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Original Research

Evaluation of platelet count and their indices as a marker of neonatal sepsis

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ABSTRACT:
Background: In this study, we wanted todetermine platelet count and their indices (PDW, MPV) as a marker of neonatal sepsis, to determine there is difference in platelet indices among: Term and pre-term neonates with sepsis, early versus late onset sepsis, monitoring of platelet count and their indices in neonatal sepsis in relation to sepsis organism. **Methods:** This was a hospital based cross sectional study conducted among 96 neonates to establish the relationship between neonatal sepsis and platelet and its indices, admitted to the NICU at District Hospital, Tumkur, over a period of 2 years from August 2022 to August 2024 after obtaining clearance from institutional ethics committee and written informed consent from the study participants. **Results:** The mean platelet count (PLT in Lakhs) in G +VE bacteria was 1.40± 0.867 and in G –VE bacteria was 1.32±0.521, and the difference was statistically highly significant (p=0.015)
The mean platelet volume (MPV in fL) in G +VE bacteria was 11.13±1.226 and in G –VE bacteria was 10.64±1.068 (p-value=0.039).
The mean Platelet Distribution Width (PDW in fL) in G +VE bacteria was 14.17± 3.690 and in G –VE bacteria was 12.42± 2.698(p-value=0.009).
The mean C-Reactive Protein (CRP in mg/L) in G +VE bacteria was 27.83± 26.930 and in G –VE bacteria was 11.80±14.619(p-value<0.001).
With a sensitivity of 68.30% and specificity of 70.17%, platelet count offers a balanced approach for identifying and ruling out bacterial types. The PPV of 34% and a high NPV of 86% suggest that platelet count is particularly effective in confirming the absence of Gram-positive infections when the count is normal or high (p-value =0.031).
MPV had a sensitivity of 75%, specificity of 39.29%, Positive Predictive Value (PPV) of 46.88% and Negative Predictive Value (NPV) of 68.8%. MPV provides higher sensitivity but lower specificity, making it more useful in identifying Gram-positive infections but less reliable in ruling out false positives (p-value <0.000).
PDW's sensitivity (52.5%) and specificity (23.21%) are lower, indicating it is less effective as a standalone marker for bacterial differentiation. Its PPV (32.81%) and NPV (40.6%) also suggest limited predictive power, making PDW more suitable as a supplementary diagnostic tool rather than a primary marker (p-value =0.012).
CRP had sensitivity of 62.5%, specificity of 62.5%, PPV of 54.35% and NPV of 70%. With a sensitivity and specificity of 62.5%, CRP is moderately effective in identifying Gram-positive infections (p-value < 0.001). **Conclusion:** Platelet and their indices can be used as sensitive markers to identify septic babies and may be combined with existing sepsis screening to specifically exclude nonseptic cases. E Coli was the most common organism causing thrombocytopenia in our study.
Keywords: Platelet count, indices, marker, neonatal sepsis.

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INTRODUCTION

Neonatal sepsis (NS) is a major cause of neonatal morbidity and mortality worldwide contributing around 38% of all deaths in neonates. According to WHO" Sepsis is a life-threatening syndromic response to infection and a final common pathway to

death for many infectious diseases worldwide". Neonatal septicemia is a clinical syndrome which is characterized by signs and symptoms of bloodstream infections with or without accompanying bacteremia, in newborn infants less than 28 days old. It remains a leading cause of morbidity and mortality,especially in middle- and lower-income countries.[1]It is caused by various organisms invading the blood stream. Neonates are fragile and can deteriorate rapidly, necessitating rapid diagnosis and prompt management is required. Blood culture and sepsis screening are the currently used methods but blood culture results are often available too late to make immediate decisions. To overcome these limitations, sepsis screening is usually relied upon despite its variable sensitivity and specificity. The negative predictive value of these parameters is too low to effectively rule out sepsis. The limitations of blood culture, its low positivity rates, and poor diagnostic capability of sepsis screening in neonates make the diagnosis of sepsis challenging, highlighting the need for better diagnostic parameters. Due to these limitations we need to find parameters which will increase the sensitivity and specificity. Haematological changes in neonatal sepsis have been utilized for early diagnosis and to detect complications. Changes in platelet count and platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) induced by neonatal sepsis have been the focus of various studies. Thrombocytopenia (below 150000 cells/mm3) is used as an early but nonspecific marker of sepsis in neonates.[2]Platelet size can be analysed using MPV and PDW, and it correlates with platelet activity. MPV is the measurement of average size of platelets; large platelets are highly active and have greater thrombotic potential. High MPV indicates an increased quantity of young platelets in the circulation.[3] In neonatal period, MPV ranges from 10 -12 fl. Elevated MPV levels are associated with condition such as destructive thrombocytopenia whereas low MPV levels indicates hypo proliferative thrombocytopenia. Platelet distribution width (PDW) indicates variation in platelet size normal values ranging between 10 % and 17.9%.[4]

