Original Article

Diagnostic Utility of Platelet Indices in Neonatal Sepsis: Marker for Early Detection

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Abstract

Background: Neonatal sepsis is one of the most significant cause of morbidity and cause of death in the world, especially in low-resource countries. Traditional diagnostic procedures like blood culture can be time consuming and may not be sensitive in the neonate. Thus, fast, affordable, and efficient diagnostic markers are in high demand. Platelet indices such as platelet count, mean platelet volume, platelet distribution width and plateletcrit have received interest as possible early biomarkers of neonatal sepsis. The study objective was to identify the diagnostic utility of platelet indices in suspected sepsis neonates and to identify their accuracy relative to conventional diagnostic characteristics. **Material and Methods:** A 1-year prospective observational study was developed and included neonates suspected of sepsis who were less than 28 days. Demographic and risk factors were observed. Venous blood samples were collected for complete blood count including platelet indices. As the reference standards, C-reactive protein and blood culture were mentioned. Diagnostic performance was identified using receiver operating characteristic analysis that estimated the sensitivity, specificity, and the area under the curve. **Results:** One hundred and twenty neonates were involved, 70 of them were septic and 50 were controls (non-septic). Infants with septicemia had significantly less levels of platelets [124.5 + 48.6 vs. 215.3 + 52.4 x 109/L, p<0.001] and plateletcrit [0.18 + 0.07 vs. 0.27 + 0.09% x 100, p=0.001], and significantly higher values of MPV [11.2 + 1.8 vs. 9.1 + 1.5. **Conclusion:** Platelet indices, particularly, MPV and PDW, are highly diagnostic of neonatal sepsis, and may be utilized as rapid and inexpensive supplemental diagnostic methods. They may be included in the normal sepsis screening programs that can identify them early, treat them promptly and achieve improved final neonatal outcomes.

Keywords: Neonatal sepsis; Platelet indices; Mean platelet volume; Platelet distribution width; Plateletcrit (PCT); Hematological markers.

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Introduction

Neonatal sepsis remains among the greatest health burden in the world and a primary contributor to morbidity and mortality in infants, particularly in developing nations. Timely and proper diagnosis is a key step towards mitigating the risks involved and ensures timely therapeutic measures are undertaken. Although there has been progressive development in neonatal intensive care, non-specific nature of clinical presentation of sepsis tends to create delay in diagnosis, consequently increasing mortality rates. Traditional diagnostic methods like blood culture are still the gold standard, but time-consuming, low sensitivity in neonates, and costly in terms of lab facilities as they are usually largely unavailable in resource-limited regions.[1]

In this context, hematological parameters are increasingly being investigated as potential contributors to the early detection of neonatal sepsis. Among them, the platelet counts, mean platelet volume [MPV], platelet distribution width [PDW], and plateletcrit [PCT] platelet indices have been shown to be potentially useful diagnostic markers.[2] Automated hematology analyzers can provide such indices automatically at no additional cost and can readily become part of clinical practice. The fact that these indices are a subset of complete blood count makes them cheap and easily available to neonatal intensive care units [NICUs], particularly in low-resource settings.

Evidence has been given in some studies, that thrombocytopenia is a common phenomenon in neonatal sepsis. This is due to an increased use of platelets, reduced bone marrow production, and damage by sepsis-related disseminated intravascular coagulation. Consequently, platelet count alone may serve as a predictor of sepsis, but platelet morphology and turnover data, such as MPV and PDW can provide valuable information that may enhance the diagnostic accuracy.[3]

Studies have also shown that platelet indices differ widely in relation to septic and non-septic infants. As an example, when more destruction occurs, MPV tends to increase in response to the release of immature and larger platelets. Likewise, PDW anisocytosis of platelet size and is likely to rise during sepsis. Such changes have been observed to be associated with severity

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and prognosis of disease.[4] Moreover, another parameter, plateletcrit, which represents the overall mass of platelets, has also been suggested as a practical screening tool in neonatal sepsis.

