Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

## ORIGINAL RESERCH

# A Study of Mean Platelet Volume as a Prognostic Marker in Acute Kidney Injury

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Received: 12 June, 2023 Accepted: 16 July, 2023

**Abstract**

**Introduction:** Acute kidney injury (AKI) is a significant health concern that leads to high rates of morbidity and mortality. Studies have shown that platelets are a marker of inflammation, and mean platelet volume (MPV) is the average volume of all platelets counted in a Coulter machine.

**Aims and objectives:** The study aimed to obtain the MPV in AKI patients and use MPV as a marker to predict the progression of AKI.

**Materials and methods:** This was a cross-sectional study conducted in the in-patient department of general medicine at a tertiary care center in patients with AKI over the age of 18 years. The cause of AKI and MPV were recorded.

**Results:** The study population consisted of 100 patients, with the majority being in the age group of 56-67 years (26%) and male predominance (58%). The most common causes of AKI were sepsis (43%), hepatorenal syndrome (18%) and dengue (10%). Patients with malaria and burn had the lowest average MPV. Patients with oliguria (p value-0.0001), who had a hospital stay of five or more days (p value-0.003), required dialysis (p value-0.0001), or passed away (p value-0.0001) had significantly lower MPV values.

**Conclusion:** This study found that MPV can be used as a marker to predict the progression of AKI. Patients with oliguria who had a hospital stay of five or more days, required dialysis, or passed away had significantly lower MPV values.

**Keywords:** Acute kidney injury, mean platelet volume, platelet, inflammation, predictor, hospital stay, dialysis, mortality.

## Introduction

Acute kidney injury (AKI) is a significant global health concern that leads to high rates of morbidity and mortality. In recent years, the United States has seen a 30% increase in the prevalence of chronic kidney disease.[1] However, there is a lack of longitudinal studies and limited data on the prevalence of chronic kidney disease in India. The occurrence of AKI can differ by geographic location and demographic factors, leading to varying rates of AKI within and between countries. In low-income and middle-income countries, like India, AKI is more commonly seen in rural and smaller towns, caused by infectious diseases, traditional medicine and poor obstetric care, and affects young and previously healthy individuals.[2,3]

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

Studies have shown that platelets are a marker of inflammation.[4]Platelets play an important role as an inflammatory marker because the turnover of platelets in the bone marrow increases with inflammation. As the turnover of platelets increases, more immature platelets are released into circulation. The maturation of platelets is influenced by various factors. Mean platelet volume (MPV) is the average volume of all platelets counted in a Coulter machine. The normal range for MPV is between 7.2-11.2 fL.[5]

This study aimed to obtain the MPV in AKI patients. The primary objective was to use MPV as a marker to predict the progression of AKI. Secondary objectives included comparing the value of MPV with AKI outcome and to study the MPV value for predicting the duration of hospital stay in a patient who presents with AKI.

## Materials and methods

This was a cross-sectional study conducted in the in-patient department of general medicine at our tertiary care center. The study was initiated after obtaining approval from the institutional research review board and conducted between April 2021 to June 2021.

The sample size for this study was calculated as 100 cases based on a previous study that showed a minimal detectable difference of mean 2.63, SD-1.88 for 80% power and 0.05 alpha error.[8]Inclusion criteria for the study were patients with AKI over the age of 18 years. The cases were included after written informed consent. Exclusion criteria included patients who had taken any antiplatelet agents during the last one week, patients with terminal malignancy, patients who have received platelet transfusion within 24 hours, patients with chronic kidney disease (CKD) on chronic dialysis, patients with associated hematological disorders, patients on drugs known to cause bone marrow suppression, and patients who refused to give written consent.

Blood samples of 5 mL were drawn for a complete hemogram including MPV, urea, creatinine, serum electrolyte level, uric acid. Urine samples were taken for albumin level and microscopic analysis. The clnico-epidemiological data of patients were recorded in a prestructured proforma. The cause was noted in each patient. The duration of hospital stay, need for dialysis, the number of days in the hospital and patient outcome were noted. A complete hemogram including mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR), and hemoglobin was recorded. Urine output was measured. Oliguria was labeled if the daily urinary output was less than 400 ml.

Qualitative data were summarized in the form of percentages and proportions, while quantitative data were expressed in mean ± S.D. The significance of the difference of proportion was determined using the chi-square test and the significance of the difference in mean ± S.D. using an unpaired T-test. For the comparison of multiple groups, an analysis of variance (ANOVA test) was done. P value <0.05 were considered statistically significant.

## Results

The study population consisted of 100 patients, with the majority being in the age group of 56-67 years (26%) and 36-45 years (23%). The least represented age group was 18-25 years (9%) and 26-35 years (9%) (figure 1). In terms of gender, 58 (58%) cases were male and 42 (42%) were female. The male to female ratio 1.38:1.

