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# CONVENTIONAL PHOTOTHERAPY FOR HYPERBILIRUBINEMIA AND ITS RELATIONSHIP WITH THROMBOCYTOPENIA IN NEONATES

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## ABSTRACT

**Background:** Thrombocytopenia as a side effect of phototherapy has not been mentioned in standard literature but was described briefly as isolated case reports after the phototherapy. Though there are few studies on effect of phototherapy on platelet count with conflicting results. **Aim and Objective:** This study was done to determine the relationship between thrombocytopenia and its severity in neonates with uncomplicated indirect hyperbilirubinemia receiving conventional phototherapy. **Materials and Methods:** This prospective observational study was carried out over a period of one year (1st September 2020 to 1st September 2021) on 56 neonates admitted with idiopathic unconjugated hyperbilirubinemia needing phototherapy through consecutive enrolment. Serum bilirubin (total, conjugated and unconjugated) and platelet count were done before initiation, twenty-four hours after phototherapy and just after completion of phototherapy. Appropriate statistical tests were used to make statistical comparisons with a p-value of < 0.05 taken as significant. **Results:** Among 56 neonates, 30(53.6%) were males and 26(46.4%) were females; 23(41.1%) were preterm neonates and 33(58.9%) were term neonates. Mean birth weight was (2493.3 ± 420.2) g. Mean gestational age was (36.94 ±1.6) weeks. The mean duration of phototherapy required was (32.87±5.7) hours. Mean platelet count before initiation, 24 hours after phototherapy and just after completion of phototherapy were (286.25 ±46.3) $\times 10^9$/L, (249.82±78.7) $\times 10^9$/L and (233.96±94.1) $\times 10^9$/L respectively. Decrease in platelet count 24 hours after phototherapy and just after completion of phototherapy was statistically significant (P-value=0.0001). Thrombocytopenia was seen in 14 neonates (25%) and type of severity was mild and moderate in 10(71.4%) and 4(28.6%) respectively but none developed sever thrombocytopenia. None having thrombocytopenia manifested with clinical bleed. Fall in platelet count was found to have a positive association with increased duration of phototherapy and in preterm neonates (P-value<0.05).However there was no statically significant association (P-value>0.05) between reduction in platelet count with gender and birth weight. **Conclusion:** we found that there was a significant association between phototherapy and thrombocytopenia in hyperbilirubinimic neonates but the thrombocytopenia was mostly mild and transient, and clinically insignificant. There was significant association between decrease of platelet count with duration of phototherapy and preterm neonates.

**KEYWORDS:** Thrombocytopenia; phototherapy; indirect hyperbilirubinemia.

## INTRODUCTION

Neonatal jaundice is a common problem, and in most cases being physiological does not require active intervention. Jaundice is observed in first week of life in approximately 60% full-term and 80% pre-term neonates.[1-2] Phototherapy though safe, is not free of side effects. Neonates receiving phototherapy have increased insensible water loss, redistribution of blood flow, watery diarrhea, irritability, rise in temperature, retinal damage, bronze baby syndrome, gonadal toxicity, impaired maternal-infant interaction, hypocalcaemia, riboflavin deficiency, DNA strand breakage, chromosomal mutations damage, and in few studies even thrombocytopenia.[1-2]

Thrombocytopenia has not yet been mentioned as an adverse consequence of phototherapy in any of the standard textbooks of pediatric medicine or neonatology.

Though few studies have been published on this topic, results are conflicting.[3] So, this study was done to determine the relationship between thrombocytopenia and its severity in neonates with uncomplicated indirect hyperbilirubinemia receiving conventional phototherapy.

## MATERIALS AND METHODS

### Study population and data collection

In this prospective observational study 56 neonates with indirect hyperbilirubinemia who received conventional phototherapy in neonatal intensive care units (NICU) in the Division of Neonatology under the Department of Pediatric Medicine, Tishreen Medical College and Hospital, Lattakia,Syria. Total study period was one year (1st September 2020 to 1st September 2021).

### Inclusion Criteria were as follows

Apparently healthy neonates in the age group of 2-14 days with negative DCT(Direct Coomb's test) , normal CRP (C-Reactive Protein), normal peripheral blood smear, having phototherapeutic level unconjugated hyperbilirubinemia per as the guidelines from American Academy of Pediatrics 2004,[4] and a base line platelet count of more than 150 $\times 10^9$/L were included in the study.

