Section: Medicine

Original Research Article

MEAN PLATELET VOLUME AND IT'S CORRELATION WITH SOFA SCORE FOR DETERMINING SEVERITY AND PROGNOSIS IN SEPSIS

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ABSTRACT

Background: Sepsis is a major cause of morbidity and mortality, and early assessment of disease severity is essential for improving outcomes. Mean platelet volume (MPV), a routinely available haematological parameter, reflects platelet activation and systemic inflammatory response and may have prognostic significance in sepsis. **Materials and Methods:** This hospital based prospective longitudinal study was conducted in a tertiary care teaching hospital and included 147 adult patients diagnosed with sepsis. Clinical findings, laboratory parameters including mean platelet volume (MPV) and Sequential Organ Failure Assessment (SOFA) scores were recorded at admission and 72 hours after admission. The correlation between MPV and SOFA score was analysed using Pearson correlation. Paired t-test was used to compare changes in SOFA score and MPV from admission value to 72 hours of admission. A p-value of less than 0.05 was considered statistically significant. **Results:** The mean SOFA score at the time of admission was 6.30 ±2.83 and the mean MPV was 8.71 ±0.70. MPV showed a strong positive correlation with SOFA score (r=0.710, p=0.01). After 72 hours of admission, the mean SOFA score (8.69 ±4.89), and the mean MPV (9.08 ±0.91) increased as compared to admission value, p value <0.001. Higher MPV values were associated with increased disease severity as indicated by higher SOFA scores. **Conclusion:** Mean platelet volume demonstrates a significant positive correlation with SOFA score in patients with sepsis. MPV, being a simple, inexpensive and readily available laboratory parameter, may serve as a useful adjunct marker for addressing severity and prognosis in sepsis.

INTRODUCTION

Sepsis has been referred to as the quintessential medical disorder of our time. This is due to the fact that it is not only the leading cause of morbidity and mortality in hospitalized patients, but it is also frequently the direct result of improvements in medical care for patients who suffer from a variety of disorders for which, up until recently, there were no treatments available.[1] The definition of the term "sepsis" has developed over the course of thousands of years via the course of history. In the ancient definitions provided by Hippocrates, the term "sepsis" was defined as the process of decay or disintegration of biological matter. Hippocrates further added that "when continuing fever is present, it is dangerous if the outer parts are cold, but the inner parts are burning hot." In the year 1992, sepsis was classified as a syndrome that is characterized by a systemic inflammatory response to an infection. This illness is characterized by specific characteristics such as increased temperature, white blood cell count, pulse rate and respiratory rate.[2] Under the current circumstances, sepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection in which septic shock is a subset of sepsis in which underlying circulatory and cellular/ metabolic abnormalities are profound enough to substantially increase mortality.[3,4]

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According to the current definition of sepsis, the words dysregulated and host response are not clearly defined. Instead, they are regarded as maladapted reactions within the immune and non-immune systems that are along the causal pathway to organ failure and mortality. According to a research that was published not too long ago by the Global Burden of Diseases, sepsis is rather prevalent, with almost 50 million cases globally each year.[5] Although the site of infection and the organism that causes sepsis might vary depending on geographic area and age, the most frequent types of sepsis are caused by bacterial infections of the respiratory system and the gastrointestinal system. Sepsis can effect anyone of any age. The mortality rate associated with sepsis was projected to be 11 million in the year 2017, which corresponds to an age-standardized mortality rate of 148 per 100,000 people. This figure accounts for approximately twenty percent of all fatalities that occur worldwide.[5] The mortality rate among patients with sepsis who require admission to critical care units is one in three and they do not survive for thirty days,[6,7] and mortality rates vary depending on factors such as age, the presence of concomitant conditions, the number of organ dysfunctions and the kind of dysfunction.[8,9]

As a result of these findings, the World Health Organization (WHO) decided to make sepsis a priority in terms of global health. This alarming increase in incidence can be attributed to a number of different factors, including (i) the advanced average age among patients, particularly in western countries; (ii) the increased number of invasive procedures; (iii) the widespread utilization of immunosuppressive drugs and chemotherapy and (iv) antibiotic resistance. Septic patients have a high risk of in-hospital mortality (IHM), which accounts for approximately 20% of all deaths worldwide. This combined ailment is one of the conditions that is encountered in the emergency department (ED) that has the highest mortality rate. This is despite the significant advancements that have been made in therapeutic management.[10]

