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Evaluation of Platelet Indices and Sepsis Markers in Neonates with Different Types of Sepsis

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ABSTRACT

Sepsis in neonates was the main reason for morbidity and mortality globally, primarily in developing countries. The World Health Organization (WHO) approximates that sepsis affects approximately 3 million neonates annually, causing about 750,000 deaths. Platelet indices such as Platelet Crit distribution width (PCT), Platelet Width Volume (PWV), and Mean Platelet Distribution (MPD) were considered major biomarkers for diagnosis. **Objective:** To evaluate the alterations in platelet indices and septic markers (CRP) in neonates with sepsis as compared to established reference values. **Methods:** This cross-sectional study was conducted at the Department of Hematology and Transfusion Medicine in the Children's Hospital and University of Child Health Sciences, Lahore, from November 2023 to February 2024. 57 neonates of the Neonatal Intensive Care Unit (ICU) were sampled. Platelet indices, including PCT, PDW, MPV, and C-reactive protein (CRP), were measured using automated hematology analyzers. Data were analyzed by using SPSS V-23.0. One sample T-test was used to compare the means with the reference value. **Results:** The mean platelet count was significantly lower. MPV and PDW were significantly elevated in neonates with sepsis compared to the reference value, while PCT was considerably lower. CRP levels were significantly elevated in neonates with sepsis. **Conclusions:** This study concluded that platelet indices and CRP levels were valued biomarkers for diagnosing and treating neonatal sepsis. These well-established inflammatory markers suggest a strong systemic inflammatory response typically associated with sepsis.

INTRODUCTION

Sepsis in neonates is one of the main causes of morbidity and mortality globally, particularly in developing and underdeveloped countries, where it causes a quarter of all neonatal deaths [1]. It is estimated by the WHO that around 3 million newborns are affected by sepsis every year, leading to about 750,000 mortalities [2]. Platelets have a very vital role not only in blood clotting but also in the body's immune response to infections [3]. Low platelet count (Thrombocytopenia), is often associated with neonatal sepsis [4, 5]. Studies identify that 20% to 49% of neonates develop thrombocytopenia with sepsis, depending upon the severity of their condition [6]. Low platelet count in neonatal sepsis is a marker of disease seriousness, with exaggerated thrombocytopenia signifying worse results [7]. Despite platelet count, specific markers like mean MPV, PDW, and PCT are used for early diagnosis of neonatal sepsis [8-10]. The average size of platelets, MPV, is increased during infections as more reactive and larger platelets are produced in bone marrow [11]. Literature suggests that septic newborns have increased MPV levels than healthy ones, suggesting it can be a useful marker for predicting sepsis [12]. Current research demonstrated that neonates with sepsis had pointedly higher MPV levels related to healthy controls, signifying its utility as a predictive marker [13]. PDW, which looks at variations in platelet size, has also been explored as a diagnostic tool for neonatal sepsis [10]. An increase in PDW may indicate the production of immature or abnormal platelets, driven by inflammatory responses during sepsis, like those caused by interleukin-6 and tumor necrosis factor-α [11]. Several

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studies have found a positive link between higher PDW and neonatal sepsis, further emphasizing its potential role in early diagnosis [12]. PCT is another marker that measures the percentage of blood volume made up of platelets. It may help to evaluate the risk of sepsis-associated complications. Although there are limited studies on PCT in neonatal sepsis, early outcomes suggest that low PCT values may indicate high risks of complications. As it states its role in platelet function and turnover, PCT may help evaluate platelet utilization in septic neonates. The availability of advanced laboratory services in tertiary care hospitals allows for complete evaluations of platelet indices, enabling early diagnoses and management of sepsis in tertiary care hospitals [13]. Diagnosis and initial treatment are important, decreasing sepsis-associated problems, yet aggravating due to general clinical indications [14]. This has enforced research into biomarkers that can help in the primary detection and management of neonatal sepsis, with platelet indices and platelet count developing as major parameters [15].

However, despite the availability of such possessions, neonatal sepsis remains an important risk in tertiary care hospitals, mainly in Low and Middle-Income Countries (LMICs). Considering the link between platelet indices, platelet count, and sepsis in such situations is important for refining clinical outcomes. The objective of this research was to evaluate the alterations in platelet indices and septic markers (CRP) in neonates with sepsis compared to established reference values.

