

Original Research Article

FREQUENCY OF THROMBOCYTOPENIA IN NEONATES FOLLOWING PHOTOTHERAPY IN NEONATOLOGY UNIT OF TERTIARY CARE HOSPITAL

ABSTRACT

Aim: To determine the frequency of thrombocytopenia and its severity in relation to level of indirect hyperbilirubinemia in neonates following phototherapy at tertiary care hospital.

Study Design: Descriptive study

Place and duration: This study was conducted at Paediatric department (neonatal ward), Liaquat University Hospital, Hyderabad, from 1st August 2020 till 31st Jan 2021

Methodology: All neonates who fulfilled the inclusion criteria presented at pediatric department (neonatal ward), Liaquat University Hospital Hyderabad were included in the study. After written consent, brief history was taken from the mother or family member and complete blood count (CBC) was sent to check the baseline platelet count along with total serum bilirubin, it was repeated after 48 hours of phototherapy.

Result: Out of 231 neonates 70 (30.3%) developed thrombocytopenia after phototherapy. In our study 117 neonates (50.6%) were males & 114 neonates (49.4%) were females with the mean age of 5.9307 ± 1.6640 days. The thrombocytopenia was seen in 70 neonates (30.3%) and type of severity was mild, moderate & severe in 52(22.5%), 13(5.6%) & 5(2.2%) respectively.

Conclusion: There was a decline in mean platelet count after phototherapy but it was not statistically significant. The treating doctor should also keep in mind, other causes of thrombocytopenia when the patient is receiving phototherapy.

Key words: Prematurity, Thrombocytopenia, Phototherapy, Low Birth Weight, Neonatal jaundice

INTRODUCTION:

Although jaundice in neonates is very common but , most of the time it is physiological and don't need any treatment.¹ Neonatal jaundice is treated by phototherapy, exchange transfusion, and various drugs like Phenobarbitone and intravenous immunoglobulin .² Phototherapy is widely used for the treatment of unconjugated hyperbilirubinemia.³ Although it is safe but, it is not free of side effects, like increased insensible water losses, watery diarrhea, irritability, fever , retinal damage, bronze baby syndrome, gonadal toxicity, hypocalcaemia and thrombocytopenia.⁴ Although in standard textbooks there is nothing about phototherapy induced thrombocytopenia but many authors found it in their studies. Maurer HM, et al. and Pishwa N, et al. observed in their studies that phototherapy causes thrombocytopenia.^{5,6} Zieve PD, et al. found effects of phototherapy on platelet.⁷ During phototherapy platelets lost the ability to aggregate and release potassium, acid phosphatase, serotonin and adenosine triphosphate.⁸ Electron microscope revealed depletion of cytoplasmic organelles in platelets as compared to controls.⁹ Unlike other side effects, a very few international studies are currently available which depict the effect of phototherapy on platelet count with controversial & variable observations.¹⁰

The local literature in our population is still scarce hence; the present study is relevant and specific for determining the effect of phototherapy on platelet count so that appropriate management plans can be designed to predict thrombocytopenia. The findings of study will be

helpful to determine any association between the duration of exposure to phototherapy and the degree of thrombocytopenia. So, further recommendations may be made to bring changes in treatment modality as intermittent phototherapy or to decrease the duration of phototherapy with increased intensity (double phototherapy).

Material and Methods:

Operational definitions:

Thrombocytopenia: The blood platelets count $<150,000/\text{mm}^3$

Mild Thrombocytopenia: Decrease in platelet count from $<150,000\text{mm}^3$ to $100,000/\text{mm}^3$

Moderate Thrombocytopenia: Decrease in platelet count from $<100,000/\text{mm}^3$ to $50,000/\text{mm}^3$

Severe Thrombocytopenia: Platelets count $<50,000/\text{mm}^3$

Phototherapy: It is the most common intervention for reducing raised bilirubin levels in a newborn in which baby is placed under high intensity of white light in the visible spectrum, blue light, and special narrow spectrum (super) blue light in the range of 420-470 nanometers at a distance of 15 cm to 20 cm.

