



A Study of Platelet Indices in Neonatal Sepsis from a Rural Tertiary Care Hospital of North India

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Abstract

Objectives: To Study the effect of sepsis on the platelet counts and other platelet indices in neonates.

Patient and Methods: This observational study was conducted prospectively over a period of one year from November 2014 to October 2015 in neonatal division of department of Paediatrics, MMIMSR, Mullana. A total of 100 neonates, who had positive septic screen and/or positive blood culture and/or clinical features suggestive of neonatal sepsis, were included in the study and were compared with appropriately matched control of 100 healthy neonates. The complete septic workup along with indices like platelet distribution width (PDW), mean platelet volume (MPV) was also done.

Results: A total of 100 neonates were enrolled for the study (85 were with positive septic screen/culture proven and 15 were of clinical sepsis). We found that in cases mean platelet count was 1.09 lakh/mm³, mean PDW was 12.1% and MPV was 16.7fL. In control group mean platelet count was 2.70 lakh/mm³, mean PDW 10.8% and MPV was 16.3fL. Difference in these indices was statistically significant (platelet count P value .004, PDW P value < .001, and MPV P value .003). Birth weight and type of onset of sepsis had no effect on platelet indices in septic babies (platelet count P value .341, PDW .560 and MPV .452). Among sepsis cases, no significant difference was found in term and preterm babies as regard to platelet indices. Also, there is no significant effect on platelet count by the type of causative organism.

Conclusion: Low platelet counts, high mean platelet volume and platelet distribution width was observed in sepsis cases with a statistically significant difference as compared to controls.

Keywords: platelet indices, neonatal sepsis.

Introduction

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection in neonatal period of life. It covers various systemic infections of newborn such as

septicaemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections. It is estimated that 20% of neonates develop sepsis and approximately 1% deaths are related to sepsis^[1]. Though blood culture is gold standard for

diagnosis but it is not always positive even in presence of clinical features of sepsis in a neonate. A high index of suspicion and its confirmation are necessary for early diagnosis of sepsis. Various tests are traditionally applied.^[2] The negative predictive value of various sepsis screen parameters is too low to confidently rule out sepsis. There is no ideal test or combination of tests which are bench markers of an excellent test.^[3-5] Due to these drawbacks we need to find parameters which can increase the sensitivity and specificity of sepsis diagnosis in an inexpensive and easy manner. Platelet indices (platelet counts, platelet distribution width-(PDW), mean platelet volume- (MPV)) are one such set of parameters which can be helpful for the diagnosis and hence early treatment of neonatal sepsis. Advantages of platelet indices are that the sample for these can be drawn at the same time as that for other investigations and require no special sampling techniques and are easily available. Few studies have documented significant changes in platelet indices in neonatal sepsis as well as older children and adults.^[6-18] Still, there is no clear consensus, so more studies are needed on this subject. At present, there is paucity of literature regarding platelet indices in neonatal sepsis. The present study was carried out to identify any co-relation between platelet indices and neonatal sepsis.

Material & Methods

This was an observational case- control study conducted over a period of one year from November 2014 to October 2015 in neonatal division of Department of Paediatrics in collaboration with Department of Microbiology, MMIMSR, Mullana, Ambala, Haryana. The aim of study was to evaluate platelet indices i.e platelet count (PC), platelet distribution width (PDW), mean platelet volume (MPV) in neonatal sepsis and to determine the effect of gestation, birth weight, type of sepsis and causative organisms, on platelet indices in neonatal sepsis. A total of 100 neonates admitted in the neonatal intensive care unit with clinical symptoms or signs

suggestive of neonatal sepsis [lethargy, decreased feeding, fever, hypothermia, vomiting, difficult breathing, apnoea, bulging fontanel, abdominal distension, multiple >10 skin pustules] or/and with positive septic screen or/and with positive blood culture sensitivity were included and were compared with appropriately matched control of 100 healthy neonates. Neonates with congenital and acquired cause of thrombocytopenia other than sepsis, i.e Autoimmune disorders of platelets, allo-immune disorder of platelets, mothers on anti-platelet medications, intrauterine infections were excluded. Soon after admission, two millilitre blood sample was taken and was processed for investigations total leucocyte count (TLC), peripheral blood film (PBF), differential leukocyte count (DLC), and immature to total (I:T) neutrophil ratio, C-Reactive protein (CRP). Platelet indices namely platelet count, MPV, PDW were also analysed, with an automated haematology analyser- SYMEX-XP 100 (XP series), JAPAN. Blood culture was observed for 72 hours before labelling it sterile. Other investigations like CSF analysis, urine culture obtained by supra-pubic puncture, chest X-ray were done as required. The clinical details of all cases and controls and their laboratory investigations results were recorded in structured Proforma. Data were analysed with chi-square/fisher exact test and student's t- test. Statistical analysis was performed by SPSS 15.0 statistical program (Chicago, IL, USA). P Values of < 0.05 were considered significant.