METHODS

This cross-sectional study was conducted at the Department of Hematology and Transfusion Medicine in the Children's Hospital and University of Child Health Sciences, Lahore from November 2023 to February 2024. Data were collected from neonates of the neonatal Intensive Care Unit (ICU) of Children's Hospital, Lahore. Patients' guardian consent was taken before sample withdrawal. A consecutive sampling technique was used to collect data from 57 neonates in the neonatal ICU. The sample was calculated as follows:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Confidence Interval = Z = 1.96, Prevalence = p = 28.6% = 0.286, Margin of error = d = 11.7% = 0.117, n = 57 [16]. Postnatal age from birth to 28 days and neonates with signs and symptoms of sepsis, along with either positive culture or other laboratory findings suggestive of bacterial infection without positive culture, were included in the study. At the same time, Neonates with congenital anomalies or congenital and acquired causes of thrombocytopenia other than sepsis were excluded from the study. After approval from the IRB (1256/SAHS), data from neonatal patients admitted to the hospital will be gathered. We extracted roughly 2 milliliters of venous blood from each newborn via peripheral veins into an ethylene diamine tetra acetic acid tube for these assays. Peripheral blood smears were prepared, stained with Leishman's stain, and analyzed to verify thrombocytopenia. An automated device (Sysmex XE 2100, Celltac, and Celltac g) was used to gather platelet indices. Gram staining and blood culture were used to identify bacterial and fungal organisms. Clinical evaluations and a thorough history from the mother were used to assess the newborns. Every infant had peripheral venous blood drawn, which was then sent for testing for platelets, platelet indices, CRP, and blood cultures. Data were entered and analyzed using IBM SPSS version 23.0. Continuous variables such as age, platelet count, MPV, PDW, and PCT were described as mean SD, whereas categorical variables like gender were described as frequencies and percentages. One sample T-test was used to compare the means of controls and cases. P-values less than 0.05 were taken as statistically significant. Ethical clearance was obtained from the ethical committee of the School of Allied Health Sciences, Children's Hospital and Institute of Child Health (ICH), Lahore.

RESULTS

Table 1 showed that 47 neonates were able to tolerate oral feeding with 50-100 ml of milk, while 10 tolerated 100-150 ml. Additionally, 41 neonates were admitted to the NNE Ward, and 16 were admitted to the Special Newborn Intensive Care Unit (NICU).

Table 1: Feeding Tolerance and Ward Distribution of Neonates with Sepsis

Feeding Tolerance (Milk Volume)	Number of Neonates
50–100 ml	47
100–150 ml	10
Ward Locations	**Number of Neonates**
NNE Ward	41
Special Newborn Intensive Care Unit (NICU)	16

The mean platelet count in neonates with sepsis was significantly lower than the reference value ($p < 0.001$). This reduction in platelet count (thrombocytopenia) could be associated with the systemic inflammatory response seen in sepsis. MPV was significantly elevated in neonates with sepsis compared to the reference value ($p < 0.001$). An increased MPV suggests larger platelet size, potentially indicating platelet activation and destruction, which was commonly observed in sepsis. PDW was significantly higher than the reference value ($p < 0.001$). Elevated PDW reflects increased variability in platelet size, indicating platelet activation, which may occur due to the inflammatory process in sepsis. The PCT was significantly lower than the reference value ($p < 0.001$). This reduced platelet crit indicated a lower total platelet mass in the blood, which could be due to decreased platelet production or increased destruction, commonly observed in septic neonates. CRP levels were significantly elevated in

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neonates with sepsis ($p < 0.001$). CRP was a well-established inflammatory marker, and its marked elevation suggests a strong systemic inflammatory response typically associated with sepsis (Table 2).

Table 2: One-Sample t-Test: Neonatal Sepsis Variables versus Reference Values

Variables	Reference Value	Mean ± SD	p-Value	Mean Difference	95% C.I of Difference (L)	95% C.I of Difference (U)
Platelets (Lac/µL)	3	2.246 ± 1.106	<0.001	-0.754	-1.048	-0.461
MPV (fL)	9	11.074 ± 1.247	<0.001	2.074	1.743	2.405
PDW (%)	13.5	18.337 ± 1.144	<0.001	4.837	4.533	5.14
PCT (%)	0.23	0.113 ± 0.089	<0.001	-0.117	-0.141	-0.093
CRP (mg/L)	6	32.066 ± 14.012	<0.001	26.066	22.348	29.784

