

## **An Observational Prospective Evaluation Platelet Count and its Indices-Effectiveness in Early Diagnosis of Neonatal Sepsis**

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### **Abstract**

**Aim:** The aim of the study was to evaluate the efficacy of platelet count (Platelets) and its indices in the early diagnosis of sepsis.

**Methods:** This was a prospective study conducted at Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India for the period of one year. Sample size of 100 patients was recruited as per hospital neonatal intensive care unit work load during the period of study. The study protocol was presented to Institutional Ethics Committee and all the data were collected after taking the informed consent of parents.

**Results:** The general characteristics of a study group showing 100 patients including 60 males and 40 females. On the basis of NNF guidelines, the patients were divided in three groups - 50% were clinically suspected sepsis (probable sepsis), 35% were with blood culture positive (culture positive sepsis), and remaining 15% in blood culture negative but CRP positive group (culture negative sepsis). The patients were divided into early and late onset. EOS was seen more in males (65%) as compared to females (35%). However, in LOS both male and females were equally affected.

**Conclusion:** Platelets can be considered as an early diagnostic tool for neonatal sepsis as it is cheap, rapid, and easily available and does not require additional equipment.

**Keywords:** Neonatal sepsis, Platelet indices, Thrombocytopenia.

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### **Introduction**

Neonatal sepsis is major cause of neonatal morbidity and mortality worldwide contributing around 38% of all deaths in neonates. Situation is even more worsened in low income underdeveloped countries. As per the National Neonatal Perinatal Database 2002-2003, the incidence of neonatal sepsis is 30 per 1000 live births.[1] Globally, the Neonatal mortality

rate has declined by 47% between 1990 and 2015 from 36 to 19 deaths per 1000 live births.[2] India contributes to one-fifth of global live births and more than a quarter of neonatal deaths.[3] Neonatal sepsis is one of the major causes of morbidity and mortality among newborns in the developing world and is more common when compared with developed

countries.[4] In 2013, the global analysis revealed that the major contributing factors for mortality in neonates were infections and preterm with associated complications in developing countries. Host defense against infection is based on two crucial mechanisms: the inflammatory response and the activation of coagulation. Platelets are involved in both hemostasis and immune response. These mechanisms work together in a complex and synchronous manner making the contribution of platelets of major importance in sepsis and platelet count (Platelets) has been used as a marker of sepsis historically. National Neonatal Forum of India (NNF) has classified sepsis into probable, culture-negative, and culture-positive sepsis.[5]

Based on the onset of sepsis, neonatal sepsis is classified into early (<72 h) and late (more than 72 h) onset. In early-onset sepsis (EOS), infants acquire infection by a vertical transmission that is through the bacterial flora of the mother. In late-onset sepsis (LOS), the acquisition of infection is predominantly through the infant's environment.[6] Coagulase-negative Staphylococci (30.27%) were the most common organisms isolated followed by *Acinetobacter* sp (15.1%), *Klebsiella* sp (5.4%), *Staphylococcus aureus* (4.8%), and *Escherichia coli* (4.8%) in a study conducted by Asifa Nazir.[7] For a definite diagnosis of sepsis blood culture has always been the gold standard.[8] However, the blood culture has a huge disadvantage of delay in availability of the result along with other chances of false-negative results.[9] Other tests such as Procalcitonin and IL-6 are very expensive and not easily affordable by most of the patients in developing countries.[10]

The aim of the study was to evaluate the efficacy of platelet count (Platelets) and its indices in the early diagnosis of sepsis.

### Materials and Methods

The study was conducted in the division of Neonatology in the Department of Paediatrics and in the Department of Pathology at Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India. The study was conducted in 1 year and written informed consent was taken from the parents. It was a Cross-sectional Analytical study and 100 patients were recruited for the statistical purposes for convenient sampling method.

