

Original Research Article

Mean platelet volume to platelet count ratio as a predictor of mortality in septic patients

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Received: 11 January 2021

Accepted: 10 February 2021

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ABSTRACT

Background: Sepsis is a major cause of mortality among critically ill patients. The complex pathophysiology involves infection with systemic inflammatory response. Early detection of sepsis, helps not only in stratification of risk, but also for monitoring its progression and efficacy of therapeutic interventions. At present there are only few reliable prognostic tools to predict severity and mortality in sepsis. This study evaluates the usefulness of mean platelet value in prognosticating patient admitted with sepsis.

Methods: We enrolled 200 patients prospectively, that have been admitted to our Medical ICU for sepsis over 2 years from 2018–2020. Changes in platelet indices, including mean platelet volume to platelet count ratio, were compared between survivors and non-survivors by using student's t test. The prognostic value of mean platelet volume to platelet count ratio for 28-day mortality was ascertained by multivariate logistic regression.

Results: Total 39 (19.5 %) patients expired within 28 days of ICU admission. MPV increased during the first 72 hours of hospital stay for both survivor and non survivors. Mean platelet volume to platelet count ratio was significantly higher in non survivors ($P < 0.001$) as compared to survivors. In multivariate cox regression, mean platelet volume to platelet count ratio was an independent predictor of 28-day mortality, after adjusting for plausible confounders.

Conclusions: Mean platelet volume to platelet count ratio is an independent risk factor for poor clinical outcomes. Hence monitoring mean platelet volume can prove as a simple tool to stratify the risk of mortality in septic patients.

Keywords: Mean platelet volume, Sepsis, Shock

INTRODUCTION

Sepsis is one of the leading causes of death in the ICU patients.¹ Despite the extensive research over the last two decades, few specific treatments have been shown to improve the outcome but great inroads have been attained in identifying various correctable abnormalities and markers within the disease process. The sepsis syndrome represents a progression in clinical and pathophysiological severity. However, it is a continuum with definable, albeit arbitrary, phases that place the patients at risk for morbidity and mortality.² The complex pathophysiology of sepsis involve infection with systemic inflammatory response.³

Thrombocytopenia may arise from reduced central production or from peripheral destruction. Among its multiple causes, Sepsis is a clear risk factor with an incidence of more than 35 %.⁴

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The mean platelet volume describes the average size of platelet in blood sample and represents the reactivity of the platelets. It is measured automated hematology analyzers employing impedance and optical effects.⁵ Platelets with high mean platelet volume and usually larger and active.

Their prothrombotic nature results in platelet adhesion and aggregation.⁶ Several studies suggest that changes in MPV are nonspecific and are seen in severe clinical conditions such during infection, sepsis and chronic inflammatory conditions.^{7,8}

There are few studies that are done on the effects of MPV in sepsis and are found to have conflicting results. Moreover, only little is known of the MPV on mortality in patients with sepsis. Hence, in our study, we aimed to look at the response of Mean Platelet volume to platelet count ratio in patients admitted with sepsis and its capability in prognostication.

METHODS

This was a case control study and was carried out over a 2-year period from 2018–2020, at Amrita Institute of Medical Sciences and Research Center, Kochi, Kerala.

Selections and description of the participants

A total of 200 patients with sepsis were admitted into the Medical ICU directly from the ER, were chosen for the study randomly. The patients were followed up for 28 days and were divided into two categories based on survival.

Inclusion criteria

Minimum age requirement was 18 years of age. No maximum age limit was set. Patients were identified in the emergency room (ER) on arrival as cases of sepsis and septic shock as per the guidelines provided by the Society of critical care medicine's latest recommendations provided with the sepsis care bundle on survivingsepsiscampaign.org

Exclusion criteria

Patients with suspected or known case of haematological malignancies or primary marrow disorders, known case of Immune Thrombocytopenic Purpura (ITP), Acute Splenic sequestration, known case of platelet structural and functional disorders, those on chemotherapy and those patients who require Linezolid for their treatment during the ICU stay.

Only direct admissions into the ICU meeting the above inclusion and exclusion criteria were chosen for the study.

Sample size calculation

Based on the results of mean Mean Platelet volume to platelet count ratio after admission, of survivors and non survivors (0.26 ± 0.89 , 0.80 ± 1.30) among septic patients observed in an earlier publication⁹ and with 90 % power and 95 % confidence, the minimum sample size comes to 200. Sample size would be in the ratio of 1:5, non survivors to survivors

Methods of data collection

After identification of such cases in the ER, their details were entered into a software developed by the IT department. The patient's lab details were automatically stored and pulled into the database.

