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Dr. Dipika Parmar
Second Year Pathology
Resident, B.J Medical College
and Civil Hospital,
Ahmedabad, Gujarat, India

Dr. Hemina Desai
Associate Professor,
Department of Pathology, B.J
Medical College and Civil
Hospital, Ahmedabad,
Gujarat, India

Dr. Hansa Goswami
Professor and Head of
Department, B.J Medical
College and Civil Hospital,
Ahmedabad, Gujarat, India

Corresponding Author:
Dr. Hemina Desai
Associate Professor,
Department of Pathology, B.J
Medical College and Civil
Hospital, Ahmedabad,
Gujarat, India

Study of thrombocytopenia and platelet indices in neonatal sepsis

Dr. Dipika Parmar, Dr. Hemina Desai and Dr. Hansa Goswami

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Abstract

Introduction: Neonatal Sepsis is major cause of neonatal morbidity and mortality contributing around 38% of all deaths in neonates worldwide. Neonatal Sepsis is clinical syndrome with or without accompanying bacteremia in the first month of life. Sepsis in neonates often results in thrombocytopenia and changes in platelet indices.

Aims & Objectives: The current study was undertaken to correlate degree of thrombocytopenia and platelet indices variation in neonates with sepsis. It gives an overview of potential utility of importance of platelet count and platelet indices in diagnosis of neonatal sepsis.

Materials and Methods: The present study was conducted on 100 neonates admitted in NICU, Civil hospital, BJMC Ahmedabad with clinical signs and symptoms of sepsis along with positive blood culture. Peripheral blood was drawn from all study subjects under aseptic precautions in EDTA container and study was done for thrombocytopenia and platelet indices variation in neonatal sepsis. All samples were processed in fully automated hematology analyzer HORIBA PENTA XLR (5 part) with standard calibration.

Results: In our study among 100 cases with neonatal sepsis, thrombocytopenia was present in 48% cases. High MPV seen in 58.34% cases and High PDW seen in 72.9% cases.

Keywords: Thrombocytopenia, platelet indices, neonatal sepsis

Introduction

Neonatal Sepsis, Sepsis Neonatorum and Neonatal Septicemia are terms that are used to describe the systemic response to infection in the newborn infants. Infection is more common in neonatal period than any other time in life due to exposure to a large number of organisms and relatively weak neonatal host defence to clear the microorganisms from blood and tissue. Clinical features of sepsis are nonspecific in neonates and high index of suspicion is required for its identification^[1]. Neonatal sepsis can be detected by blood culture and hematological parameters called as sepsis screen which includes following tests; total leucocyte count (TLC), absolute neutrophil count, peripheral smear for band cells, Micro ESR, CRP (C reactive protein). Sepsis screen will be considered positive if 2 or more parameters are positive^[2]. Although blood culture is the "Gold Standard" for diagnosis of sepsis, reports are usually available after 48-72 hours & yields positive results in 25-70% of cases. Blood culture may be affected by intrapartum antibiotic administration to mother. So, hematological changes induced in neonatal sepsis have been used to make an early diagnosis and to detect complications^[3].

Thrombocytopenia is used as an early but nonspecific marker of sepsis in Neonates. Important platelet indices available for clinical utility include mean platelet volume (MPV), platelet distribution width (PDW) in neonatal sepsis. All these indices are readily available with no additional cost while performing routine blood counts, using autoanalyzers^[4].

The present study was undertaken to evaluate the correlation of thrombocytopenia and alterations in platelet indices with blood culture as these parameters aid in the in early diagnosis of neonatal sepsis.

Aims and Objectives

- To study degree of thrombocytopenia in Neonatal sepsis.
- To correlate variation in platelet indices in Neonatal sepsis.

Materials and Methods

The present study is a prospective analysis of neonates admitted in NICU at civil hospital, BJMC Ahmedabad. This study includes 100 cases belonged to 0-28 day age group with clinical signs and symptoms of sepsis along with positive blood culture. Peripheral blood was drawn from all patients under aseptic precautions in EDTA container. The routine hematological investigations were performed in fully automated hematology analyzer Horiba Penta XLR (5

part) with standard calibration.

Observations

- The present study was conducted on total 100 neonates (0-28 days) with sepsis and positive blood culture for microorganisms.

The blood culture isolates in present study were shown in Table.1

Table 1: Blood culture isolates

Organisms isolated	Number of cases	%
Coagulase negative Staphylococci	49	49%
Klebsiella pneumoniae	26	26%
Acinetobacter Species	8	8%
Enterococcus Faecium	7	7%
Pseudomonas aeruginosa	5	5%
Candida	4	4%
Proteus Mirabilis	1	1%
Total	100	100%

In our study, out of 100 neonates with sepsis; Coagulase negative Staphylococci was isolated in 49 cases. Klebsiella pneumoniae was isolated in 26 cases. Acinetobacter species was isolated in 8 cases. Enterococcus Faecium was isolated in 7 cases. Pseudomonas aeruginosa was isolated in 5 cases. Candida was isolated in 4 cases. Proteus Mirabilis was

isolated in 1 case.