AIMS AND OBJECTIVES

- This study aims to evaluate platelet count and their indices as a marker of neonatal sepsis.
- To determine platelet, count and their indices (PDW, MPV) as a marker of neonatal sepsis
- To determine there is difference in platelet indices among-
  - Term and pre-term neonates with sepsis,
  - Early versus late onset sepsis
- Monitoring of platelet count and their indices in neonatal sepsis in relation to sepsis organism.

METHODS

This was a Hospital Based Cross Sectional Study conducted among 96 neonates to establish the relationship between neonatal sepsis and platelet and its indices, admitted to the NICU at District Hospital, Tumkur, over a period of 2 years from August 2022 to August 2024 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

All newborns admitted to the neonatal unit of Hospital with

a) Clinical signs and symptoms of sepsis: Hypothermia or hyperthermia, lethargy, poor cry, refusal to suck, poor perfusion, prolonged capillary refill time, hypotonia, absent neonatal reflex, bradycardia (<100/min), tachycardia (>200/min), hypotension, respiratory distress, apnea, tachypnea, bluish skin color and gasping respiration, hypoglycemia or hyperglycemia, metabolic acidosis.

and /or

b) Sepsis screen positive (which include absolute neutrophil count, immature to total neutrophilic ratio, micro ESR, CRP, WBC)

with

c) blood culture positivity

Exclusion Criteria

1. Neonates having platelet or bleeding disorders
2. Neonates with congenital anomalies, congenital heart disease, IUGR, maternal drugs (indomethacin, antihistamines)
3. Neonates whose parents or guardians did not agree to be a part of study

Sample size

Based on article by Dr Hajira, 60 % neonates having neonatal sepsis have thrombocytopenia

d: desired level of Precision or margin of error(e) = 0.10(10 %) Expected prevalence (p) = 0.6 (60%) z-value for 95% CI = 1.96

Minimum sample required(n)= 92

STATISTICAL METHODS

Data was collected and entered and tabulated in MS Excel spread sheet. Statistical analysis was done using statistical software SPSS. After assessment of the ratios of thrombocytopenia, high MPV, and PDW, the qualitative variables were compared by using chi-square test and quantitative variables were compared by using t test, fischer exact test, and ANOVA. Outcomes were expressed in proportions.

Data was also represented using appropriate diagrams like bar.

P value <0.005 was considered statistically significant.

RESULTS

TYPE OF ORG FOUND IN BLOOD CULTURE		N	Mean	Std. Deviation	" t " Value	P Value
WBC (X10 ^3)	G +VE	40	18.42	7.761		
					0.409	0.684
	G -VE	56	17.76	7.694		
NEUT (%)	G +VE	40	55.56	19.311		
					1.265	0.209
	G -VE	56	60.13	15.986		
LYM (%)	G +VE	40	39.14	16.286		
					2.358	0.020
	G -VE	56	31.40	15.539		

Distribution of cases according to White blood cell count, Neutrophil and Lymphocyte

TYPE OF ORG FOUND IN BLOOD CULTURE		N	Mean	Std. Deviation	" t " Value	P Value
PLT(Lakhs)	G +VE	40	1.40	0.867	1.138	0.015
	G -VE	56	1.32	0.521		

Table 1 :Distribution of cases according to Platelet Count

In the study, the mean White Blood Cell Count (WBC in x10^3) in G +VE was 18.42± 7.761 and in G –VE was 17.76± 7.694 and the difference was not statistically significant (p=0.684). The mean Neutrophil in G +VE was 55.56± 19.311 and in G –VE was 60.13± 15.986 and the difference was not statistically significant (p=0.209). The mean Lymphocyte in G +VE was 39.14±16.286 and in G –VE was 31.40± 15.539 and the difference was statistically significant (**p=0.020**).

