ORIGINAL RESEARCH

Role of Platelet Indices in Neonatal Sepsis

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ABSTRACT

Background: Neonatal sepsis is major cause of neonatal morbidity and mortality worldwide. Blood culture and sepsis screening are currently used method, but their utility is limited due to delayed reporting and increased cost. Platelet indices are one such set of parameters which can be helpful in the future diagnosis of neonatal sepsis. This study was aimed to evaluate the significance of platelet indices as a marker of neonatal sepsis.

Methods: Neonates with culture-positive sepsis or clinical sepsisas per Centre for Disease Control (CDC) definition were categorized as cases and neonates initially suspected of having sepsis. Inborn and outborn babies admitted in NICU with clinical suspicion of neonatal sepsis were included. Babies with congenital and acquired causes of thrombocytopenia other than sepsis (e.g. autoimmune disorders of platelets, allo-immune disorders of platelets) and congenital anomalies, congenital heart disease and Inborn Error of Metabolism were excluded from the study.All babies enrolled were investigated for blood culture, platelet indices (platelet count, MPV, PDW, PCT).Chi square test has been used for significantly and p value less than 0.05 has been taken to be significant.**Results:** A total of 120 babies were enrolled,platelet count has highest sensitivity (97.7%), NPV (96.5%) but PDW has highest specificity (77.7%), PPV (68.6%). All the test results were statistically significant with P value <0.001 except for PCT count which was not significant (p =0.18). Combined all makers platelet count + MPV have highest sensitivity (79.1%) and Platelet count + MPV + PDW + PCT have highest specificity (90.2%), PPV (76.6%) but Platelet count + PDW have highest NPV (81.9%).

Conclusions: It may be concluded that platelet indices are sensitive markers to identify septic babies. The platelet count decreased with development of sepsis and PDW and MPV increased in septic babies. Thrombocytopenia was the most sensitive marker for culture-positive sepsis, and the highest specificity of platelet indices was seen when all the platelet indices (platelet count + MPV + PDW + PC) or (MPV + PDW + PCT) were combined.

Keywords:Neonatal sepsis,Platelet indices, ThrombocytopeniaMean platelet volume, platelet distribution width.

INTRODUCTION

Systemic infection in the neonatal period is called neonatal sepsis. It is still a major cause of NICU admission and morbidity and mortality of newborns especially in developing countries [1]. Early diagnosis and treatment is essential to reduce morbidity and mortality [2].

Early-onset sepsis is defined as the onset of symptoms before 7 days of age, although some experts limit the definition to infections occurring within the 1st 72 hr of life.

Late-onset sepsis is generally defined as the onset of symptoms at ≥7 days of age. Similar to early onset sepsis, there is variability in the definition, ranging from an onset at >72 hr of life to ≥7 days of age. [3].

It has been noted that only 20% of symptomatic neonates with suspected early onset sepsis (EOS) have a positive blood culture and only 30% neonates who were clinically suspected to have late onset sepsis (LOS) in neonatal intensive care unit (NICU) setting have a positive blood culture [4,5]. Sepsis had been reported to be more common in premature babies than in full term [6-8].

Neonatal sepsis often accompanied by thrombocytopenia and late onset sepsis, remains an important cause of thrombocytopenia in neonates [9-13]. However, the blood culture report is not immediately available and it cannot be relied upon for making immediate decisions. To overcome these limitations, we usually rely on the sepsis screening, but it has a variable sensitivity and specificity. The negative predictive value of these parameters is too low to confidently rule out sepsis [14,15].

Thrombocytopenia has been used as an early indicator but a non-specific laboratory marker for sepsis [16,17]. For this purpose, some hematological findings can be

helpful as blood culture is not available before 48 - 72 hours.

Platelet indices are biomarkers of platelet activation. These indicators have diagnostic and prognostic utility in a range of situations, including sepsis, without incurring any additional costs. These platelet indices include Platelet count, mean platelet volume, platelet distribution width, platelet crit, mean platelet component, mean platelet mass, platelet component distribution width, platelet large cell ratio and immature platelet fraction.

There have been studies showing significant changes in platelet indices in patients with neonatal sepsis [8,18-22]. These studies have measured platelet count, mean platelet volume (MPV) and platelet distribution width (PDW). It has been shown by these studies, that platelet count decreases and MPV and PDW increases in neonates with sepsis [19].

