

Phototherapy in Hyperbilirubinemic Neonates; Does it Affect Platelet Count?

Aisha Sajid,¹ Tahir Mahmood,² Sohaib Riaz,³ Saba Ghulam Nabi⁴

Abstract

Objective: To determine the effect of phototherapy on platelet count in neonates having unconjugated hyperbilirubinemia.

Patients and Methods: This cross sectional study was conducted in the Neonatology unit of a Hospital, Faisalabad during a period of nine months i.e., January to September 2015. All the neonates having unconjugated hyperbilirubinemia and requiring phototherapy with normal initial platelet count were included in the study. Platelet count was evaluated before the start of phototherapy and then during phototherapy at 24 hrs, 48 hrs and 72 hrs interval. Platelet counts were compared after 24, 48 and 72 hours of phototherapy. P value < 0.05 was considered significant.

Results: Total 150 newborns having unconjugated hyperbilirubinemia were included with mean age of 3.95 ± 1.71 days. After 24 hours of phototherapy, about 8.1% of the patients were having severe thrombocyto-

penia (platelet count $< 50 \times 10^9/L$); this percentage rose to 18.4% after 48 hours and 33.3% after 72 hours of phototherapy. None of the patients developed clinical manifestation of bleeding. The number of patients with normal platelet count ($1,50 \times 10^9/L - 400 \times 10^9/L$) after 24 hours of continuous phototherapy was 50%, gradually reducing to 38% after 48 hours and only 33% after 72 hours of completion of phototherapy (p value < 0.05).

Conclusion: Hyperbilirubinemic neonates undergoing phototherapy had a fall in platelet count without any clinical manifestation of bleeding.

Key Words: Hyperbilirubinemia, Phototherapy, platelet count

Introduction

Neonatal jaundice due to unconjugated perbilirubinemia is quite common condition that affects about 60% of term and 80% of preterm infants during first week of life.^{1,2} Once unconjugated hyperbilirubinemia crosses the upper limits of physiological jaundice (unconjugated serum bilirubin level 5 – 6 mg/dl), it may be harmful for the brain. Bilirubin encephalopathy may affect brain resulting in permanent developmental delay.³ Treatment options available for unconjugated hyperbilirubinemia include phototherapy, exchange transfusion, IV immunoglobulins and metalloporphyrin. Out of these options, phototherapy which is a non-invasive technique has been used widely for the treatment of neonatal jaundice. In 1985 National Institute of Child Health and Human Development documented that efficacy of phototherapy is comparable to exchange transfusion in prevention of neurological sequelae.⁴ Hence, Phototherapy is being considered world wide as first line treatment for neonatal Jaundice.⁵

Regarding the adverse effects of phototherapy, previously certain studies have documented various

¹ Associate Professor/HOD of Pediatrics
University Medical and Dental College, Faisalabad

² Assistant Professor/HOD/Pediatrics
Aziz Fatima Medical & Dental College, Faisalabad

³ Assistant Professor /Pediatrics
University Medical and Dental College, Faisalabad

⁴ PGR Pediatrics, Allied Hospital, Faisalabad

Date of Submission 03-12-2015

Date of Revision Received 19-01-2016

Date of 2nd Revision Received 15-04-2016

Date of Acceptance for Publication 02-08-2016

Conflict of Interest: None

Funding Source: None

Contribution

All Authors have contributed in Study Design, Data Collection, Data Analysis, Data Interpretation, Manuscript Writing and Approval.

adverse effects including insensible water loss, inability to maintain body temperature, electrolyte imbalance, loss of circadian rhythm, skin rash, increased incidence of allergies including allergic rhinitis, bronchial asthma and retinopathy of prematurity.⁶⁻¹² Phototherapy may also affect the hematological system. Certain past and recent studies have documented thrombocytopenia as a side effect of phototherapy as well^{13,14} Thrombocytopenia in neonates is very well documented condition and is commonly due to multiple etiologies including septicemia, alloimmune antibody mediated thrombocytopenia, maternal ITP (Immune thrombocytopenic purpura), TAR (thrombocytopenia absent radius) syndrome, toxoplasmosis, others (syphilis, parvovirus B₁₉, varicella zoster) rubella, cytomegalovirus, herpes infections, congenital a megakaryocytic thrombocytopenia or other congenital causes.¹⁵ Thrombocytopenia in any neonate may be life threatening and not only requires multiple investigations to rule out the above mentioned causes but also the aggressive management according to severity of the condition.

