Study to Evaluate the Effectiveness of Platelet Count (Referred to as Platelets) and its Indices as Diagnostic Tools for Early Detection of Sepsis in a Hospital Setting

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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 department of pediatrics for the period of one year. Sample size of 200 patients was recruited as per hospital neonatal intensive care unit work load during the period of study.

Results: The general characteristics of a study group showing 200 patients including 130 males and 70 females. On the basis of NNF guidelines, the patients were divided in three groups - 52% were clinically suspected sepsis (probable sepsis), 34% were with blood culture positive (culture positive sepsis), and remaining 14% in blood culture negative but CRP positive group (culture negative sepsis). Probable sepsis was more among preterm babies whereas culture negative and culture positive were more in term babies. Sensitivity and accuracy for Platelets were 54.6% and 60% in the culture positive group, whereas sensitivity and accuracy for Platelets in the probable sepsis group was 68% and 57.8%. 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. 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 were found to be significant in all groups.

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.

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. [3] 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]

Neonates are fragile and can deteriorate rapidly, so rapid diagnosis and prompt management is required. Blood culture and sepsis screening are currently used method, but their utility is limited due to delayed reporting and increased cost. [6]

Due to these limitations we need to find parameters which will increase the sensitivity and specificity. Platelet indices can be helpful in the future diagnosis of neonatal sepsis. Despite being a promising and convenient marker for sepsis, there have been only a few studies on the utility of platelet markers in neonatal sepsis. 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]

Testing of newer biomarkers from readily available tests and establishing their diagnostic accuracy to improve the precision in an early diagnosis of neonatal sepsis needs to be done. A CBC is one such affordable and readily available investigation. Platelets have been recognized as a key player in inflammation and thrombosis. Mean platelet volume (MPV) is a surrogate marker of platelet activity and is easily available in automated cell counters. In many physiological and pathological states, platelet activation is indirectly measured from MPV. MPV has been reported to have diagnostic and prognostic values in perinatal infections and inflammation. [11,12] In a recent study by Hayato et al [13] a high MPV was shown to correlate with neonatal mortality in preterm neonates less than 32 weeks of age.

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

This was a prospective study conducted at department of pediatrics, SKMCH, Muzaffarpur, Bihar, India for the period of one year. Sample size of 200 patients was recruited as per hospital neonatal intensive care unit work load during the period of study.

Neonates delivered in SKMCH, Muzaffarpur, Bihar, 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. [14,15]

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%
Gender	
Male	130 (65)
Female	70 (35)
Types according to NNF	
Suspected Sepsis	104 (52)
Culture positive sepsis	68 (34)
Culture Negative sepsis	28 (14)

The general characteristics of a study group showing 200 patients including 130 males and 70 females. On the basis of NNF guidelines, the patients were divided in three groups - 52% were clinically suspected sepsis (probable sepsis), 34% were with blood culture positive (culture positive sepsis), and remaining 14% in blood culture negative but CRP positive group (culture negative sepsis). 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	70	62.6	64.6	6.2	70	64	62.5	6.25
Sensitivity	68	28	34	86	54.6	16	25.5	18
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	60	30	38	14

Sensitivity and accuracy for Platelets were 54.6% and 60% in the culture positive group, whereas sensitivity and accuracy for Platelets in the probable sepsis group was 68% and 57.8%. 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
Platletcrit	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 were 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. [16]

The general characteristics of a study group showing 200 patients including 130 males and 70 females. On the basis of NNF guidelines, the patients were divided in three groups - 52% were clinically suspected sepsis (probable sepsis), 34% were with blood culture positive (culture positive sepsis), and remaining 14% in blood culture negative but CRP positive group (culture negative sepsis). Probable sepsis was more among preterm babies whereas culture negative and culture positive were more in term babies. 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. [17] In a study conducted by Salama et al. 39.8% of

neonates had probable sepsis and were culture positive. [18]

Naik et al. reported thrombocytopenia in 66.25% of neonates with sepsis having 66.25% sensitivity and 87% specificity. [19] Sensitivity and accuracy for Platelets were 54.6% and 60% in the culture positive group, whereas sensitivity and accuracy for Platelets in the probable sepsis group was 68% and 57.8%. 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. 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. [20] 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. 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. [21]

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 were found to be significant in all groups. 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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