In addition, people who survive sepsis have a greater likelihood of going back to the hospital and dying in the long run.[11,12] Nearly half of those who survive sepsis are readmitted to the hospital at least once within a year, and one in six people who survive sepsis do not make it through the first year of treatment.[13,14] We have not yet developed a single medication that has been shown to reliably save the lives of sepsis patients, despite the fact that we have conducted more than three decades of study and more than two hundred randomized controlled studies.[15] In most cases, the treatment for sepsis consists of straightforward measures such as controlling the source of the infection, administering antibiotics at the appropriate time, performing resuscitation and supportive care for organ failure.[16]

The frequency of microorganisms that may be identified in sepsis and septic shock has changed throughout the course of time. Gram-positive bacteria are now the most prevalent, while fungal sepsis has become increasingly significant in terms of both clinical and epidemiological relevance. Staphylococcus aureus and Streptococcus pneumoniae are the Gram-positive bacteria that are most frequently isolated as pathogens. On the other hand, among the Gram-negative bacteria, those most frequently detected include Escherichia coli, Klebsiella and various species of Pseudomonas. Candida spp. which can frequently be seen in immunosuppressed or neoplastic patients who are having long-term therapy with chemotherapeutic and immunosuppressive medicines, play the most important role among the fungal infections. The respiratory tract and pulmonary parenchyma account for 43 percent of all infections that are linked with sepsis. The urinary system accounts for 16 percent, the abdominal infections accounts for 14 percent and other sites like brain parenchyma accounts for 13 percent.[17]

When viewed from a pathogenetic perspective, sepsis is presently thought to be the outcome of many pathways that concurrently include a large variety of mediators that are both pro-inflammatory and anti-inflammatory. In addition, the cellular alterations that are associated with sepsis have recently been characterized and the significance of microcirculation has been stressed in the transition from sepsis to septic shock. In this respect, the endothelium has been recognized as the main functional unit in the pathophysiology of sepsis due to its role in the regulation of microcirculation and the modulation of coagulation mechanisms as well as inflammatory and anti-inflammatory signalling pathways. This is because of the endothelium's ability to regulate microcirculation. Composed of proteoglycans and glycoproteins, the glycocalyx is a component of the endothelium membrane that is included in the membrane. There are a variety of tasks that it mediates, including the building of a mechanical barrier that regulates vascular permeability, the activation of leukocytes and platelet adhesion and the control of the inflammatory and anti-inflammatory response. It is possible for oxidizing agents, cytokines, exotoxins and bacterial endotoxins to cause damage to the morpho-functional integrity of the glycocalyx, which is referred to as "glycocalyx shedding." Because of this occurrence, leukocytes undergo diapedesis and there is an increase in vascular permeability. Additionally, oedema occurs, which causes an increase in interstitial pressure and a decreased level of tissue perfusion.[18]

Patients who have infections that originate from any infectious source should be suspected of having sepsis, as stated by the third international consensus on sepsis and septic shock (Sepsis-3). In the case of these individuals, it is advisable to take into consideration a quick Sequential Organ Failure Assessment (qSOFA), wherein a result of two or more suggests patients who are at a greater risk of dying while they are still in the hospital. The 2021

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recommendations, on the other hand, not only oppose the use of qSOFA as the primary screening tool, but they also encourage the use of the National Early Warning Score (NEWS) or the systemic inflammatory response syndrome (SIRS) score instead. This is because both scores have a higher sensitivity than qSOFA when it comes to predicting the fate of sepsis patients. The confirmation of a diagnosis of sepsis is achieved when the Sequential Organ Failure Assessment (SOFA) score is equal to or greater than 2. The condition known as septic shock is characterized by the use of a vasopressor to keep a patient's mean arterial pressure (MAP) at a level of 65 mmHg or higher and a serum lactate level of 2 mmol/L or higher.[19]