Although most of the studies have documented thrombocytopenia as a result of phototherapy, but few other studies have proven the opposite effect of phototherapy on platelet count i.e., phototherapy exposure results in increased platelet count.^{16,17} So, the ultimate effect of phototherapy on platelet count still needs to be investigated further in various clinical settings.

To our knowledge, there is hardly any local study reporting the effect of phototherapy exposure over platelet count. Keeping in view this background we conducted this study to determine the effect of phototherapy on platelet counts of hyperbilirubinemic neonates in our set up.

Patients and Methods

It was a cross sectional study conducted in the Neonatology unit of the Pediatrics department. The Duration of study was nine months starting from January 2015 to September 2015. Research proposal was approved by the Board of Research and Advance Studies and the Ethical Review Committee. Informed consent was taken from the parents or caretakers of the patients. All the neonates being admitted in Neonatal unit having clinical jaundice were observed. Initial investigations were performed including complete blood counts, serum/bilirubin levels and blood groups of baby and mother. The newborns with unconjugated hyperbilirubinemia requiring phototherapy for 72 hours or

more were included in the study after confirming normal platelet count at the start of phototherapy.

All those hyperbilirubinemic patients having thrombocytopenia due to other known causes like septicemia, DIC (Disseminated intravascular coagulation), Toxoplasmosis, others (varicella zoster, Parvovirus B₁₉) Rubella, cytomegalovirus. Herpes infection and other congenital causes of thrombocytopenia were excluded from the study. Total and direct bilirubin levels were measured by Diazo method (Diazotized sulfanilic test) and Platelets were measured by Hydrodynamic focusing method. Platelet count was performed before start of phototherapy and then during phototherapy at intervals of 24, 48 and 72 hrs subsequently. Thrombocytopenia was defined as platelet count below $150 \times 10^9/L$. It was further categorized as mild (platelet count $< 150 \times 10^9/L - 100 \times 10^9/L$), moderate platelet count $< 100 \times 10^9/L - 50 \times 10^9/L$) and severe thrombocytopenia (platelet count $< 50 \times 10^9/L$). Data were entered in predesigned proforma and statistical analysis was performed by SPSS version 19. Platelet counts of the patients were compared after 24 hours, 48 and 72 hours of undergoing continuous phototherapy. Chi square test was applied for comparison of categorical data, and P value < 0.05 was considered significant.

Results

In our study total 124 newborns having unconjugated hyperbilirubinemia were included with mean age of 3.95 ± 1.71 days. Mean value of total serum bilirubin level of the newborns at the start of phototherapy was 16.6 ± 3.25 mg/dl. The demographic profile of the participants is shown in table 1.

Frequency and percentages of patients having thrombocytopenia after phototherapy are shown in figures 1, 2 and 3. After continuing the phototherapy for 24 hours, about 8.1% of the patients were having severe thrombocytopenia (platelet count $< 50 \times 10^9/L$), the number gradually rose to 18.4% after 48 hours and 33.3% after 72 hours of phototherapy. (P value < 0.05). Similarly, after 24 hours of phototherapy 50% of total patients didn't have thrombocytopenia that number decreased to 38 % after 48 hours and 33% after 72 hours of completion of phototherapy. (P value < 0.05). None of the patients developed any bleeding manifestations in the form of hematuria, malena, petechial purpuric spots, bleeding from umbilical cord or any other site.

Frequency of thrombocytopenia was compared between premature and full term babies but statistically no significant difference was observed between the two groups at any time during phototherapy (p value = 0.94, 0.072, 0.34 at 24 , 48 and 72 hours intervals respectively during continued phototherapy).