The primary cause of Acute Kidney Injury (AKI) in the study population was sepsis (43%), followed by hepatorenal syndrome (18%), dengue (10%), toxin and cardiac failure (8%), diarrhea and glomerulonephritis (3%), malaria, contrast nephropathy and post renal obstruction (2%), and burns (1%). The mean hemoglobin level was 11.19 ±2.05 gm/dl, the mean total leucocyte count 17.19 ±2.05 /µl, the mean neutrophil-lymphocyte ratio (NLR)was 10.97 ±8.38, mean platelet 1.51 ±0.65 lac/ µl, Mean MPV 9.98 ±1.25, mean urea 121.23

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

±51.28, mean creatinine was 3.28 ±1.47 were observed.The study found that 26% of patients had oliguria, and 74% had normal urine output.

Out of 100 patients, 82% recovered from AKI, while 18% expired. 27% of patients required dialysis, while 73% did not. The majority of patients (80%) required 1-5 days of hospital stay, with 17% requiring 5-10 days, and only 3% requiring more than 10 days. The mean hospital stay was 4.37 ± 2.44 days.

The mean values of MPV in different age and sex groups were also analyzed. In terms of age groups and mean values of MPV, the highest mean MPV was seen in the age group of 56-67 years (10.2 ± 1.19) and the lowest mean MPV was seen in the age group of 18-25 years (9.93 ± 1.14) (table 1). There was a statistically insignificant difference in the MPV according to age (p value-0.66). The mean values of MPV in different gender were 9.88 ± 1.24 for male and 10.12 ± 1.19 for female, the difference was statistically insignificant (p value-0.33).

Statistically significant differences were observed in patients with different levels of urine output, recovery status, need for dialysis, and hospital stay. Patients with oliguria (p value-0.0001), requiring dialysis (p value-0.0001), requiring ≥5 days (p value-0.003) and those who expired (p value-0.0001) had significantly lower MPV (table 3).

In terms of the causes of AKI, the highest average MPV values was seen in contrast nephropathy (11.3 ± 1.39), by toxins (10.33 ± 1.19), and diarrhea (10.20 ± 1.23). While the lowest average MPV value were seen in malaria (8.3 ± 1.20) and burns (8.8 ± 0.01) (8.9 ± 0.14) (table 2).

While assessing urine output, the average MPV in normal urine output patients (10.29 ± 1.25) was higher thantheaverage MPV in patients with oliguria (9.08 ± 1.59). The difference was statistically significant (p value-0.0001). The average MPV in recovered patients (10.22 ± 1.25) was higher than the average MPV of cases who expired (8.87 ± 1.44).The difference was statistically significant (p value-0.0001). Similarly, the average MPV of cases who didn’tneed dialysis (10.33 ± 1.25) was higher than the average MPV of cases requiring dialysis (9.01 ± 1.15). The difference was statistically significant (p value-0.0001). Additionally, the average MPV of patients with <5 days of hospital stay (10.28 ± 1.25) was higher than the average MPV of patients with a hospital stay of ≥5 days (9.29 ± 1.59). The difference was statistically significant (p value-0.003).

**Table 1. MPV according to demographic characteristics**

| **Age groups** | **MPV** | | |
|---|---|---|---|
| | **Mean** | **SD** | **P value*** |
| 18 – 25 years | 10.2 | 1.19 | 0.66 |
| 26 – 35 years | 9.67 | 1.14 | |
| 36 – 45 years | 10.23 | 1.22 | |
| 46 – 55 years | 9.93 | 1.14 | |
| 56 – 67 years | 9.96 | 1.14 | |
| **Gender** | **Mean** | **SD** | **P value**** |
| Male | 9.88 | 1.24 | 0.33 |
| Female | 10.12 | 1.19 | |
| *One-way ANOVA test<br>**Unpaired T test | | | |

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**Table 2. MPV according to the cause of AKI**

| Cause | MPV | |
|---|---|---|
| | Mean | SD |
| Contrast nephropathy | 11.30 | 1.39 |
| Toxin | 10.33 | 1.19 |
| Diarrhea | 10.20 | 1.23 |
| Sepsis | 10.04 | 1.22 |
| Dengue | 9.99 | 1.25 |
| Cardiac failure | 9.98 | 1.14 |
| Hepatorenal syndrome | 9.90 | 1.17 |
| Glomerulonephritis | 9.67 | 1.25 |
| Post renal obstruction | 8.90 | 0.14 |
| Burns | 8.80 | 0.01 |
| Malaria | 8.30 | 1.20 |

