Original Article

Hematological Abnormalities in Neonates Diagnosed with Neonatal Sepsis

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ABSTRACT

Objective: To determine the mean value of hematological parameters including red blood cell distribution width, platelet distribution width, mean platelet volume, white blood cell count, red blood cell count and platelet count in neonates diagnosed with neonatal sepsis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, Sahiwal Teaching Hospital, Sahiwal from 1st February 2025 to 31st July 2025.

Methods: In this study 70 neonates were enrolled. Blood samples were taken in a 3cc disposable syringe and sent to the laboratory for assessment of hematological parameters

Results: The mean age was 11.6±7.4 days, and 39 (55.7%) neonates were males. Early-onset sepsis was present in 42 (60%) cases. Raised red cell distribution width was observed in 46 (65.7%) neonates, abnormal white blood cell count in 38 (54.3%), raised platelet distribution width in 39 (55.7%), raised mean platelet volume in 34 (48.6%), and thrombocytopenia in 29 (41.4%). Late-onset sepsis was associated with significantly higher red cell distribution width, platelet distribution width, and mean platelet volume and a significantly lower platelet count.

Conclusion: Hematological abnormalities were frequent among neonates with sepsis. Red cell and platelet indices may provide useful supportive information, particularly in neonates with late-onset sepsis and low birth weight.

Key Words: Neonatal sepsis, Hematological abnormalities, Red cell distribution width, Mean platelet volume, Platelet distribution width, Thrombocytopenia

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INTRODUCTION

Sepsis is one of the most common infectious diseases of newborns, which mostly occurs in premature and low birth weight babies. Sepsis is the third most common cause of neonatal death with a high morbidity and mortality rate particularly in the developing countries, causing over a quarter of neonatal deaths (25%).[1,2] It may be diagnosed by the presence of a positive blood culture and/or cerebrospinal fluid culture.[3] The hemogram or blood count includes the quantitative (counting) and qualitative (formula) examination of the counted elements of blood (erythrocytes, leukocytes and platelets). The first years of life have a dramatic effect on the blood count parameters, which vary according to the developmental stage.[4]

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Most common haematological abnormalities in neonatal sepsis are anaemia, leukocytosis, thrombocytopenia and shortened coagulation time. Mean platelet volume (MPV) and red blood cell distribution width (RDW), which are components of the complete blood count, are, however, routinely measured, inexpensive, and are readily available but there is little information on the haematological abnormalities in neonatal sepsis.[3] The correlation of MPV and RDW with inflammatory diseases. The mean platelet volume is a direct measure of platelet activation due to inflammation.[5] Red blood cell distribution width is one of the red blood cell indices that are rapidly and automatically calculated by all modern hematological analysers.[6] Ahmed et al[7], conducted a study in Sudan and found that among neonates with neonatal sepsis, the mean RDW was 18.366±2.1%, which was significantly higher than neonates without neonatal sepsis (17.464±18%). Similarly, mean MPV was 10.604±0.95 vs. 8.894±0.85 and platelet count was 60.289±52.0 vs 212.030±162.6.

Neonatal sepsis, a serious systemic infection during the first 28 days of life, is a major cause of the morbidity and mortality of the newborns worldwide.[8] The very immature immune responses and limited physiological reserves, as well as constant exposure to maternal, environmental and health care-associated pathogens

make newborns especially vulnerable. Clinical signs are often subtle and vague such as poor feeding, temperature instability, lethargy, respiratory symptoms, apnea, altered perfusion, and glucose disturbances.[9] This often results in progressive deterioration, multi-organ failure, disseminated intravascular coagulation and death within 24 hours of onset.[10] Currently, more than half a million neonates per year die from neonatal infections, such as sepsis, pneumonia and meningitis, with the highest rates in low- and middle-income countries (LMICs).[11]

