Platelet Indices as Indicators of Severity of Sepsis

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Abstract

Aims: To compare Platelet indices with SOFA scores of patients with sepsis in order to assess the relationship between platelet indices like MPV and PDW and the severity of sepsis. *Settings and Design:* A total of 100 patients with sepsis or septic shock as cases and 95 patients as controls (with out sepsis) were considered for this study. *Patients and Methods:* The SOFA scoring of the patients (both cases and controls) was done at the time of admission. The relationship between platelet indices and severity of sepsis obtained by prognosis of the patient using admission SOFA score was assessed. *Statistical Analysis:* Statistical analysis was performed using SPSS for Windows version 17.0. *Results:* In patients with sepsis, there was a significant difference (P<0.05) between the baseline values of platelet counts as well as platelet indices amongst the two groups. *Conclusion:* The findings of this study suggest that platelet indices are significant indicators of severity of sepsis. Intense supervision and aggressive treatment of sepsis patients with higher baseline platelet indices may prevent progression of disease.

Keywords: Sequential Organ Failure Assessment (SOFA) Score; Mean Platelet Volume (MPV); Platelet Distribution Width (PDW); Platelet Indices; Sepsis.

Introduction

Sepsis is a major disease affecting millions of people worldwide each year [1,2]. It is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [3]. Septic shock is a subset of sepsis, in which, underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality [3].

Sepsis is the primary cause of death from infection, especially if not recognised and treated promptly and its recognition mandates urgent attention. The main differentiating factors between sepsis and any other infection are an aberrant host response and the presence of organ dysfunction [3].

The Sequential Organ Failure Assessment (SOFA) score is one of the most widely available scores, to describe organ dysfunction and predict survival [4]. It is a means to clinically characterize a septic patient. SOFA has widespread familiarity within the critical care community and a well-validated relationship to mortality risk. It can be scored retrospectively, either manually or by automated systems, from clinical and laboratory measures often performed routinely as part of acute patient management [3].

One of the systems frequently affected in sepsis is the haemostatic system.Thrombocytopenia (platelet count < 150,000/µl) is common in critically ill patients, with an estimated incidence of 20%–40% at some point during the intensive care unit (ICU) stay [5, 6]. Sepsis is a major risk factor for the development of thrombocytopenia.Generally, platelet production increases as platelet count decreases. An increased number of young platelets are also functionally more active than older platelets [1,7].

In addition to their important role in haemostasis and thrombosis, accumulating evidence demonstrates that platelets contribute to the inflammatory process, microbial host defense, wound healing, angiogenesis, and remodeling [8].

Changes in the coagulation system are manifested by the prolongation of the Activated partial thromboplastin time (aPTT) and Prothombin time (PT), and decreased platelet (PLT) count [9]. The extent of the platelet fall is correlated to the prognosis in many studies, and platelet count has been shown to return towards normal values as the patient recovers.

Platelet indices like Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) are related to PLT and hence vary with variation in platelet counts.

Thus, a prospective study was conducted by us with an aim to compare Platelet indices with SOFA scores of patients with sepsis in order to assess the relationship between platelet indices like MPV and PDW and the severity of sepsis.

Materials and Methods

Eligible adult patients admitted in the ICU were considered for the study based on the following Inclusion and Exclusion Criteria:-

Inclusion Criteria

- Patients - Those in the ICU diagnosed as sepsis, severe sepsis, and septic shock at the first medical examination.

- Control Group - Patients in the ICU without sepsis.

Exclusion Criteria

- Pregnant women or women who had recently given birth
- Patients with active hemorrhage
- Patients with hematological diseases
- Patients who had infused with blood or platelets prior to their admission
- Patients who had used anti-platelet drugs prior to their admission.

A total of 100 patients with sepsis or septic shock as cases and 95 patients as controls were considered for this study.

Data Collection

After taking the patients' informed consent, their baseline characteristics, including demographic information were noted. The SOFA scoring of the patients (both cases and controls) was done at the time of admission based on assessment of the following systems – respiratory, coagulation, hepatobiliary, cardiovascular, neurologic and renal systems.

Blood samples were collected from the patients and platelet counts and indices were estimated at initial presentation of the patients to the hospital. All blood samples were obtained from the venous system and stored in tubes containing ethylenedia-minetetraacetic acid (EDTA) and assayed automatically using internationally certified devices - Sysmex XE-2100 and Sysmex XT-2000i. These devices work by utilizing the power of fluorescent flow cytometry and hydrodynamic focusing technologies.