Discussion

In our study 50% of the patients were found having low platelet count after 24 hours of phototherapy and this number of patients increased with increasing the duration of phototherapy. Our results are comparable to the study performed by Pisva et al, that demonstrated thrombocytopenia in 49% of patients after 24 hours of phototherapy.¹³ They related the thrombocytopenia with increased platelet turnover and damage during phototherapy. Another study performed by Kera M.S reported the incidence of thrombocytopenia in 35% of children after 48 hours of exposure to photo-

Table 1: Demographic profile of the neonates undergoing phototherapy (n = 124).

Demographic Features	Frequency	Percentage
Sex of the patients		
Male	78	63
Female	46	37
Weight of the patients		
< 2.5 kg	62	50
2.5 – 3.5 kg	52	42
> 3.5 kg	10	8
Gestational age of the patients		
Full term	106	85.5
Preterm	18	14.5
Mode of delivery		
C-section	42	34
Normal vaginal delivery	82	66

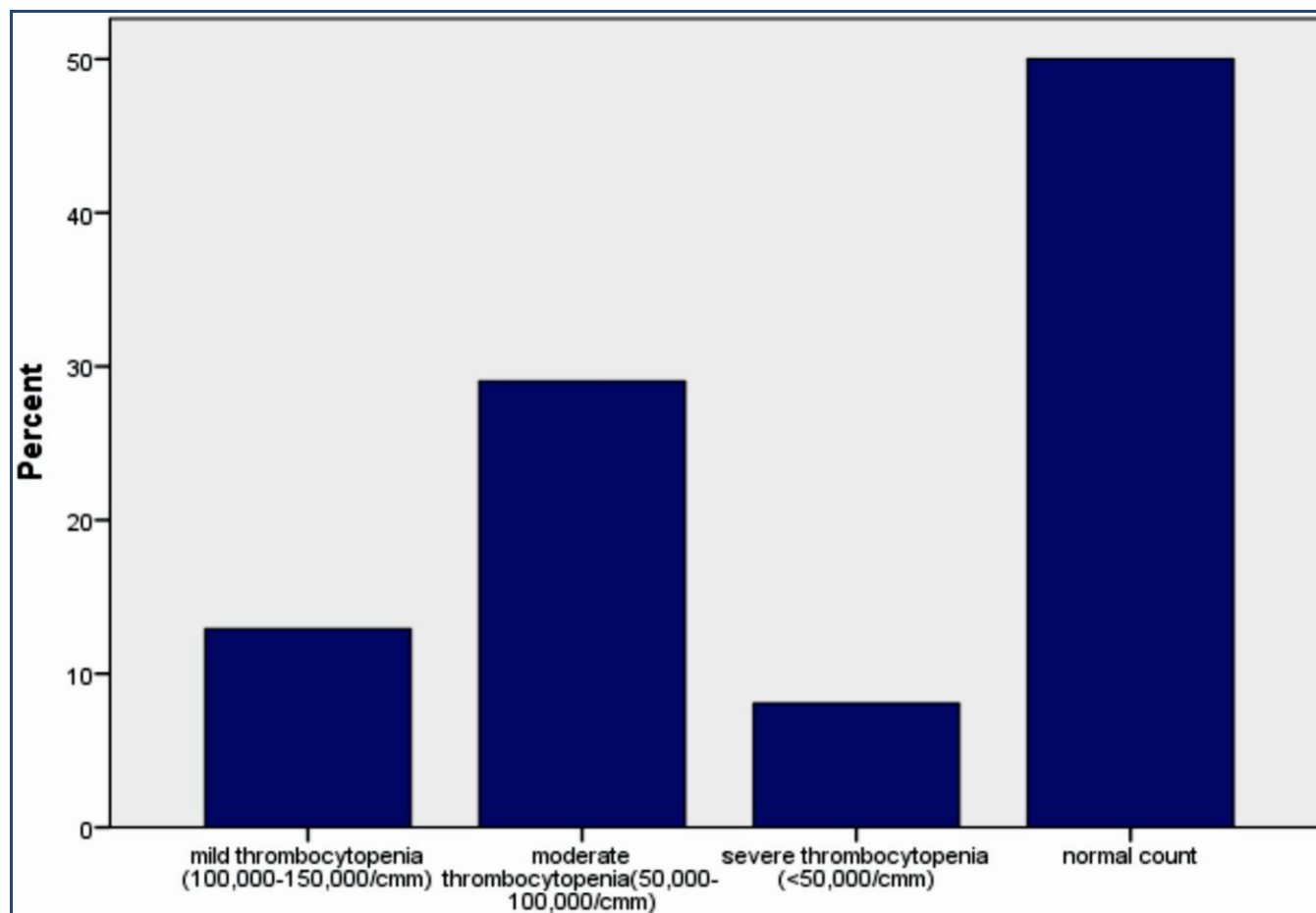


Fig 1: Frequency of thrombocytopenia after 24 hours of starting phototherapy.