METHODS

This was an observational cross-sectional study carried out in Department of Pediatric Medicine, Sahiwal Teaching Hospital, Sahiwal from 1st February 2025 to 31st July 2025. The study was approved by CPSP/REU/PED-2022-143-7117, dated 17 January 2025. The sample size was determined using a sample-size calculator from the World Health Organization. The minimum sample size of 70 neonates was determined by selecting a 95% confidence level with absolute precision 0.05, based on the mean red cell distribution width of 18.366±2.1 in neonates with sepsis reported earlier.[7] All neonates, irrespective of gender, diagnosed to have neonatal sepsis and meeting the eligibility criteria, during the study period, were included. Neonates (1-28 days) of either sex were included if they were clinically and laboratory based diagnosed as neonatal sepsis within the defined criteria. Neonates born before 37 weeks gestation were excluded. Induced abortions and neonates with congenital anomalies, inborn errors of metabolism, severe neonatal jaundice, respiratory distress syndrome, surfactant deficiency or extremely low birth weight (<1 kg) were also excluded. Mothers with pregnancy induced hypertension (BP > or = 140/90 mmHg and dipstick proteinuria > +1) did not have their babies included. Neonates who had birth asphyxia (Apgar score less than 7 at 5 minutes) were also excluded. Demographic and clinical data were recorded. Data provided included neonatal age, sex, birth weight, current weight, mode of delivery, gestational age at birth, and site of birth, as well as the Apgar score at 5 minutes and whether the baby had been diagnosed with early- or late-onset neonatal sepsis. Venous blood samples were drawn from each neonate after performing aseptic measures and placed into an appropriate ethylenediaminetetraacetic acid tube. The sample was sent straight to the hospital laboratory for full blood count and haematological examination. The parameters that were measured were red cell distribution width, platelet distribution width, mean platelet volume, white blood cell count, red blood cell count, and platelet count. Any laboratory data obtained was documented. The main outcome was the nature of hematological abnormalities in neonates who were diagnosed with neonatal sepsis. The hematological parameters assessed were red cell distribution width, platelet distribution width, mean platelet volume, white blood cell count, red blood cell count and platelet count. These parameters were also compared among appropriate demographic and clinical subgroups.

The data was analyzed through SPSS-25. Normality of quantitative variables was determined by Shapiro-Wilk test. Neonatal age, birth weight, current weight, gestational age, Apgar score, RDW, PDW, MPV, WBC, RBC and platelet count, all quantitative variables, were presented as mean ± SD (normally distributed). Data that did not fit the normal distribution were presented as median (interquartile range). Qualitative data such as gender, mode of delivery, place of birth and type of neonatal sepsis were represented as frequencies and percentages. Data were stratified by the following variables: place of birth, birth weight, current weight, neonatal sepsis (early- and late-onset), gender, mode of delivery, gestational age at birth and Apgar score. Mean hematological parameters were compared between two groups after stratification using independent-samples t-test. One-way analysis of variance was used to make comparisons between more than two groups. When the data were not parametric the Mann-Whitney U test or the Kruskal-Wallis test were used. A p-value of <0.05 was deemed as statistically significant.

RESULTS

Their mean age was 11.6±7.4 days. Males were slightly more common, accounting for 39 (55.7%) neonates, while 31 (44.3%) were females. The mean birth weight was 2.78±0.46 kg, whereas the mean current weight was 2.69±0.45 kg. The mean gestational age at birth was 38.6±1.1 weeks, and the mean Apgar score at 5 minutes was 8.1±0.8. Vaginal delivery was reported in 41 (58.6%) cases and caesarean section in 29 (41.4%). Most neonates were hospital-born, 44 (62.9%), while 26 (37.1%) were home-born (Tables 1-2).

Table No. 1: Baseline demographic and clinical characteristics of neonates with sepsis (n=70)

Variable	No.	%
Gender		
Male	39	55.7
Female	31	44.3
Clinical characteristics		
Vaginal delivery	41	58.6
Caesarean section	29	41.4
Hospital-born	44	62.9
Home-born	26	37.1
Early-onset sepsis	42	60.0
Late-onset sepsis	28	40.0

The mean red cell distribution width was 18.42±2.16%, with values ranging from 14.2% to 23.8%. The mean platelet distribution width was 16.91±2.37 fL, ranging

from 12.1 to 22.4 fL, while the mean platelet volume was 10.84±1.29 fL, with a range of 8.1-13.9 fL. The mean white blood cell count was 17.62±6.84 $\times 10^9$/L and ranged from 4.2 to 34.8 $\times 10^9$/L. The mean red blood cell count was 4.36±0.71 $\times 10^{12}$/L, with values between 2.8 and 5.9 $\times 10^{12}$/L (Table 3).

Table No. 2: Descriptive statistics of neonates with sepsis (n=70)

Variable	Mean±SD
Age (days)	11.6±7.4
Birth weight (kg)	2.78±0.46
Current weight (kg)	2.69±0.45
Gestational age (weeks)	38.6±1.1
Apgar score at 5 minutes	8.1±0.8

Raised platelet distribution width was present in 39 (55.7%), while raised mean platelet volume was identified in 34 (48.6%) cases. An abnormal total white blood cell count was found in 38 (54.3%) neonates, including leukocytosis in 27 (38.6%) and leukopenia in 11 (15.7%). A low red blood cell count was recorded in 22 (31.4%) neonates. Thrombocytopenia was present in 29 (41.4%) cases, including severe thrombocytopenia in 8 (11.4%) [Table 4].

