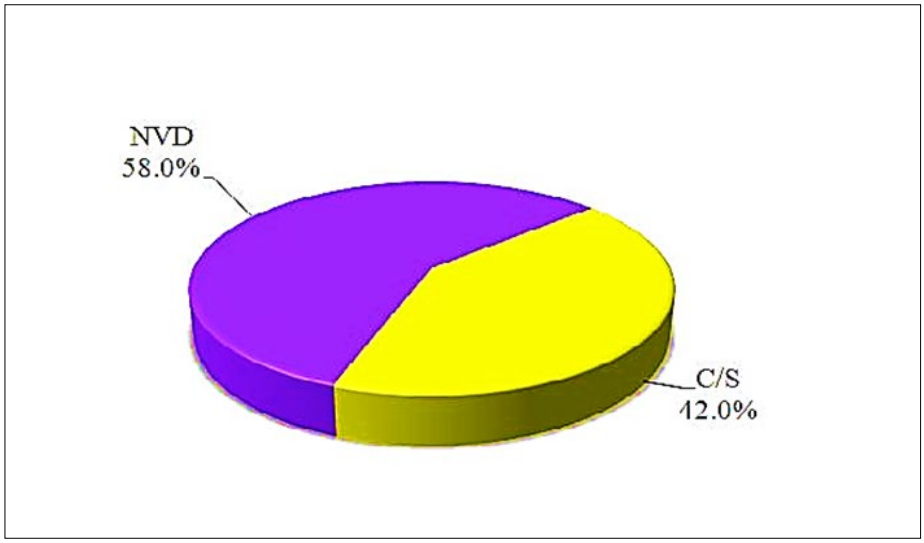

Figure (1). Distribution of babies according to mode of delivery

The serum bilirubin levels ranged from 15-18mg/dl with a mean of 16.72±1.41 SD before phototherapy, and 4-11mg /dl with a mean of 8.87±1.71 SD after phototherapy, and there was a significant drop in serum bilirubin p=<0.001 (Table 3).

Table (3). Distribution of the babies according to TSB mg/dl.

TSB	Before photo	After photo	T	p
Min	15	4	32.384	P<0.001
Max	18	11		
Mean ±SD	16.72±1.41	8.87±1.71		
Median (IQR)	16.8	9.5		

t: paired t-test

There is a significant association between phototherapy and a drop in serum calcium levels with a mean of 8.89± 0.99 SD before phototherapy and a mean of 8.14±1.22 SD after phototherapy. 32 (64%) of the babies developed hypocalcemia after phototherapy and among them, 16 (32%) had a deficiency in calcium before phototherapy. 4/32 babies developed symptoms of hypocalcemia, one convulsion, one irritability, and 2 developed jitteriness. Statistical analysis shows a significant association between phototherapy and a drop in serum calcium level with p = 0.00 (Table 4). In contrast, 1(2%) developed hypercalcemia after phototherapy.

Table (4). Distribution of the babies according to S. Ca.

S. Ca mg/dl	Before photo		After photo		T	P
	NO	%	No	%		
4-8	18	36	32	64	t=8.321	0.001
8-11	31	62	17	34		
>11	1	2	1	2		

Of babies who developed hypocalcemia, 53% were female, and only one female patient developed hypercalcemia. Statistical analysis shows no significant association between gender and changes in serum calcium P=0.914 (Table 5).

Table (5). Correlation between S. Ca after phototherapy and gender

S. Ca mg/dl	Male		Female		Total
	NO	%	NO	%	
4-8	15	46.2%	17	53.1%	32
8-11	7	41.9%	10	58.8%	17
>11	0	0.0	1	100	1
P=0.914					

DISCUSSION

A suitable and secure way to lower a newborn's indirect bilirubin level is through phototherapy. The link between phototherapy and hypocalcemia in newborns was initially proposed by (Romagnodi et al., 1979).

In the studied groups, the mean total serum bilirubin (TSB) was 16.72 ± 1.41 SD, compared to a study by (Karamifar et al., 2002). which showed 18.0±2.4 SD, and (Alizadeh-Taheri et al., 2013), where the mean TSB was 20.1±3.3 SD. The duration of phototherapy was between 24 and 48 hours (39.36±11.64 SD), in contrast to the (Eghbalian & Monsef, 2002), where it was 3 days.