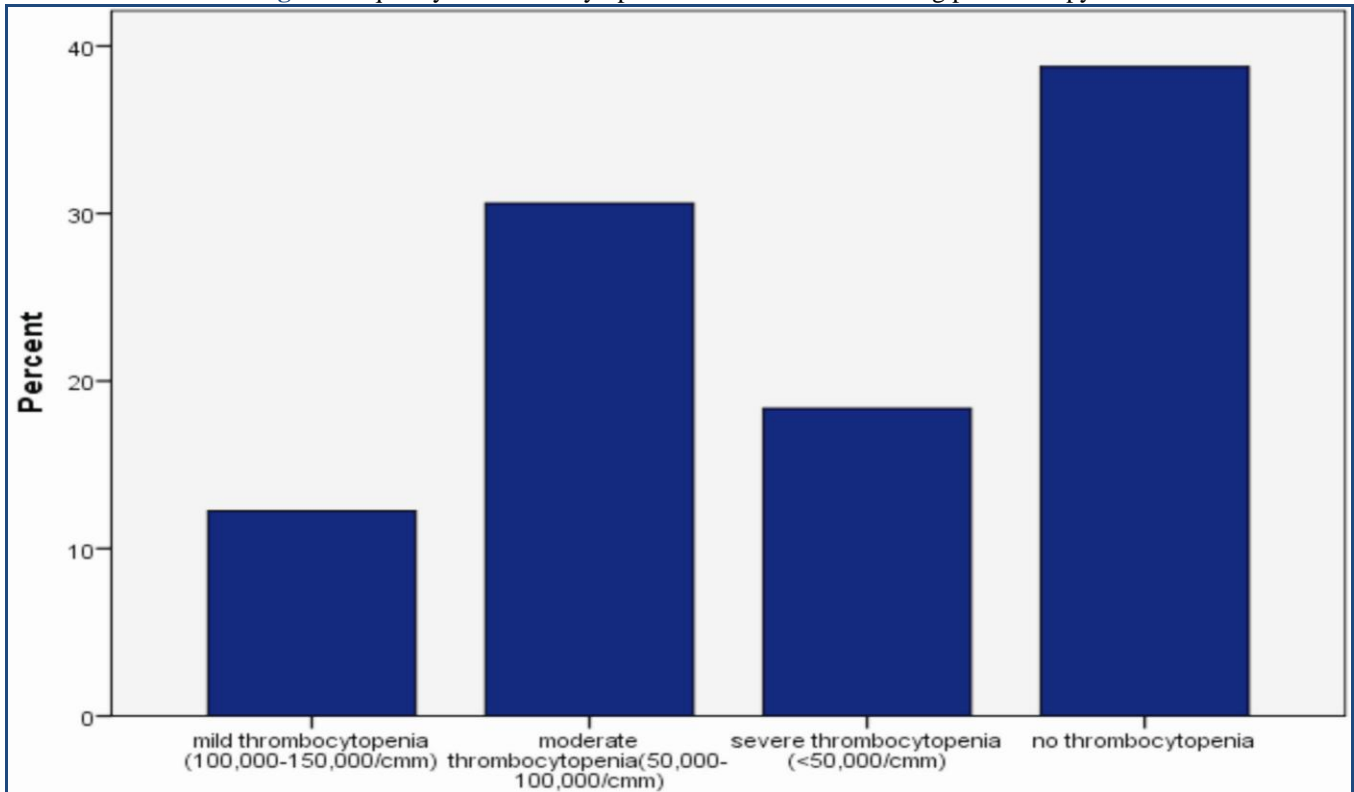


Fig. 2: Frequency of thrombocytopenia after 48 hours of starting phototherapy