This descriptive study was conducted at Paediatric department (neonatal ward), Liaquat University Hyderabad by Non probability consecutive technique from 31st July to 2020 31st Jan 2021. The Sample size was calculated through Rao soft by taking the prevalence of severe thrombocytopenia after phototherapy is found to be 3%,¹ with the margin of error of 2.2% and sample size was 231. **Permission was taken from the ethical review committee of university.**

All neonates of either gender who were exposed to phototherapy for more than 48 hours for treatment of jaundice were included in the study. Neonates having features of sepsis, birth asphyxia, renal failure, IUGR, TORCH infection or congenital heart diseases (as per record of patient) were excluded from the study. The neonates already having thrombocytopenia before

phototherapy, the preterm neonates with gestational age less than 34 weeks were also excluded from the study.

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. All neonates who fulfilled the inclusion criteria presenting in the pediatric department with yellowish discoloration of the skin and need phototherapy as per recommended guidelines were enrolled in the study. CBC with reticulocyte count and peripheral blood smear, Coomb's test, Serum bilirubin (total, direct, indirect), mother's blood group and baby's blood group were sent before starting phototherapy. Full thorough examination of the newborn was performed to exclude neonatal sepsis or other co-morbidities. The phototherapy was started if needed as per recommended guidelines. After 48 hours of exposure to phototherapy, CBC report was repeated to determine any change in platelet count. At the end, researcher noted the outcome on predesigned proforma in order to determine the presence and severity of thrombocytopenia.

The data of all patients were analyzed in SPSS version 22. The frequency and percentage (%) were calculated for qualitative variables such as gender, status of gestational age, thrombocytopenia, and severity of thrombocytopenia. Mean and standard deviation was calculated for age, gestational age, duration of phototherapy, birth weight, and platelet counts before and after phototherapy. The effect modifiers like age, gender, gestational age, gestational age status, birthweight, and duration of phototherapy was addressed through stratification. The post-stratification chi-square test was applied and a p-value ≤ 0.05 was considered as statistically significant.

RESULTS

A total of 231 neonates exposed to phototherapy for > 48 hours were selected to conduct this study. The mean age was 5.9307 ± 1.6640 days (Table 1). The mean gestational age was 38.251 ± 2.0381 weeks. The mean birth weight was 3.8537 ± 0.409 kg (Table 1). The mean duration of phototherapy was 75.6190 ± 14.775 hours. The mean baseline platelet count before phototherapy was $244346.3203 \pm 62062.74155$. The mean platelet count after 48 hours of phototherapy was $162541.1255 \pm 44653.222$. (Table 1)

In our study 117 neonates (50.6%) were males & 114 neonates (49.4%) were females (as shown in Table-2). The gestational age status was late preterm in 62 patients (26.8%), term in 151 patients (65.4%) & post term in 18(7.8%) patients, as shown in Table-2. The study outcome is thrombocytopenia which was seen in 70 neonates (30.3%) and the type of severity was mild in 52(22.5%), moderate in 13(5.6%) & severe in 5 neonates (2.2%) as shown in Table-3. In our study thrombocytopenia was not significantly associated with age, gestational age, gestational age status, birth weight & duration of phototherapy with the P-value of 0.174, 0.715, 0.796, 0.889 & 0.538 respectively. Thrombocytopenia was associated with gender (P-value 0.006).

Table-1**Descriptive statistics of age, gestational age, & birth weights, duration of phototherapy and baseline platelet count before phototherapy and after 48 hours of phototherapy)**

Statistics	Age (days)	Gestational age (weeks)	Birth weights (kg)
Mean	5.930	38.251	3.853
Std. Deviation	1.664	2.038	0.409
Statistics	Duration of phototherapy	Baseline platelet count before phototherapy baseline	Platelet count after 48 hours of phototherapy
Mean	75.619	244346.320	162541.125
Std. Deviation	14.775	62062.741	44653.222

