

A Clinicopathological Study of Thrombocytopenia and Platelet Indices in Neonatal Sepsis

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ABSTRACT

Background and Objective: Neonatal sepsis is a growing health problem in third world countries, like India. The present clinic pathological study was performed to assess the grade of thrombocytopenia and platelet indices in patients with neonatal sepsis. **Materials and Methods:** A prospective cross-sectional study was conducted in the Neonatal Intensive Care Unit, Department of Pediatrics and Pathology JNMC, Aligarh from 2019-2021 in 172 babies (cases = 142, controls = 30). Neonates who presented with clinical signs or symptoms of sepsis were taken as the case group and healthy neonates were taken as the control and grade of thrombocytopenia and platelet indices ascertained. **Results:** The most common symptom in neonates with sepsis was respiratory distress, 108 (76.4%) followed by poor suckling in 96 (67.6%) and lethargy in 87 (61.0%). Moderate thrombocytopenia was seen in 47 (33.1%) cases. Blood culture was positive in 58 (40.8%) of the sepsis patients. The average Mean Platelet Volume (MPV) was 8.51 ± 1.60 fL in culture-positive neonates and 8.50 ± 1.45 fL in culture-negative cases ($p = 0.94$). The mean platelet crit (PCT) was $0.09 \pm 0.06\%$ in culture-positive neonates and $0.11 \pm 0.05\%$ in culture-negative cases ($p = 0.13$). **Conclusion:** Thrombocytopenia is one of the early but non-specific indicators of neonatal sepsis. Therefore, hematological parameters like mean platelet volume and platelet crit can be an added tool to detect early onset neonatal septicemia.

KEYWORDS

Neonatal sepsis, thrombocytopenia, mean platelet volume, plateletcrit platelet distribution width

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INTRODUCTION

Neonatal sepsis is a severe form of illness in the first month of life with or without accompanying bacteremia¹. The incidence of the disease is 30 per 1000 live births, which amounts to 19.0% of all neonatal deaths in India and is one of the commonest causes of neonatal mortality^{2,3}.

Neonatal sepsis may be caused by various organisms invading the bloodstream which may be bacterial, viral and fungal. Among the organisms, *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella* species are the predominant ones⁴. The clinical features are vague and ill-defined in neonates and a high degree of clinical suspicion is required for its identification. An early but nonspecific manifestation is altered feeding behavior⁵.



Diagnosis of sepsis in neonates is based on blood culture, which is considered the gold standard, but the results of culture are available after a period of 48-72 hrs, which are frequently falsely negative. So, hematological and laboratory parameters serve as fast diagnostic methods, which could be beneficial for the diagnosis of neonatal sepsis⁶.

Thrombocytopenia is a non-specific indicator of neonatal sepsis. The prevalence of thrombocytopenia in neonates varies from 1.0-5.0% with a higher incidence in newborns admitted to the intensive care unit. Bleeding is a major complication of thrombocytopenia⁷. The aims and objectives of the present study were the clinicopathological analysis of thrombocytopenia and platelet indices in neonatal sepsis.

MATERIALS AND METHODS

This study was a hospital-based prospective cross-sectional study conducted in the Neonatal Intensive Care Unit, Department of Pediatrics in collaboration with the Department of Pathology JNMC, Aligarh from 2019-2021 in 172 babies (cases = 142, controls = 30). Neonates with clinical signs or symptoms of sepsis served as the case group and healthy neonates were as control. The ethical clearance was obtained from the institutional ethics committee (D.No.165/FM/IEC) and proper consent was taken from the parents of neonates.

Study design and data collection: The study groups comprised cases and controls. The cases included 142 neonates, who were culture positive: Neonates having positive blood culture along with clinical or laboratory evidence of sepsis and culture negative with neonates having clinical criteria of sepsis as per/World Health Organization criteria or having positive sepsis screen but without positive blood culture. While 30 neonates were taken as controls, who were without any clinical or laboratory evidence of sepsis.

Observed parameters: The observed haematological parameters like mean platelet volume, platelet distribution width, plateletcrit, total leucocyte count and platelet count were assessed by an automated 5-part sysmex hematology analyzer and a general blood picture was performed after Leishman staining of smears.

Statistical analysis: Statistical analysis was done using the SPSS software version 25 and $p < 0.05$ was considered statistically significant.

RESULTS

Among the case group, 83 (58.5%) were males and 59 (41.5%) were females. Babies with birth weight < 2.5 kg were 47 (33.1%) and those with ≥ 2.5 kg were 95 (66.9%). The caesarean section comprised 74 (52.1%) cases. Gender, birth weight, mode of delivery and gestational age were compared between septic patients and the control group (Table 1).

