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Evaluation of phototherapy effects on platelet numbers and volumes in neonates with unconjugated hyperbilirubinemia in Sulaimani city/Kurdistan region/Iraq

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Abstract:

BACKGROUND: Unconjugated hyperbilirubinemia is a rather common disease that affects 60% of term and 80% of preterm infants within their 1st week of life. Phototherapy is considered the safest method for the treatment of unconjugated hyperbilirubinemia in neonates, which is the most common problem in the neonatal period.

OBJECTIVES: To identify the effect of phototherapy on platelet numbers and volumes, and if the duration of treatment, gestational age, birth weight and other factors have some influences on this effect.

PATIENTS, MATERIALS AND METHODS: A prospective cohort study was conducted from November 1, 2023, to April 1, 2024. Seventy-four neonates were enrolled in this study including males and females (1.39:1), with different gestational ages and birth weights. Neonates were selected according to the specific inclusion and exclusion criteria. Thorough history and physical examination performed with several laboratory investigations sent. Total serum bilirubin measured before starting phototherapy, after 24 hours, 48 h, 72 hours, and 4 days later. SPSS program was used to code, enter, and process the gathered data.

RESULTS: Platelet number in general decreased with increasing duration of phototherapy regardless of other parameters (P = 0.045). In correlation to the duration of phototherapy and time of jaundice appearance, it was statistically significant for only neonates who required phototherapy for more than 4 days and time of jaundice appearance between 1 and 3 days (P = 0.042). Platelets number decreased with increasing duration of phototherapy especially in low birth weight and very low birth weight neonates, P value 0.028 and 0.047 respectively. There were statistically significant values (P = 0.002 and P = 0.001) in the correlation of decreasing platelet numbers to gestational age and duration of phototherapy, especially more evident with gestational age below 37 weeks (preterm) and in periods after 24 h and 72 h. There were no statistically significant values in platelet volumes in correlation to any of the previous parameters.

CONCLUSIONS: Platelets number decreased with phototherapy management, and it is more evident with longer phototherapy duration, low birth weight and early onset, while platelet volume not affected. Hence, it is recommended to avoid unnecessary prolongation of phototherapy.

Keywords:

Neonates, phototherapy, platelets counts, unconjugated hyperbilirubinemia

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Introduction

Unconjugated hyperbilirubinemia is a rather common disease that affects 60% of term and 80% of preterm infants within their 1st week of life.[1]

Unconjugated hyperbilirubinemia may be detrimental to the brain and cause a persistent developmental delay if it exceeds the maximum limits of physiological jaundice.[2]

For unconjugated hyperbilirubinemia, exchange transfusion, intravenous immunoglobulin, and phototherapy are viable treatment options. Among these possibilities, phototherapy, a noninvasive technique, has been used extensively to treat jaundice in newborns. For neonates, phototherapy is generally highly safe and may not have any negative long-term side effects.[3]

Despite being safe, phototherapy might have negative effects. The following problems and adverse consequences have been reported: loose stools, retinal damage, increased insensible water loss, bronze baby, skin rash, hypocalcemia, decreased mother–infant contact, and gonadal toxicity. When phototherapy is combined with hyperbilirubinemia, it can result in DNA strand breaks and other impacts on the genetic material of cells.[1,3]

While the majority of studies have shown that phototherapy causes thrombocytopenia, only a small number of studies have shown that phototherapy has the opposite effect on platelet count. Therefore, more research in a variety of clinical contexts is still required to determine the exact impact of phototherapy on platelet count.[2]

In the modern era of postnatal discharge from the hospital, neonatal hyperbilirubinemia is the most frequent cause of readmission for neonates in the 1st week of life. It is a reflection of the liver's underdeveloped bilirubin excretory pathway. Pediatricians and parents alike are concerned about neonatal hyperbilirubinemia.[4]

Phototherapy acts by converting unconjugated bilirubin into water-soluble photoproducts that can be excreted in urine directly without hepatic metabolism. These photoproducts are speculated to be nonneurotoxic based on the observations that these are polar and do not cross blood–brain barrier. The range of 460–490 nm is most effective for phototherapy (blue-green light).[5,6]

Thrombocytopenia is considered one of the most common hematological abnormalities in neonates. Severe thrombocytopenia was found in around 26% of neonates and nearly 11% of thrombocytopenic neonates presented with hemorrhage. Intracranial hemorrhage percentage was found in 5.9% and mostly in preterm neonates. Death occurred in 4.5% of neonates. Hence, monitoring platelet count during phototherapy is crucial.[7] This study aimed to identify the effect of phototherapy on platelet numbers, volumes, the duration of treatment, and other associated factors.