### Exclusion Criteria

Neonates with conjugated hyperbilirubinemia, ABO and Rh incompatibility, Neonates having features of sepsis, TORCH infection, birth asphyxia, hemangioma, antiplatelet drugs given to mother or baby and congenital anomalies.

CBC and peripheral blood smear, Direct Coomb's test, CRP, Serum bilirubin (total, direct, indirect), mother's blood group and neonate's blood group were sent before starting phototherapy.

After initial history taking, clinical examination and laboratory investigations, all neonates were put to continuous conventional phototherapy with interruption only during breast feeding.

Serum bilirubin and platelet count were measured before initiation of phototherapy, 24 hours later and just after completion of phototherapy. Neonates showed a fall of platelet count were recorded, then followed up after one week to asses any change in platelet count if present.

Platelet count before initiation of phototherapy was taken as control value for respective neonate.

### Definitions

Platelet count <150 $\times 10^9$/L was taken as the definition of thrombocytopenia. Mild, moderate and severe thrombocytopenia were graded when platelet counts were between (100 to 150$\times 10^9$/L) (50–100 $\times 10^9$/L) and less than 50 $\times 10^9$/L respectively. Platelet count above 450$\times 10^9$/L was considered as thrombocytosis.

Various factors like, duration and epidemiological factors such as sex, birth weight, gestational age, were studied. Serum bilirubin was measured by diazo method (Diazotized sulphanilic test). Platelet count was measured by automated hematology analyzer and was confirmed by microscopy.

### Statistical methods

For statistical analysis data were entered into a Microsoft excel spread sheet and then analyzed by IBM SPSS (version 20). Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Friedman test was applied for analyzing the difference in mean involving several dependent groups. Chi-square test or Fisher exact was used for categorical variables .P-value < 0.05 was considered for statistically significant.

## RESULTS

A total of 56 neonates were included in the present study, 30 neonates (53.6%) were males & 26 neonates (46.4%) were females, 23(41.1%) were preterm neonates and 33(58.9%) were term neonates. The mean gestational age was 36.94 ± 1.6 weeks. The mean birth weight was 2493.3± 420.2 g. The mean duration of phototherapy required was 32.87 ± 5.7 hours (Table 1).The mean baseline platelet count before phototherapy was 286.25 ± 46.3$\times 10^9$/L. The mean platelet count after 24 hours of phototherapy was 249.82 ± 78.7$\times 10^9$/L. The mean platelet count just after completion the phototherapy was 233.96 ± 94.1$\times 10^9$/L (Table 2 and Figure 3). Decrease in mean platelet count was found after 24 hours of phototherapy and just after completion the phototherapy, and the results were statistically significant (P-value<0.05) (Table 2). Thrombocytopenia was noted in total 14 neonates (25%) (Figure 1) and the type of severity was mild in 10(71.4%) and moderate in 4(28.6%) but none developed sever thrombocytopenia (Figure 2). The minimum platelet count in the study population following phototherapy was 95 $\times 10^9$/L but none of the neonates developed bleeding manifestations. In the present study, fall in mean platelet count just after completion of phototherapy was more prominent among preterm neonates (P-value=0.0001).In our study thrombocytopenia following phototherapy was not significantly associated with gender, birth weight (with the P-value of 0.09, 0.4 respectively). Fall in platelet count was positively associated with increasing duration of phototherapy (P-value =0.002) (Table 3).

## DISCUSSION

In the present study, the overall incidence of thrombocytopenia was 25%, this came in agreement with Khera and Gupta,[5] Shah MH et al,[6] and Sarkar et al,[3] who showed that phototherapy was complicated with thrombocytopenia in 35%, 45.6% and 31.1% respectively of neonates who received phototherapy. In disagreement with our study, the study done by Monsef et al,[7] which reported that there was an increase in the

platelet count after phototherapy. Naqvi et al,[8] showed that the decline in mean platelet count after phototherapy was not statistically significant.

As regarding to severity of thrombocytopenia, our study showed that 10 neonates (71.4%), 4 neonates (28.6%) of neonates who developed thrombocytopenia had mild and moderate thrombocytopenia respectively. In agreement with our study, the study of Khera and Gupta.[5] Who showed that majority of neonates had mild thrombocytopenia (74%), moderate thrombocytopenia was seen in 23% of cases. Shah MH et al,[6] showed that 66% had mild thrombocytopenia, and 21.3% developed moderate thrombocytopenia.