The mean red cell distribution width was significantly higher in late-onset than early-onset sepsis, at 19.18±2.27% versus 17.91±1.94% (p=0.015). Similarly, platelet distribution width was higher in late-onset sepsis, 17.86±2.45 fL compared with 16.28±2.11 fL (p=0.006), while mean platelet volume was 11.47±1.22 fL versus 10.42±1.17 fL (p=0.001). The mean platelet count was significantly lower in late-onset sepsis than in early-onset sepsis, 148.9±76.2 $\times 10^9$L versus 194.8±75.4 $\times 10^9$/L (p=0.015) [Table 5].

The mean red cell distribution width was significantly higher than that of neonates weighing 2.5 kg or more, 19.41±2.28% versus 18.08±2.02% (p=0.021). The mean red blood cell count was significantly lower in the low-birth-weight group, 4.05±0.73 $\times 10^{12}$/L compared with 4.47±0.67 $\times 10^{12}$/L (p=0.028). Similarly, the mean platelet count was lower in neonates weighing below 2.5 kg, 139.3±70.1 $\times 10^9$/L versus 189.2±77.6 $\times 10^9$/L (p=0.018) [Table 6].

Table No. 3: Hematological parameters among neonates with sepsis (n=70)

Hematological parameter	Mean±SD	Minimum–Maximum
Red cell distribution width (%)	18.42±2.16	14.2-23.8
Platelet distribution width (fL)	16.91±2.37	12.1-22.4
Mean platelet volume (fL)	10.84±1.29	8.1-13.9
White blood cell count ($\times 10^9$/L)	17.62±6.84	4.2-34.8
Red blood cell count ($\times 10^{12}$/L)	4.36±0.71	2.8-5.9
Platelet count ($\times 10^9$/L)	176.4±78.6	38-356

Table No. 4: Frequency of hematological abnormalities among neonates with sepsis (n=70)

Hematological abnormality	No.	%
Raised red cell distribution width	46	65.7
Raised platelet distribution width	39	55.7
Raised mean platelet volume	34	48.6
Leukocytosis	27	38.6
Leukopenia	11	15.7
Abnormal total white blood cell count	38	54.3
Low red blood cell count	22	31.4
Thrombocytopenia	29	41.4
Severe thrombocytopenia	8	11.4

Table No. 5: Comparison of hematological parameters according to type of neonatal sepsis

Parameter	Early-onset sepsis (n=42)	Late-onset sepsis (n=28)	p-value
Red cell distribution width (%)	17.91±1.94	19.18±2.27	0.015
Platelet distribution width (fL)	16.28±2.11	17.86±2.45	0.006
Mean platelet volume (fL)	10.42±1.17	11.47±1.22	0.001
White blood cell count ($\times 10^9$/L)	18.54±6.41	16.24±7.35	0.171
Red blood cell count ($\times 10^{12}$/L)	4.48±0.68	4.18±0.72	0.083
Platelet count ($\times 10^9$/L)	194.8±75.4	148.9±76.2	0.015

Table No. 6: Comparison of hematological parameters according to birth weight

Parameter	Birth weight <2.5 kg (n=18)	Birth weight ≥2.5 kg (n=52)	p-value
Red cell distribution width (%)	19.41±2.28	18.08±2.02	0.021
Platelet distribution width (fL)	17.78±2.51	16.61±2.26	0.069
Mean platelet volume (fL)	11.34±1.31	10.67±1.25	0.054
White blood cell count ($\times 10^9$/L)	16.13±6.94	18.13±6.79	0.283
Red blood cell count ($\times 10^{12}$/L)	4.05±0.73	4.47±0.67	0.028