Patient Materials and Methods

This was a prospective cohort study conducted from November 1, 2023, to April 1, 2024, in multiple locations (in the neonatal intensive care unit [NICU] in Dr. Jamal Ahmed Teaching Hospital for Pediatrics, in the NICU of Obstetric Teaching Hospital, private clinic, and two private hospitals) in Sulaimani city/Kurdistan region/Iraq.

The study enrolled (74) neonates, who were complaining of unconjugated hyperbilirubinemia. Both gender included with male to female ratio (1.39:1) as shown in Figure 1. All term (completed 38–42-week gestational age from the 1st day of the last menstrual period), preterm (those born before 37-week gestational age), and postterm (those born after 42-week gestational age) were included in this study.

Birth weights were considered normal (birth weight: 2.5–4.5 kg), low birth weight (1.5–<2.5 kg), very low birth weight (1–<1.5 kg), extremely low birth weight (<1 kg), and large birth weight (>4.5 kg).[8]

Inclusion criteria

1. Neonates (term, preterm, and postterm) with unconjugated hyperbilirubinemia, whether pathological (such as Rh and ABO incompatibilities) or exaggerated physiological jaundice that required phototherapy according to phototherapy guidelines[9]
2. Neonates with platelet numbers within the normal range at the time of diagnosis.

Exclusion criteria

1. Neonates with any comorbidities such as septicemia, respiratory distress syndrome, sepsis, birth asphyxia, or any congenital anomalies
2. Those who were confirmed as conjugated hyperbilirubinemia
3. If exchange transfusion performed or indicated
4. Neonates with platelet number below the lower limits of normal range (when platelets count <150,000/mm^3)
5. Extremely low birth weight (<1 kg)
6. When data were not enough to be included in the study
7. Those that refused to be included in this study.

History was taken from all, with complete physical examination (with particular attention paid to; gestational age, postnatal age, duration and time of appearance of

jaundice, blood group of mother and baby, family history of hemoglobinopathies, or red blood cells enzyme deficiencies, or other blood disorders and family history of previous similar conditions).

All patients were sent for complete blood count, total serum bilirubin (TSB), at time of diagnosis (before starting phototherapy), after 24 from starting phototherapy, 48 h, 72 h, and for some patients after 4 days later (for those required phototherapy more than 3 days).

Some of the patients were sent for a direct and indirect fraction of bilirubin, reticulocyte count, thyroid function tests, and other tests depending on presentation and differential diagnoses, to exclude other conditions and to differentiate the causes of direct and indirect hyperbilirubinemia, respectively.

Platelet counts were taken using a (Medonic M32 hematology analyzer, Sweden). Thrombocytopenia was considered when platelet count was <150,000/mm^3, whereas mild, moderate, and severe thrombocytopenia were 100,000–150,000/mm^3, 50,000/mm^3, and <50,000/mm^3, respectively. While thrombocytosis when platelet count more than 450,000/mm3. Regarding platelet volume: normal range 7-11 fl, small when <7 fl, and large if >11 fl respectively.[8]

T.S.B. levels measured by taking capillary blood sample using the red capillary tube (microhematocrit tube) into the spectrophotometer Apel Br 501's machine type.

Ethical considerations

Following international criteria, this study was carried out. Every phase of the work process adhered to the 2008 Helsinki Declaration. Participants' confidentiality was maintained. It was approved by the Ethical Committee of Sulaimani Medical College.

Verbal informed consents were obtained from the parents of neonates enrolled in this study. The research has been approved by scientific and ethical committee in college of medicine/ University of Sulaimani (on 3rd of January 2024, number 111).

Statistical analysis

SPSS program (Statistical Package for the Social Sciences) version 23 (IBM SPSS) (Armonk, NY, IBM Corp, USA) was used to code, enter, and process the gathered data. Following their representation in tabular and diagrammatic formats, the results were interpreted. When applicable, the mean, median, standard deviation (SD), and percentage were used to statistically characterize the data. The Chi-square tests were used to statistically assess the difference between two means and to tabulate and statistically analyze all of the data from different groups. $P < 0.05$ was considered statistically significant, $P < 0.01$ strongly significant, and $P > 0.05$ nonsignificant.

Results

The total number of neonates enrolled in this study was 74, of which 43 (58.1%) were male and 31 (41.9%) were female.

The demographic parameters of the neonates with unconjugated hyperbilirubinemia treated by phototherapy are shown in Table 1.

Male to female ratio was 1.39:1. As shown in Figure 1.

The mean of postnatal age 6.88 ± 3.276 SD, the minimum 3 days while maximum 15 days.

The mean of gestational age 36.51 ± 4.295 SD, the minimum 27 weeks while maximum 44 weeks. The majority of neonates were preterm (50%), followed by term (37.8%) and then post-term (12.2%).