In the present study, we didn't find severe thrombocytopenia, in disagreement with Khera and Gupta,[5] and Shah MH et al,[6] who found in their studies sever thrombocytopenia in 3%, 12.8% respectively.

None of the neonates with thrombocytopenia, in ours had manifestations of bleeding. Similar findings were noted in studies by Maurer et al,[9] and Khera and Gupta.[5] The reason for the same could be the fact that thrombocytopenia was transient and rarely found to be severe in all the three studies.

This study observed that preterm neonates who received phototherapy had significantly higher incidence of thrombocytopenia than term neonates. In agreement with our study, the studies conducted by, Shah MH et al,[6] Sonawane P et al,[10] and Sarkar et al.[3] Khera and Gupta,[5] showed that term neonates had higher incidence of thrombocytopenia, but the results were not statistically significant.

Our study showed that, there was no statistically significant difference in the incidence of thrombocytopenia following phototherapy based on gender and birth weight, in agreement with the studies of Sarkar et al,[3] and Vafaie M et al.[11]

In the present study, the incidence of thrombocytopenia increased with increasing duration of phototherapy received (Table3) similar findings were noted in studies by Sarkar et al,[3] and Shah MH et al.[6]

The drop in platelet counts following Phototherapy may be due to the photochemical reaction in the vascular bed and direct platelet injury by the ultraviolet light of phototherapy leading to reduction in platelet life span and an increase in platelet turnover.[11-12] Thrombocytopenia is expected to be more marked when bone marrow compensation is inadequate, as in the case of preterm neonates.

**Table 1: Range, median, mean and standard deviation of various parameters (n=56).**

| Attribute | Min-Max | Median | Mean ± SD |
|---|---|---|---|
| Gestational age (week) | 34-39 | 37.5 | 36.94±1.6 |
| Birth weight (g) | 1750-3000 | 2640 | 2493.3±420.2 |
| Platelet count before initiation of Phototherapy | 225-385 | 276 | 286.25±46.3 |
| Duration of phototherapy(hours) | 24-40 | 37 | 32.87±5.7 |

**Table 2: Mean platelet count before initiation of phototherapy, 24 hours later, and just after completion of phototherapy.**

| Platelet count | Min-Max | Mean ± SD | P-value |
|---|---|---|---|
| Before initiation of phototherapy | 225-385 | 286.25±46.3 | 0.0001 |
| 24 hours after phototherapy | 125-372 | 249.82±78.7 | |
| Just after completion of phototherapy | 95-294 | 233.96±94.1 | |

**Table 3: Thrombocytopenia according to various factors (n=56).**

| variable | Neonates with Thrombocytopenia N (%) | neonates without Thrombocytopenia N (%) | P-value |
|---|---|---|---|
| ***Gender*** | | | |
| Male | 9(64.3%) | 21(50%) | 0.09 |
| Female | 5(35.7%) | 21(50%) | |
| ***Gestational age*** | | | |
| Term | 3(21.4%) | 30(71.4%) | |
| Preterm | 11(78.6%) | 12(28.6%) | 0.0001 |
| ***Birth weight*** | | | |
| ≥2500 grams | 6(42.9%) | 31(73.8%) | |
| <2500 grams | 8(57.1%) | 11(26.2%) | 0.4 |
| ***Duration of phototherapy*** | | | |
| 24-36 hours | 4(28.6%) | 17(40.5%) | |
| 36-48 hours | 10(71.4%) | 25(59.5%) | 0.002 |

