

# Frequency of Thrombocytopenia in Septic Neonates

Rana Mubarik Ali<sup>1</sup>, Waseem Asghar<sup>1</sup>, Humayun Amjad<sup>2</sup> and Aamir Furqan<sup>3</sup>

## ABSTRACT

**Objectives:** To find the frequency of Thrombocytopenia in Septic Neonates.

**Study Design:** Observational / Descriptive study

**Place and Duration of Study:** This study was conducted at the Department of Pediatrics, Nishtar hospital, Multan from December 2015 to December 2016.

**Materials and Methods:** A total number of two hundred and twelve (n=212) enrolled in the study. Data was analyzed with statistical software SPSS version 21.1. Mean  $\pm$  SD were calculated for quantitative data and frequencies (percentages) were calculated for qualitative data. Chi square test and logistic regression was applied to see association between thrombocytopenia and septicemia. SPSS software was used to analyze the data and p value  $\leq$  0.05 was considered as significant.

**Results:** A total number of 100% (n=212) neonates were included in this study, either genders. Gender distribution showed that there were more males i.e., 61.8% (n=131) and 38.2% (n=81) were females. The mean age of the patients was 11.80 days with S.D 6.37. The main outcome variable of this study was thrombocytopenia. Out of 100% (n=212) patients, all were sepsis patients, in our study, it was observed that 86.3% (n=183) patients have thrombocytopenia.

**Conclusions:** we concluded that thrombocytopenia is a major and early predictor of sepsis but not sufficient for the diagnosis of septicemia, so other parameters must be ruled out.

**Key Words:** Thrombocytopenia, Septicemia, Neonates, Blood.

**Citation of article:** Ali RM, Asghar W, Amjad H, Furqan A. Frequency of Thrombocytopenia in Septic Neonates. Med Forum 2017;28(5):85-88.

## INTRODUCTION

Sick, premature and neonates in the intensive care unit confront common hematological problems and thrombocytopenia which is usually a manifestation of an underlying pathologic process. About 20% to 40% of the neonates can suffer a high rate of morbidity and mortality in our setups due to that cause. Premature and ill neonates mostly have low platelet count<sup>1</sup>. It is narrated by various studies that bacteria, rickettsia, protozoa, fungi and viruses are the main etiological factors underlying neonatal septicemia and leading to thrombocytopenia. Immune mediated, genetic disorders and chromosomal anomalies are the remaining culprits of thrombocytopenia<sup>2</sup>.

Disseminated intravascular coagulation (DIC) is a coagulopathy arising in few patients of bacterial

septicemia. Thrombocytopenia is not only seen in disseminated intravascular coagulation but also in early sepsis<sup>3,4</sup>. Diagnosis of thrombocytopenia is based entirely on CBC (complete blood count) and peripheral blood smear. To rule out common variable immune deficiency as an underlying causative agent for thrombocytopenia immunoglobulin assay is commonly performed laboratory test in pediatric population<sup>5</sup>. Cure is yet to be found for thrombocytopenia. Even successful medical or surgical management is failed to bring down and reduce relapses frequency arising many years after treatment.<sup>6</sup> Thrombocytopenia can resolve spontaneously on its own without the need for its treatment in most of the children<sup>7</sup>. Though, in neonates, sepsis is the main causative agent for thrombocytopenia but Birth asphyxia, folic acid deficiency and vitamin B6 are also included in its known causes. Better prognosis of thrombocytopenia is associated with a relatively longer follow-up and lower age at the time of diagnosis of this hematological problem<sup>8</sup>. Immunosuppression with the use of Azathioprine (150 mg/d) and or cyclophosphamide (50-100 mg/d) is considered as an essential part of treatment of this abnormality. However, early use of rituximab in the treatment regime is found to be associated with delaying or even avoiding surgery altogether in young patients in a meta-analysis of various studies of adult patient with the same problem<sup>9</sup>. In addition to this benefit, relapses can also be averted with Rituximab therapy<sup>10</sup>. A study conducted by Arif SH, on the topic of bacterial sepsis

<sup>1</sup>. Department of Cardiology, Ch. Pervaiz Ellahi Institute of Cardiology, Multan.

<sup>2</sup>. Department of Research Centers, Ibn-e-Sina Hospital and Medical Research centre, Multan.