The mean birth weight was 3.003 ± 0.9488 SD. The minimum was 1 kg, and the maximum was 5 kg.

Sixty-two percent of neonates were within the normal range of birth weights, whereas 35.2% were below the normal range, and around 2.7% of neonates were above normal.

Most neonates were delivered by C-section (70.3%), and around 25.7% of neonates were delivered by normal vaginal delivery, whereas instrumental delivery was 4.1% only.

Mixed feeding was the common mode of feeding (56.8%), followed by formula (32.4%) and then breast (10.8%).

Physiological jaundice was the most common etiology (52.7%), ABO incompatibility (25.7%), and G6PD deficiency (10.8%), followed by other etiologies.

All patients were Kurdish and Muslim.

Table 2 shows the platelet number and volume in neonates with unconjugated hyperbilirubinemia before phototherapy in correlation to different parameters.

No neonates enrolled in this study have platelets count nor number below the normal range according to exclusion criteria.

Table 3 shows some statistical values of different parameters.

Table 1: Demographic parameters of the neonates with unconjugated hyperbilirubinemia treated by phototherapy (*n*=74)

Demographic parameters	*n* (%)	Total, *n* (%)
Gender		
Male	43 (58.1)	74 (100)
Female	31 (41.9)	
Postnatal age (age of jaundice appearance) (days)		
1–3	8 (10.8)	74 (100)
4–7	36 (48.6)	
8–11	20 (27.0)	
12–>12	10 (13.5)	
Gestational age (weeks)		
Term 38–42	28 (37.8)	74 (100)
Preterm 33–37	24 (32.4)	
Preterm 28–32	10 (13.5)	
Preterm<28	3 (4.1)	
Postterm>42	9 (12.2)	
Birth weight (kg)		
2.5–4.5	46 (62.2)	74 (100)
1.5–<2.5	21 (28.4)	
1–<1.5	5 (6.8)	
>4.5	2 (2.7)	
Mode of delivery		
Normal vaginal delivery	19 (25.7)	74 (100)
Cesarean section	52 (70.3)	
Instrumental delivery	3 (4.1)	
Mode of feeding		
Breast feeding	8 (10.8)	74 (100)
Formula feeding	24 (32.4)	
Mixed feeding	42 (56.8)	
Vitamin K IM		
Received	59 (79.7)	74 (100)
Not received	15 (20.3)	
Family history of neonatal jaundice		
Positive	40 (54.1)	
Negative	34 (45.9)	
Etiology of hyperbilirubinemia		
Rh incompatibility	3 (4.1)	74 (100)
ABO incompatibility	19 (25.7)	
G6PD deficiency	8 (10.8)	
Family history of Hb pathies	4 (5.4)	
Pyruvate kinase deficiency	1 (1.4)	
Physiological jaundice or unknown	39 (52.7)	
Address		
Urban	66 (89.2)	74 (100)
Rural	8 (10.8)	

Hb=Hemoglobin, IM=Intra-muscular injection, G6PD=Glucose 6 phosphate dehydrogenase deficiency

The mean of jaundice presentation in neonates in this study was 6.88 days (minimum of 3 days and maximum of 15 days).

We did not include neonates with extremely low birth weight in this study (minimum of 1 kg).

The lowest gestational age was 27 weeks and the highest was 44 weeks.

The lowest level of bilirubin that required phototherapy was 5.7 (the decision of treatment with phototherapy was according to protocol as mentioned in patients' materials and methods).

No neonates enrolled in this study presented with severe anemia (the lowest level of Hb before starting phototherapy was 12.5 g/dL).

Statistics of platelet numbers and volumes in relation to the duration of phototherapy are shown in Table 4.

Platelet number in general decreased with increasing duration of phototherapy regardless to other influences, while platelet volume not.

P value for platelet number statistically significant in this correlation, but not significant for platelet volume.

Table 5 shows the platelet number and volumes in correlation to the duration of phototherapy and time of jaundice appearance.

All neonates under phototherapy did not develop critical thrombocytopenia (<50,000) nor severe thrombocytosis (>650,000).

P value was statistically significant for platelet numbers in correlation with the duration of phototherapy and time of jaundice appearance, but not significant for platelet volumes.

Table 6 shows the platelet number and volumes in correlation to the duration of phototherapy and birth weights.

In Table 6, *P* value was statistically significant for platelet numbers in relation to duration of phototherapy and birth weights, but not significant for platelet volumes.

Again, no neonate developed significant thrombocytopenia, and only one neonate developed a platelet level below 100,000 μL, but was not clinically evident.