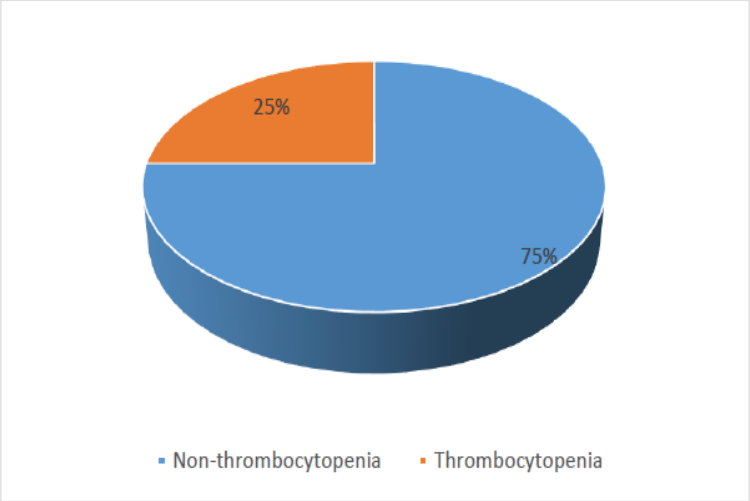


**Figure 1: Incidence of thrombocytopenia.**

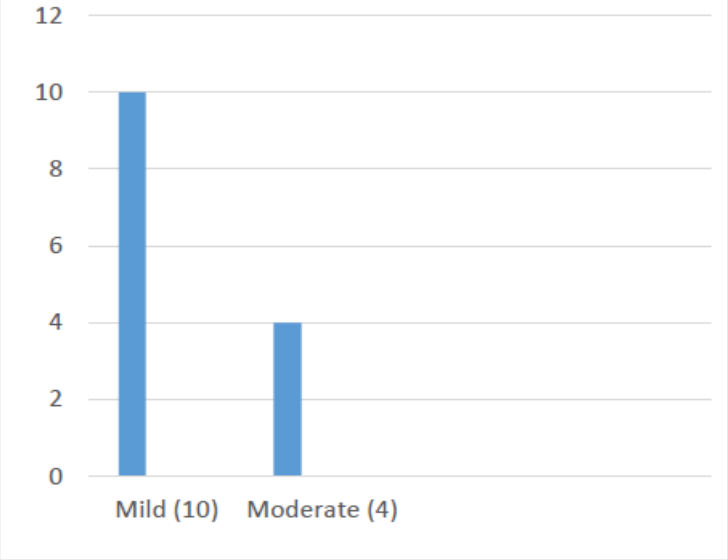


**Figure 2: Severity of thrombocytopenia.**

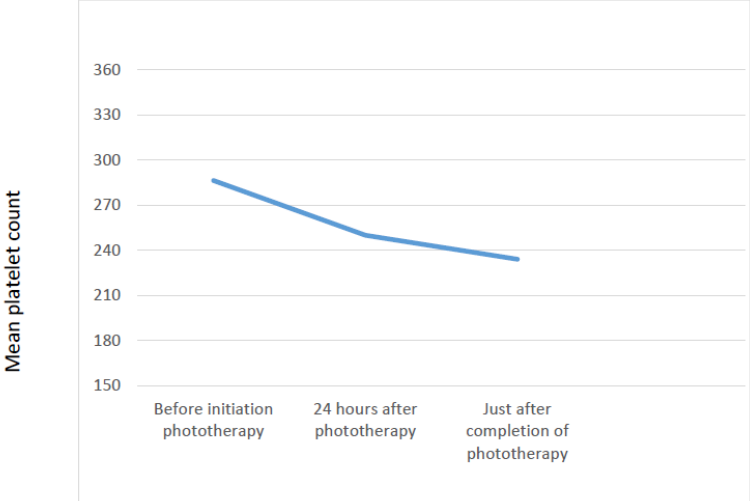


**Figure 3: Mean platelet count before initiation of phototherapy, 24 hours later, and just after completion of phototherapy.**

## CONCLUSION AND RECOMMENDATIONS

We found that there was a significant association between phototherapy and thrombocytopenia in hyperbilirubinimic neonates but the thrombocytopenia was mostly mild and transient, and clinically insignificant. There was significant association between decrease of platelet count with duration of phototherapy and preterm neonates. Hence the treatment should be initiated based on the standard guidelines. Unnecessary use and prolongation of phototherapy should be avoided considering the possible side effects.

### Declarations Competing of Interests

All the authors do not have any possible conflicts of interest.

### Ethical consideration

Permission was taken from the ethical review committee of university. Written and verbal informed consent was taken from the guardian (mother or father) after explaining them the purpose and procedure of the study in detail and ensuring the confidentiality.

### Availability of data and materials

Most of the data was in the article, and other data can be asked from the corresponding author.

### Funding

Not applicable.

### Author contributions

All authors performed the measurements and wrote the article. Literature review was done by Dr. Arwa Youssef, and all authors performed analytic calculations and performed the numerical simulations.

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