Platelet count

Neonates with platelet count <150x10³/uL were identified as having thrombocytopenia. The degree of thrombocytopenia observed in present study was shown in Table.2

Table 2: Degree of thrombocytopenia

Platelet count-Degree of thrombocytopenia	No of Neonates
Mild((100 – 150x10 ³ /uL)	20
Moderate (50-100x10 ³ /uL)	18
Severe (<50x10 ³ /uL)	10
Total	48

Out of 100 cases with sepsis; 48 neonates had thrombocytopenia and out of 48 neonates 20 had mild degree thrombocytopenia, 18 had moderate degree

thrombocytopenia, 10 had severe degree thrombocytopenia. The degree of thrombocytopenia varied with different organisms isolated in blood culture is shown in Table.3

Table 3: Degree of thrombocytopenia with different organisms

Organisms	Degree Of Thrombocytopenia			Total cases (%)
	Mild	Moderate	Severe	
Gram positive organisms				
Coagulase negative Staphylococci	8	8	2	18 (38%)
Enterococcus Faecium	1	0	0	1 (2%)
Total				19 (40%)
Gram negative organisms				
Klebsiella pneumoniae	9	9	8	26(54%)
Acinetobacter Species	0	1	0	1 (2%)
Pseudomonas aeruginosa	2	0	0	2 (4%)
Total				29 (60%)

Incidence of thrombocytopenia is more common in gram negative sepsis comparing to gram positive sepsis. In Our study, total 48 cases had sepsis associated with thrombocytopenia. Out of these 48 cases, gram positive organisms were cultured in 19 cases and gram negative organisms were cultured in 29 cases. Gram positive organisms associated with thrombocytopenia comprises of 40% cases whereas gram negative organisms associated with thrombocytopenia in 60% cases. This shows thrombocytopenia is more commonly seen in gram negative septicemia than gram positive septicemia.

MPV as shown in Table.4

Table 4: Correlation of degree of thrombocytopenia & mpv (mean platelet volume)

	MPV	
	Increased	Normal/Decreased
Mild(100 – 150x10 ³ /uL)	12 (60%)	8 (40%)
Moderate (50-100x10 ³ /uL)	10 (56%)	8 (44%)
Severe (<50x10 ³ /uL)	6 (60%)	4 (40%)
Total	28 (58%)	20 (42%)

28 out of 48 cases with sepsis had increased values of MPV (58%). 6 out of 28 cases with increased MPV values showed

Platelet indices variation

In our study we correlated degree of thrombocytopenia with

severe degree of thrombocytopenia.

In our study we also correlated degree of thrombocytopenia with PDW as shown in Table.5

Table 5: Correlation of degree of thrombocytopenia & pdw (platelet distribution width)

	PDW	
	Increased	Normal
Mild(100 – 150x10 ³ /uL)	15 (75%)	5 (25%)
Moderate (50-100x10 ³ /uL)	13 (72%)	5 (28%)
Severe (<50x10 ³ /uL)	7 (70%)	3 (30%)
Total	35 (73%)	13 (27%)

35 out of 48 cases with sepsis had increased values of PDW (73%).7 out of 35 cases with increased PDW values showed

Table 6: There have been studies which shows incidence of different organisms in neonatal sepsis.

	Rekha N <i>et al.</i> [1]	Krishna <i>et al.</i> [7]	Kumhar <i>et al.</i> [8]	Tripti K. Karne <i>et al.</i> [9]	Present study
Klebsiella pneumoniae	41.6%	37.9%	33.8%	10%	60.41%
Coagulase negative staphylococci	13.8%	-	7.9%	17.5%	11.6%
Pseudomonas	5.5%	10.3%	10.2%	40%	4.1%

In our study among the neonates with gram negative sepsis Klebsiella pneumoniae was most common cultured organism and in gram positive sepsis, Coagulase negative staphylococcus aureus was the most common cultured organism.

In the study conducted by Rekha N *et al.* [1] and Krishna *et al.* [7], Kumhar *et al.* [8]; Klebsiella pneumonia was the commonest organism identified and In the study conducted by Tripti K. Karne *et al.* [9], Pseudomonas aeruginosa was the most common organism followed by staphylococcus aureus.

Sepsis is the commonest cause of neonatal mortality and is probably responsible for 38% of total neonatal deaths each year in developing countries [10]. Neonatal sepsis is associated with high mortality as diagnosis of sepsis in neonates presents as challenge because the clinical signs of sepsis are nonspecific and it mainly depends upon investigation. To overcome this limitation and to guide early diagnosis of neonatal sepsis, Sepsis screens are used. In neonatal sepsis there is leucopenia of less than 4000/cumm, absolute neutrophil count less than 1500/cumm, Immature(band cell)/total neutrophil ratio is equal or more than 0.2, micro ESR equal or more than 15 in first hour and C reactive protein equal or more than 8-10mcg/ml considered significant. Sepsis screen will be considered positive if 2 or more parameters are positive mentioned from above [2]. The negative predictive value of various sepsis screen parameters is too low to confidently rule out early onset of sepsis. In addition their use will increase the cost of investigations significantly [3].