Approximately forty percent of patients who are suffering from severe sepsis have platelet counts that are less than eighty thousand per microlitre. Platelets play a crucial role in the thromboembolic, inflammatory and immunomodulatory processes that occur in sepsis. People who did not survive sepsis have been shown to have significant thrombocytopenia as a result of the consumption of platelets and depletion of coagulation factors that occurs during the condition. Mean platelet volume (MPV) is a reliable method for determining the size of platelets and shows the degree to which platelets are reactive. Platelets can become more prothrombotic, leads to platelet adhesion and aggregation when their MPV is increased. Platelets that have an elevated MPV are also more active and bigger. In most cases, a larger MPV is a reflection of compensatory production in the bone marrow following stress-induced platelet death, such as that which takes place during sepsis. Changes in MPV have been seen in a number of different conditions, including infection, sepsis, coronary artery disease, cerebrovascular illnesses, arterial and venous thrombosis and chronic inflammatory disorders, according to a number of investigations.[20]

One of the characteristics of inflammation is the presence of increased MPV. Endothelial dysfunction is a component of the route that leads to organ dysfunction and may be connected with platelet activation and consumption. In recent studies, it was shown that the mean platelet volume was increasing in tandem with the levels of IL-6 and CRP in patients with sepsis and that this increase was connected with the severity of the sepsis.[21]

The Mean Platelet Volume (MPV), which is measured in femtoliters (fL), is an anatomical biomarker that is generated from platelets. Although it is not often utilized, it is recorded in standard blood counts. It is garnering interest as a sign of progression to multiple organ dysfunction, clinical severity and death in septic conditions.[22,23] Using the MPV as a predictor of mortality and severity in patients with sepsis, the purpose of this study is to demonstrate the utility of the MPV and compare it with SOFA.

Objectives

1. To determine the usefulness of Mean Platelet Volume (MPV) in sepsis for illness severity.
2. To compare the effectiveness of Mean Platelet Volume with Sequential Organ Failure Assessment (SOFA) Score in determining severity of sepsis.

MATERIALS AND METHODS

Study design: Prospective longitudinal study

Study setting: The study was carried out in the Department of Medicine, RIMS, a tertiary care hospital in Imphal, Manipur, India.

Study population: All the patients of both gender between the age of 18 to 75 years admitted in ICU and Medicine ward with sepsis.

Inclusion criteria:

1. Sepsis defined by SOFA score ≥ 2.
2. Length of hospital stay more than 72 hours.

Exclusion criteria:

1. Patients with active haemorrhage.
2. Patients who had used anti-platelet drugs such as clopidogrel, aspirin prior to admission.
3. Patients who had received radiotherapy or chemotherapy or bone marrow transplantation 1 month prior to admission.
4. Patients who refuse to participate in the study.

Study duration: The study was conducted from September, 2023 to October, 2024.

Sample size and Sampling: The study was conducted on 147 eligible patients admitted in ICU under the Department of Medicine, Regional Institute of Medical Sciences, Imphal who were diagnosed with sepsis and stayed for more than 72 hours, during the study period were included in the study. Patient diagnosed with sepsis by SOFA score ≥2 and eligible for the study were recruited from the in-patient ICU, Department of Medicine, RIMS, Imphal based on convenient sampling method.

Data source:

a) Primary data were collected using a structured proforma.
b) Secondary data were collected from records provided by Department of Medicine, RIMS, Manipur

Study variables: Socio-demographic characteristics like age, sex, religion, etc., clinical signs, mean platelet volume and SOFA score at the time of admission, were the independent variables. Outcome variables were mean platelet volume and SOFA score after 72 hours of hospital stay.

Study instruments:

1. 5 part Automated Hematology Analyzer (Mindray BC-5150)
2. Pretested predesigned proforma
3. Automated biochemistry analyser for blood investigation reports
4. SOFA score

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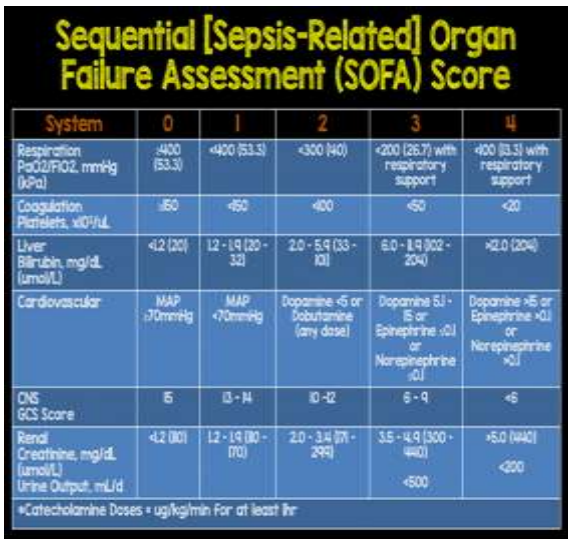

Working Definition: Sepsis was defined in our study patients by Sequential Organ Failure Assessment (SOFA) score ≥ 2.