Table 7 shows the platelet number and volumes in correlation with the duration of phototherapy and gestational age.

P value was statistically significant for platelet numbers in relation to the duration of phototherapy and gestational ages, but not significant for platelet volumes. The number of platelets decreased with increasing

Table 2: Platelet number and volume in neonates with unconjugated hyperbilirubinemia before phototherapy in correlation to different parameters (*n*=74)

Parameters	Platelet numbers				Platelet volumes			
	150,000–450,000, *n* (%)	451,000–650,000, *n* (%)	Total, *n* (%)	*P* value	7–11 fL, *n* (%)	>11 fL, *n* (%)	Total, *n* (%)	*P* value
Gender								
Male	26 (35.1)	17 (22.97)	43 (58.1)	0.63	39 (52.7)	4 (5.4)	43 (58.1)	0.057
Female	17 (22.97)	14 (18.9)	31 (41.89)		23 (31)	8 (10.8)	31 (41.89)	
Family history of neonatal jaundice								
Positive	23 (31)	17 (22.9)	40 (54.05)	0.90	32 (43.24)	8 (10.81)	40 (54.05)	0.33
Negative	20 (27.02)	14 (18.9)	34 (45.94)		30 (40.54)	4 (5.4)	34 (45.94)	
Etiology of neonatal jaundice								
Rh incompatibility	1 (1.35)	2 (2.7)	3 (4.05)	0.86	3 (4.05)	0	3 (4.05)	0.83
ABO incompatibility	12 (16.21)	7 (9.45)	19 (25.67)		15 (20.27)	4 (5.4)	19 (25.67)	
G6PD deficiency	5 (6.75)	3 (4.05)	8 (10.81)		6 (8.1)	2 (2.7)	8 (10.81)	
Family history of Hb pathies	2 (2.7)	2 (2.7)	4 (5.4)		3 (4.05)	1 (1.35)	4 (5.5)	
Pyruvate kinase deficiency	1 (1.35)	0	1 (1.35)		1 (1.35)	0	1 (1.35)	
Physiological jaundice or unknown	22 (29.72)	17 (22.97)	39 (52.7)		34 (45.94)	5 (6.75)	39 (52.7)	
Postnatal age (days)								
1–3	2 (2.7)	6 (8.1)	8 (10.81)	0.17	6 (8.1)	2 (2.7)	8 (10.81)	0.19
4–7	24 (32.43)	12 (16.21)	36 (48.64)		32 (43.24)	4 (5.4)	36 (48.64)	
8–11	12 (16.21)	8 (10.81)	20 (27.02)		14 (18.91)	6 (8.1)	20 (27.02)	
12–>12	5 (6.75)	5 (6.75)	10 (13.51)		10 (13.51)	0	10 (13.51)	
Gestational age (weeks)								
Term 38–42	22 (29.72)	6 (8.1)	28 (37.83)	0.83	25 (33.78)	3 (4.05)	28 (37.83)	0.43
Preterm 33–37	12 (16.21)	12 (16.21)	24 (32.43)		19 (25.67)	5 (6.75)	24 (32.43)	
Preterm 28–32	4 (5.4)	6 (8.1)	10 (13.51)		9 (12.16)	1 (1.35)	10 (13.51)	
Preterm <28	1 (1.35)	2 (2.7)	3 (4.05)		3 (4.05)	0	3 (4.05)	
Postterm >42	4 (5.4)	5 (6.75)	9 (12.16)		6 (8.1)	3 (4.05)	9 (12.16)	
Birth weight (kg)								
2.5–4.5	32 (43.24)	14 (18.91)	46 (62.16)	0.047	40 (54.05)	6 (8.1)	46 (62.16)	0.27
1.5–<2.5	9 (12.16)	12 (16.21)	21 (28.37)		16 (21.62)	5 (6.75)	21 (28.37)	
1–<1.5	2 (2.7)	3 (4.05)	5 (6.75)		5 (6.75)	0	5 (6.75)	
>4.5	0	2 (2.7)	2 (2.7)		1 (1.35)	1 (1.35)	2 (2.7)	
Mode of feeding								
Breastfeeding	6 (8.1)	2 (2.7)	8 (10.81)		7 (9.46)	1 (1.35)	8 (10.81)	0.75
Formula feeding	15 (20.27)	9 (12.16)	24 (32.43)	0.43	21 (28.37)	3 (4.05)	24 (32.43)	
Mixed feeding	22 (29.72)	20 (27.02)	42 (56.75)		34 (45.94)	8 (10.81)	42 (56.75)	
Mode of delivery								
Normal vaginal delivery	9 (12.16)	10 (13.51)	19 (25.67)	0.21	18 (24.32)	1 ((1.35)	19 (25.67)	0.20
Cesarean section	31 (41.89)	21 (28.37)	52 (70.27)		41 (55.4)	11 (14.86)	52 (70.27)	
Instrumental delivery	3 (4.05)	0	3 (4.05)		3 (4.05)	0	3 (4.05)	
IM Vitamin K								
Received	38 (51.35)	21 (28.37)	59 (79.72)	0.029	50 (67.56)	9 (12.16)	59 (79.72)	0.65
Not received	5 (6.75)	10 (13.51)	15 (20.27)		12 (16.21)	3 (4.05)	15 (20.27)	