In the present study, the mean Platelet Count (PLT in Lakhs) in G +VE was 1.40± 0.867 and in G –VE was 1.32±0.521, and the difference was statistically highly significant (**p=0.015**).

TYPE OF ORG FOUND IN BLOOD CULTURE		N	Mean	Std. Deviation	" t " Value	P Value
MPV (fL)	G +VE	40	11.13	1.226	2.091	0.039
	G -VE	56	10.64	1.068		

Distribution of cases according to Mean Platelet Volume

TYPE OF ORG FOUND IN BLOOD CULTURE		N	Mean	Std. Deviation	" t " Value	P Value
PDW(FL)	G +VE	40	14.17	3.690	2.686	0.009
	G -VE	56	12.42	2.698		

Distribution of cases according to Platelet Distribution Width

TYPE OF ORG FOUND IN BLOOD CULTURE		N	Mean	Std. Deviation	" t " Value	P Value
CRP	G +VE	40	27.83	26.930	3.751	<0.001
	G -VE	56	11.80	14.619		

Table 2 :Distribution of cases according to C-Reactive Protein

In the present study, the Mean Platelet Volume (MPV in fL) in G +VE was 11.13±1.226 and in G –VE was 10.64±1. 068.And the difference was statistically significant (**p=0.039**).

In the present study, the mean Platelet Distribution Width (PDW in fL) in G +VE was 14.17± 3.690 and in G –VE was 12.42± 2.698. And the difference was statistically highly significant (**p=0.009**).

In the present study, the mean C-Reactive Protein (CRP in mg/L) in G +VE was 27.83± 26.930 and in G –VE was 11.80±14.619. And the difference was statistically highly significant (**p<0.001**).

		ONSET				TOTAL		CHISQUARE VALUE	P VALUE
		EOS		LOS					
		NO.	%	NO.	%	NO.	%		
PLATELET COUNT	<150000	24	50	24	50	48	100	12.000	<0.000
	≥150000	8	16	40	84	48	100		
MPV	> 10.4	13	30	31	70	44	100	0.524	0.307
	≤ 10.4	19	36	33	64	52	100		
PWD	≤ 19	16	25	48	75	64	100	6.000	0.014
	> 19	16	50	16	50	32	100		

Correlation of cases according to onset of sepsis

		TYPE OF ORG FOUND IN BLOOD CULTURE				TOTAL		CHISQUARE VALUE	P VALUE
		G +VE		G -VE					
		NO.	%	NO.	%	NO.	%		
PLATELET COUNT	<150000	25	52	23	48	48	100	4.286	0.031
	≥150000	15	32	33	68	48	100		
MPV	> 10.4	10	22	34	78	44	100	11.988	<0.000
	≤ 10.4	30	58	22	42	52	100		
PWD	≤ 19	21	32	43	68	64	100	6.193	0.012
	> 19	19	60	13	40	32	100		

Table 3 :Correlation of cases according to type of organism

In the study, significant correlation between low platelet counts and early onset sepsis was noted. MPV and PDW values show varying levels of significance, indicating their potential utility in differentiating EOS and LOS.

In the present study, a strong correlation between higher MPV and Gram-negative infections was noted. And there was significant PDW and MPV differences between Gram-positive and Gram-negative organisms.