<sup>3</sup>. Department of Anesthesia, Nishtar Medical College, Multan.

Correspondence: Dr. Aamir Furqan, Assistant Professor, Department of Anesthesia, Nishtar Medical College, Multan.

Contact No: 0333 6203152

Email: draamir2009@hotmail.com

Received: March 22, 2017;

Accepted: April 19, 2017

and thrombocytopenia in patients admitted to neonatal intensive care unit, showed that thrombocytopenia was present in 83.5% of patients and positive blood culture in only 41.1 % of studied patients<sup>11</sup>.

This study was planned to provide basic literature for the sole purpose of providing precise investigation and treatment of thrombocytopenia because despite of common occurrence of thrombocytopenia, no local study was available to show the frequency of occurrence of thrombocytopenia in septic neonates.

**MATERIALS AND METHODS**

This study was started after approval from ethical committee of Nishtar Hospital, Multan. Duration of study was from December 2015 to December 2016. Informed consent was sought from patient’s guardian in order to include the patient’s data in research. Guardians were ensured about the confidentiality of information. Their Addresses and telephonic contacts were taken. BD Vacutainer ethylene diamine tetra acetic acid (EDTA) tubes were used for the purpose of collecting and transporting blood samples to the respective laboratory for platelet count under strict aseptic measures. Automatic hematological cell counter was used to calculate platelet count as a part of complete blood count. All the concerned data was entered on the Performa of each patient. Thrombocytopenia was measured in terms of laboratory investigation, if Platelet count is less than 1, 50000  $\mu\text{l}^{-1}$  it was labeled as thrombocytopenia.

Sepsis was labeled positive on the basis of positive septic screen and Septic screen was considered positive if any two of the following was present (i) Total Leukocyte count (TLC) of  $<5000/\text{cc}$  mm<sup>3</sup> or  $>20000/\text{mm}^3$ , (ii) Absolute Neutrophils Count of  $<1800/\text{mm}^3$ , (iii) Immature /Total Neutrophils ratio of  $>0.2$ , (iv) Micro ESR  $>15\text{mm}$  in 1 hour, (v) Platelet Count of  $<150000/\text{mm}^3$ , (vi) CRP value of  $>1\text{mg/L}$ . Preterm babies of  $<2.5$  kg weight and whose parents were not willing to give permission were excluded from the study. Computer software SPSS version 16 was used for entering and analyzing all the data. Mean and standard deviation was calculated for quantitative variables like age of patients. Frequency and percentage was calculated for qualitative variables like gender, sepsis and thrombocytopenia. Effect modifier like gender was controlled by stratification of data. Post stratification chi square test was applied. A p value of  $<0.05$  was considered statistically significant.

**RESULTS**

A total number of 100% (n=212) neonates were included in this study, both genders. Gender distribution showed that there were more males i.e. 61.8% (n=131) and 38.2% (n=81) were females. The mean age of the patients was 11.80 days with S.D 6.37. The main outcome variable of this study was

Thrombocytopenia. Out of 100% (n=212) patients, in our study, it was observed that 86.3% (n=183) patients have Thrombocytopenia.

When patients were grouped into different age categories, it was noted that 27.8% (n=59) patients were 1 to 7 days, 41% (n=87) were 8 to 14 days, 21.2% (n=45) were 15 to 21 days and 9.9% (n=21) were 22 to 28 days of age. When Chi-Square was applied to check the effect modification, it was noted that gender and stratified age were significantly associated with Thrombocytopenia with P-values 0.000 and 0.004 respectively. When logistic regression was applied to find the predictors of Thrombocytopenia, it was noted that gender was the predictor of Thrombocytopenia and age was not the predictor of Thrombocytopenia with P-values 0.000 and 0.225 respectively. Odd ratios of age and gender also showed this trend i.e. 1.04 and 5.29 respectively.