Clinical details of the patient were followed up during their hospital stay and further up to 28 days. These details were entered into the software and stored on the database for further analysis manually.

Individual SOFA and APACHE II score elements were assessed and entered into the software which was stored for later evaluation.

Sample collection

The day 1 samples of MPV and CRP were taken on admission from the ER and sent to the lab within 15 minutes of admission. The sample for MPV was the same sample for CBC and were collected in EDTA vacutainers at admission. The samples for Complete Blood Count (CBC) which includes the MPV were analysed in the Hematology lab using Abbott Cell-Dyn model 3700 hematology analyzer and reported within 40 minutes of sample collection.

SOFA score on admission were calculated within 2 hours of admission after initial evaluation and emergency management including fluid resuscitation, mechanical ventilation (invasive/ non-invasive)

The outcome was taken as either death of the patient (in this study referred to as "non survivors") or the patients who were alive during their hospital stay and at follow up at 28 days (referred to as "survivor"). All the details were stored in the data base until the required sample size was reached and was then taken for analysis. Data analysis was done with the help of a statistician.

Statistical analysis

The statistical analysis was done using the IBM SPSS version 20.0 software. The categorical variables were expressed using percentage and frequency. Numerical variables were denoted using mean and standard deviation. ROC curve analysis was used to determine the cut-off values for change in Mean platelet volume.

Chi-square was used to test the statistical significance of the association of all categorical variables with mortality. Independent sample t test was used to study the statistical significance of the difference in the mean values of all continuous variables with mortality. Multivariate logistic regression analysis was used to identify the independent predictor of mortality. A p value of <0.05 was considered to be statistically significant.

RESULTS

Demographic data

Total of 200 patients were selected after passing through the inclusion criteria. Of these patients, there were 127 male patients and 73 female patients (Table 1). Patient's outcome was followed for 28 days. Outcome taken were the death to the patient due to sepsis and septic shock.

The most common reason for admission to the hospital was pneumonia (83 patients), followed by urinary tract infection (61 patients). 18 patients with pneumonia expired with 21 patients having other sources of sepsis.

Mean platelet volume was taken on the day of admission and on the 72 hours post admission. Mean platelet volume on day 1 in expired patients was 9.64 with standard deviation of 0.95, mean MPV at 72 hours was 11.48 with standard deviation of 1.09 and mean change in MPV (72

hours–adm) was 1.81 with standard deviation of 0.66 (Table 2).

Table 1: Distribution of demographic and clinical parameters.

Parameters	Frequency	Percentage
Gender		
Male	127	63
Female	73	36
Duration of hospital stay		
<12 days	138	69
>12 days	62	31
Distribution of site of infection		
Pneumonia	83	41
UTI	61	30
Intra-abdominal	16	8
Others	35	18
Multiple	5	3
Mortality		
Survivors	161	80.5
Non-survivors	39	19.5

APACHE score calculated at the time of admission had a mean of 29.39 with standard deviation of 17.36 (Table 2).

SOFA was also calculated on Day 1. In the “non – survivors” category, SOFA Day 1 mean was found to be 7.41 with standard deviation of 2.66 (Table 2).

Table 2: Comparison of continuous clinical and demographic parameters with mortality.

Variables	Survivors (n=161)	Non-survivors (n=39)	P value
Age	64.96±15.12	67.87±10.42	0.159
BMI	23.65 ±2.55	23.79±2.09	0.746
MAP	76.13±10.15	62.33±8.15	<0.001
Comorbidity	3.12±2.01	3.67±1.45	0.058
APACHE II	8.47±6.61	29.38±17.36	<0.001
SOFA	3.92±1.85	7.41±2.66	<0.001
Total count	16.02±.86	13.36±6.42	0.04
Hemoglobin	11.45±2.05	10.51±2.31	0.013
Platelet count	281.9±105.9	127.8±47.4	<0.001
MPV(adm)	9.60±0.99	9.64±0.95	0.838
MPV/Platelet	38.95±18.79	91.97±51.06	<0.001
CRP	158.5±92.29	171.0±89	0.448
Creatinine	1.75±0.92	3.23±1.66	<0.001
Total bilirubin	1.13±0.88	1.53±1.86	0.192
Albumin	3.27±0.52	2.84±0.43	<0.001
pH	7.37±0.86	7.00±0.00	<0.001
Bicarbonate	20.22±2.50	16.85±2.87	<0.001
Lactate	1.75±0.61	2.58±1.18	<0.001