The relationship between platelet indices and severity of sepsis obtained by prognosis of the patient using admission SOFA score was assessed.

Statistical Analysis

All the quantitative variables like age, mean platelet volume, etc. are presented in terms of descriptive statistics such as Median and Interquartile range (IQR). All the qualitative variables are presented using Percentage.

Baseline characteristics as well as Platelet counts, MPV and PDW were compared between cases and controls using Mann-Whitney test. Chi square test was used to compare the categorical variables between cases and controls.

Patients were grouped into two categories based on their SOFA scores at the time of admission – a) those with SOFA scores < 9, and b) those with SOFA scores > 11. Platelet count, MPV and PDW between these two groups were compared independently using Mann-Whitney test.

Receiver operating characteristic (ROC) curve was used to find the cut off point for MPV and PDW for determining severity of sepsis. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for MPV and PDW.

All tests were two sided and a P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS for Windows version 17.0.

Results

A total of 100 sepsis patients were included in the study consisting of 64 males and 36 females. Also, 95 patients (64 males and 31 females) were included in the control group.

Age, gender and other baseline characteristics such as respiratory rate, heart rate, and haematocrit were statistically similar between the two groups (P>0.05). However, a statistically significant difference (P<0.05) was found in the temperature, white blood cell count, Prothrombin Time and Activated partial thromboplastin time between cases and controls [Table 1].

The cases exhibited a significantly lower baseline platelet count (P<0.05) when compared to controls at the time of admission. Patients with sepsis had higher values of platelet indices compared to controls at the time of admission to the ICU, however, this was not statistically significant (P>0.05) [Table1].

The cases and controls were further divided into two groups based on their SOFA score at the time of admission – those with a score < 9 and those with a score > 11. The trends in platelet count and indices in these two groups are shown in Table 2.

In patients with sepsis, there was a significant difference (P<0.05) between the baseline values of platelet counts as well as platelet indices amongst the two groups [Table 2].

There was no significant difference (P>0.05) observed between the platelet counts and indices amongst the two groups in case of controls [Table 2].

Figure 1 and Figure 2 show the results of ROC curve analysis for finding out the cut off point for

Table 1: Demographic characteristics and trends in baseline platelet counts and indices of cases and controls

	Cases	Controls	P Value
Age (years)			0.107
≤ 30	7.00%	17.90%	
31 – 45	21.00%	22.10%	
46 – 60	28.00%	26.30%	
≥ 60	44.00%	33.70%	
Sex			0.621
Males	64.00%	67.40%	
Females	36.00%	32.60%	
Period of stay in ICU (Days)	7.00 (5.00 - 11.00)	6.00 (3.00 - 11.00)	0.075
Temperature			0.001
Febrile	47.00%	23.20%	
Afebrile	53.00%	76.80%	
Respiratory rate (cpm)	21.50 (18.00 - 26.75)	20.00 (18.00 - 26.00)	0.052
Heart rate (bpm)	100.50 (88.00 - 110.00)	94.00 (82.00 - 108.00)	0.097
Hematocrit (%)	32.00 (28.25 - 38.00)	35.00 (29.00 - 42.00)	0.055
White cell count (/mm³)	14015.00 (7802.50 - 18225.00)	10210.00 (7550.00 - 13740.00)	0.01
Prothrombin time (s)	14.20 (12.60 - 16.25)	12.80 (11.70 - 14.60)	0.001
Activated partial thromboplastin time (s)	38.75 (32.00 - 51.45)	30.00 (24.70 - 36.20)	<0.001
Platelet Count (lakhs/mm³)	1.46 (0.595 - 2.15)	2.21 (1.34 - 2.935)	<0.001
Mean Platelet Volume (fl)	10.45 (9.40 - 11.30)	9.90 (9.15 - 10.80)	0.053
Platelet Distribution Width (%)	11.90 (10.0 - 14.35)	10.80 (9.95 - 12.20)	0.124