		TYPE OF ORG FOUND IN BLOOD CULTURE				TOTAL		CHISQUARE VALUE	P VALUE
		G +VE		G -VE					
		NO.	%	NO.	%	NO.	%		
CRP	POSITIVE (≥10 mg/L)	25	54	21	46	46	100	5.843	0.016
	NEGATIVE (<10 mg/L)	15	30	35	70	50	100		
Total		40	42	56	58	96	100		

Correlation between the blood culture and C-reactive Protein

		TYPE OF ORG FOUND IN BLOOD CULTURE				TOTAL		CHISQUARE VALUE	P VALUE
		G +VE		G -VE					
		NO.	%	NO.	%	NO.	%		
PLATELET COUNT	<150000	25	52	23	48	48	100	4.286	0.031
	≥150000	15	32	33	68	48	100		
	Total	40	42	56	58	96	100		

Table 4 :Correlation between the blood culture and platelet count

In the present study, majority Gram-positive bacteria (54%) were found in samples with high CRP levels. A higher proportion of Gram-negative bacteria (70%) were seen in samples with low CRP levels. There was significant relationship between CRP levels and the type of bacteria (**p-value = 0.016**).
In the present study, lower platelet counts (< 150,000/μL) tend to be associated with Gram positive infections (50%), while higher counts (≥ 150,000/μL) are more linked to Gram negative infections (50%). There was significant relationship between platelet count levels and the type of bacteria (**p-value = 0.031**

		TYPE OF ORG FOUND IN BLOOD CULTURE				TOTAL		CHISQUARE VALUE	P VALUE
		G +VE		G -VE					
		NO.	%	NO.	%	NO.	%		
MPV	> 10.4	30	58	22	42	52	100	11.988	0.000 < 0.001
	≤ 10.4	10	23	34	77	44	100		
Total		40	40	42	56	58	96		

Correlation between the blood culture and mean platelet volume

		TYPE OF ORG FOUND IN BLOOD CULTURE				TOTAL		CHISQUARE VALUE	P VALUE
		G +VE		G -VE					
		NO.	%	NO.	%	NO.	%		
PDW(FL)	≤ 19	21	33	43	67	64	100	6.193	0.013
	> 19	19	59	13	41	32	100		
Total		40	42	56	58	96	100		

Table 5: Correlation between the blood culture and platelet distribution width

In the present study, majority of Gram-positive bacteria (58%) were found in samples with MPV greater than 10.4 fL. A higher percentage of Gram-negative bacteria (77%) were observed in samples with MPV equal to or less than 10.4 fL. There was significant association between MPV and the type of bacteria (p-value < 0.000). There is a higher proportion of Gram-negative bacteria in samples with lower MPV values.
In the present study, majority of Gram-negative bacteria (58%) were found in samples with PDW lesser than or equal to 19 fL. A higher percentage of Gram-positive bacteria (59%) were observed in samples with PDW greater than 19 fL. There is significant association between PDW and the type of bacteria (p-value = 0.013).

DISCUSSION

Parameters gender

In the present study, 59(61.5%) participants were males and 37(38.5%) were females. In culture positive sepsis, 21(36%) were males & 19(51%) were females. In culture negative sepsis, 38(64%) were males & 18(49%) were females. A slightly higher percentage of males than females were observed. However, the two groups did not differ with respect to distribution of sex, (p=0.127). Platelet indices did not differ significantly with gender (p>0.05 for MPV, PDW and platelet counts) so this difference in male and female distribution did not affect our results with respect to platelet indices.
In a study conducted by **Gupta et al**[5], the demographic analysis revealed that out of the total sample population, 148 individuals (72.2%) were male, while 57 individuals (27.8%) were female.

Mode of delivery

In the present study, 44(46%) were delivered by NVD and 52(54%) were delivered by LSCS. Slightly higher LSCS deliveries were noted than NVD deliveries but the difference was not statistically significant (p= 0.332).
A study by **Gupta BK et al**[5], reported that among the mothers in their study, 108 (52.68%) underwent normal vaginal deliveries, while 97 (47.31%) required lower segment caesarean sections.

Type of admission

In the present study, 35(36.5%) participants were inborn and 61(63.5%) were outborn in terms of type of admission. More admissions were outborn than inborn and the difference was not statistically significant (p= 0.123).

