

An Observational Study of Frequency of Thrombocytopenia Following Phototherapy in Neonatal Hyperbilirubinemia Conducted in a Tertiary Care Hospital in Maharashtra

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ABSTRACT:

Background and Objective: Phototherapy is the standard treatment for neonatal hyperbilirubinemia. Although some studies have suggested an association between phototherapy and acquired thrombocytopenia during the early neonatal period, the evidence remains inconclusive. This study evaluated the frequency of thrombocytopenia following phototherapy and the factors associated with its occurrence.

Materials and Methods: This prospective observational study included 200 neonates with physiological hyperbilirubinemia admitted to the NICU of a tertiary care hospital. Phototherapy was initiated according to the American Academy of Pediatrics guidelines. Serum bilirubin and platelet counts were measured before starting phototherapy and repeated every 24 hours during treatment and immediately after its completion using an automated Coulter LH 750 analyzer, with microscopy used for confirmation. Data on sex, birth weight, gestational age, age at onset of jaundice, timing of phototherapy initiation, phototherapy dose and duration, and initial serum bilirubin levels were recorded and statistically analyzed.

Results: Among the 200 neonates studied, 70 (35%) developed thrombocytopenia following phototherapy, while 130 (65%) maintained normal platelet counts. Statistical analysis demonstrated that the observed reduction in platelet count was not significant. Furthermore, no significant association was found between thrombocytopenia and sex, birth weight, gestational age, age at onset of jaundice, timing of phototherapy initiation, phototherapy dose, duration of

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phototherapy, or initial serum bilirubin levels.

Conclusion: Thrombocytopenia was observed in 35% of neonates receiving phototherapy for physiological hyperbilirubinemia; however, the association was not statistically significant. Routine phototherapy does not appear to be an independent risk factor for clinically significant thrombocytopenia.

Keywords: Neonatal hyperbilirubinemia, phototherapy, thrombocytopenia, neonate, platelet count.

INTRODUCTION

Neonatal jaundice, or neonatal hyperbilirubinemia, is one of the most common clinical conditions encountered during the neonatal period, affecting approximately 60% of term and 80% of preterm infants within the first week of life.[1] Clinically apparent jaundice develops when serum bilirubin levels exceed approximately 5 mg/dL and is characterized by yellow discoloration of the skin, sclera, and mucous membranes. Although physiological jaundice is generally benign and resolves spontaneously within one to two weeks, nearly 10% of breastfed infants experience prolonged jaundice requiring further evaluation. Severe or untreated hyperbilirubinemia may result in bilirubin encephalopathy and kernicterus, making timely diagnosis and management essential.[2]

Neonatal hyperbilirubinemia primarily results from increased bilirubin production due to accelerated red blood cell turnover, immature hepatic bilirubin conjugation, and reduced bilirubin excretion. Additional risk factors include hemolytic disorders, prematurity, infections, increased enterohepatic circulation, genetic conditions affecting bilirubin metabolism, and maternal factors such as diabetes mellitus. Management of neonatal jaundice is guided by serum bilirubin levels, gestational age, and associated clinical risk factors, with the American Academy of Pediatrics providing evidence-based recommendations for initiating treatment.[3]

Among the available treatment modalities, phototherapy remains the cornerstone for managing unconjugated hyperbilirubinemia

because of its efficacy, non-invasive nature, and favorable safety profile. Phototherapy converts unconjugated bilirubin into water-soluble photoisomers that can be excreted without hepatic conjugation, thereby reducing serum bilirubin levels and preventing the need for exchange transfusion. Effective phototherapy is delivered using blue light with wavelengths between 420 and 470 nm at an appropriate distance from the infant to maximize irradiance.[4]

Despite its widespread use and overall safety, phototherapy is associated with several recognized adverse effects, including increased insensible water loss, diarrhea, temperature instability, retinal injury, hypocalcemia, bronze baby syndrome, impaired maternal-infant bonding, oxidative stress, and DNA damage. An additional but less well-established adverse effect is thrombocytopenia. Although thrombocytopenia has been described in isolated case reports and a few observational studies, it is not routinely recognized as a complication of phototherapy in standard pediatric or neonatology textbooks.[5]