The most common symptom found in neonates with sepsis in this study was respiratory distress, 108 (76.4%) followed by poor suckling in 96 (67.6%), lethargy in 87 (61.0%) and bleeding in 60 (42.3%) cases. Other symptoms included poor crying, vomiting and abnormal movements (Table 2).

Blood culture was positive in 58 (40.8%) of the sepsis patients and 84 (59.2%) had culture-negative sepsis. Gram-negative bacteria were present in 46 (79.3%) cases followed by gram-positive bacteria in 9 (24.1%) cases and fungus constituted 3 (5.2%) cases. In this study, *Klebsiella pneumoniae* (32.8%) was the most commonly isolated organism, followed by Coagulase negative staphylococcus (18.9%) and *Pseudomonas* in 17.2% of cases.

Table 1: Demographic comparison between cases and controls

Parameters	Case	Control	p-value
Gender			
Male	83 (58.5%)	16 (53.3%)	0.77
Female	59 (41.5%)	14 (46.7%)	
Birth weight			
<2.5 kg	47 (33.1%)	13 (43.3%)	0.23
≥2.5 kg	95 (66.9%)	17 (56.7%)	
Types of delivery			
Normal delivery	68 (47.9%)	17 (56.7%)	0.38
Caesarean section	74 (52.1%)	13 (43.3%)	
Gestational age			
Preterm	45 (31.7%)	08 (26.7%)	<0.001
Term	85 (59.8%)	19 (63.3%)	
Post term	12 (8.5%)	03 (10.0%)	

Table 2: Distribution of cases according to general presenting complaints

Symptoms	Number of cases	Percentage
Poor suckling	96	67.6
Lethargy	87	61.0
Respiratory distress	108	76.4
Hypothermia	33	23.1
Hyperthermia	17	12.2
Hypoglycemia	46	32.6
Bleeding	60	42.3
Poor cry	59	41.7

Table 3: Distribution of cases according to hematological parameters

Parameters	Case	Control	p-value
Hemoglobin (g dl⁻¹)			
<14	39 (27.4%)	3 (10.0%)	0.04
≥14	103 (72.6%)	27 (90.0%)	
TLC (x10⁹)			
<5	31 (21.8%)	03 (10.0%)	0.01
5-19	52 (36.6%)	20 (66.7%)	
>19	59 (41.6%)	07 (23.3%)	
Thrombocytopenia			
Mild	31 (21.8%)	4 (13.3%)	0.04
Moderate	47 (33.1%)	0 (0%)	
Severe	24 (16.9%)	0 (0%)	

TLC: Total leucocyte count

Hematological parameters showed Hemoglobin of less than 14 g dL⁻¹ in 39 (27.4%) neonates in the case group. Total leukocyte counts of $<5 \times 10^9 \text{ L}^{-1}$ were found in 31 (21.8%) cases whereas increased TLC was seen in 59 (41.6%) cases. Thrombocytopenia was found in 102 (71.8%) cases. It was graded as mild, moderate and severe. Moderate thrombocytopenia was seen in the majority, 47 (33.1%) cases followed by mild thrombocytopenia in 31 (21.8%) cases and severe thrombocytopenia in 24 (16.9%) neonates in the case group ($p = 0.04$) (Table 3).

Peripheral smear findings were toxic granules in neutrophils, seen in 61 (42.9%) cases. Cytoplasmic vacuolations were present in 27 (19.0%) and a shift to left with immature cells was found in 48 (33.8%) cases. Nucleated RBC has seen in 36 (25.4%) neonates in the case group (Table 4).

The average mean platelet volume (MPV) was $8.51 \pm 1.60 \text{ fL}$ in culture-positive neonates and $8.50 \pm 1.45 \text{ fL}$ in negative culture-negative cases ($p = 0.94$). The mean platelet distribution width (PDW) was $17.2 \pm 1.70\%$ in culture-positive cases and $17.0 \pm 1.93\%$ in culture-negative cases ($p = 0.45$). The mean platelet crit (PCT) was $0.09 \pm 0.06\%$ in culture-positive neonates and $0.11 \pm 0.05\%$ in culture-negative cases ($p = 0.13$) (Table 5).