Hb=Hemoglobin, IM=Intra-muscular injection, G6PD=Glucose 6 phosphate dehydrogenase deficiency

duration of phototherapy, and it was more evident with decreasing gestational age. Fortunately, there was no neonate developed critical thrombocytopenia.

Discussion

Neonatal hyperbilirubinemia accounts for the most common cause of admission to the NICU in our locality, and all over the world, it is up to 60% in term and 80% in preterm neonates. Phototherapy is regarded as a first option of management in mild-to-moderate hyperbilirubinemia in most of the NICU and it is considered to be safer than other treatment modalities.[8,10,11] This study is carried out to identify the possible effect of phototherapy on platelet number and volumes.

In current study males more than females with male to female ratio (1.39:1). The time of clinical jaundice presentation mostly between 4–7 days old in (48.6%) of cases, and 8–11 days in (28%), respectively. On the other hand, preterm were (50%) of cases, term (37.8%), and post-term (12.2%) respectively. The majority of our

Table 3: Some statistical values of different parameters (*n*=74)

Attribute	Mean±SD	Minimum	Maximum	Median
Age of presentation (days)	6.88±0.381	3	15	6
Birth weight (kg)	3.003±0.110	1	5	3
Gestational age (weeks)	36.51±0.499	27	44	37.5
TSB before phototherapy (mg/dL)	13.88±0.397	5.7	19.4	14
TSB after completing phototherapy (mg/dL)	11.18±0.349	5.6	17.6	11.2
Hb before phototherapy (mg/dL)	19.48±0.299	12.5	25.3	19.55
Hb after completing phototherapy (mg/dL)	17.43±0.316	11.1	24.4	17.05

SD=Standard deviation, TSB=Total serum bilirubin, Hb=Hemoglobin

Table 4: Statistics of platelet numbers and volumes in relation to the duration of phototherapy (*n*=74)

Parameters	Mean±SD	Minimum	Maximum	Median	*P*	*t*-test*
Platelet numbers per μL						
Before phototherapy	458,770.27±76,210.693	230,000	650,000	450,000.00	0.045	0.036
After 24 h	338,391.89±97,708.375	120,000	510,000	340,000.00		
After 48 h	243,905.41±106,418.426	110,000	460,000	230,000.00		
After 72 h	243,658.54±112,403.650	99,000	430,000	300,000.00		
Platelet volumes per fL						
Before phototherapy	10.491±0.9004	6.9	11.7	10.850	0.662	0.583
After 72 h	10.893±0.7778	7.8	12.0	11.000		

**t*-test measured in correlation between the level of total bilirubin before starting phototherapy and after 72 h from starting phototherapy. SD=Standard deviation

cases have a normal birth weight (62.2%), while (35.2%) are below the normal, and only (2.7%) above the normal, these findings are convenient with a study in Duhok/Iraq by Shabo *et al*., a study in Bahrain by Isa *et al*., and a study in Nigeria by Onyearugha *et al*.[12-14]

Fifty-two (70.3%) of neonates included in this study were delivered by cesarean section, 19 (25.7%) by normal vaginal delivery, and 3 (4.1%) by instrumental. The majority of neonates in this study depending on mixed feeding (56.8%), followed by formula feeding (32.4%), then exclusive breastfeeding (10.8%). Overall, the finding is supported by a study in Iraq by Shabila.[15]

Most of neonates received IM Vitamin K prophylaxis (79.7%) for preventing hemorrhagic disease of newborns, and this was established by the Ministry of Health in the Kurdistan region as a protocol for all newborns regardless to the decision of what mode of feeding will be used later.

Positive family history of previous neonatal jaundice was found in (54.1%). The main etiology of indirect hyperbilirubinemia in our cases is physiological or unknown (52.7%), followed by ABO incompatibility (25.7%), G6PD deficiency (10.8%), hemoglobinopathies (5.4%), Rh incompatibility (4.1%), and one case suspected to have pyruvate kinase deficiency (1.4%); these statistics quite similar to researches carried out in Saudi Arabia and in Iran.[16-18]

In correlation of different parameters with the platelet number and volume at the time of diagnosis (first reading) show no statistically significant in most of the parameters except for birth weight and prophylactic Vitamin K to platelet number only.