Table 2: Trends in platelet counts and indices among cases and controls

		SOFA score ≤ 9*	SOFA score ≥ 11*	P Value
Cases	Platelet count (lakh/mm³)	1.715 (0.68 - 2.6475)	0.705 (0.35 - 1.1225)	0.002
	Mean Platelet Volume (fl)	10.00 (9.00 - 11.00)	11.90 (10.98 - 12.65)	<0.001
	Platelet Distribution Width (%)	11.15 (9.85 - 13.50)	15.80 (13.10 - 16.725)	<0.001
Controls	Platelet count (lakh/mm³)	2.21 (1.425 - 2.92)	1.145 (0.375 - 3.48)	0.36
	Mean Platelet Volume (fl)	9.80 (9.20 - 10.80)	9.95 (6.30 - 10.90)	0.619
	Platelet Distribution Width (%)	10.90 (10.00 - 12.20)	10.70 (6.75 - 12.525)	0.452

*Data are median (IQR)

Table 3: Results of ROC curves of Platelet Indices

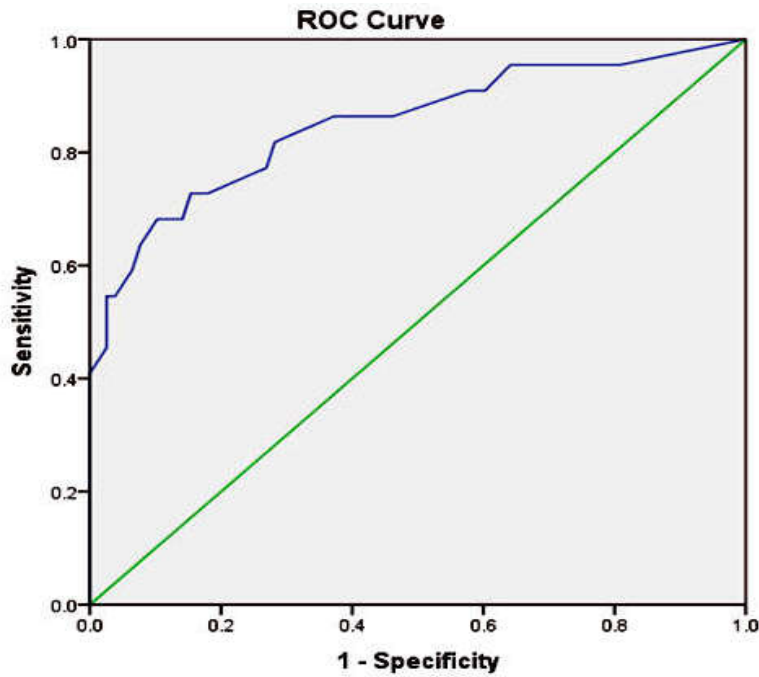|	Platelet Indices	
	Mean Platelet Volume	**Platelet Distribution Width**
Cut off point	11.2 fl	14.50%
Sensitivity	72.70%	72.70%
Specificity	84.60%	92.30%
Positive Predictive Value	57.10%	72.70%
Negative Predictive Value	91.70%	92.30%
Area Under Curve	85%	85.90%
P Value	<0.001	<0.001

Fig. 1: ROC curve for Baseline Mean Platelet Volume

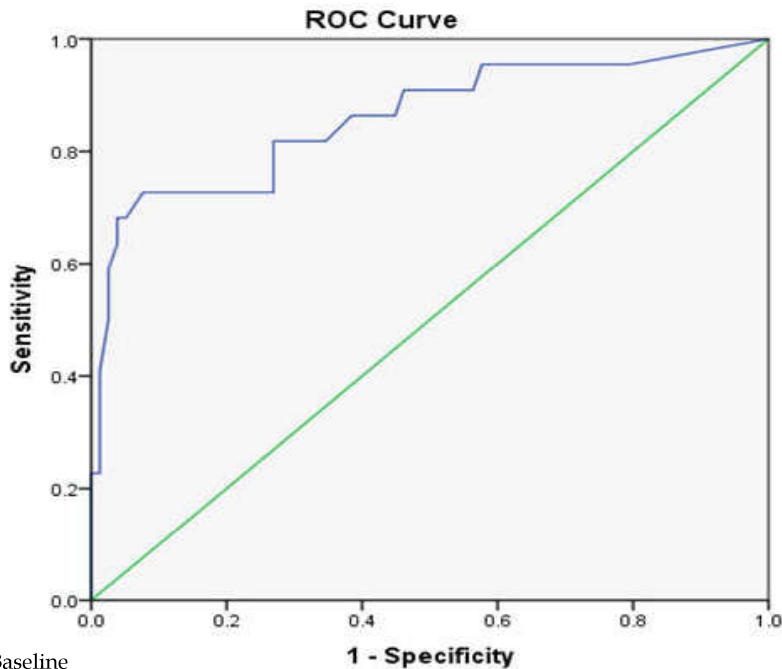Diagonal segments are produced by ties.