MATERIALS AND METHODS

This is a hospital based observational study, which was conducted in Neonatal Intensive Care Unit of Chirayu Medical College and Hospital (CMCH) a tertiary care hospital in Bhopal Madhya Pradesh.over a period of 18 month. Clearance was obtained from institutional ethics committee.

Neonates with culture-positive sepsis or clinical sepsisas per Centre for Disease Control (CDC) definition were categorized as cases and neonates initially suspected of having sepsis. Inborn and outborn babies admitted in NICU with clinical suspicion of neonatal sepsis were included. Babies with congenital and acquired causes of thrombocytopenia other than sepsis (e.g. autoimmune disorders of platelets, allo-immune disorders of platelets) and congenital anomalies, congenital heart disease and Inborn Error of Metabolism were excluded from the study.

All babies enrolled were investigated for blood culture, platelet indices (platelet count, MPV, PDW, PCT). For this, approximately 2 mL of venous blood was drawn from each neonate through peripheral veins with all aseptic precautions, prior to administration of any antibiotic therapy.

Chi square test has been used for significancy and p value less than 0.05 has been taken to be significant.

RESULTS

A total of 120 babies were enrolled, of which 64% and 36% cases belonged to EOS (<72 hr) and LOS (>72 hr) respectively, 53% were males and 47% were females, 62% and 38% were preterm and term respectively, 4%, 18%, 48%, and 30% belonged to ELBW (<1000gms), VLBW (<1500-1000 gms), LBW (1501-2500 gms), and (>2500gms) respectively [Table 1].

Table 1:Distribution of patients by Age, Gender, Gestation age and Birth weight

Parameter	Frequency	Percentage	Mean ± SD
Age (hour)			
<72	77	64%	34.22 ± 19.31
>72	43	36%	151.65 ± 98.72
SEX			
Male	64	53%	
Female	56	47%	
Maturity			
Preterm	75	62%	32.32 ± 2.41
Term	45	38%	38.13 ± 1.30
Weight in gm			
500-1000	5	4%	797 ± 108.25
1001-1500	22	18%	1267.85 ± 132.13
1501-2500	57	48%	2034.29 ± 178.44
>2500	36	30%	2825 ± 209.34
Total	120	100%	

Mean ±Standard Deviation

There were 48 patients who had Gram-positive or Gram-negative growth on blood culture. Out of 48 culture positiveEOS were 44% and LOS were 56%. Age of babies were significantly associated with culture positive (P<0.001). 25 babies were male and 23 were female with p value = 0.94 (p value> .05), hence there was no significant difference between male and female babies. 79.10% babies were low birth weight. Weight of babies were significantly associated with culture positive (P<0.001). 70% were preterm and 30% were term babies shown culture positive [Table 2].

Table 2: Correlation between Age, weight, maturity with positive blood culture (n= 48)

Parameter	Blood culture positive	Percentage	Blood culture negative	Percentage	Total	P value
Age (hour)						
< 72 hr	21	44%	56	78%	84	< 0.001
> 72 hr	27	56%	16	22%	36	
Sex						
Male	25	52%	38	53%	63	0.94
Female	23	48%	34	47%	57	
Weight (gm)						
500-1000	5	10.40%	1	1.40%	6	< 0.001
1001-1500	19	39.60%	2	2.70%	21	
1501-2500	14	29.20%	43	59.80%	57	
>2500	10	20.8	26	36.10%	36	
Maturity						
<37	34	70%	43	60%	75	
≥ 37	14	30%	29	40%	45	
Total	48	100%	72	100%	120	

Platelet count has highest sensitivity (97.7%), NPV (96.5%) but PDW has highest specificity (77.7%), PPV (68.6%). All the test results were statistically significant with P value <0.001 except for PCT count which was not significant (p =0.18). Combined all makers platelet count + MPV have highest sensitivity (79.1%) and Platelet count + MPV + PDW + PCT have highest specificity (90.2%), PPV (76.6%) but Platelet count + PDW have highest NPV (81.9%). All the test results were statistically significant with P value <0.001 except for Platelet count + PCT which were not significant (p =0.05) [Table 3].