TABLE – 2**Frequency distribution of gender and thrombocytopenia**

Characteristics	Frequency(n)	Percentage (%)
Gender		
Male	117	50.6%
Female	114	49.4%
Neonate		
Late preterm	62	26.8%
Term	151	65.4%
Post term	18	7.8%
Thrombocytopenia		
Yes	70	30.3%
No	161	69.7%
If yes severity of thrombocytopenia		
Mild	52	22.5%
Moderate	13	5.6%
Severe	5	2.2%
No thrombocytopenia	161	69.7%

TABLE – 3**Thrombocytopenia according to various factors**

(n=231)

Age (days)	Thrombocytopenia according to age		Total	P-value
	Yes	No		
4-8	62(26.8%)	151(65.4%)	213(92.2%)	0.174
9-12	8(3.5%)	10(4.3%)	18(7.8%)	
Total	70(30.3%)	161(69.7%)	231(100%)	
Gender	Thrombocytopenia according to gender		Total	P-value
	Yes	No		
Male	45(19.5%)	72(31.2%)	117(50.6%)	0.006
Female	25(10.8%)	89(38.5%)	114(49.4%)	
Total	70(30.3%)	161(69.7%)	231 (100%)	
Gestational age (weeks)	Thrombocytopenia according to gestational age		Total	P-value
	Yes	No		
35-38	36(15.6%)	87(37.7%)	123(53.2%)	0.715
39-42	34(14.7%)	74(32%)	108(46.8%)	
Total	70(30.3%)	161(69.7%)	231 (100%)	
Late preterm	17(7.4%)	45(19.5%)	62(26.8%)	0.796
Term	48(20.8%)	103(44.6%)	151(65.4%)	
Post term	5(2.2%)	13(5.6%)	18(7.8%)	
Total	70(30.3%)	161(69.7%)	231 (100%)	
Birth weights	Thrombocytopenia according to birth weight		Total	P-value

(kg)	Yes	No		
3-3.5	18(7.8%)	40(17.3%)	58(25.1%)	0.889
3.6-5	52(22.5%)	121(52.4%)	173(74.9%)	
Total	70(30.3%)	161(69.7%)	231 (100%)	
Duration of phototherapy	Thrombocytopenia according to duration of phototherapy		Total	P-value
	Yes	No		
49-72	37(16%)	78(33.8%)	115(26.5%)	0.538
73-96	33(14.3%)	83(35.9%)	116(50.2%)	
Total	70(30.3%)	161(69.7%)	231 (100%)	

DISCUSSION

In our study thrombocytopenia was seen in 70 neonates (30.3%), and type of severity was mild in 52(22.5%), moderate in 13 (5.6%) & severe in 5 (2.2%) neonates. In a similar local study there was insignificant decrease in platelets after phototherapy. Mild thrombocytopenia was seen in 7 (2.23%) neonates, while moderate thrombocytopenia was present in 2 (0.64%) neonates¹¹. In another similar Indian study 35 (35%) neonates had thrombocytopenia among them 74% had mild thrombocytopenia. In 26 (74%) neonates thrombocytopenia was present during the first day of phototherapy¹². In a study from Nepal the mean platelet count also decreased from 258×10³ cells/mm³ to 241×10³ cells/mm³ with a p-value of 0.041 which was significant¹³.

The phototherapy causes decreased platelet life span along with increased production of platelets but when bone marrow is compromised then thrombocytopenia occurs¹⁴.

In our study thrombocytopenia was common in term neonates. In Premature neonates mean Platelet Count was decreased on the first day of Phototherapy when compared with no Phototherapy which was statistically significant ($p = 0.018$). In a similar study Mean Platelet Count 24 Hr after Phototherapy was significantly decreased (in preterm and term neonates both) as compared to the Mean Platelet Count before starting Phototherapy ($p = 0.008$)¹⁵.

In our study thrombocytopenia was predominant in male gender. In a study among 190 neonates, 108(56.8%) were male and 82(43.2%) were female; Mean platelet count before initiation and just after completion of phototherapy were $(2, 49,321.0526 \pm 89,460.2101)/\mu\text{L}$ and $(2, 22,436.8421 \pm 88,538.7173)/\mu\text{L}$ respectively. Decrease in platelet count just after completion of phototherapy was statistically significant ¹¹. The limitation of our study was single center study and smaller sample size. Further studies with larger sample sizes are required.