PV leaking

In the present study, leaking PV >24 Hours was present in 3 (3.1%) and absent in 93 (96.9%) cases. Minimal occurrences of foul-smelling discharge and leaking PV > 24 hrs were observed and there was no significant correlation (p-value = 0.766).
A study by **Gupta et al**[5], reported that per vaginal (PV) leakage was observed in 22 cases (10.7%), while it was absent in 183 cases (89.3%)

Onset of sepsis

In the current study, the onset of sepsis was LOS in 64(68%) and EOS in 32(32%). LOS more common than that of EOS, but there was no significant correlation (p-value = 0.168).
A study by **Patil A et al**[6], found that early-onset sepsis (EOS) was more prevalent, occurring in 59% of

cases, compared to late-onset sepsis (LOS), which accounted for 41% of cases.

Gestation

In the current study, based on gestation, the majority of the neonates were born at term
65(67%), followed by preterm 31(33%). And there was no significant correlation (p-value = 0.266).
In the study by **Majumdar A et al**[7], 56% of the neonates were preterm, while the remaining 44% were term neonates.

Organism

In the present study, out of 96 neonates with sepsis, E Coli 54 (54%), Klebsiella species 16(16%) and Staph aureus species 15 (15%) were the most common Gram positive and Gram-negative organisms followed by Acinetobacter, CONS and fungal species.
A study by **Mevundi GN et al**[8], identified the most common causative organism as Staphylococcus aureus (43.3%) followed by E. coli (21.7%), Klebsiella (20.0%), Pseudomonas (8.3%) and Candida (5%).

Anthropometry and vitals

In the present study, the mean birth weight (in kg) in G +VE was 2.71± 0.520 and in G – VE was 2.56± 0.342 with the difference not being statistically significant(p=0.080).
In the study by **Mevundi et al**[8], the mean weight of neonates with Gram-positive bacterial infections was 2.26 kg (±0.60 kg), while those with Gram-negative bacterial infections had a mean weight of 2.29 kg (±0.62 kg). The difference in mean weight between the two groups was not statistically significant (p=0.764) similar to our study.
The mean height (in cm) in G +VE was 48.90±1.033 and in G –VE was 48.86± 0.841 and the difference was not statistically significant(p=0.823).
The mean weight (in kg) in G +VE was 2.69± 0.466 and in G –VE was 2.57±0.328 and the difference was not statistically significant(p=0.130).

Investigations

In the study, the mean white blood cell count (WBC in x10^3) in G +VE group was 18.42± 7.761 and in G –VE group was 17.76± 7.694 with the difference not being statistically significant (p=0.684).
The mean Neutrophil count in G +VE group was 55.56± 19.311 and in G –VE group was 60.13± 15.986 with the difference not being statistically significant (p=0.209).
The mean Lymphocyte in G +VE group was 39.14±16.286 and in G– VE group was 31.40± 15.539 with the difference being statistically significant (p=0.020).
In the present study, the mean hemoglobin (HB in g/dL) in G +VE group was 17.49± 2.800 and in G – VE group was 16.87± 2.642 with the difference not being statistically significant (p=0.275).

CRP

In the present study, in neonates with sepsis the mean C-Reactive Protein (CRP in mg/L) in G +VE group was 27.83± 26.930 and in G –VE group was 11.80±14.619 with the difference being statistically highly significant (**p<0.001**). CRP had a sensitivity and specificity of 62.5%. Sensitivity indicates that 62.5% of the cases with Gram-positive bacteria had CRP levels ≥ 10 mg/L, correctly identified as positive by this marker. Specificity suggests that 62.5% of the cases with Gram-negative bacteria had CRP levels < 10 mg/L, correctly identified as negative by this marker.
In clinical diagnosis, sensitivity and specificity are crucial metrics for assessing the accuracy of a test. Sensitivity measures the proportion of true positives correctly identified by the test, while specificity measures the proportion of true negatives correctly identified. High sensitivity and specificity indicate that the test is reliable in distinguishing between the conditions being tested.
In similar studies, **Naher et al**[9], reported a sensitivity of 55% and specificity of 100% and **Koksal et al**[10] reported a sensitivity of 48% and specificity of 87%.
In the present study, CRP is moderately effective in identifying Gram-positive infections. Its positive predictive value indicates that over half of the patients with high CRP levels have Gram-positive bacteria. The negative predictive value is higher, suggesting that CRP is more reliable in ruling out Gram-positive infections when the levels are low.
In the present study, CRP offers balanced sensitivity and specificity, making it a useful marker for preliminary screening.