Table 4: Distribution of cases according to peripheral smear findings

Peripheral smear findings	Cases	Control	p-value	Chi ²
Toxic granules	61 (42.9%)	01 (3.3%)	<0.001	16.90
Cytoplasmic vacuolations	27 (19.01%)	02 (6.67%)	0.10	2.69
Shift to left with immature cells	48 (33.8%)	03 (10.0%)	0.009	6.73
NRBCs	36 (25.4%)	03 (10.0%)	0.06	3.33

NRBCs: Nucleated red blood cells

Table 5: Correlation of blood culture with platelet indices in cases with sepsis

Platelet indices	Culture positive	Culture negative	p-value
MPV (fl)	8.51±1.60	8.50±1.45	0.94
PDW (%)	17.2±1.70	17.0±1.93	0.45
PCT (%)	0.09±0.06	0.11±0.05	0.13

Mean±SD, MPV: Mean platelet volume, PDW: Platelet distribution width and PCT: Plateletcrit

DISCUSSION

The most common symptom in neonates with sepsis in this study was respiratory distress in 76.4% of cases. A positive microbial culture from a normally sterile site (blood) is frequently used as the gold standard to define neonatal sepsis. In the current study, blood culture was positive in 58 (40.8%) neonates in the study group, with *Klebsiella* as the most common organism isolated in 32.8% of cases. Platelet count is an important haematological indicator of neonatal sepsis and platelet indices aid in a more reliable and rapid diagnosis. In this study, thrombocytopenia was found in 102 (71.8%) neonates. The current study findings also revealed that MPV was a significant parameter in septic patients with a mean value of 8.50±1.51 fL in the case group and 7.50±0.82 fL in the control group. However, platelet distribution width and plateletcrit values were not significant. Detection of the degenerative changes of neutrophils in peripheral blood smears can be of value in identifying neonates with infection. This study observed some degenerative changes like toxic granules, cytoplasmic vacuolation and shift to left with immature cells along with nucleated RBCs.

Samreen *et al.*⁴ and Ayub *et al.*⁶ have also stated the most common symptom of respiratory distress in the form of tachypnea, grunting, retractions and increased work of breathing in 83.0 and 63.0% of neonates, respectively. Lim *et al.*⁸ reported a higher incidence of poor activity, lethargy and increased respiratory effort. Shoukry *et al.*⁹ showed that *Klebsiella pneumoniae* was the most frequent bacteria. Arif *et al.*¹⁰ reported blood culture positivity in 24 cases (33.8%) and negative in 47 (66.1%) cases. Hassan *et al.*¹¹ found 63.0% positive blood culture cases. Samreen *et al.*⁴ and Arif *et al.*¹⁰ have reported thrombocytopenia in 83.5 and 81.7% of their studies, respectively. This study was also concordant with Guida *et al.*¹² and Prathyusha *et al.*¹³, who reported that MPV showed a statistically significant difference between the study groups. Mitsiakos *et al.*¹⁴ explained that the variation in MPV affects PCT. Panwar *et al.*¹⁵ stated that immature polymorphonuclear leucocytes (PMNs) were 21 (45.6%) and toxic granules were 15 (32.6%) in the culture-positive group. Annam *et al.*¹⁶ observed toxic granules in 38.3% of cases, which was consistent with this study. Al-Gwaiz and Babay¹⁷ have reported band cells and toxic granulation in 50.0% of neonatal sepsis.

Thrombocytopenia and platelet indices aid in the early diagnosis of neonatal septicaemia, but more proactive indicators like acute phase reactants and blood culture could be more sensitive markers of sepsis.

This study serves as a guide to the early diagnosis of neonatal septicaemia. The present study provides insight into the haematological parameters to be assessed in cases of neonatal sepsis so as to initiate early treatment and a better prognosis. Easy haematological tests like thrombocytopenia with platelet indices could guide in the diagnosis and help in a better cure of the ailment.

A larger sample size and long duration of follow-up could serve better for more accurate statistical analysis.

CONCLUSION

The clinical features of sepsis are non-specific and ill-defined and a high degree of clinical suspicion is required for its identification. The presence of leukopenia or leukocytosis and thrombocytopenia are early but non-specific indicators of neonatal sepsis. However, when present, they are strong pointers to the presence of sepsis. Therefore, hematological parameters like mean platelet volume and platelet crit can be an added tool to detect early onset septicemia.

SIGNIFICANCE STATEMENT

The present study highlights the clinicopathological analysis of thrombocytopenia and platelet indices in neonatal sepsis, which is a rampant burden load of severe infections in this age group. The presence of leukopenia or leukocytosis and thrombocytopenia are early but non-specific indicators of neonatal sepsis. Therefore, hematological parameters like mean platelet volume and platelet crit with blood culture can be an added tool to detect early onset septicemia. A larger sample size and long duration of follow-up could serve better for more accurate statistical analysis.

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