**Table No.1: Demographics and frequency of Thrombocytopenia**

Characteristics	Frequency	Percentage (%)
<b>Gender</b>		
Male	131	61.8
Female	81	38.2
Age in days	11.80 $\pm$ 6.37	
<b>Thrombocytopenia</b>		
Yes	183	86.3
No	29	13.7
<b>Age Groups</b>		
1-7 Days	59	27.8
8-14 Days	87	41.0
15-21 Days	45	21.2
22-28 Days	21	9.9

**Table No.2: Inferential Results**

Gender	Thrombocytopenia		P Value
	No	Yes	
Female	21	60	0.000
Male	8	123	
<b>Total</b>	29	183	

**Table No.3: Inferential Results**

Age Groups	Thrombocytopenia		Total
	No	Yes	
1-7 Days	12	47	0.001
8-14 Days	6	81	
15-21 Days	11	34	
22-28 Days	0	21	
<b>Total</b>	29	183	

<b>Odd ratios</b>	
Age	1.0431
Gender	5.2905

## DISCUSSION

Sick babies both pre and full term suffer a great deal of morbidity and mortality by a frequently encountered problem called thrombocytopenia<sup>12</sup>. In different studies, about 20 to 40% of NICU admitted newborns had thrombocytopenia<sup>13</sup>. Though bacterial septicemia has various manifestations but thrombocytopenia is the common one. Neonates are more prone to infection in virtue of their weak immune system. Moreover, neonates are made more susceptible to infections by the complex interaction of several identified risk factors in both neonates and their mother. Rapid treatment following early suspicion and accurate diagnosis is necessary for the better prognosis of neonatal septicemia. Occurrence of thrombocytopenia early in the course of septicemia make it an early predictor of septicemia<sup>14,15</sup>.

In our study, 212 neonates of both genders were included. Males constituted about 61.8% compared to 38.2% of females with the overall mean age of 11.80 days with S.D of 6.37. Thrombocytopenia was the main outcome variable in our study. All selected study patients were septic and 86.3% (n=183) of them showed thrombocytopenia. On applying Chi-Square it was noted that gender and stratified age were significantly associated with Thrombocytopenia with P-values 0.000 and 0.004 respectively. Similarly, in a previous study 83.5% of sick neonates admitted in NICU had a platelet count of  $<150 \times 10^3/\mu\text{l}$ . Only 33.8% of these cases were narrated to have positive blood culture results. Low platelet count is a significant change present in bacterial septicemia observed even in the patients with negative blood culture results<sup>16</sup>. That's why; it was also shown by that study that platelet count is a good indicator of septicemia irrespective of blood culture report.

Though data is not shown but gram positive bacteria were isolated more commonly than gram negative in neonates suffering from septicemia, same as found in a study by Jack et al.<sup>17</sup> But these findings are in total contrast to several Indian studies in which gram negative bacteria are the most commonly isolated organisms. But another fact is worthy of mentioning that thrombocytopenia was much intense in severity in neonates who get infected by gram negative bacteria compared to gram positive and almost every patient of gram negative septicemia had thrombocytopenia with a strong tendency to develop DIC compared to its rival group. A study done by Riedler et al.<sup>18</sup> showed more prevalence of thrombocytopenia reaching up to 80% in gram negative septicemia compared to gram positive septicemia ( 65% ).

Growth of organism on blood culture is different in various studies depending upon the local prevalence's and conditions favoring a specific organism. Out of numerous organism in different studies Coagulase

negative staphylococcus growth ranges from 4.46 to 90% in various studies conducted by Batisti et al<sup>19</sup> and Simpson et al<sup>19</sup>. In earlier times it was not considered pathogenic and was discarded but now the development of thrombocytopenia and other complications proves the pathogenicity of that organism. The virulence, ability of colonization, ability to acquiring antibiotic resistance, its survival in inanimate environment and its acquirement in neonates especially premature born without normal flora in first few weeks make Klebsiella one of the important organisms on cultures of NICU admitted neonates and in several outbreak. In few cases, Acinetobacter, Citrobacter and Pseudomonas can also be isolated. Despite the suspicion of nosocomial outbreak most of these cases can be attributed to incidental findings.

Mortality rate in septic patients is considerably greater in preterm and low birth weight neonates. The most virulent of all the organisms in term of causing mortality is Klebsiella. Out of many complications of septicemia, DIC is a fatal one needing intensive treatment. Consumptive coagulopathy in DIC makes thrombocytopenia an important finding. But it is suggested by Nosen et al that majority of cases of septicemia show thrombocytopenia without the development of full blown DIC<sup>20</sup>. Not only bacteria but protozoa, fungi, virus and rickettsia can be the cause of underlying infections leading to thrombocytopenia. Most of the studies were done only for bacterial isolate, thrombocytopenia in patients with no bacterial growth in culture might be attributed to above mentioned causes.