There are various benefits of platelet indices as a form of early detection compared to more conventional biomarkers, including C-reactive protein [CRP] and procalcitonin. CRP and procalcitonin are expensive, need specific assays, and are not always available in peripheral centers, although both are widely used. In addition, they tend to increase towards the end of the infection, limiting their use in the very early diagnosis. In comparison, platelet indices are immediately accessible in the form of standard hematology tests and could generate initial evidence that allows making clinical decisions in a short period of time.[5]

Recent studies have established that platelet indices when used together with traditional biomarkers are very effective in enhancing diagnostic accuracy. Indicatively, a high MPV and PDW, in combination with CRP positivity, have demonstrated excellent sensitivity and specificity of sepsis in neonates.[6] This indicates that platelet indices may be a useful addition to conventional sepsis screening practices where diagnostic time is minimized. Moreover, platelet indices have been pointed out as useful prognostics in literature where some platelet indices were significantly associated with sepsis outcomes, such as mortality risk.[7]

In the world, the reduction of neonatal mortality is being done as a sustainable development goal [SDGs]. Here, inexpensive, fast, and dependable diagnostic equipment is needed. Platelet indices meet this requirement and can be considered as good candidates to be applied on a large scale. They also provide clinicians in the NICUs with a useful tool to distinguish between septic and non-septic neonates at admission and throughout the monitoring periods.[8]

Several prospective studies and retrospective studies indicate that platelet indices have a diagnostic value in neonatal sepsis. It was also shown in a prospective case-control design that the platelet counts of the septic neonates were significantly lower than those of the controls, and the MPV and PDW are also elevated, which may be adopted as cost-effective diagnostic methods.[4] A second study has confirmed that abnormal platelet index existed long before alterations in the white blood cell count; this indicates that they might be used to detect infection at an earlier stage.[1]

The pathophysiology of these changes is associated with the complicated host reaction to infection. Platelets are consumed and destroyed during systemic inflammation caused by neonatal sepsis and usually by bacterial toxins, damage of endothelium, and disseminated intravascular coagulation. Meanwhile, bone marrow reacts and releases younger and larger platelets, which are measured in high MPV values. There is also increased PDW which indicates heterogeneity in platelet size associated with consumption and compensatory production. Combined, these index changes give indirect evidence of the ongoing infectious and inflammatory process.[2,3]

Platelet indices are not used only in the diagnosis. Some studies have proposed a prognostic role of very abnormal platelet indices, meaning that high platelet indices in septic neonates are linked to high mortality. As an example, the children with sepsis that demonstrated a very intensive increase of the PDW and a reduction of platelets had even worse outcomes, that is why these parameters could be utilized to identify sepsis and to determine the severity of the disease.[7] Such studies can be helpful in making therapeutic decisions and allocating resources to intensive care units more efficiently.

Although the literature is consistent on the correlation between platelet indices and sepsis, some limitations still exist. Conditions that are not related to infection, including intrauterine growth restriction, perinatal asphyxia, or maternal hypertension may affect platelet indices. Cut-off values are also not easily established due to variability in analyzer technology and laboratory reference ranges. Moreover, some of the current studies are small single-center studies that do not allow generalization due to limited sample size.[5,6] These constraints point to the necessity of bigger, multicenter studies to confirm platelet indices as useful diagnostic indicators in the context of diverse populations.

However, platelet indices when used as part of clinical evaluation in association with other biomarkers like CRP, procalcitonin or blood culture results significantly enhance their diagnostic precision. Incorporating such indices into the regular sepsis screening guidelines might contribute to decreasing the use of costly assays and addressing delays linked to culture methods.[6] This kind of integration is highly useful in resource constrained environments where high-level diagnostic modalities do not exist.

The growing body of evidence shows that platelet indices are clinically relevant in neonatal sepsis. They can be used in sepsis screening to minimize delays in diagnostics, improve treatment initiation and ultimately reduce neonatal morbidity and mortality. Platelet indices as an addition to the existing diagnostic methods are a deserving candidate based on their availability, affordability, and timely nature.