Data Collection: A detailed structured proforma was used. The proforma includes detailed clinical history of patients with SOFA score ≥2 who were admitted at the Department of Medicine, RIMS, Imphal. Informed consent were taken from all the participants. The participants were reassured of their anonymity at the time of data collection and the importance of an honest answer was stressed. The proforma also records findings of a complete general physical and clinical examination. Further, the patients were assessed by biochemical test, platelet count, mean platelet volume, SOFA score were evaluated at the time of admission and after 72 hours of follow up period. Collected data were checked for completeness and consistency before discharge of the patient and necessary rectifications were made.

Statistical Analysis: The collected data were entered and analysed in SPSS (IBM) version 21. Summarizations of data for age, gender, religion were carried out by using descriptive statistics such as mean, standard deviation and percentages. Paired t test was used to compare changes in SOFA score and mean platelet volume from admission value to after 72 hours of admission. P-value of less than 0.05 was taken as statistically significant.

Ethical issues: Ethical approval was obtained from the Research Ethics Board, RIMS, Imphal before the beginning of the study. Written informed consent were taken from the participant and their participation was completely voluntary and right to refuse to participate in the study was respected. A unique code number was given and no names were taken to maintain confidentiality. All the information collected for the study were utilized only for the purpose and not disclosed to anyone outside the research team.

RESULTS

A total of 147 patients between the age of 18 to 75 years admitted in Medicine wards and ICU with sepsis, with 72 hours of hospital stay who were included in this study.

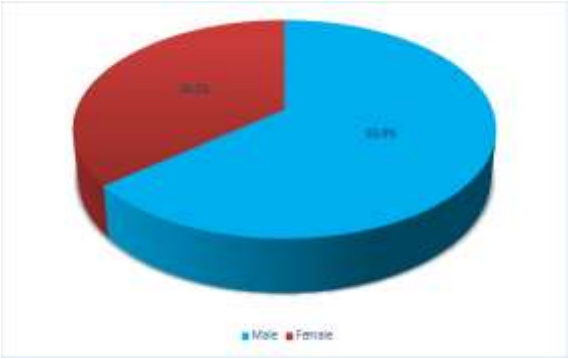

Figure 1: Distribution of patients by gender (N=147)

Majority of the patients, 94(63.9%) were males and remaining 53(36.1%) were females.

Table 1: Distribution of the patients by mean age among the gender (N=113)

Sl.no.	Gender	Mean age in years	Standard deviation	P value
1.	Male	53.93	15.07	0.581
2.	Female	52.45	16.24	
3.	Total	53.39	15.47	

The mean age of male patients were higher than female patients but the difference was not significant. The mean age of the patients was 53.39 ±15.47 years.

Table 2: Distribution of the patients by age in years (N=147)

Sl.no.	Age group	No. of participants	Percentage
1.	18-30 years	15	10.2
2.	31-40 years	23	15.6
3.	41-50 years	22	15.0
4.	51-60 years	25	17.0
5.	61-70 years	41	27.9
6.	> 70 years	21	14.3
7.	Total	147	100

The group 61 years to 70 years has the maximum number of patients, 41 (27.9%) followed by 51 to 60 years, 25 (17%). Minimum number of patients was seen in the group 18-30 years, 15 (10.2%).

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Table 3: Distribution of the patients by source of infection (N=147)

Sl.no.	Source of infection	No. of participants	Percentage
1.	Gastrointestinal tract	49	33.3
2.	Respiratory tract	48	32.7
3.	Urinary tract	38	25.9
4.	Others	12	8.2
5.	Total	147	100

Major source of infection was from the gastrointestinal, 49(33.3%) and respiratory, 48(32.7%) which is followed by urinary tract, 38(25.9%). Only 12(8.2%) were from other sources like CNS infections, etc.

Table 4: Mean SOFA score and MPV at the time of admission (N=147)

Sl.no.	Characteristics	Mean	Standard deviation
1.	SOFA score	6.30	2.83
2.	Mean Platelet Volume (MPV)	8.71	0.70

The mean SOFA score at the time of admission was 6.30 ± 2.83 and the mean platelet volume was 8.71 ± 0.70.