Platelet count

In the present study**,** the mean Platelet Count (PLT in Lakhs) in G +VE was 1.40± 0.867 and in G –VE was 1.32±0.521, and the difference was statistically highly significant (p=0.015).
Lower platelet counts (< 150,000/µL) tend to be associated with Gram-positive infections, while higher counts (≥ 150,000/µL) are more linked to Gram-negative infections.
With a sensitivity of 68.30% and specificity of 70.17%, platelet count offers a balanced approach for identifying and ruling out bacterial types. The PPV of 34% and a high NPV of 86% suggest that platelet count is particularly effective in confirming the absence of Gram-positive infections when the count is normal or high.
In a study by **Choudhary RR et al**[11], reported that platelet count <1.5lacs/mm3 was the most sensitive marker for sepsis, with a sensitivity of 83.70% and specificity of 65%.
Platelet count provides a significant but less strong correlation with bacterial type.
Lower counts are more commonly associated with Gram-positive infections.

MPV

In the present study, in neonates with sepsis, the Mean Platelet Volume (MPV in fL) in G +VE was 11.13±1.226 and in G –VE was 10.64±1.068 with the difference being statistically significant (p=0.039) implying MPV may vary with the type of bacterial infection. MPV levels greater than 10.4 fL were considered positive.

There is a strong correlation between higher MPV values and the presence of Grampositive bacteria. Specifically, when MPV >10.4 fL, there is a significantly higher likelihood (58%) of the infection being caused by Gram-positive bacteria.

Conversely, lower MPV values (≤ 10.4) are more likely associated with Gram-negative bacteria (77%).

MPV's sensitivity (75%) and specificity (60.71%) suggest it is a fairly reliable marker for distinguishing between Gram-positive and Gram-negative infections. The predictive values also support its use, particularly the NPV of 77.3%, which indicates a good probability that patients with lower MPV do not have Gram-positive infections.

A study by **Arad ID et al**[12], found that the sensitivity and specificity of increased MPV in neonatal sepsis is 54% and 46% respectively.

In the present study, MPV provides higher sensitivity but lower specificity, meaning it is more useful in identifying Gram-positive infections but less reliable in ruling out false positives. On the other hand, MPV does not show a significant association with the type of bacterial infection, although there is a noticeable trend where lower MPV values are more commonly associated with Gram-negative bacteria.

PDW

In the present study, the mean Platelet Distribution Width (PDW in fL) in neonates with sepsis was 14.17± 3.690 for G+VE and 12.42± 2.698 for G-VE. The difference was statistically highly significant (p=0.009). PDW levels greater than 19 fL were used as cutoff threshold and considered positive.

The sensitivity (52.5%) and specificity (23.21%) of PDW are lower, making it a less reliable marker than MPV for predicting the type of bacterial infection. The PPV and NPV also indicate limited predictive power, with values of 32.81% and 40.6%, respectively.

PDW values >19 fL are more frequently associated with Gram-positive bacteria (59%), whereas values ≤ 19 are more commonly found in Gram-negative infections (67%).

In a similar study, **Majumdar, et al**, the sensitivity and specificity of PDW for diagnosing neonatal sepsis were 79.5% and 36.6% respectively, and the PPV and NPV were 40.9% and 77.7%

CONCLUSION

High PDW, high MPV and low platelet count are more associated with neonatal sepsis. MPV stands out as a robust marker with high sensitivity and specificity for differentiating between Gram-positive and Gram-negative infections. While PDW is significant, it is better suited as a supplementary marker. Platelet count provides balanced diagnostic insights, enhancing the overall accuracy when used in conjunction with MPV and PDW. Integrating MPV with PDW and platelet count could enhance diagnostic accuracy, allowing for more precise and timely interventions. Thus, platelet and their indices can be used as sensitive markers to identify septic babies and may be combined with existing sepsis screening to specifically exclude nonseptic cases. E Coli was the most common organism causing thrombocytopenia in our study.

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