Results

A total of 100 neonates admitted in the neonatal intensive care unit with clinical symptoms or signs suggestive of neonatal sepsis or/and with positive septic screen or/and with positive blood culture sensitivity were evaluated during the study period. Table 1 summarizes the demographic profile of the control and sepsis groups. Table 2 shows the conventional laboratory parameters results in cases and control groups. There were significant differences between control and sepsis group in

terms of platelet count (P value .004) in addition to significant differences between control and sepsis group related to MPV (P value .003) and PDW (P value .001). Table 3 summarizes the laboratory parameters used in sepsis screen between confirmed and clinical sepsis. No significant differences were found between confirmed and clinical sepsis groups in terms of CRP, TLC, Micro ESR, I/T ratio. Significant difference was found in platelet counts of confirmed and clinical sepsis (P value .023) but no significant difference was seen in PDW and MPV among the confirmed sepsis group and clinical sepsis group.

Table 4 shows comparison of the laboratory characteristics of neonates of <34weeks, 34-37

weeks and >37 weeks of gestation of the septic neonates. No significant differences were seen in platelet and platelet indices in relationship with gestational age. Table 5 depicts that, no significant differences were seen in laboratory parameters among different birth weight groups. Out of total 100 cases including confirmed and clinical sepsis cases, 66 cases had EONS and 34 developed LONS. No significant difference was observed in platelet indices in response to time of onset of sepsis. Also, No significant differences were seen in conventional laboratory parameters and platelet indices in relation to the type of organism causing infection.

Table 1. Demographic profile of included patients

Variables	Control(n=100)	Cases(n=100)
Male/Female	59(59%)	61 (61%)
	41(41%)	39 (39%)
In born/Out born	96(96%)	89 (89%)
	4 (4%)	11 (11%)
LBW YES	44(44%)	34(34%)
	56(56%)	66(66%)
Term/Preterm	55(55%)/45(45%)	45(45%)/55(55%)
AGA	81 (81%)	75 (75%)
SGA	19 (19%)	25 (25%)
Mode of delivery-NVD	85 (85%)	82 (82%)
	LSCS	15 (15%)
Booked/ Unbooked	80 (80%)	33 (33%)
	20 (20%)	67 (67%)
Maternal infections PROM	10 (10%)	51 (51%)
Parity Primigravida	50(50%)	40(40%)
	Multigravida	50 (50%)
H/O Multiple P/V examinations	1 (1%)	9 (9%)
Resuscitation at birth	2(2%)	28 (28%)

Table 2 comparison of Laboratory parameters of study population

Variables	Control	Case	P value
Platelet count(Lakhs)	270100+/- 95006	109270+/-113126	.004
PDW(%)	10.8+/-1.9	12.1+/-2.5	.001
MPV(fl)	16.3+/-0.4	16.7+/-2.1	.003

Table 3. Comparison of Laboratory parameters of sepsis screen in confirmed and clinical sepsis

Variables	Confirmed sepsis (n=85)	Clinical sepsis(n=15)	P value
CRP(%)	36	7	.759
TLC/mm ³	4982+/- 6330	13900+/-15645	.105
Micro ESR	10.52+/- 4.3	9.60+/-3.3	.439
I/T Ratio >0.2	13 (15%)	2 (13%)	.803
Platelet count(L)	108552 +/- 1063	134000+/-1339	.023
PDW(%)	12.05+/- 2.4	12.8 +/-3.19	.280
MPV(fL)	11.7+/-2.8	11.5+/-2.6	.869

Table 4 Laboratory parameters comparison in various groups (Gestation wise)

Variables	Gestation			P value
	<34wks	>34wks	>37 wks	
CRP(%)	.61+/- .49	.56+/- .5	.54+/- .4	.644
TLC/mm ³	12475+/-6522	14113+/-9019	15415+/-7105	.383
Micro ESR	10.8+/- 4.3	10.2+/-4.1	9.4+/-4.0	.516
I/T Ratio>0.2	6	13	2	.699
Significant ANC	7704+/-5569	9070+/- 5963	9460+/-5467	1.00
Platelet count(L)	171588+/-10981	196550+/-96547	195660+/-95500	0.45
PDW(%)	11.5+/-2.4	11.4+/-2.3	11.2+/-2.1	0.63
MPV(fL)	11.4+/-2.6	11.5+/-2.4	11.7+/-2.3	0.24

Table 5. Laboratory parameters comparison in various groups' (birth weight wise)

Variables	Birth weights			P value
	=/<1500n=	1501-2500	>2501	
TLC/mm ³	11856+/-6332	13346+/-8902	13591+/-5635	.560
Micro ESR	10.25+/-4.2	9.4+/-3.5	9.36+/-3.2	.234
ANC	7979 +/5736	8431+/-5568	9280+/-5058	.143
Platelet count(L)	172204+/-113613	192076+/-106582	198435+/-85022	.341
PDW(%)	11.8+/-2.4	11.5+/-2.5	11.2+/-2.2	.560
MPV(fL)	11.4+/-2.7	11.67+2.4	11.4+/-2.4	.452

Discussion

In the developing world, neonatal septicaemia remains as the major cause of mortality and morbidity in spite of recent advances in the technology and therapeutics.^[15] As neonates are fragile and can rapidly deteriorate, so the treatment should be initiated in a neonate suspected to have sepsis without any delay.