In present study, 100 cases of neonatal sepsis are evaluated. The current study was undertaken to evaluate thrombocytopenia and platelet indices variation in neonatal septicemia and to look into various hematological parameters both individually and in combination as a part of sepsis screening.

There have been studies showing the significant changes in platelet count and platelet indices in patients with neonatal sepsis. These parameters may increase the sensitivity and specificity of the existing sepsis screen when combined with it. It has been seen that platelet count decreases and

severe degree of thrombocytopenia

Discussion

Neonatal sepsis is a clinical syndrome characterized by systemic signs and symptoms of infection in the first month of life. Neonatal sepsis can be divided in to 2 main classes depending on the onset of symptoms related to sepsis; early onset sepsis usually presents within the first 72 hours of life and the source of infection is generally the maternal genital tract and in late onset sepsis usually presents after 72 hours and the source of infection is either nosocomial or community acquired [5]. The “Immune deficiency” of the newborn is relative rather than absolute. Most infectious being caused by organisms that are also capable of causing infection in older children, but neonatal infection is usually more severe and more likely to disseminate [6].

MPV&PDW increases in neonates with sepsis. High MPV&PDW show more specificity for detecting septicemia (95% and 79% respectively) and have good negative predictive value [11].

Thrombocytopenia commonly accompanies systemic infection in neonates. Initial changes occur in leucocytes, this is soon followed by a drop in platelet count. The various mechanisms that may be responsible for thrombocytopenia are as follows:

1. Endothelial damage that occurs during sepsis, with platelet adhesion and aggregation
2. Removal of platelets by the reticuloendothelial system.
3. Decreased platelet production may be a contributing factor.
4. Some infections are associated with DIC leading to thrombocytopenia [12].

The normal platelet count for neonates is approximately 224x10³/ul. Platelets of the neonates are slightly larger than those of adults. This reflects an increased proportion of young forms. Platelet count of less than 150x10³/ul are considered low [13]. Thrombocytopenia can be graded to different severity for the risk assessment and management as following [14].

1. Normal- >150x10³ /ul
2. Mild degree thrombocytopenia – 100-150x10³/ul
3. Moderate degree thrombocytopenia- 50-100x10³/ul
4. Severe degree thrombocytopenia- <50x10³/ul

In Our study out of total sepsis positive cases, thrombocytopenia presented in 48 % cases and in mild, moderate and severe thrombocytopenia presented in 18%, 20% and 10% respectively. Rekha N *et al.*[1] showed that in their study thrombocytopenia was present in 72.2% cases with sepsis, while Bhat Y R *et al.* [15] showed thrombocytopenia in 39.5 % cases, and Tripti K Karne *et al.* noted thrombocytopenia in 57.5% cases [9].

In neonatal sepsis variation in platelet indices i.e. high MPV and high PDW.

Mean platelet volume: MPV is a measurement of average size of platelets. Normal value of MPV in neonatal period is

10-12 fl. MPV is inversely proportional to platelet count in normal subjects. The platelet volume is regulated by cytokine dependent megakaryocyte ploidy and platelet number. In the sepsis there is decreased platelet count and young platelets which are bigger and more active enter the circulation and hence MPV is increased. Increased MPV indicates increased platelet diameter. Therefore increased MPV is useful clinically as a marker of production rate and platelet activation [15].

In Present study elevation in Platelet indices seen in neonatal sepsis proven cases which is correlated and compared with other study. In our study elevation in MPV seen in 54.47% cases. In study conducted by Rekha N *et al.* [1] showed elevation in MPV in 47.7% cases, and in study of Bhat Y R *et al.* [15] showed elevation in MPV in 13.9% cases whereas Tripti K. Karne *et al.* [9] showed elevation in MPV in 35.92% cases.

Platelet distribution width is an indicator of variation in platelet size. Normal value of PDW in neonatal period is 10%-17.9%. A platelet distribution width can be calculated just as the RDW and is correlated with platelet count and MPV [16]. PDW is an indicator of volume variability in platelets size and reflects the heterogeneity in platelet morphology. PDW is increased in sepsis and it is useful indicator for diagnosis of neonatal sepsis [15].

In our study elevation PDW seen in 72.9 % cases. In study conducted by Rekha N *et al.* [1] showed elevation in PDW 47.7% cases, and in study of Bhat Y R *et al.* [15] showed elevation in PDW in 72.1% cases whereas Tripti K. Karne *et al.* [9] showed elevation in PDW in 43.69% cases.

Conclusion

It was concluded from this study that platelet count and platelet indices may serve as an important tool to aid sepsis screening. The platelet count is decreased with development of sepsis and PDW and MPV are increased in septicemia. There is correlation of high MPV and PDW with thrombocytopenia in neonatal sepsis. Thus, platelet count and platelet indices may be used as diagnostic and prognostic biomarkers for neonatal sepsis.

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