## CONCLUSION

We concluded that thrombocytopenia is a major and early predictor of sepsis but not sufficient for the diagnosis of septicemia, so other parameters must be ruled out.

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Durand-Zaleski I, Schlegel N, Blum-Boisgard C, Uzan S, Dreyfus M, Kaplan C, et al. Screening primiparous women and newborns for fetal/neonatal alloimmune thrombocytopenia: a prospective comparison of effectiveness and costs. *Am J Perinatol* 1996;13(07):423-31.
2. Sinha N, Deb A, Mukherjee A. Septicemia in neonates and early infancy. *IndJ Pediatr* 1986; 53(2):249-56.
3. Levi M. Treatment of Disseminated Intravascular Coagulation (DIC). *Anticoagulation and Hemostasis in Neurosurgery*: Springer; 2016.p.167-82.
4. Boral BM, Williams DJ, Boral LI. Disseminated intravascular coagulation. *Am J Clin Pathol* 2016;

- aqw195.
5. Neunert C, Lim W, Crowther M, Cohen A, Solberg L, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood* 2011;117(16):4190-207.
  6. Ahn YS, Harrington WJ. Treatment of idiopathic thrombocytopenic purpura (ITP). *Ann Review Med* 1977;28(1):299-307.
  7. Gernsheimer T, James AH, Stasi R. How I treat thrombocytopenia in pregnancy. *Blood* 2013;121(1):38-47.
  8. Shim YJ, Kim UH, Suh JK, Lee KS. Natural course of childhood chronic immune thrombocytopenia using the revised terminology and definitions of the international working group: a single center experience. *Blood Res* 2014;49(3):187-91.
  9. Auger S, Duny Y, Rossi JF, Quittet P. Rituximab before splenectomy in adults with primary idiopathic thrombocytopenic purpura: a meta-analysis. *Bri J Haematol* 2012;158(3):386-98.
  10. Tsai HM, Lian ECY. Antibodies to von Willebrand factor-cleaving protease in acute thrombotic thrombocytopenic purpura. *New Engl J Med* 1998;339(22):1585-94.
  11. Arif S, Ahmad I, Ali S, Khan H. Thrombocytopenia and bacterial sepsis in neonates. *IndJ Hematol Blood Transfusion* 2012;28(3):147-51.
  12. Roberts I, Murray N. Neonatal thrombocytopenia: causes and management. *Archives of Disease in Childhood-Fetal and Neonatal Edition* 2003; 88(5):F359-F64.
  13. Sparger K, Deschmann E, Sola-Visner M. Platelet transfusions in the neonatal intensive care unit. *Clin Perinatol* 2015;42(3):613-23.
  14. de Stoppelaar SF, van't Veer C, van der Poll T. The role of platelets in sepsis. *Thromb Haemost* 2014;112(4):666-77.
  15. Storm W. Use of thrombocytopenia for the early identification of sepsis in critically ill newborns. *Acta paediatr Acad Scientiarum Hungaricae* 1981;23(3):349-55.
  16. Takahashi T, Maeda K, Suzuki T, Ishido A, Shigeoka T, Tominaga T, et al. The first identification and retrospective study of severe fever with thrombocytopenia syndrome in Japan. *J Infect Dis* 2014;209(6):816-27.
  17. Guida JD, Kunig AM, Leef KH, McKenzie SE, Paul DA. Platelet count and sepsis in very low birth weight neonates: is there an organism-specific response? *Pediatr* 2003;111(6):1411-5.
  18. Riedler G, Straub P, Frank P. Thrombocytopenia in septicemia. A clinical study for the evaluation of its incidence and diagnostic value. *Helvetica Medica Acta* 1971;36(1):23-38.
  19. Battisti O, Mitchelson R, Davies PA. Changing blood culture isolates in a referral neonatal intensive care unit. *Arch Dis childhood* 1981;56(10):775-8.
  20. Neame PB, Kelton JG, Walker IR, Stewart I, Nossel H, Hirsh J. Thrombocytopenia in septicemia: the role of disseminated intravascular coagulation. *Blood* 1980;56(1):88-92.

Electronic  
COPY