Table 3: Correlation of Platelet count, MPV, PDW and PCT in relation to Culture findings (Growth/ No growth)

Parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value
Platelet count	97.7	38.8	51.6	96.5	< 0.001
MPV	79.1	48.6	50.6	77.7	0.002
PDW	72.9	77.7	68.6	81.1	< 0.001
PCT	58.3	54.1	45.9	66.1	0.18
Combination					
Platelet count + MPV	79.1	58.3	55.8	80.6	< 0.001
Platelet count + PDW	72.9	81.9	72.9	81.9	< 0.001
Platelet count + PCT	54.1	63.89	50	67.6	0.05
Platelet count + MPV + PDW + PCT	47.9	90.2	76.6	72.2	< 0.001
MPV + PDW + PCT	47.9	84.7	67.6	70.9	< 0.001
MPV + PCT	50	68	51	67.1	0.04
PDW + PCT	47.9	84.7	67.7	70.9	< 0.001

PPV: Positive predictive value; NPV: Negative predictive value;
MPV: Mean platelet volume; PDW: Platelet distribution width; PCT: Platelet crit

DISCUSSION

We have seen that the groups differed in terms of prevalence of thrombocytopenia and increased MPV and PDW, which was statistically higher ($P < 0.001$). In the study group, 98% of cases of neonatal sepsis developed thrombocytopenia. Abdulla *et al.* [23] in their study showed that 42.8% babies with sepsis developed thrombocytopenia. In another study by Ahmad *et al.* [24] it was seen that mortality rate was higher among children with thrombocytopenia and its prevalence was 24.7% in neonatal sepsis.

Guida et al. [10] had reported that 54% septic Very Low Birth Weight (VLBW) neonates developed thrombocytopenia. Akarsu et al. [25] had shown higher initial platelet count in gram positive sepsis compared to gram negative sepsis., In our study Sensitivity, specificity, PPV, NPV of platelet count were 97.7%, 38.8%, 51.60%, 96.50% respectively when compared with other studies where sensitivity was 24.7%.[24] MPV in our data was increased in 78% of neonatal sepsis which was far greater when compared with the results of the study by Abdulla *et al.* [23] where 27.8%

children suffering from sepsis had an increase in MPV. It was also seen that sensitivity and specificity of increase in MPV in diagnosis of neonatal sepsis were found to be 78.4% and 33.3%, respectively.

In a study by Arad *et al*. [26] it was seen that sensitivity and specificity of an increase in MPV in diagnosis of neonatal sepsis were 54% and 46%, respectively. In our study was also seen that Sensitivity, specificity, PPV, NPV of MPV were 79.10%, 48.6%, 50.6%, 77.7% respectively.Guida*et al* [10]. was reported a statistically significant increase in MPV with neonatal sepsis from baseline values (mean change in MPV 0.30 femtoliters; 95% CI: 0.12–0.47).

Catal*et al*. [1] found a MPV value of 10.35 fL was identified as the cut off value in patients probably resulting in sepsis with a sensitivity of 97.8% and specificity of 78.7% (AUC = 0.949; $P < 0.001$), and a MPV value of 10.75 fL was determined as the cut off value at diagnosis in patients possibly resulting in death with a sensitivity of 95.2% and a specificity of 84.9% (AUC = 0.944; $P< 0.001$).

Akarsu*et al*.[25]Found that 39.5% were associated with thrombocytopenia, 13.9% with an elevation in baseline MPV and PDW, 11.6% with an elevation in baseline MPV and 72.1% with an elevation in baseline PDW.

PDW was found to be increased in 73% cases. An increase in PDW was far greater when compared with the results of the study by Abdulla *etal*.[23] which show that PDW increased in 38% cases of sepsis. Mittal,*etal*.[27] Thrombocytopenia was the most predictive marker for culture positivity in septic babies (83.08%), and when all the platelet indices (MPV + PDW + PC) or (MPV + PDW) were combined (46.34%) it was found to be highly specific marker for prediction of sepsis. Platelet indices had a better sensitivity (83.08%) than sepsis screen (60%). When sepsis screen and platelet indices were combined, it increased the specificity (62.6%).

CONCLUSIONS

It was concluded from this study that platelet indices may serve as an important tool to aid sepsis screening. The platelet count decreased with development of sepsis and PDW and MPV increased in septic babies. Platelet indices did not differ significantly with gestational age nor with Gram-positive or Gram-negative blood culture. Thrombocytopenia was the most sensitive marker for culture-positive sepsis, and the highest specificity of platelet indices was seen when all the platelet indices (platelet count + MPV + PDW + PC) or (MPV + PDW + PCT) were combined. The incidence of sepsis was high among preterm (70%), low birth weight babies 79.1%. Male babies were more prone for septicaemia. Male and female observed was 52% and 48% respectively. The blood culture positivity was 40% in our study group.

Thus, it may be concluded that platelet indices are sensitive markers to identify septic babies.

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Nil

CONFLICTS OF INTEREST

There are no conflicts of interest.

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