Neonates delivered in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India and referred from outside with features of suspected septicemia or probable sepsis as per NNF criteria of poor feeding, irritability, excessive cry, lethargy poor cry and reflexes, fever, hypothermia, jaundice, vomiting, abdominal distension, tachypnea and grunting, convulsions, diarrhea, pustules, cyanosis, bulge fontanelle, disseminated intravascular coagulation, bleeding, poor perfusion, shock, and apnea were included in the study. Neonates who developed sepsis during the period of hospitalization for other reasons and proved to have sepsis by positive blood culture, cerebrospinal fluid (CSF), and urine culture were also included in the study while neonates with congenital anomalies of Gastrointestinal Tract system such as trachea-esophageal fistula, malrotation of gut, anomalies of the cardiovascular system or respiratory system, central nervous system, and inborn error of metabolism were excluded from the study.

At admission, thorough history was taken and clinical examination was done. Sepsis profile was sent including hemoglobin, total leukocyte count, differential leukocyte count, Platelets and its indices-MPV, PDW and PCT, absolute neutrophil count (ANC), C-reactive protein (CRP), band cell ratio (BCR), and blood culture for all the patients. BECKMAN COULTER LS-750 Analyzer was used and as when required X-ray chest, Urine C/S, and CSF culture was done. The

patients were categorized into three groups-Clinically suspected sepsis (probable sepsis), culture positive sepsis, and culture negative as per NNF criteria of sepsis screen comprising of total leukocyte count, I/T ratio (BCR), ANC, m-ESR e, and CRP.[11,12]

Statistical Package for the Social Sciences 20.0 version of statistical analysis was used. Sensitivity, Specificity, Positive predictive value (PPV) and Negative

predictive value (NPV) of Platelets and its indices were evaluated and compared between probable sepsis with culture negative sepsis and probable sepsis with culture positive sepsis. Non-parametric tests like the Chi-square test were applied to see the association between the variables. The three groups were compared for Platelets and its indices with Analysis of variance (ANOVA) test.

**Results**

**Table 1: Patient details**

Variables	N%
<b>Gender</b>	
Male	60 (60)
Female	40 (40)
<b>Types according to NNF</b>	
Suspected Sepsis	50 (50)
Culture positive sepsis	35 (35)
Culture Negative sepsis	15 (15)

The general characteristics of a study group showing 100 patients including 60 males and 40 females. On the basis of NNF guidelines, the patients were divided in three groups - 50% were clinically suspected sepsis (probable sepsis), 35% were with blood culture positive (culture positive sepsis), and remaining 15% in blood culture negative but CRP positive group (culture negative sepsis). The

patients were divided into early and late onset. Out of 40 preterm subjects, 25 (62.5%) were male and 15(37.5%) were female whereas out of 60 term subjects 36(60%) were male and 24(40%) were females. EOS was seen more in males (65%) as compared to females (35%). Probable sepsis was more among preterm babies whereas culture negative and culture positive were more in term babies.

**Table 2: Sensitivity and specificity of platelet count and its indices in probable sepsis and culture positive sepsis**

Parameters	Probable sepsis				Culture positive sepsis			
	Platelet count	PDW	MPV	Plateletcrit	Platelet count	PDW	MPV	Plateletcrit
Specificity	68	62.5	62.5	6.2	68	62	62.5	6.25
Sensitivity	69	28	34	86	52.9	14	26.4	17
NPV	21.5	21.7	23.2	12.5	40.7	25.6	28	3.4
PPV	66.6	70	73.9	74.1	78.2	45	60	28.5
Accuracy	57.8	36	40.9	66.6	58	30	38	14

Sensitivity and accuracy for Platelets were 52.9% and 58% in the culture positive group, whereas sensitivity and accuracy for Platelets in the probable sepsis group was 69% and 57.5%. Specifically, NPV

and PPV was 68%, 40.7%, and 78.2% in culture positive whereas it was 68%, 21.5%, and 66.6% in the probable sepsis group

**Table 3: Comparison of normal with probable sepsis and culture positive**

Parameters	Normal	Probable sepsis (mean)	Culture + ve sepsis (mean)	Culture negative CRP + ve (mean)	p-value
Platelet count	150–400	219.2	174.8	205.78	0.030
PDW	8.3–56.6%	12.5	15.1	11.05	0.170
MPV	7.2–11.7fl	10.9	9.94	11.9	0.550
Plateletcrit	0.22–0.24%	2.5	1.46	3.2	0.60

Analysis on the basis of ANOVA for three groups-culture positive, culture negative, and probable sepsis was done for Platelets and its indices (MPV, PDW, and PCT). Platelets was found to be significant in all groups.