Experimental studies have demonstrated that exposure of platelets to high-intensity light may impair platelet aggregation, secretion, and survival. Clinical studies have also reported reductions in platelet counts following phototherapy, possibly due to shortened platelet lifespan and increased splenic sequestration of damaged platelets. [6,7] However, the available evidence remains inconsistent, with several investigations reporting conflicting findings regarding both the incidence and clinical significance of phototherapy-associated thrombocytopenia.

Given these conflicting reports and the limited availability of well-designed studies, further evaluation is warranted. The present study was therefore undertaken to determine the frequency of thrombocytopenia among neonates receiving phototherapy for neonatal hyperbilirubinemia and to identify demographic and clinical factors associated with its occurrence.

MATERIAL AND METHODS

Study design: It is an observational study.

Sample Size (n) = $(Z^2 * p * (1-p)) / E^2$ Let's calculate the sample size:
 $n = (1.96^2 * 0.15 * (1-0.15)) / 0.05^2$ $n = (3.8416 * 0.15 * 0.85) / 0.0025$

$n = 0.4906464 / 0.0025$

$n = 196.25856$

Rounding up to the nearest whole number, the recommended sample size for this calculation is 197. Therefore, a sample size of 200 participants would be required for this study to achieve a 95% confidence level with a 5% absolute error, assuming an estimated proportion (p) of 15%.

INCLUSION CRITERIA:

- Neonates requiring phototherapy for indirect hyperbilirubinemia irrespective of gender, age at onset of jaundice and birth weight after taking written informed consent.

EXCLUSION CRITERIA

- babies with features of severe hemolysis
- Babies with direct hyperbilirubinemia
- Babies with sepsis, birth asphyxia
- Babies with platelet count $<1, 50,000 / \text{mm}^3$ at admission
- Baby or mother on any drugs causing thrombocytopenia
- Babies requiring exchange transfusion
- Babies with hemangiomas or any congenital anomalies
- Neonates who developed signs suggestive of sepsis during phototherapy

Place of study: Tertiary Care Hospital

Duration of study: 18 months

Sampling method: Snow ball/ convenient sampling method

Sampling Size: 200

To calculate the sample size with a Z value of 1.96 (corresponding to a 95% confidence level), an absolute error of 5%, and an estimated proportion (p) of 15%, we can use the following formula:

• Parents not giving informed written consent

Detailed procedure of study conduct:

After approved by institutional ethical committee, informed consent is obtained from the parent. Study will be conducted among neonates admitted for Neonatal hyperbilirubinemia in NICU of tertiary care hospital setting. Serum bilirubin value and platelet count will be documented prior to starting phototherapy. Decision to start phototherapy is based on guidelines from American academy of pediatrics. Once started, phototherapy is interrupted only for feeding and nursing for 20 minutes every 3 hours. Repeat platelet count and serum bilirubin is performed at every 24 hours interval as long as phototherapy is given and just after stopping phototherapy by automated coulter LH 750 analyzer based on flowcytometry and electrical impedance principle and reconfirmed by microscopy. Data regarding birth weight, maturity, mode of delivery, dose of phototherapy, duration of phototherapy, hours of life phototherapy was started and bleeding manifestations is collected and entered in Microsoft Excel for comparison and statistical analysis will be made.

STATISTICAL ANALYSIS:-

Statistical package for IBM SPSS for Windows, Version 22.0. Released 2013. Armonk, NY: IBM

Corp., will be used to perform statistical analyse. Microsoft 2019 excel book will be used for tables and graphs.

normal platelet levels after phototherapy.