After phototherapy, 32(64%) individuals in our study were hypocalcemia which is statistically

significant p<0.001. The study by (Karamifar et al., 2002). was correlated with the current study with the significant decrease in serum calcium levels reported in term newborns following phototherapy. In premature neonates, (Romagnodi et al., 1979) were the first to propose a link between hypocalcemia and phototherapy in 1979, and they found hypocalcemia in 52.3% of newborns. According to (Sethi et al., 1993) 75% of full-term newborns developed hypocalcaemia after phototherapy. These studies support the findings of the current study.

Correlation of hypocalcemia with other studies

Study	Year	No. of participants	Hypocalcemia after photo	P
Sethi et al.	1993	40	75%	p<0.05
Jain et al.	1998	40	30%	p<0.05
Karamifar et al.	2002	153	8.7%	p<0.018
Yadav RK et al.	2012	30	66.6%	p<0.05
Arora et al.	2014	100	56%	P<0.05
Our study	2022	50	64%	p<0.001**

(Jain et al., 1998), following phototherapy, 30% of full-term newborns experienced hypocalcemia. In (Dutta, 2001) findings, phototherapy caused hypocalcemia in 75% of full-term infants. (Karamifar et al., 2002) reported that the prevalence of hypocalcemia in full-term infants was 8.7% (p=0.018). (Eghbalian & Monsef, 2002) study discovered a statistically significant difference (p<0.05) between serum calcium levels before and after phototherapy. Romagnoli, C. 1979, Phototherapy-induced hypocalcemia. Journal of Pediatrics, 94: 815-816. (Yadav et al., 2012) study following 48 hours of phototherapy, 66.6% of term neonates developed a decrease in their calcium levels p<0.05. (Alizadeh-Taheri et al., 2013) studied the prevalence of phototherapy-induced hypocalcemia in 147 term neonates and found a decrease in serum calcium levels in 56% of babies out of which 7% developed significant hypocalcemia (p=0.03) after 48 hours of phototherapy.

(Arora et al., 2014) study concluded that hypocalcemia was more frequently observed in term neonates. A much higher incidence of hypocalcemia was observed by (Sethi et al., 1993) and the lowest incidence was reported by (Karamifar et al., 2002). The reason for this difference is not 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 the (Arora et al., 2014). Symptomatic hypocalcemia was observed in (Arora et al., 2014; Jain et al., 1998; Sethi et al., 1993) In the present study, it was observed that phototherapy induces a considerable decline in serum calcium levels in icteric newborn therapy. This decline may continue down to the threshold of hypocalcemia and be accompanied by signs and symptoms of hypocalcemia such as jitteriness, apnea, irritability, and or convulsion which was in comparison to the (Karamifar et al., 2002) study.

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	Afterphototherapy	
Eghbalian et al.	9.85±1.23	9.09±0.93	<0.001
Karamifar et al.	9.53±0.92	9.30±1.11	0.043
Taheri et al.	9.8±0.80	9.5±0.90	<0.05
Our Study	8.89±0.99	8.14±1.22	<0.001**

In our study, there was a significant decline in mean serum calcium levels following phototherapy in term neonates, also ($p<0.001$) which was similar to the other studies done by (Alizadeh-Taheri et al., 2013; Eghbalian & Monsef, 2002; Karamifar et al., 2002).

CONCLUSION

Among newborns treated with phototherapy who are jaundiced, hypocalcemia is a common occurrence. When working with newborns in this situation, we should be mindful that institutional policy and research priorities should take serial monitoring for hypocalcemia and its consequences into account.

Our study explains the significant effect of phototherapy on calcium levels in term neonates (64%) with jaundice receiving phototherapy. The range of ca was <8.5 mg/dl. Although the signs were not remarkable, some infants developed complications like convulsions, jitteriness, and irritability.

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ETHICS

Informed consent was obtained from the patient's parents regarding the study objectives and methods.

Duality of interest: Yes, there is a conflict of interest in this manuscript.

Author contributions: A. developed the theoretical formalism. B supervised the project. A, C, and D performed the analytic calculations and performed the numerical simulations. All authors read, reviewed, and approved the final manuscript

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