In the present investigations, neonates with platelets count falling below the normal range were excluded, resulting in finding that diverge from other research identifying thrombocytopenia in low-birth-weight infants. It is widely recognized that low birth weight is predominantly linked to prematurity and its associated complications. Therefore, the result of this study should not be regarded as definitive scientific evidence.[19,20]

There is no scientific evidence demonstrating a connection between the prophylactic vitamin K and neonatal platelet numbers and volumes; while some data suggest that vitamin K may improve the platelet function but it does not appear to have an impact on platelets counts and volumes; therefore finding in the current study, even it is statistically significant but cannot be considered as definitive scientific evidence.[21,22]

The reduction in levels of unconjugated bilirubin and hemoglobin is observed following phototherapy, aligning with scientific evidence indicating that effective phototherapy may reduce the level of bilirubin in a rate of 1–2 mg/dL over 4–6 h, while hemoglobin level naturally start to decline physiologically after birth.[8,9,23]

It is worth mentioning that platelet numbers, in general, decreased with increasing duration of phototherapy regardless to other influences with ($P = 0.045$), while it is statistically nonsignificant for platelet volume ($P = 0.662$), this finding in agreement with a study in Egypt by

Table 5: Platelet number and volumes in correlation to duration of phototherapy and time of jaundice appearance (*n*=74)

Parameters	Time of jaundice appearance (days)	Platelet numbers (μL)				Platelet volumes (fL)			*P*
		50,000–<100,000, *n* (%)	100,000–<150,000, *n* (%)	150,000-450,000, *n* (%)	>450,000–650,000, *n* (%)	<7, *n* (%)	7–11, *n* (%)	>11, *n* (%)	
Duration of phototherapy									
Before the phototherapy	1–3	0	0	2 (2.7)	6 (8.1)	0	19 (25.7)	11 (14.9)	For platelet number=0.51
	4–7	0	0	24 (32.4)	12 (16.2)	1 (1.4)	25 (33.8)	10 (13.5)	
	8–11	0	0	12 (16.2)	8 (10.8)	0	7 (9.5)	0	Platelets volume=0.30
	12 and more	0	0	5 (6.8)	5 (6.8)	0	0	1 (1.4)	
After 24 h	1–3	0	1 (1.4)	26 (35.1)	1 (1.4)	-	-	-	For platelet number=0.91
	4–7	0	2 (2.7)	31 (41.9)	3 (4.1)	-	-	-	
	8–11	0	3 (4.1)	6 (8.1)	0	-	-	-	
	12 and more	0	0	1 (1.4)	0	-	-	-	
After 72 h	1–3	0	14 (18.9)	16 (21.6)	0	0	4 (5.4)	4 (5.4)	Platelet number=0.60
	4–7	0	12 (16.2)	23 (31.1)	1 (1.4)	0	26 (35.1)	10 (13.5)	Platelets volume=0.56
	8–11	0	1 (1.4)	6 (8.1)	0	1 (1.4)	13 (17.5)	6 (8.1)	
	12 and more	0	0	1 (1.4)	0	0	8 (10.8)	2 (2.7)	
After 4 days*	1–3	0	11	8 (19.5)	0	-	-	-	Platelet number=0.042
	4–7	0	0	0	0	-	-	-	
	8–11	1 (1.4)	2	15 (36.6)	0	-	-	-	
	12 and more	0	1 (1.4)	3 (7.3)	0	-	-	-	

*We have enough data for 41 patients only after 4 days of phototherapy because most patients required no more phototherapy after 72 h, and in other patients, we did not get the required data (unfortunately, data were not enough for platelet numbers and volumes after 4 days of phototherapy)

Table 6: Platelet number and volumes in correlation to duration of phototherapy and birth weights (*n*=74)