RESULTS

In our study a total of 200 neonates were included. All of the neonates had physiological jaundice and were evaluated for the study. 35 % of the neonates (70) had thrombocytopenia after phototherapy while 65% of neonates (130) had

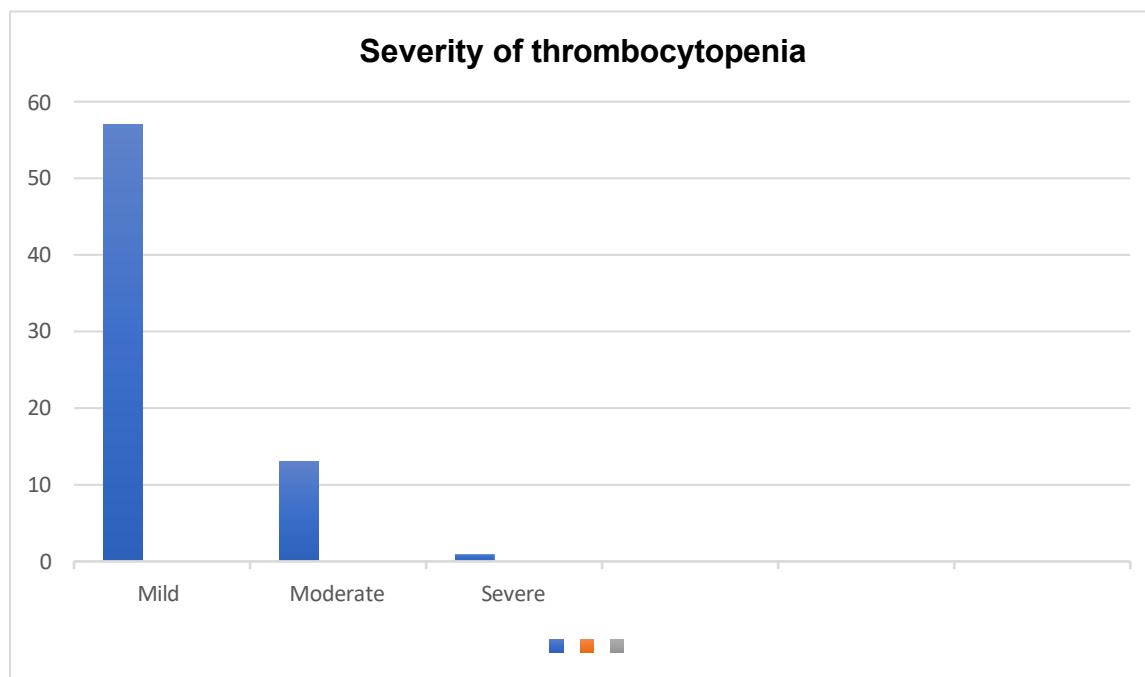


Figure No: 1- Severity of thrombocytopenia after phototherapy

Among 70 neonates who developed thrombocytopenia after phototherapy, 57 (81.4%) of the neonates have developed mild thrombocytopenia, 13 (18.5%) of the neonates have developed moderate thrombocytopenia and 1 (1 %) neonate have developed severe thrombocytopenia. None of the neonates have developed bleeding manifestations. Out of the

total 200 neonates who had been evaluated, 120 neonates were male and 80 neonates were females. Among 120 male neonates 50 (41.6 %) had thrombocytopenia while 70 (58.3%) of them did not have thrombocytopenia. Among 80 females 20 (25%) females had thrombocytopenia while 60 (75%) females did not have thrombocytopenia.

Table No :1 – Comparison of thrombocytopenia among normal birth weight and low birthweight babies

Sl. No.	Characteristics	With thrombocytopenia (group A, $n = 70$)	Without thrombocytopenia (group B, $n = 130$)	Total $n = 200$

			=130)	
	Birth weight (g)			
	< 2,500	12	40	52
	> 2,500	58	90	148

According to birth weight , out of the 200 neonates who were evaluated, 52 neonates were less than 2500 grams (low birth weight) while, 148 neonates had weight above 2500 grams.(Normal birth weight babies). 23 % of neonates among low birth weight group (< 2.5 kg)

had thrombocytopenia while 76.9 % of low birth weight group didnt have thrombocytopenia. Among normal weight neonates (>2.5 kg), 39.1% had thrombocytopenia while 60.8 % didnt have thrombocytopenia.