Platelet count ($\times 10^9$/L)	139.3±70.1	189.2±77.6	0.018

DISCUSSION

In the present study, the authors showed that neonates with neonatal sepsis had hematological abnormalities. The most common abnormalities were raised red cell distribution width (65.7%), abnormal total white blood cell count (54.3%), raised platelet distribution width (55.7%), raised mean platelet volume (48.6%) and thrombocytopenia (41.4%). The observations suggest the widespread impact of neonatal sepsis on red cells, white cells and platelets and reinforce the use of commonly available hematological parameters in the evaluation of affected neonates. The mean age of the study population was 11.6±7.4 days and 60.0% of cases were early onset sepsis. Such an excess could be due to maternal and perinatal transmission of infection in early neonatal period. Neonatal sepsis can cause a rapid onset of respiratory and systemic signs and symptoms because of underdeveloped immune system and reduced physiological reserves. Increased early onset sepsis is also highlighting the need for maternal risk assessment, as well as aseptic delivery and early postnatal surveillance.[12] Almost 2/3 of the neonates had elevated RDW levels, and the total mean RDW was 18.42±2.16%. RDW measures the variation in size of RBC and may rise in response to alterations in red cell survival, hemolysis, oxidative stress, impaired erythropoiesis or inflammation. Systemic infection may interfere with iron metabolism and may impair function of the bone marrow, leading to a release of cells of varying sizes into the blood. The present study showed elevated levels of RDW occurred frequently; this indicates that RDW might be a valuable supportive marker of haematological stress in neonatal sepsis. The mean RDW was also significantly higher in late onset compared to early onset sepsis (19.18±2.27% vs. 17.91±1.94%). This may be due to a longer period of inflammatory exposure, extended hospitalisation, repeated blood sampling, nutritional disturbances or the severity of illness in neonates with late onset infection. Late-onset sepsis is also linked to the use of healthcare-related organisms and is more likely to be associated with invasive procedures that could result in a greater systemic inflammatory response. Platelet indices also were significantly modified.[13] The mean platelet distribution width was 16.91±2.37 fL, while the mean platelet volume was 10.84±1.29 fL. 55.7% neonates had raised PDW and 48.6% had raised MPV. These indices measure the size of platelets and the release of newer and larger platelets from the bone marrow. Sepsis can trigger platelet activation, consumption, endothelial damage, and inflammatory cytokines, which can lead to the production of larger platelets. Thus, elevated MPV and PDW can be a sign of the elevated platelet turnover and inflammation.[14] Both PDW and MPV were significantly higher among neonates with late-onset sepsis. Mean PDW increased from 16.28±2.11 fL in early-onset sepsis to 17.86±2.45 fL in late-onset sepsis, while MPV increased from 10.42±1.17 fL to 11.47±1.22 fL. These results indicate that platelet activation and consumption may be increased in the late onset disease. Additionally, the more significant shifts in platelet indices could be due to a longer duration of infection, invasive procedures, and increased severity of illness.[15]

The rate of neonates with thrombocytopenia was 41.4% and severe thrombocytopenia was 11.4%. Sepsis can decrease platelets in a variety of ways: peripheral destruction, platelet consumption, endothelial activation, disseminated intravascular coagulation, immune-mediated destruction, and decreased bone-marrow production. The clinical significance of thrombocytopenia is that it may be associated with greater bleeding tendency and more severe infections. The mean platelet count was significantly lower in late-onset and early-onset sepsis groups and was 148.9±76.2 $\times 10^9$/L and 194.8±75.4 $\times 10^9$/L respectively. This is again evidence of more platelet consumption in the late onset disease. Neonatal anemia (RBC <4.5 x 106/ul) was found in 31.4% of the neonates.[16] The anemia or decrease in RBC in neonatal sepsis may result from depressed erythropoiesis, hemolytic process, shortened red cell survival, multiple phlebotomy, bleeding or nutritional deficits. The mean RBC count was also lower in late onset sepsis, but this did not achieve statistical significance. The lack of significance could be due to the relatively small number of infants studied, disease duration, or because very premature and extremely low birth neonates were excluded, which are more susceptible to anemia.[17]

The results of the present study have clinical relevance, as these are the parameters that are currently available in the routine laboratory examination of automated analysis of complete blood count These parameters are cost-effective and can be measured quickly, which is useful in situations where use of advanced biomarkers or rapid microbiological tests is restricted. None of these indices, however, are stand-alone and should not be used alone.[18] The most important use of these is to complement clinical evaluation, to facilitate the identification of high-risk neonates, and to monitor for changes occurring while in treatment. Late onset sepsis was associated with increased RDW, PDW, and MPV and decreased platelet count, thus indicating that platelet and red cell indices might be indicators of the severity or duration of systemic inflammation. Likewise, the low-birth-weight neonates had poorer hematological data, which further underscores the need to closely monitor this vulnerable population. A single value may not be as informative as serial measurements, which can show a trend of progression, treatment response or complication.[19,20]

CONCLUSION

Hematological abnormalities were common among neonates diagnosed with neonatal sepsis. Raised red cell distribution width was the most frequent finding, while altered platelet indices, abnormal white blood cell count, reduced red blood cell count, and thrombocytopenia were also frequently observed. Neonates with late-onset sepsis had significantly higher red cell distribution width, platelet distribution width, and mean platelet volume, together with a lower platelet count, indicating more pronounced hematological disturbance. Low-birth-weight neonates also showed higher red cell distribution width and lower red blood cell and platelet counts.Routine complete blood count parameters may therefore provide useful and readily available supportive information in the assessment of neonatal sepsis, particularly where advanced diagnostic facilities are limited.

Limitations: This was undertaken in one centre, and the relatively small number of children may restrict the findings to a relatively small population. The cross-sectional design did not permit the evaluation of time course changes in hematological parameters nor the relationship of the parameters to treatment response. The study did not include any septic neonates in a non-septic control group and there was no assessment of microbiological organisms, inflammatory biomarkers, disease severity, transfusion history or mortality outcome. There were also some hematological abnormalities that could have been affected by nutritional status, maternal factors or undiagnosed clinical conditions.

Author's Contribution:

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Drafting or Revising Critically:	Nimra Gull, Muhammad Yasin
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