CONCLUSION

In conclusion there was a decline in mean platelet count after phototherapy but it was not statistically significant. The treating doctor should also keep other causes of thrombocytopenia when the patient is receiving phototherapy.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References

1. Bratton, S., Cantu, R.M. and Stern, M., 2019. Breast milk jaundice.
2. Farhan MA, Ali MI, Faraz A, Kazmi SY, Sami W, Irfan A. Efficacy of newer modalities in the management of indirect hyperbilirubinemia at a secondary care hospital: A prospective study from 2015-2018. JPMA. The Journal of the Pakistan Medical Association. 2020; 70(10):1753-7.
3. Faulhaber FR, Procianoy RS, Silveira RC. Side effects of phototherapy on neonates. American journal of perinatology. 2019; 36(03):252-7.
4. Abdelhakeem AM, Radwan MS, Eldahshan TA. Effect of phototherapy on peripheral blood cell count in full term newborns with neonatal hyperbilirubinemia. Al-Azhaarassiut Med J. 2015; 13(1):159-64.
5. Maurer HM, Haggins JC, Still WJ. Platelet injury during phototherapy. Am J Hematol. 1976; 1:89-96.
6. Pishva N, Pishva H. Incidence of thrombocytopenia in hyperbilirubinemic neonates during phototherapy. Acta Medica Iranica. 2000; 38:7-9
7. Zieve PD, Solomon HM, Krevans JR. The effect of hematoporphyrin and light on human platelets. I. Morphologic, functional, and biochemical changes. J Cell Physiol. 1966; 67:271-279
8. Diogo P, Faustino MA, PMS Neves MG, Palma PJ, P Baptista I, Gonçalves T, Santos JM. An insight into advanced approaches for photosensitizer optimization in endodontics—A critical review. Journal of functional biomaterials. 2019; 10(4):44.

9. Gaertner F, Ahmad Z, Rosenberger G, Fan S, Nicolai L, Busch B, Yavuz G, Luckner M, Ishikawa-Ankerhold H, Hennel R, Benechet A. Migrating platelets are mechano-scavengers that collect and bundle bacteria. *Cell*. 2017; 171(6):1368-82.
10. Schlappi C, Kulkarni V, Palabindela P, Bemrich-Stolz C, Howard T, Hilliard L, et al. Outcomes in Mild to Moderate Isolated Thrombocytopenia. *Pediatrics*. 2018; 142(1):e20173804
11. Bashir A, Kumar A, Maheshwari N, Hingorjo B, Ahmed S, Fatima S. Phototherapy in full term neonates suffering from unconjugated hyperbilirubinemia; Does it affect platelet count?. *The Professional Medical Journal*. 2020; 27(09):1911-5.
12. Khera S, Gupta R. Incidence of thrombocytopenia following phototherapy in hyperbilirubinemic neonates. *Medical Journal Armed Forces India*. 201; 67(4):329-32.
13. Timilsina M, Gauchan E, Ganesh BK. Effect of phototherapy on hematological profile of newborns with unconjugated hyperbilirubinemia. *Journal of Chitwan Medical College*. 2021; 11(2):15-8.
14. Maurer HM, Fratkin M, McWilliams NB. Effects of phototherapy on platelet counts in low-birthweight infants and on platelet production and life span in rabbits. *Pediatrics*. 1976; 57:506-512
15. Sonawane P, Bhaisara B, Bhatawdekar A. Effect of conventional phototherapy on platelet count in full term and preterm neonates with indirect hyperbilirubinemia-A prospective cohort study. *J Med Sci Clin Res*. 2018; 6(03):959-66.
16. Sarkar SK, Biswas B, Laha S, Sarkar N, Mondal M, Angel J, Abhisek K, Kumar V, Acharya A, Biswas P, Mal S. A study on effect of phototherapy on platelet count in

neonates with unconjugated hyperbilirubinemia: a hospital based prospective
observational study. Asian Journal of Medical Sciences. 2021; 12(5):41-6.

UNDER PEER REVIEW