The mean age among the “non–survivors” category was 67.87 with standard deviation of 10.42. With a p value of >0.05, we can conclude there is no significant difference

in the mean age between the “survivors” and “non survivors” category (Table 2)

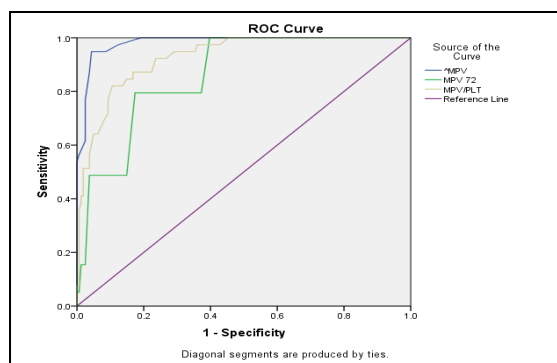


Figure 1: ROC Curve.

With the above data, we can conclude safely that basic demographic does not influence the MPV levels and therefore will not be a variable in the rest of the study.

Main study results

Among the total 39 patients, who have expired, Mean Platelet Volume day 1 had a mean of 9.64 with standard deviation of 0.95. Among the survivors the Mean Platelet Volume at admission was mean of 9.60 with standard deviation of 0.99. Comparison done with student's t-test showed no statistical difference between the two groups with p value of 0.838 (Table 2).

Meanwhile, mean platelet volume at 72 hours, change in mean platelet volume and mean platelet volume to platelet count ratio showed promising results with mean of 11.48 with standard deviation of 1.09, 1.81 with standard deviation of 0.66 and mean of 9.197 with standard deviation of 5.106 respectively in the "non-survivors" category. These variables were found to be statistically significant $p < 0.01$ (Table 2).

Mean APACHE scoring and SOFA score calculated at admission in "non-survivors" category was 29.38 with standard deviation of 17.36 and mean of 7.41 with standard deviation of 2.66 respectively (Table 2). Both the variables were found to be statistically significant.

As we can see above mean platelet volume at 72 hours, change in mean platelet volume, mean platelet volume to Platelet count ratio, APACHE and SOFA score had significant differences in the mean values among the two groups suggesting these variables better predicted their respective outcomes.

An ROC curve analysis was done, after ascertaining that Mean Platelet Volume showed a significant difference between the "survivors" and "non survivors" group. The ROC curve analysis was done, cut off for mean platelet volume to platelet count ratio was 5.3, with sensitivity of 84 %, specificity of 84 and positive predictive value of 55%.

A logistic regression analysis was done to find out the best predictor of outcomes. On analysis the B (Beat) value of MPV to platelet count ratio was found to be significant (p value < 0.005) as compared to APACHE and SOFA scoring (p value 0.15, 0.41) (Table 4). This shows that mean platelet volume to platelet count ratio are better predictors of mortality as compared to SOFA and APACHE.

It was also decided to see if the change in mean platelet volume, mean platelet volume to platelet count ratio, SOFA and APACHE had an influence on the duration of hospital stay. On analysis, it was found that none of the variables were found to be significant $p > 0.05$. This means the duration of hospital stay was independent of change in mean platelet volume, mean platelet volume to platelet count ratio, and SOFA and APACHE II scores.

Table 3: Association of MPV/ platelet ratio with mortality.

MPV/PLT Ratio	Mortality		P value
	Non Survivors n(%)	Survivors n(%)	
<5.3 (140)	6(4)	134 (95)	<0.001
≥5.3 (60)	33 (55)	27(54)	

Table 4: Logistic regression.

Variables	B	Wald	p Value	OR
APACHE (>25)	1.599	5.253	0.022	4.896
SOFA (>5)	1.540	4.03	0.020	4.666
MPV baseline	1.937	5.708	0.017	6.941
MPV at 72 hours	1.559	3.015	0.082	4.756
MPV/Plt ratio (>5.3)	2.797	16.471	0.000	16.391

In table 1 out of the 200 cases, 127 (63 %) were male and 73 (36%) were female. Predominant causes of hospital stay were attributed to Pneumonia 83 (41 %), followed by UTI 61 (30 %).

In figure 1 area under the curve (AUC) of MPV 72h, Δ MPV72h-adm and MPV/Platelet ratio were 0.86, 0.98 and 0.92, and the cutoffs chosen are 11.9, 1.45 and 53.5 respectively.