Table No :2 – Comparison of thrombocytopenia among term babies and preterm babies

Sl. No.	Characteristics	With thrombocytopenia (group A, <i>n</i> = 70)	Without thrombocytopenia (group B, <i>n</i> = 130)	Total <i>n</i> = 200
	Period of gestation (wk)			
	< 37	5	38	43
	> 37	65	92	157

In terms of period of gestation, 43 neonates were less than 37 weeks and 157 neonates were greater than 37 weeks. Among preterms(<37 weeks) , 11.6 % had thrombocytopenia while 88.3 % didnt

have thrombocytopenia. Among term babies 41.4 % didnt have thrombocytopenia while 58.5 % have thrombocytopenia

Table :3 – Comparison of thrombocytopenia according to day of onset of jaundice

Sl. No.	Characteristic s	With thrombocytopenia (group A, <i>n</i> = 70)	Without thrombocytopenia (group B, <i>n</i> = 130)	Total <i>n</i> = 200
4	Neonatal age of onset of jaundice (d)			

	2–3	30	61	91
	4–5	28	52	80
	> 6	12	17	29

Among 200 neonates studied, 91 neonates had onset of jaundice from 2nd to 3rd day, while 80 neonates had onset of jaundice from 4th to 5th day and rest 29 neonates had onset of jaundice after 6th day. Among neonates with age of onset of jaundice between 2-3 days, 32.9% had thrombocytopenia and 67.03 % had no

thrombocytopenia. Among neonates with age of onset of jaundice between 4-5 days, 35 % had thrombocytopenia while 65 % didn't have thrombocytopenia. Among neonates with age of onset of jaundice >6 days, 41.3% had thrombocytopenia while 58.6 % didn't have thrombocytopenia.

Table :4 – Comparison of thrombocytopenia according to Dose of Phototherapy

Sl. no.	Characteristics	With thrombocytopenia (group A, $n = 70$)	Without thrombocytopenia (group B, $n = 130$)	Total $n = 200$
1	Dose of phototherapy			
	DSPT	41	69	110
	SSPT	29	61	90

Out of total 200 patients studied, 106 of them received DSPT while 94 of them received SSPT. Among neonates who received DSPT, 37.2% developed thrombocytopenia while 62.8% didn't

develop thrombocytopenia. Among those received SSPT, 32.2% developed thrombocytopenia while 67.7 % didn't develop thrombocytopenia.

Table :5- Comparison of thrombocytopenia according to Duration of Phototherapy

Sl. no.	Characteristics	With thrombocytopenia (group A, $n = 70$)	Without thrombocytopenia (group B, $n = 130$)	Total $n = 200$
2	Duration of phototherapy (hr)			
	< 48	40	75	115
	> 48	30	55	85

Among 200 neonates, 115 out of total neonates received phototherapy for less than 48 hours

while 85 of them received phototherapy for >48 hours. Those infants who received phototherapy

<48 hrs ,34.7% developed thrombocytopenia while 65.2% didnt develop phototherapy.Among those received phototherapy greater than 48 hrs

,35.2% developed thrombocytopenia, while 64.7% didnt develop thrombocytopenia.

Table :6 – Comparison of thrombocytopenia according to initial serum bilirubin levels

Sl. no.	Characteristics	With thrombocytopenia (group A, n = 70)	Without thrombocytopenia (group B, n = 130)	Total n = 200
3	Serum bilirubin (mg/dL)			
	< 18	56	118	174
	> 18	14	12	26

Out of 200 neonates, 174 neonates had serum bilirubin <18mg/dl at the time of admission while 26 of them had serum bilirubin >18 mg/dl at the time of admission. Those neonates who had serumbilirubin <18 mg/dl at the time of admission, 32.1% developed thrombocytopenia while 67.8% didnt develop thrombocytopenia. Among those neonates who had serum bili >18 mg/dl at the time of admission 53.8% developed thrombocytopenia while 46.1% didnt have thrombocytopenia.