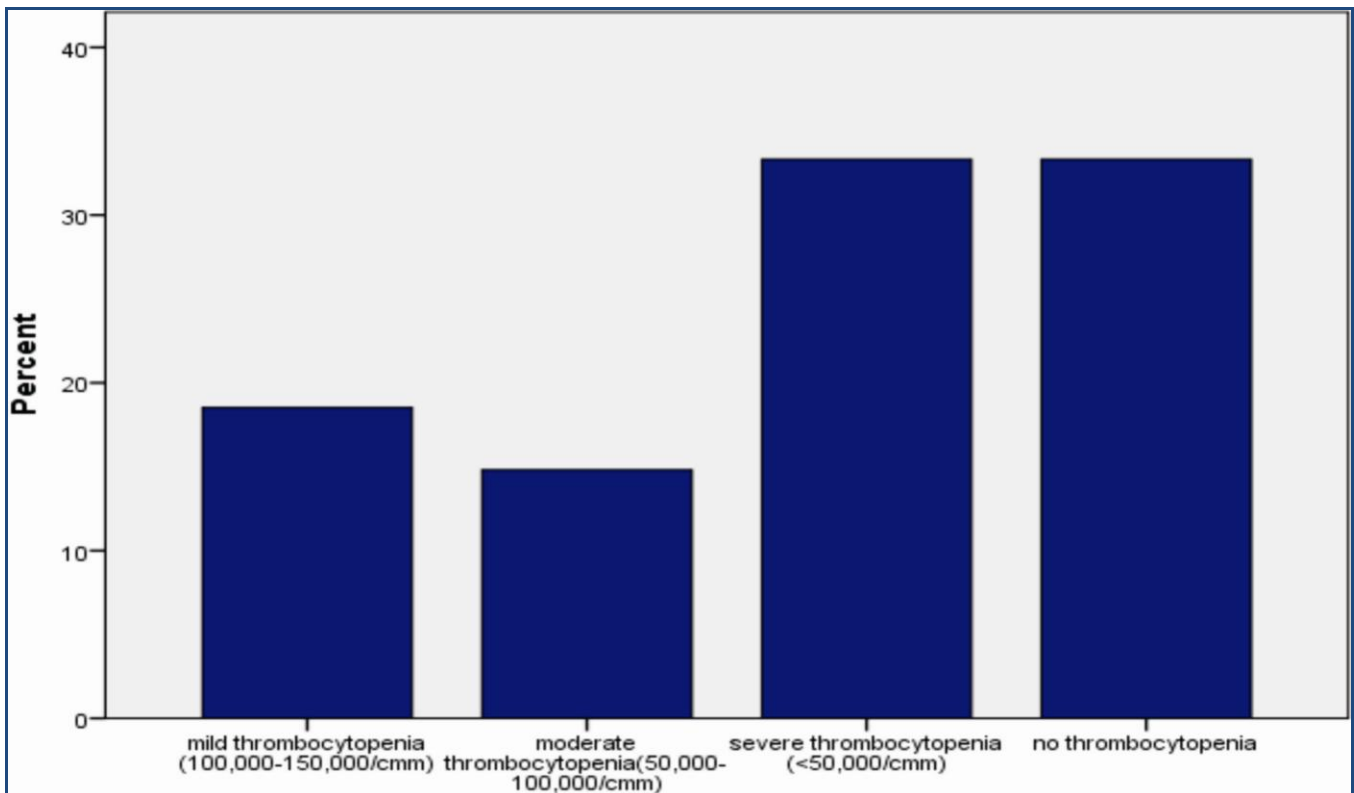


Fig 3: Frequency of thrombocytopenia after 72 hours of starting phototherapy.