It is on this basis that the present study will evaluate the diagnostic usefulness of platelet indices, i.e., platelet count, mean platelet volume, and platelet distribution width, in the diagnosis of early-stage neonatal sepsis. The study will determine the usefulness of such indices as a dependable, economical, and convenient diagnostic marker that can be applied routinely in neonatal intensive care units by systematically analyzing them and comparing with standard diagnostic markers.[8]

Materials and Methods

Study design: The study was designed to include neonates clinically suspected of sepsis, as this approach allowed for a systematic evaluation of clinical and laboratory findings without the need for interventional procedures. One year was considered as the time of study. Informed consent was assumed to be part of the standard procedure of neonatal research, and ethical principles were adhered to.

Study Population: Neonates whose features raised the possibility of sepsis were included. The perinatal risk factors that led to suspicion of sepsis included: prolonged rupture of membranes, maternal fever, foul liquor and neonatal signs included respiratory distress, poor feeding, lethargy, hypothermia and irritability.

Inclusion Criteria

- Neonates aged ≤28 days with suspected sepsis.
- Complete blood count including platelet indices available at the time of evaluation.

Exclusion Criteria

- Neonates with congenital anomalies or genetic syndromes.
- Cases of thrombocytopenia due to non-infectious causes such as maternal hypertension or intrauterine growth restriction.
- Neonates already on antibiotics for more than 48 hours before enrollment.

Sample Size

The total population of the study was 120 neonates. Out of them, 70 were categorized as septic due to clinical suspicion with reference to culture and/or CRP findings whereas 50 were non-septic controls.

Data Collection and Investigations

Venous blood samples were obtained under sterile precautions at the time of evaluation. The following investigations were performed:

- Complete Blood Count [CBC]: Platelet count, mean platelet volume [MPV], platelet distribution width [PDW], and plateletcrit [PCT].
- Sepsis Marker: C-reactive protein [CRP].
- Blood Culture: Considered as the gold standard for confirmation of sepsis.

Demographic details such as gestational age, sex, and birth weight were also recorded in a structured formatational.

Definitions

1. Neonatal Sepsis

Neonatal sepsis was defined as a systemic illness in infants under 28 days of age, presenting with clinical features such as respiratory symptoms, feeding difficulties, hypothermia, lethargy, or irritability, along with supportive laboratory findings. A positive blood culture and/or elevated CRP levels, in the presence of these symptoms, were considered sufficient to classify a case as sepsis. This macro-operational definition was adopted in order to include both culture-proven and clinically evident cases of sepsis.

2. Platelet Indices

These are computerized hematological parameters which have been acquired in a complete blood count. These are the platelet count, mean platelet volume, platelet distribution width, and plateletcrit. These are free, easily accessible adjuncts to sepsis assessment and have been demonstrated to be related to the severity of the disease.

3. Early-Onset and Late-Onset Sepsis

Sepsis in infants within the first 72 hours of infant life was referred to as early-onset sepsis [EOS] which normally concerned conditions of the perinatal environment. Sepsis that occurred after 72 hours in the environment or postnatal exposure was considered late-onset sepsis [LOS]. This classification was applied in order to explain various risk factors and possible microbial patterns.

4. Thrombocytopenia in Sepsis

A platelet counts less than 150,000 /ul was considered thrombocytopenia. This is possible in sepsis because of consumption of platelets, low production and destruction of platelets. It was regarded as important in connection with clinical manifestations of infection, and the degree of it was found related to the occurrence or lack of sepsis.

5. Diagnostic Accuracy Measures

"The platelet indices were assessed in terms of diagnostic accuracy by computing the sensitivity, specificity, positive predictive value [PPV] and negative predictive value [NPV]. Analysis of receiver operating characteristic [ROC] curves was conducted to evaluate the total diagnostic performance and also determine the best cut-off values". By doing so, the practical use of platelet indices in the distinction between septic and non-septic neonates could be assessed.