Parameters	Birth weight (kg)	Platelet numbers (µL)				Platelet volumes (fL)			*P*
		50,000–<100,000, *n* (%)	100,000–<150,000, *n* (%)	150,000–450,000, *n* (%)	>450,000–650,000, *n* (%)	<7, *n* (%)	7–11, *n* (%)	>11, *n* (%)	
Duration of phototherapy									
Before phototherapy	2.5–4.5	0	0	32 (43.3)	14 (18.9)	0	40 (54.1)	6 (8.1)	Platelet number=0.047
	1.5–<2.5	0	0	9 (12.2)	12 (16.2)	0	16 (21.6)	5 (6.8)	Platelets volume=0.27
	1–<1.5	0	0	2 (2.7)	3 (4.1)	0	5 (6.8)	0	
	>4.5	0	0	0	2 (2.7)	0	1 (1.4)	1 (1.4)	
After 24 h	2.5–4.5	0	2 (2.7)	43 (58.1)	1 (1.4)	-	-	-	Platelet number=0.028
	1.5–<2.5	0	3 (4.1)	17 (22.9)	1 (1.4)	-	-	-	
	1–<1.5	0	1 (1.4)	3 (4.1)	1 (1.4)	-	-	-	
	>4.5	0	0	1 (1.4)	1 (1.4)	-	-	-	
After 72 h	2.5–4.5	0	11 (14.9)	34 (49.9)	1 (1.4)	0	32 (43.2)	14 (18.9)	Platelet number=0.045
	1.5–<2.5	0	14 (18.9)	7 (9.5)	0	1 (1.4)	13 (17.6)	7 (9.4)	Platelets volume=0.501
	1–<1.5	0	2 (2.7)	3 (4.1)	0	0	5 (6.8)	0	
	>4.5	0	0	2 (2.7)	0	0	1 (1.4)	1 (1.4)	
After 4 days*	2.5–4.5	0	4 (9.8)	18 (43.9)	0	-	-	-	Platelet number=0.056
	1.5–<2.5	1 (2.4)	9 (27.9)	4 (9.8)	0	-	-	-	
	1–<1.5	0	1 (2.4)	2 (4.9)	0	-	-	-	
	>4.5	0	0	2 (4.9)	0	-	-	-	

*We have data for 41 patients only after 4 days of phototherapy because most patients required no more phototherapy after 72 h (unfortunately, data were not enough for platelet volumes after 4 days of phototherapy)

Elsaeed *et al*. (P = 0.001), a study in India by Khera and Gupta and another in Turkey by Shabo *et al*.[2,3,12]

The study conducted by Venaktamurthy *et al*. in India, however, contradicted the findings of the present study (P = 0.150). This discrepancy may be attributed to variations in research methodologies, as our study and those in concurrence with it assessed platelet count at least three times over different time periods, while Venaktamurthy *et al*. only measured platelet count twice - upon admission and after discontinuation of phototherapy.[4]

We were able to collect data from 41 neonates only who were on phototherapy for more than 4 days because other neonates required less duration to get the safe level of phototherapy and discharged. There is a statistically significant correlation (P = 0.042) between the duration of phototherapy and the time of jaundice appearance for neonates who needed phototherapy for more than 4 days and had jaundice appear between 1 and 3 days (41 neonates only). This could be attributed to the scientific fact that jaundice appearing within the first 3 days of life is more likely to be associated with complications than jaundice appearing after 3 days of life, leading to a longer duration of phototherapy for most cases.[1,8,23]

In the present study, a significant correlation was found between birth weights and a decrease in platelet numbers with duration, particularly in low birth weight and very low birth weight infants between 24 h and 72 h (P = 0.028 and P = 0.047, respectively). However, there were no statistically significant relations between platelet volumes and birth weights or durations. These results are consistent with previous studies by Elsaeed *et al*., Khera and Gupta, and Shabo *et al*., although Venaktamurthy *et al*. have conflicting findings.[2-4,12]

Platelet numbers were found to decrease in relation to gestational age and the duration of phototherapy. This trend was particularly noticeable in babies born before 37 weeks of gestation and in the periods following 24 hours and 72 hours of phototherapy (P = 0.002 and P = 0.001, respectively). However, platelet volume did not show any statistically significant differences across all gestational ages and durations of phototherapy. These results align closely with the studies conducted by Elsaeed *et al*., Khera and Gupta, Shabo *et al*., Abd El Moktader *et al*., and Sarkar et al. Venaktamurthy *et al*., on the other hand, reported a P value of 0.150, which was deemed statistically nonsignificant.[2-4,12,24,25]

Despite platelet numbers not dropping to dangerous levels in neonates of varying gestational ages and birth weights, it is evident that phototherapy affects platelet numbers without impacting volumes. Prolonged use of

Table 7: Platelet number and volumes in correlation with duration of phototherapy and gestational age (*n*=74)