therapy and out of them majority (76%) had mild thrombocytopenia. Moderate and severe thrombocytopenia was seen only in 23% and 3% respectively, while in our study 18.5% of the patients developed severe thrombocytopenia at 48 hours of continuous phototherapy.¹⁶ A study conducted in Iran discovered that 36% of the patients with idiopathic hyperbilirubinemia showed thrombocytopenia simultaneously, irrespective of their treatment with phototherapy.¹⁷

Although phototherapy is a frequently used treatment modality in neonatal hyperbilirubinemia, its side effects are still being studied in many recent trials. Two latest studies performed in India proved the association of thrombocytopenia with phototherapy although that thrombocytopenia was subclinical with no significant symptoms.^{18,19} A comparative study performed in Bangalore compared the effects of phototherapy between preterm and term infants and found that both term and preterm infants developed thrombocytopenia after phototherapy without any significant association between gestational age and incidence of thrombocytopenia.²⁰ None of these studies show clinically significant bleeding manifestation in any patient like our study.

Thrombocytopenia as a side effect of phototherapy has not been documented in the textbooks, as yet. On the other hand few studies have documented the opposite effect of phototherapy on platelet counts. There are certain studies that found increased mean platelet count of infants in response to phototherapy.^{21,22} They considered the increased platelet turnover and marrow releases as responsible mechanism for platelet rise.

As far as the etiology of thrombocytopenia in phototherapy is concerned, various mechanisms have been suggested. A study done in the past showed exposure of platelets to light resulted in loss of potassium and the ability to adhere. Cytoplasmic depletion of granules was evident by electron analysis.²³ Lifespan of platelets may be reduced secondary to phototherapy which results in increased production rate and when bone marrow fails to meet that deficiency, thrombocytopenia results.²⁴

Keeping in view the transient and subclinical nature of thrombocytopenia in newborns receiving phototherapy, extensive investigations for thrombocytopenia may be delayed in these neonates.

The limitation in our study was that it was a single center study and many patients lost their follow up afterwards once their platelet count was in safe range,

so we couldn't determine the exact time pattern of recovery of platelet count. So, further studies may be carried to find out the recovery pattern of platelet count after discontinuation of phototherapy and also the intensity of exposure to phototherapy light responsible for thrombocytopenia.

Conclusion

Our study establishes the association of phototherapy with decreased platelet count in hyperbilirubinemic neonates without any serious bleeding manifestations.

References

1. Ambalavnan N, Corlo WA. Jaundice and Hyperbilirubinemia in the Newborn. In: Kliegman, Stanton, Schor SG, Behrman. Nelson's Text Book of Pediatrics. 20th ed. Philadelphia: WB Saunders; 2015: p. 871-80.
2. Rennie J, Burman – Roy S, Murphy MS. Neonatal jaundice: summary of NICE guidance. *BMJ*. 2010; 340: c2409.
3. Maisels MJ, McDonagh AF. Phototherapy for neonatal jaundice. *N Engl J Med*. 2008; 358: 920–8.
4. Bryla DA. Randomized, controlled trial of phototherapy for neonatal hyperbilirubinemia. Development, design, and sample composition. *Pediatrics*, 1985; 75: 387–92.
5. Waterham M, Bhatia R, Donath S, Molesworth C, Tan K, Stewart M. Phototherapy in transport for neonates with unconjugated hyperbilirubinaemia. *Journal of paediatrics and child health*, 2016 Jan. 1; 52 (1): 67-71.
6. Aspberg S, Dahlquist G, Kahan T, Kallen B. Is neonatal phototherapy associated with an increased risk for hospitalized childhood bronchial asthma? *Pediatr Allergy Immunol*. 2007; 18: 313–9.
7. Aspberg S, Dahlquist G, Kahan T, Kallen B. Confirmed association between neonatal phototherapy or neonatal icterus and risk of childhood asthma. *Pediatr Allergy Immunol*. 2010; 21: 733–9.
8. Boo NY, Chew EL. A randomised control trial of cling-film for prevention of hypothermia in term infants during phototherapy. *Singapore Med J*. 2006; 47: 757–62.
9. Kumar P, Murki S, Malik GK. Light emitting diodes versus compact fluorescent tubes for phototherapy in neonatal jaundice: a multi center randomized controlled trial. *Indian Pediatr*. 2010; 47: 131–7.
10. Mehta S, Kumar P, Narang A. A randomized controlled trial of fluid supplementation in term neonates with severe hyperbilirubinemia. *J Pediatr*. 2005; 147: 781–5.
11. Chen A, Du L, Xu Y. The effect of blue light exposure on the expression of circadian genes: *bmal1* and *crypto-*