Neonatal patients were classified into three groups based on culture: gram-positive culture, gram-negative culture, and fungal sepsis. The test examines several parameters: weight, platelet count, platelet count (MPV), Platelets Distribution Width (PDW), Platelet Crit (PCT), and C-Reactive Protein (CRP). The average number of platelets was slightly higher in gram-negative cultures (2.30) compared to gram-positive cultures (2.11), and fungal sepsis was (2.50). The p-value of 0.803 indicated no statistically significant difference in platelet count. Platelet count alone does not significantly vary with the type of sepsis, indicating that it may not be a strong standalone marker for differentiating between the types of sepsis. MPV was slightly higher in the Gram-positive culture (11.49 fl) compared to the Gram-negative culture (10.86 fl) and fungal sepsis (11.30 fl). The p-value of 0.201 suggests that the differences in MPV across the groups were not statistically significant. MPV does not show a strong correlation with the type of sepsis in neonates. DW was highest in the fungal sepsis group (19.45%), followed by the gram-positive culture (18.82%) and gram-negative culture (18.04%). The p-value of 0.021 indicated a statistically significant difference in PDW among the groups. PDW appears to be a more sensitive marker in differentiating between the types of neonatal sepsis. Higher PDW values might be associated with more severe or different types of infections, such as fungal sepsis. PCT was higher in the Gram-negative culture group (0.13%) compared to the Gram-positive culture (0.08%) and fungal sepsis (0.04%). A p-value of 0.039 indicated a statistically significant difference in PCT between the groups. PCT indicated that there is a significant difference between sepsis types, suggesting that this may be a valuable marker for evaluating severe or characteristic neonatal sepsis. CRP levels were highest in the fungal sepsis group (51.69 mg/l), Gram-positive culture (36.66 mg/l), and Gram-negative culture (28.77 mg/L). A P-value of 0.016 indicated a statistically significant difference in CRP levels. CRP was an important marker in this study, with elevated levels potentially indicative of more serious or specific infections, especially in cases of fungal sepsis. PDW, PCT, and CRP were the main parameters showing statistically significant differences in neonates of different types of sepsis. These findings suggest that these markers might be useful in clinical settings to differentiate between types of neonatal sepsis and potentially to assess the severity of the condition. Platelet count and MPV do not exhibit significant differences across the groups, indicating that they might not be as effective in distinguishing between different types of neonatal sepsis (Table 3).

Table 3: Comparison of Platelet Count, and Platelet Indices across Different Types of Neonatal Sepsis

Characteristics	N	Mean ± SD	p-Value
CRP (mg/L)			
Gram Positive Culture	18	36.66 ± 12.44	0.016
Gram Negative Culture	37	28.77 ± 13.76	
Fungal Sepsis	2	51.69 ± 0.40	
Total	57	32.07 ± 14.01	
Platelets (Lac/µL)			
Gram Positive Culture	18	2.11 ± 0.83	0.803
Gram Negative Culture	37	2.30 ± 1.24	
Fungal Sepsis	2	2.50 ± 0.71	
Total	57	2.25 ± 1.11	
MPV (fL)			
Gram Positive Culture	18	11.49 ± 1.34	0.201
Gram Negative Culture	37	10.86 ± 1.14	
Fungal Sepsis	2	11.30 ± 2.12	
Total	57	11.07 ± 1.25	
PDW (%)			
Gram Positive Culture	18	18.82 ± 0.83	0.021
Gram Negative Culture	37	18.04 ± 1.20	
Fungal Sepsis	2	19.45 ± 0.21	
Total	57	18.34 ± 1.14	
PCT (%)			
Gram Positive Culture	18	0.08 ± 0.05	0.039
Gram Negative Culture	37	0.13 ± 0.10	
Fungal Sepsis	2	0.04 ± 0.03	
Total	57	0.11 ± 0.09	

Platelet count has a weak positive correlation with PCT ($r = 0.242$, $p = 0.070$) and MPV ($r = 0.108$, $p = 0.423$), though these correlations were not statistically substantial. The weak negative association with PDW ($r = -0.247$, $p = 0.064$) suggests that higher platelet counts might be related to lower PDW, but this relationship was also not statistically significant. The correlation between platelet count and CRP was minimal ($r = -0.065$, $p = 0.632$), indicating no meaningful relationship between these two parameters. Overall, the platelet count does not show strong or significant correlations with the other parameters, suggesting that while the platelet count was an important

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marker, it may not directly correlate with these specific platelet indices or CRP levels in neonatal sepsis (Table 4).