Parameters	Gestational age (weeks)	Platelet numbers (μL)				Platelet volumes (fL)			*P*
		50,000–<100,000, *n* (%)	100,000–<150,000 , *n* (%)	150,000–450,000, *n* (%)	>450,000–650,000, *n* (%)	<7, *n* (%)	7–11, *n* (%)	>11, *n* (%)	
Duration of phototherapy									
Before phototherapy	38–42	0	0	22 (29.7)	6 (8.1)	25 (33.8)	3 (4.1)	28 (37.8)	Platelet number=0.083
	33–37	0	0	12 (16.2)	12 (16.2)	19 (25.7)	5 (6.8)	24 (32.4)	
	28–32	0	0	4 (5.4)	6 (8.1)	9 (12.2)	1 (1.4)	10 (13.5)	Platelets volume=0.433
	<28	0	0	1 (1.4)	2 (2.7)	3 (4.1)	0	3 (4.1)	
	>42	0	0	4 (5.4)	5 (6.8)	6 (8.1)	3 (4.1)	9 (12.2)	
After 24 h	38–42	0	0	28 (37.8)	0	-	-	-	Platelet number=0.002
	33–37	0	5 (6.8)	18 (24.3)	1 (1.4)	-	-	-	
	28–32	0	0	10 (13.5)	0	-	-	-	
	<28	0	1 (1.4)	1 (1.4)	1 (1.4)	-	-	-	
	>42	0	0	7 (9.5)	2 (2.7)	-	-	-	
After 72 h	38–42	0	4 (5.4)	24 (32.4)	0	0	20 (27)	8 (10.8)	Platelet number=0.001
	33–37	0	16 (21.6)	8 (10.8)	0	1	15 (20.3)	8 (10.8)	
	28–32	0	6 (8.1)	4 (5.4)	0	0	7 (9.5)	3 (4.1)	Platelets volume=0.881
	<28	0	1 (1.4)	2 (2.7)	0	0	3 (4.1)	0	
	>42	0	0	8 (10.8)	1 (1.4)	0	6 (8.1)	3 (4.1)	
After 4 days*	38–42	0	2 (4.9)	11 (26.8)	0	-	-	-	Platelet number=0.014
	33–37	0	9 (21.9)	4 (9.8)	0	-	-	-	
	28–32	0	2 (4.9)	3 (7.3)	1 (2.4)	-	-	-	
	<28	0	1 (2.4)	1 (2.4)	0	-	-	-	
	>42	0	0	7 (17.1)	0	-	-	-	

*We have data for 41 patients only after 4 days of phototherapy because most patients required no more phototherapy after 72 h (unfortunately, data were not enough for platelet numbers and volumes after 4 days of phototherapy)

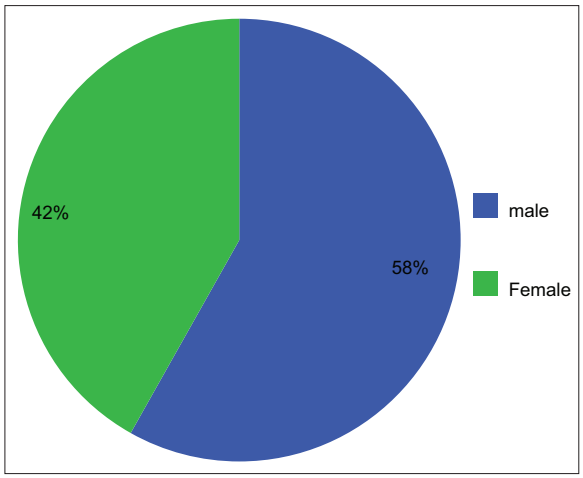

Figure 1: Male to female ratio

phototherapy for over 4 days, particularly in high-risk patient groups, could result in clinically significant thrombocytopenia. Further studies with increased sample size and longer duration are necessary to confirm this.

Therefore, it is advisable to adhere to phototherapy guidelines for the treatment of unconjugated hyperbilirubinemia, ensuring that the duration of treatment is appropriate and does not exceed the recommended timeframe.

Conclusions

Platelet number in general decreased with increasing duration of phototherapy regardless of other parameters.

In correlation to the duration of phototherapy and time of jaundice appearance, it is statistically significant for only neonates who required phototherapy for more than 4 days and time of jaundice appearance between 1 and 3 days.

Platelet number decreased in correlation to the duration of phototherapy and birth weights.

There is a statistically significant correlation between decreasing platelet numbers to gestational age and duration of phototherapy, especially more evident with gestational age below 37 weeks (preterm) and in periods after 24 h and 72 h, respectively.

There are no statistically significant for platelet volume in correlation to any of the parameters included in this study.

Recommendations

It is essential to avoid unnecessary extension of phototherapy for neonates with unconjugated hyperbilirubinemia, particularly for those born with low birth weights and preterm infants. Although no patients in this study developed serious thrombocytopenia (as it did not include patients with other conditions associated with thrombocytopenia), it could result in clinically significant thrombocytopenia values, especially in critically ill patients with concurrent conditions such as sepsis, hemolysis, asphyxia, and more. Therefore, further research is recommended to include neonates with critical conditions and hyperbilirubinemia.

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Conflicts of interest

There are no conflicts of interest.

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