DISCUSSION

In our study, out of the total 200 neonates who were evaluated , 35 % of them developed thrombocytopenia while 65 % ofthem didnt develop thrombocytopenia. In a similar study conducted by **N Pishva, H Pishva** on 101 neonates, conventional phototherapy showed thrombocytopenia among 50 patients (49.5 %). **[8] Naqvi H (2021)** determined the frequency of thrombocytopenia and its severity in relation to level of indirect hyperbilirubinemia in neonates following phototherapy at tertiary care hospital. There was a decline in mean platelet count after phototherapy, but it was not statistically significant. **[9]**

Youssef A et al (2022) determined the relationship between thrombocytopenia and its

severity in neonates with uncomplicated indirect hyperbilirubinemia receiving conventional phototherapy. Decrease in platelet count 24 hours after phototherapy and just after completion of phototherapy was statistically significant (P-value=0.0001). **[10]**

In a study by **Youssef A et al (2022)**, there was no statically significant association (P-value>0.05) between reduction in platelet count with gender. **[10]** Our study has revealed that babies with normal birth weight had more incidence of thrombocytopenia compared to low birth weight group. But these findings were not statistically significant.In a study by **Youssef A et al (2022)**, there was no statically significant association (P-value>0.05) between reduction in platelet count with birthweight. **[10]** According to **Vafaie M. et al (2018)**, there was no significant correlation between birth weight and incidence of thrombocytopenia. **[11]**

It was also observed that neonates who had onset of jaundice at higher age had more incidence of thrombocytopenia compared to the ones who had lower age of onset. However these findings were not statistically significant. In a study by **Khera S. and colleagues (2011)**, similar findings has been observed. **[12]**

In terms of relation of thrombocytopenia with phototherapy, those receiving DSPT has higher incidence of thrombocytopenia compared to those receiving SSPT. But statistical analysis revealed no significance. In our study, those neonates who have received phototherapy for a duration greater than 48 hours has slightly more incidence of thrombocytopenia compared to those who received phototherapy less than 48 hours, but results are not significant. In **Youssef A et al (2022)** study, fall in platelet count was found to have a positive association with increased duration of phototherapy (P -value <0.05). [10] According to **Shah MH et al (2019)**, more frequent platelet count monitoring is necessary for those who need to receive phototherapy for a longer period of time. [13]

Neonates who had serum bilirubin greater than 18 mg/dl at the time of admission had higher incidence of thrombocytopenia compared to the ones who had serum bilirubin <18 mg/dl at time of admission. On detailed analysis, we have found that these associations were not statistically significant. Similar findings have been observed in study by Sanjeev Khera and Rakesh Gupta. [12]

CONCLUSION

The present study demonstrated that thrombocytopenia was observed in a proportion of neonates receiving phototherapy for neonatal hyperbilirubinemia; however, the association was not statistically or clinically significant, as none of the affected neonates developed bleeding manifestations or required therapeutic intervention. These findings suggest that while a transient decline in platelet count may occur during phototherapy, routine discontinuation of treatment or unnecessary diagnostic investigations are not warranted in clinically stable neonates, and serial monitoring is generally sufficient. Furthermore, no significant association was found between thrombocytopenia and sex, birth weight, gestational age, age at onset of jaundice, initial serum bilirubin level, phototherapy dose, or duration of phototherapy. Although a higher frequency of thrombocytopenia was observed among neonates receiving double-surface phototherapy, prolonged phototherapy (>48 hours), and those with higher baseline bilirubin levels, these trends did not reach statistical significance. Larger multicenter studies are needed to further clarify the potential dose- and duration-dependent effects of phototherapy on platelet counts and to establish their clinical relevance.

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