Table 4: Correlation of Platelet Count with Sepsis Markers in Neonates

Variables	Platelets (Lac/µL)	MPV (fL)	PDW (%)	PCT (%)	CRP (mg/L)
Platelets (Lac/µL)					
Pearson Correlation	1.000	0.108	-0.247	0.242	-0.065
Significant (2-Tailed)	-	0.423	0.064	0.070	0.632
MPV (fL)					
Pearson Correlation	0.108	1.000	0.468	-0.546	0.118
Significant (2-Tailed)	0.423	-	0.000	0.000	0.380
PDW (%)					
Pearson Correlation	-0.247	0.468	1.000	-0.546	0.050
Significant (2-Tailed)	0.064	0.000	-	0.000	0.714
PCT (%)					
Pearson Correlation	-0.247	0.468	1.000	-0.546	0.050
Significant (2-Tailed)	0.064	0.000	-	0.000	0.714
CRP (mg/L)					
Pearson Correlation	-0.065	0.118	0.050	-0.164	1.000
Significant (2-Tailed)	0.632	0.380	0.714	0.222	-

DISCUSSION

The present research offers important results on platelet count, such as Platelet Width Volume (PWV), Platelet Crit distribution width (PCT), Mean Platelet Distribution (MPD), and CRP (C-Reactive Protein) in neonates with sepsis. These factors, presentation deviations from the mention values, were reliable with movements detected in current reports, representing their position in the monitoring and diagnosis of neonatal sepsis. The decreased platelet counts in this research (mean: 2.246 lacs/µL) relates to the mean value of 3 lacs/µL, providing the well-standard suggestion between neonatal sepsis and thrombocytopenia. Research such as Toro-Huamanchumo CJ et al., have stated that 20-70% of neonates with sepsis progress to thrombocytopenia reliant on the severity of the infection. Thrombocytopenia happens due to augmented platelet utilization, frequently as a result of disseminated intravascular coagulation (DIC), a general problem of sepsis [17]. The pointedly raised MPV (mean: 11.074 fL) detected in this report was consistent with the results of Kristopher May Pamudji and colleagues, who proved that a rise in MPV showed the issue of greater, more responsive, and early platelets from the bone marrow in response to systemic infection [18]. This rise in MPV proposes augmented platelet yield and a responsive thrombocytosis usually seen during septic situations. Thus, MPV can assist as a marker of infection and inflammation severity in neonates with sepsis. Also, the raised PDW values in the study (mean: 18.337%) align with those stated in Wu J *et al.*, in 2019, where a rise in PDW was related to better variability in platelet size, showing higher platelet destruction and production during sepsis [19]. The important change in PDW among diverse sepsis forms in this report ($p = 0.021$) provides the hypothesis that PDW can help as a sensitive marker in distinguishing between forms of neonatal sepsis, mainly fungal infections. Our study also obtained a momentous decrease in PCT (mean: 0.113%) related to the mentioned value of 0.23%, with a p-value of 0.039, representing statistical importance. Low PCT in neonates with sepsis showed decreased platelet count due to high platelet utilization, mainly in severe infections. The variations in PCT among sepsis emphasize its value in evaluating the severity of the state and the level of platelet demolition in neonatal sepsis [20]. CRP stages in this report (mean: 32.066 mg/L) were markedly increased, particularly in fungal sepsis cases (mean: 51.69 mg/L), aligning with results from Eichberger J et al., who stated that increased CRP points relate with greater infection severity. Raised CRP was a well-recognized marker for fungal and bacterial infections, making it a consistent indicator for monitoring and diagnosing neonatal sepsis [21].

CONCLUSIONS

In conclusion, the study's findings confirm that the platelet indices, such as MPV, PDW, and PCT, along with CRP, were valuable in diagnosing and differentiating between types of neonatal sepsis. These markers provide clinicians with critical insights into the severity and nature of the infection, improving neonatal sepsis management and outcomes.

Authors Contribution

Conceptualization: HA
Methodology: HA, TL, MS
Formal analysis: TL
Writing, review and editing: TL, MS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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