Table 5: Mean SOFA score and MPV at 72 hours after admission (N=147)

Sl.no.	Characteristics	Mean	Standard deviation
1.	SOFA score	8.69	4.87
2.	Mean Platelet Volume (MPV)	9.09	0.91

The mean SOFA score after 72 hours was 8.69 ± 4.87 and the mean platelet volume was 9.09 ± 0.91.

Table 6: Correlation between SOFA score and MPV at the time of admission (N=147)

Correlations			
		SOFA_admission	**MPV**
SOFA_admission	Pearson Correlation	1	.710**
	Sig. (2-tailed)		.000
	Sum of Squares and Cross-products	1164.830	205.491
	Covariance	7.978	1.407
	N	147	147
MPV	Pearson Correlation	.710**	1
	Sig. (2-tailed)	.000	
	Sum of Squares and Cross-products	205.491	71.950
	Covariance	1.407	.493
	N	147	147
**. Correlation is significant at the 0.01 level (2-tailed).			

There was a significant positive correlation between SOFA score and mean platelet volume collected at the time of admission with the pearson correlation of 0.710.

Table 7: Correlation between SOFA score and MPV at 72 hours of admission (N=147)

Correlations			
		SOFA_72hrs	**MPV_72_hrs**
SOFA_72hrs	Pearson Correlation	1	.715**
	Sig. (2-tailed)		.000
	Sum of Squares and Cross-products	3471.224	461.910
	Covariance	23.776	3.164
	N	147	147
MPV_72_hrs	Pearson Correlation	.715**	1
	Sig. (2-tailed)	.000	
	Sum of Squares and Cross-products	461.910	120.083
	Covariance	3.164	.822
	N	147	147
**. Correlation is significant at the 0.01 level (2-tailed).			

There was a significant positive correlation between SOFA score and mean platelet volume collected at 72 hours of admission with the pearson correlation of 0.715.

Table 8: Mean SOFA score at admission and after 72 hours of admission (N=147)

Sl.no.	SOFA	Mean score	Standard deviation	P value
1.	At admission	6.30	2.82	< 0.001*
2.	After 72 hours	8.69	4.87	

paired t-test

The mean score of SOFA increased after 72 hours of admission (8.69 ± 4.87) when compared with mean SOFA score at admission (6.30 ± 2.82). The difference was found to be significant.

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Table 9: Mean MPV value at admission and after 72 hours of admission (N=147)

Sl.no.	MPV	Mean score	Standard deviation	P value
1.	At admission	8.71	0.70	< 0.001*
2.	After 72 hours	9.08	0.91	

paired t-test

The mean MPA increased after 72 hours of admission (9.08 ± 0.91) when compared with mean MPA at admission (8.71 ± 0.70). The difference was found to be significant.

DISCUSSION

In this study, we studied 147 patients between the age of 18 to 75 years admitted in Medicine ward and ICU with sepsis, with SOFA score ≥ 2. They were followed up till 72 hours after admission. Majority of the study population were males with 94(63.9%) and remaining 53(36.1%) were females. Vélez-Páez JL et al,[10] reported majority of their study population to be females with (61.96%) and males with (38.1%), which is in contrast to this study finding. Guclu E et al,[18] reported (57.9%) of their study population to be males and remaining (42.1%) females. Zhang S et al,[21] found male preponderance of (73.2%) among their study population admitted in ICU and Zhang Z et al,[26] too in this study found (65.6%), which is similar to this study result. Thus many of the studies reported male patients to be more than female patients which is similar with this study. This may be due to the hormonal conditions playing a part in immune system, where androgen hormones play suppressive role in immune response, while female hormones play protective role.[34,39]

In this study the group of 61-70 years has the maximum number of patients 41 (27.9%) followed by 51 to 60 years 25(17%). Minimum number of patients was seen in the group 18-30 years 15(10.2%). The mean age of the patients was 53.39 ±15.47 years in our study. Vélez-Páez JL et al,[10] and Guclu E et al,[18] reported the mean age of their study population to be 61.15 ± 20.94 years and 69 years respectively which is higher than this study population. While Zhang S et al,[21] reported the mean age of 57 years among their study population and also Zampieri FG et al,[25] reported the mean age of their study population to be 50.3 ±17.3 years, which is comparable with this study finding. Thus majority of the studies reported middle aged and older patients were more commonly affected with sepsis which is similar to our study.