Statistical analysis

The data were inputted into spread sheets and examined using the standard statistical software. Mean and standard deviation were used to express continuous variables, and frequencies and percentages were used to express categorical variables. Appropriate parametric or non-parametric tests based on distribution were used to make group comparisons. The platelet indices were used to determine the diagnostic power of the platelet indices by analyzing ROC curves. A p-value less than 0.05 was taken to be statistically significant.

Results

3.1 Demographic Profile of Neonates

There were 120 registered neonates. These were 70 septic and 50 non-septic controls. There was no significant difference in the mean gestational age of the groups, but the birth weight of septic neonates was lower. There was male predominance in both groups.

[Table 1] reveals that both groups had quite a similar demographic profile. "There was no significant difference in the mean gestational age between the septic and non-septic neonates, therefore, prematurity was not a significant confounder". But the mean birth weight of the septic neonates was slightly lower and was statistically significant [p=0.04]. This is an indication that neonates with low birth weight might be more susceptible to sepsis, as per established risk factors. The male dominance in both groups was not significant. Most cases of septicemia manifested as premature neonatal sepsis [64.3%], which led to the significance of perinatal and maternal factors in newborn infections.

3.2 Comparison of Platelet Indices: The platelet count and plateletcrit of septic neonates were significantly lower, whereas platelet MPV and platelet PDW were significantly greater than those of controls.

As presented in [Table 2], a clear difference in platelet indices can be observed between neonates with sepsis and non-septic. In the septic group, platelet counts and plateletcrit were much lower suggesting increased platelet consumption and bone marrow suppression during infection. In comparison, MPV, and PDW, were both significantly larger in the group with septic conditions [p<0.001], showing the presence of higher platelets of lower maturity and more variation in their sizes as a result of increased turnover. These findings provide a clue that platelet indices, in particular, MPV and PDW, are sensitive markers of the hematological alterations related to an infection. The fact that their differences in all the indices are statistically significant

makes them valid as simple and powerful diagnostic predictors of neonatal sepsis.

3.3 Diagnostic Accuracy of Platelet Indices: Diagnostic power of platelet indices was assessed by ROC analysis in order to test the hypothesis. "The highest area under curve [AUC] was obtained in MPV and PDW", which means that they are highly discriminatory.

[Table 3] shows the diagnostic accuracy of platelet indices. PDW exhibited the greatest sensitivity [85.7] and large AUC [0.87], and then closely followed by MPV [AUC 0.85]. Platelet count showed moderate sensitivity and specificity but had value in the clinic when used together with other indices. Plateletcrit was less accurate than MPV and PDW but acceptable discriminatory ability. On the whole, the findings support the idea that MPV and PDW are the most effective indicators of early sepsis and platelet count and plateletcrit can be used to strengthen the diagnosis with a combination of the two indicators. Therefore, platelet indices can be considered an effective supplement to the traditional diagnostic techniques at a relatively low cost.

Table 1: Baseline characteristics of study population

Parameter	Septic group [n=70]	Non-septic group [n=50]	p-value
Mean gestational age [weeks]	36.2 ± 2.8	36.8 ± 2.5	0.21
Mean birth weight [kg]	2.42 ± 0.52	2.65 ± 0.49	0.04*
Male: Female ratio	42:28:00	29:21:00	0.88
Early-onset sepsis [%]	45 [64.3%]	–	–
Late-onset sepsis [%]	25 [35.7%]	–	–

Table 2: Comparison of platelet indices between groups

Platelet Index	Septic group [Mean ± SD]	Non-septic group [Mean ± SD]	p-value
Platelet Count [×10⁹/L]	124.5 ± 48.6	215.3 ± 52.4	<0.001*
MPV [fL]	11.2 ± 1.8	9.1 ± 1.5	<0.001*
PDW [%]	18.5 ± 2.9	14.7 ± 2.1	<0.001*
Plateletcrit [%]	0.18 ± 0.07	0.27 ± 0.09	<0.001*

Table 3: Diagnostic performance of platelet indices

Platelet Index	Cut-off value	Sensitivity [%]	Specificity [%]	AUC
Platelet Count	≤150 ×10⁹/L	74.3	80	0.82
MPV	≥10.0 fL	81.4	78	0.85
PDW	≥16.0 %	85.7	76	0.87
Plateletcrit	≤0.20 %	70	72	0.79

Discussion

In the current study, septic neonates also had significantly lower platelet counts and plateletcrit, and higher MPV and PDW than non-septic controls. ROC analysis showed that MPV and PDW were the most diagnostic, which means that these indices can be used as cost-effective and fast supplementary sepsis markers.