- chrome 1 in peripheral blood mononuclear cells of jaundiced neonates. *Pediatr Res*. 2005; 58: 1180–4.
12. Gloria – Bottini F, Bottini E. Is there a role of early neonatal events in susceptibility to allergy? *Int J Biomed Sci*. 2010; 6: 8–12.
 13. Pishva N, Pishva H. Incidence of thrombocytopenia in hyperbilirubinemic neonates during phototherapy. *Acta Medica Iranica*. 2000; 38: 7–9.
 14. Tawab CN, Saldanha PR, Mithun HK. Phototherapy induced thrombocytopenia—a comparative study among breastfed term and preterm neonates with hyperbilirubinemia. *International Journal of Medical and Health Sciences*, 2014 October; 3 (4): 256-60.
 15. Scott J P. Neonatal Thrombocytopenia. In: Kliegman, Stanton, Schor SG, Behrman. *Nelson's Text Book of Pediatrics*, 2^{0th} ed. Philadelphia: WB Saunders; 2015: p.2406.
 16. Khera S, Gupta R. Incidence of thrombocytopenia following phototherapy in hyperbilirubinemic neonates. *Medical Journal Armed Forces India*. 2011 Oct. 31; 67 (4): 329-32.
 17. Boskabadi H, Mafinezhad S, Bagher F. Incidence of Thrombocytopenia in Idiopathic Hyperbilirubinemic Newborns. *Maced J Med Sci*. 2014 Jun; 7 (2): 261-4.
 18. Venaktamurthy M, Balaji M D, Reddy T K. A study on effect of phototherapy on platelet count in neonates with neonatal hyperbilirubinemia in a tertiary care rural hospital. *International Journal of Contemporary Pediatrics*. 2016 Feb; 3 (1): 253-5.
 19. Bhargava, Omprakash, et al. Incidence of thrombocytopenia in hyperbilirubinemic neonates following Phototherapy. *Asian J. Research Chem*. 2015 April; 8 (4): 221-30.A
 20. Abdul Tawab C N, Saldanha P R, Mihun H k. Phototherapy Induced Thrombocytopenia –A Comparative Study among Breastfed Term And Preterm Neonates with Hyperbilirubinemia in *Int J Med Health Sci*. 2014 Oct; 3 (4): 256-60.
 21. Monsef A, Eghbalian F. Does conventional phototherapy have any effect on platelet count in full term neonates with indirect hyperbilirubinemia? *Health*, 2011; 3 (12): 709-11.
 22. Ghafarpour SK, Sultani H. Effect of phototherapy on platelet and white blood cell count in term infants. *Medical journal of Tabriz university of medical sciences*, 2006; 28 (3): 59-62.
 23. 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: 271–9.
 24. Maurer HM, Fratkin M, McWilliams NB. Effects of phototherapy on platelet counts in low-birth weight infants and on platelet production and life span in rabbits. *Pediatrics*, 1976; 57: 506–12.