Here table 2 shows low mean arterial pressure in non-survivors is 62.33 ± 8.15 as compared to the non survivors 76.13 ± 10.15 , is statistically significant $p < 0.001$. High APACHE II in non survivors is 29.38 ± 17.36 as compared to survivors 8.47 ± 6.61 , is statistically significant $p < 0.001$. High SOFA score in non survivors is 7.41 ± 2.66 as compared to survivors 3.92 ± 1.85 , is statistically significant $p < 0.001$. MPV/ Platelet ratio is high in non survivors (91.97 ± 51.06), as compared to survivors (38.95 ± 18.79) and is statistically significant $p < 0.001$

In table 3 the mortality among MPV/PLT < 5.3 is 6 (4%) and that of MPV/PLT > 5.3 is 33 (55%), which shows statistical significance association with p value < 0.001 .

The above table 4 shows that APACHE, SOFA, MPV/platelet ratio are all predictors of mortality. But as we can clearly see that MPV/platelet ratio is superior to APACHE and SOFA in predicting mortality.

DISCUSSION

Sepsis and Septic shock remains as one of the most challenging problems in ICU settings. Despite the extensive knowledge regarding the patient response to sepsis, only limited studies have been done in evaluating the potential for platelet indices to be used as a marker in sepsis or assess its value in prognostication. Platelet count in itself though, has found its way into the SOFA scoring as one of the variables assessing coagulation parameters in those with sepsis.

Early detection of sepsis helps in risk stratification, allocation of resources and assess the efficacy of therapeutic interventions.

During the clinical course of sepsis, platelets undergo wide variations, which initially respond with hyperstimulation followed by exhaustion. The causes of thrombocytopenia, can be centrally mediated or from peripheral destruction.¹⁰ There is an inverse relationship between Mean platelet volume and platelet count, this can be seen in several physiological and pathological situations.¹¹ This inverse relationship was also found in our study.

There are several studies that have looked into MPV for critically ill patients. Zampietti et al studied 87 critically ill patients and found that MPV at 24 hours were significantly higher in the non-survivor group. They found no relationship between the prognosis and the MPV taken at admission. They also were able to conclude that MPV was better at predicting outcome than the difference in the platelet count within the first 24 hours.¹¹ Similar results were also observed by a European study done by Eberhardt et al.¹² Another study by Beechi et al published in 2008 in Italy, showed conflicting results with their analysis showing a 3 times increase in death probability (95 % CL, OR=3.04, $P < 0.05$) of patient with an MPV > 9.7 fl at recruitment time. The rationale given for this was that

sepsis resulted in a marrow disturbance which ultimately reduced platelet production.¹²

In the previous studies that were done, we have seen that MPV does in fact predict mortality in patients with sepsis. Most of the studies which has been listed above shows that a high MPV, whether at admission or through the course, was indicative of a poor prognosis. One study showed a contradicting report of a low MPV being indicative of poor prognosis.

This is a prospective study, to evaluate the usefulness of MPV to platelet count ratio on day as a mortality predictor in septic patients. We found that the mean platelet volume increased within the first 72 hours of hospital stay. This increase was high for both survivors and non survivors. But the non survivors had a much steeper rise as compared to the survivors. MPV to platelet count ratio also was found to be higher in the non survivors. Through Multivariate logistic regression, we can conclude MPV to platelet count ratio is an independent predictor of mortality. These findings were similar to the earlier publications.^{9,13}

Limitations

It doesn't entirely reflect the population of India since the patient samples only reflect a possible local subset. MPV has not been studied in the conditions included in the exclusion criteria. At this point MPV cannot be used to evaluate the prognosis in patients who are in the exclusion criteria. This study does not take into account, the other conditions that can affect MPV such as smoking, Cerebrovascular accidents (CVA) and acute coronary syndromes (ACS).

CONCLUSION

MPV/Platelet ratio, which is a part and parcel of a complete blood count, is a hidden gem in our diagnostic arsenal and can help identify a patient with a possible poor outcome on admission. MPV/ Platelet ratio more than 5.3, suggest a higher chance of mortality in patients with sepsis and septic shock. It will also help us to convey a prognosis to the patient's relatives. But for MPV to be accepted in this light, requires much larger and broader studies involving different patient groups. Meanwhile it would be prudent to keep a close watch on the MPV of these patients and tailor the treatment regimens to the possible predicted outcomes.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Thomas MM, Vasant PK, Pillai MG. Mean platelet volume to platelet count ratio as a predictor of mortality in septic patients. *Int J Adv Med* 2021;8:427-32.