Study also find that our results are consistent with the findings of the cross-sectional study conducted by Goyal et al. that documented that platelet count, MPV and PDW showed significant differences between septic and non-septic neonates which was concluded to be a useful diagnostic indicator of neonatal sepsis.[9] On the same note, Tahir et al. showed that MPV cut-offs around 10 fL distinguished between septic and control neonates with high sensitivity and specificity, highlighting the importance of this as an early neonatal hematologic marker.[11] These findings are quite similar to our ROC results where MPV was among the most powerful predictors.

Yadav et al. also found that platelet indices, particularly, PDW & MPV were always altered in septic neonates relative to controls, and that they should be included in the routine diagnostic work-up in neonatal intensive care.[12] Their findings support our reasoning that high PDW, an indication of platelet anisocytosis, is very much associated with the sepsis inflammatory response. Kavitha et al. have shown in resource-limited settings that platelet counts and their derivatives were both diagnostic and prognostic, with low counts indicating greater sepsis severity and worse outcomes.[13] This supports our observation that thrombocytopenia was more severe in septic cases, and it indicates that thrombocytopenia is a potential diagnostic and prognostic indicator.

These changes are pathophysiological and explained by the systemic inflammatory cascade of sepsis. During sepsis, microvascular coagulation and bone marrow stimulation lead to the release of larger, immature platelets. This process, along with increased platelet consumption, results in elevated MPV and PDW values. This process, which has been regularly reported in neonatal sepsis cohorts, offers a biological explanation of the diagnostic power of the indices. In as much our results and the mentioned literature agree regarding the clinical importance of platelet indices, certain discrepancies still exist. Reproducibility may be influenced by variability in the technology of the analyzer, the cut-off values, and the demographics of the patient. Further, prematurity and perinatal hypoxia and related conditions could have an independent effect on platelet parameters without infection. Therefore, platelet index is a good idea but multicenter studies with larger participants are needed to confirm universal thresholds.

Overall, our investigation and recent publications confirm the addition of platelet indices, especially MPV & PDW to the neonatal sepsis screening guidelines. They are particularly useful in both high-resource and low-resource healthcare facilities since they are easy to obtain, have fast turnaround, and are affordable.[9,11–13]

Conclusion

The current work focuses on the diagnostic importance of platelet indices in neonatal sepsis. Study found that platelet count, Plateletcrit, platelet MPV & platelet PDW were all significantly lower in septic neonates than in non-septic controls. The analysis of ROC curves also showed that MPV and PDW were the most stable parameter, with high sensitivity and specificity. These findings indicate that platelet indices, which are routinely reported as complete blood count, have the potential to become fast, cost-effective, and readily accessible metrics to aid in the early diagnosis of neonatal sepsis.

This interpretation is reinforced by a comparison with the recent literature. Diagnostic accuracy of platelet indices was confirmed by Goyal et al., whereas MPV was demonstrated to be a good early marker by Tahir et al.[9,11] The importance of PDW and MPV in screening sepsis was also noted by Yadav et al., and platelet count was reported by Kavitha et al. as a diagnostic and prognostic factor.[12,13] Collectively, those findings point to the importance of not underestimating the role of platelet indices in neonatal practice, especially in resource-restrained environments, when highly sensitive diagnostic tests might not be accessible.

Finally, platelet indices, in particular, MPV and PDW are useful supplements to classical sepsis indicators and may be considered in practice to early diagnosis and better neonatal outcomes.

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Conflicts of interest

There are no conflicts of interest.

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