### Discussion

Neonatal sepsis is major cause of neonatal morbidity and mortality worldwide contributing around 38% of all deaths in neonates. Situation is even more worsened in low income underdeveloped countries. As per the National Neonatal Perinatal Database 2002-2003, the incidence of neonatal sepsis is 30 per 1000 live births.[13]

The need for early recognition, diagnosis of neonatal septicemia, and prompt institution of treatment is paramount to prevent death (s) and complications associated with neonatal septicemia. The definitive diagnosis of sepsis is made by blood culture, which requires a minimum of 48–72 h, yields a positive result in 30–40% of cases. One of the most common hematological manifestations seen during early sepsis is thrombocytopenia. Platelet indices; PCT, MPV, and PDW are a group of derived platelet parameters obtained as a part of the automatic complete blood count. PI are biomarkers of platelet activation. Average mean cell volume is 7.2–11.7 fL Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation. During activation, platelets' shapes change from biconcave discs to spherical, and a pronounced pseudopod formation occurs that leads to MPV increase during platelet activation.

The PDW reported varies markedly, with reference intervals ranging from 8.3 to 56.6%. Under physiological conditions, there is a direct relationship between MPV and PDW; both usually change in the same direction. PCT is the volume occupied by platelets in the blood as a percentage. The normal range for PCT is 0.22–0.24%.

Platelets play an important role in inflammation. Septic patients are observed to have low Platelets due to production of many cytokines, endothelial damage and bone marrow suppression. PI have been shown to have diagnostic value in certain inflammatory diseases, such as inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis, and atherosclerosis.[14] In our study, sepsis was predominantly present in males (60%) as compared to females (40%) with early onset sepsis in 64% and 36% had late onset sepsis. In our study, there were 50% probable sepsis cases, 34% culture proven cases and 16% culture negative sepsis. In a similar study conducted by Salama et al. 39.8% of neonates had probable sepsis and were culture positive.[15]

Naik et al. reported thrombocytopenia in 66.25% of neonates with sepsis having 66.25% sensitivity and 87% specificity.[16] Culture positive patients in our study were found to have thrombocytopenia in 72% of neonates having 52.9% of sensitivity and 68% of specificity with NPV 40.7% and PPV 78.2%. Probable sepsis neonates also had decreased Platelets with sensitivity and specificity as 20% and 68%, respectively, with NPV of 21.5 and PPV of 6. In culture positive cases, in our study, PDW

sensitivity is 14% with specificity of 62% and NPV of 25.6 with PPV of 45. While in probable sepsis there was sensitivity of 62% with specificity of 62.5% with NPV of 21.7 and PPV of 70. Sangsari et al. in their study on PI in different types of germs found that PDW was elevated in all culture positive infections specifically in Gram-negative sepsis.[17] PCT in culture proven cases had sensitivity of 17% and specificity of 6.25% with NPV of 3.4 and PPV of 28.5 while in probable sepsis PCT showed sensitivity of 86% with specificity of 62% and NPV of 12.5 with PPV of 74.1 (Fig. 4). Very few studies show changes in PCT. Sandeep et al. reported high PDW, low PCT, and high but not significant MPV in preterm neonates which were compared with term neonate.[18]

The Platelets was significantly low (p value-0.030) in all three groups, probable sepsis, culture positive sepsis and culture negative sepsis; however, the PI such as PDW, MPV, and PCT did not show any significant difference in the various groups. Platelets may be considered an alternative, novel diagnostic tool for detection of early neonatal sepsis as it is cheap, rapid, and easily available and does not require additional equipment.

### Conclusion

Platelets can be considered as an early diagnostic tool for neonatal sepsis as it is cheap, rapid, and easily available and does not require additional equipment. High PDW, high MPV and low platelet count are more associated with neonatal sepsis.

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