In this study the major source of infection was from the gastrointestinal 49(33.3%) and respiratory 48(32.7%) followed by urinary tract 38(25.9%). Infections from other sources were only 12(8.2%). Similar finding was reported by Vélez-Páez JL et al,[10] in their study where majority of their patients source of infection was gastrointestinal tract (44.2%) followed by respiratory tract (30.6%) and urinary tract (15.9%). Kitazawa T et al,[19] reported majority of their patients infection was due to catheter related infection or unknown in 70% followed by intraabdominal infection in 17%, UTI in 7% and pneumonia in 2%. Zhang S et al,[21] reported in their study that the most common cause of admission in ICU was pulmonary (26.5%) followed by cardiovascular (10.3%) and neurological(9.8%). This finding is also supported by Zhang Z et al,[26] in their study where the commonest cause of admission in ICU were neurological, cardiovascular and pulmonary infections. Thus majority of the studies reported gastrointestinal and pulmonary source of infection to be the commonest cause of their admission in ICU which is similar with this study finding. Members of Enterobacteriaceae constitutes the major group of isolates. Overall, Escherichia coli was the most common isolate from GI and respiratory tracts in ward patients, followed by Staphylococcus aureus and K.pneumoniae. In ICU common organisms causing infections were E.coli, K.pneumoniae, A.baumanii and S.aureus.

In this study we found the mean SOFA score of the sepsis patient at the time of admission to be 6.30 ± 2.83 and the mean platelet volume to be 8.71 ± 0.70 fL. Keeping MPV normal at our lab at (7.5-11.5) fL all the patients received standard sepsis treatment protocol as per their disease profile and were followed up for 3 days in this study and SOFA score and MPV value were estimated again and found the mean SOFA score to be 8.69 ± 4.87 and the mean platelet volume to be 9.09 ± 0.91 fL. On further analysis it was found that the SOFA score measured at the time of admission was positively correlated with the MPV values and it was statistically significant with the pearson correlation of 0.710. Similarly, the measurements taken after 72 hours of admission were also analysed for correlation. We found a significant positive correlation between SOFA score and MPV values. This finding was supported by Puspayani IY et al,[34] in their study, they also did Pearson test to analytically associate SOFA score and MPV and showed positive correlation with medium power ($r = 0.5732$). Our result was also similar with the study conducted by Vardon-Bounes F et al,[40] that utilized multidimensional analysis with 301 subjects, that showed significant correlation between MPV and SOFA score ($r = 0.486$; $p < 0.0001$). The study by Kim CH et al,[27] also showed that MPV and SOFA were positively correlated ($r = 0.018$; $p = 0.746$). Multiple organ failures are substantially associated with septicemia-related deaths. The Surviving Sepsis Campaign (SSC) recommends SOFA (Sequential Organ Failure Assessment), which is clinically translated into the degree of organ dysfunction in sepsis and has prognostic significance.[34]

Platelet is an important component; although its primary function is in the process of hemostasis (in

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conjunction with coagulation factors), platelets are also known to have a role in inflammation, the defence of the host against pathogens, wound healing, angiogenesis, and remodeling. Platelets also known to mediate the extravasation of leukocytes and to manufacture reactive oxygen species. Furthermore, it is known that thrombocytes are activated by oxidative stress, which is a phenomenon that happens during inflammation. The capacity of platelets to exert influence over other cells demonstrates that platelets are capable of playing a wide variety of important roles in pathologic processes. Platelet indices are a collection of statistics that are derived from platelet counts and are obtained using automated blood counts. Several pieces of evidence suggested that platelet indices could have diagnostic and prognostic significance in certain diseases. Therefore, platelet indices (MPV) can be used as a reliable instrument at par with SOFA. The automated blood count is the source of platelet indices, and there are no additional expenditures involved.[41,42]

Further studies can be done with increase duration of follow up to explore the mortality predicting capacity of mean platelet volume among sepsis patient admitted in ICU for intensive care monitoring and treatment.

CONCLUSION

There is a positive correlation between mean platelet volume (MPV) and SOFA score among patients with sepsis. This shows that the increase in MPV is directly proportional to the increase in SOFA scores both at the time of admission and 72 hours after hospitalization. Therefore MPV may be used as a tool which is cheap and readily available in predicting death in sepsis patients.

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