Till today there is no single test to reliably exclude or include neonatal sepsis. Among various tests employed are TLC, DLC, Micro ESR, ANC, CRP, I:T ratio but none of them can help in immediate and early decision making. In our study all of these tests were significantly different in septic neonates.

Platelet indices (platelet counts, platelet distribution width-PDW, mean platelet volume-MPV) are laboratory parameters which can be added to battery of traditional tests for more reliable rapid diagnosis. These indices are widely available and are inexpensive laboratory investigations.

Platelet count is an important haematological parameter in neonatal sepsis. Several studies have been done in analysing platelet indices like MPV and PDW besides platelet count in neonatal sepsis. Few studies have documented significant changes in platelet indices in neonatal sepsis as well as older children and adults.^[6-14] There is

paucity of literature on this role of platelet parameters in neonatal sepsis in Indian subcontinent. This study was done for evaluation of platelet indices (platelet count, PDW, MPV) in neonatal septicaemia, in rural Indian population. Our study's results indicate that platelet count decreases, while MPV and PDW increase in response to sepsis. We interpret thus, that neonatal sepsis in general affects all platelet indices.

Various workers have determined a specific platelet response with different degrees of thrombocytopenia to sepsis in neonates^[15-17]. In the present study, results indicated that sepsis was associated with lower platelet count. Thus our results are in agreement with the available literature that thrombocytopenia is a feature of sepsis. We further analysed the platelet indices among septic neonates. No significant difference was found in MPV, PDW in septic term and preterm neonates. Also, no significant changes were found in parameters of infants with early and late on-set sepsis. Additionally, these levels were neither different between culture positive and negative sepsis, nor for different infectious agents (gram positive/negative and fungal infections) as well. There is still some controversy whether thrombocytopenia is suggestive of one (or more) causative agents of neonatal sepsis. Study by Manzoni P et al^[18] have identified that

thrombocytopenia might not be an organism-specific marker of sepsis. Whereas few authors have shown correlation of thrombocytopenia with specific microorganisms, there is paucity of literature on organism specific changes in various platelet indices, particularly Indian this study also we did not find any specific response, such as a different level and frequency of thrombocytopenia, to any different causative microorganism in infants with sepsis. This may be explained by the fact that the mechanism of thrombocytopenia in septic neonates is believed to be multifactorial.^[19,20]

MPV may be used for predicting the severity of sepsis and death with a high sensitivity and specificity at the diagnosis of sepsis. Guclu E et al showed that MPV was significantly different between sepsis and non septic patients^[14]. Results of our study are in concordance to the available literature. But there was no significant difference in relation to birth weight.

In our study we did not find a significant difference in platelet indices in relation to the organism involved. Similar to our results, Guida et al also stated that there is no statistical significance difference in these indices and gram negative or positive sepsis, neither being premature or full term^[9]. We did not find any significant differences in MPV in relation to term and preterm septic neonates. The results of the present study demonstrated that platelet indices may not be useful for discrimination of sepsis according to time of on-set (LOS and EOS).

In our study we found a significant difference in PDW between septic and non-septic neonates. Guclu E et al showed that MPV and PDW were significantly different between sepsis patients and control group^[14] Authors also concluded PDW as the only significant distinctive laboratory parameter different between survivors and non survivors.

Qayyum R et al reported only PDW to be an independent predictor of all-cause mortality hence can be used as a parameter in estimating death rate among septic patients.^[21]

We did not find any significant correlation of PDW with mortality in our study. It may be due to low number of non survivors in the septic neonates.

From our study, results indicate that platelet indices can be used in increasing the robustness of set of tests in an inexpensive manner in including or excluding the sepsis. In general, in a given situation, there is at present, still, no single test (or a combination of tests) in available panorama of laboratory tests, to reliably identify neonatal sepsis with high sensitivity and specificity. There is dearth of literature from India on platelet indices in neonatal sepsis.

Nevertheless, our study is an attempt in the direction of defining the value of this economically cheaper and widely available haematological parameter in detecting this condition with more confidence for a treating clinician.

More studies can make the role of assessing platelet indices in sepsis, more clear so that we start incorporating them in our laboratory tests along with the conventional ones. Whether other factors like prematurity, type of organism involved also affect the platelet indices, can be made clearer by more larger studies in Indian setting, where cost of expensive tests limit their usefulness in early diagnosis and hence management of neonatal sepsis.

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