Fig. 2: ROC curve for Baseline Platelet Distribution Width

Diagonal segments are produced by ties.

baseline platelet indices. A cut off point for MPV and PDW were 11.2 fl and 14.5% respsctively. [Table 3].

Discussion

Sepsis is a non specific inflammatory defence mechanism [10].The mortality rate of this condition varies from 25% to 80% depending on illness severity and the number of occurrences and the severity of organ failure [11,12,13]. Hence, early detection of sepsis will be useful for risk stratification and therefore, allocation of resources.

The present study is a prospective oneabout the prognostic value of changes in platelet indices in patients with sepsis or septic shock. The main findings of this study are mentioned below.

A comparison was made between the platelet counts and indices of the cases and controls. It was found that the patients with sepsis had significantly lower baseline platelet counts when compared to patients without sepsis. Also, their platelet indiceswere higher than the controls at the time of admission. This situation was probably due to endothelial damage, production of many cytokines, and bone marrow suppression in septic patients.Platelets release more than 300 proteins and small molecules from their granules, which can influence the function of the vascular wall and circulating immune cells [14]; and secrete microbicidal proteins and antibacterial peptides [8]. Platelets, also mediate leukocyte movement from the bloodstream through the vessel wall to tissues.They are capable of forming reactive oxygen species; the oxidative stress that accompanies inflammation can also activate platelets [15,16].

Their ability to influence other cells means that they can also play many principal roles in the pathophysiology of diseases [15].

Further, there was a significant difference in the platelet counts and indices between the sepsis patients with different SOFA scores. Patients with higher SOFA scores had higher MPV, increased PDW, and lower platelet count compared to patients with lower SOFA scores. Therefore, platelet indices and count can be used as a direct indicator of organ dysfunction and hence, predict mortality. MPV is a measurement of the average size of platelets found in the blood. It usually increases in cases of destructive thrombocytopenia. Normal value of MPV has been found to be between 7.5-11.5fl in previous studies [17]. The PDW increases during

platelet depletion when turnover is accelerated and is an indicator of differences in platelet size. It is an indicator of variation in platelet size, which can be a sign of active platelet release. Normal values of PDW are between 10% and 17.9% [1,9].

It was found that greater baseline MPV levels, higher than 11.2fl, have moderate (72.70%) sensitivity and (84.60%) specificity can be used for determining sepsis severity.Similarly, at the time of admission, PDW levels, higher than 14.5%, with moderate (72.70%) sensitivity and high (92.30%) specificity can also be used. Amoderate positive predictive value (72.70%) supports this hypothesis too. Therefore, these indices can be used as an auxiliary test in the determination of severity of sepsis.

Findings in recent studies support our results. Van der Lelie et al showed that MPV was elevated in 13 of the 25 septicaemia patients, and returned to normal values as soon as the disease was under control [18].

Another study of 10 infected patients with thrombocytopenia, found that MPV rose at the beginning and subsequently decreased, following a biphasic change [19]. An elevation of MPV therefore suggested that the infection is invasive, systemic and uncontrolled and is related to the severity of the disease [9].

In a third study, it was concluded that MPV and PDW were significant parameters in the diagnosis of sepsis and in the differential diagnosis of sepsis and severe sepsis [1]. It was found that if PDW and MPV show increased trend while Platelet count shows a decreased trend, a poor prognosis maybe indicated in patients with septic shock [20].

The present study conducted in adults demonstrated that MPV and PDW levels were higher in sepsis patients. It was observed that PDW and MPV levels increased with increase in severity of sepsis patients. The low level of thrombocytopenia in patients with severe sepsis can explain the high levels of MPV and PDW.

Conclusion

The findings of this study suggest that platelet indices are significant indicators of severity of sepsis. Further studies are required to establish their role as prognostic markers of sepsis and septic shock. However, they can be used in addition to other established markers such as SOFA score, Acute Physiology and Chronic Health Evaluation

(APACHE) II score and C- reactive protein (CRP) to measure illness severity due to their low cost and easy accessibility. Intense supervision and aggressive treatment of sepsis patients with higher baseline platelet indices may prevent progression of disease.

Acknowledgement

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