**Table 3. Association of MPV with other parameters**

| Urine outcome | MPV | | |
|---|---|---|---|
| | Mean | SD | P value* |
| Normal (n=74) | 10.29 | 1.25 | 0.0001 |
| Oliguria (n = 26) | 9.08 | 1.59 | |
| **Dialysis** | **Mean** | **SD** | **P value*** |
| Yes (n=27) | 9.01 | 1.15 | 0.0001 |
| No (n=73) | 10.33 | 1.25 | |
| **Duration of hospital stay** | | | **P value*** |
| <5(n=80) | 10.28 | 1.25 | 0.003 |
| ≥5 (n=20) | 9.29 | 1.59 | |
| **Outcome** | | | **P value*** |
| Recovered (n=82) | 10.22 | 1.25 | 0.0001 |
| Expired (n=18) | 8.87 | 1.44 | |
| *Unpaired T test | | | |

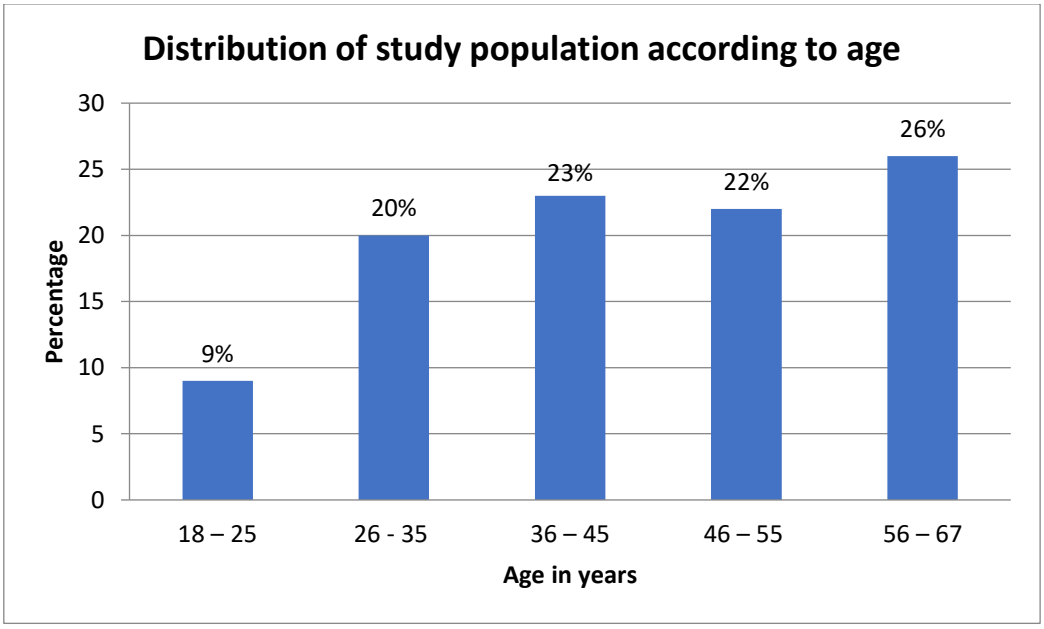


**Figure 1. Distribution of study participants according to age.**

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

**Discussion**

As an integral component of the immune system, platelets can increase in response to the "acute phase reaction" that occurs during inflammation.[7] This elevation of platelets can be indicative of increased activity in the bone marrow cells in response to the interleukins, such as IL-1 and IL-6, which are produced during the inflammatory phase.[8]

In our study, we aimed to investigate the relationship between mean platelet volume (MPV) and the various clinical and laboratory characteristics of patients with acute kidney injury (AKI).We found that the age distribution of the study population was skewed towards the older age groups, with maximum 26% of the study population being in the 56-67 years age group, followed by 23% in the 36-45 years age group, and minimum 9% in the 18-25 years age group. The mean age of the study population was 44.15 ± 12.63 years with a male predominance (58%). These findings are consistent with the observations made byPongsittisak et al.and Hans et al.who found older age and male gender to be an important risk factor for AKI.[6,9]

We also observed that the most common causes of AKI in our study population were sepsis (43%), hepatorenal syndrome (18%), dengue (10%). These findings are justified by the high burden of poor socioeconomic sector in India. All three diseases are linked to a combination of factors such as high incidence of infectious diseases, malnutrition, high prevalence of viral hepatitis and other liver diseases, presence of Aedes mosquito, high population density, inadequate sanitation, poor vector control measures and tropical climate which supports the proliferation of mosquitoes.[10-13]

In our study, we found that patients with oliguria, who had a hospital stay of ≥5 days, required dialysis, or passed away had significantly lower MPV values. In the study conducted by Han et al., involving 349 patients with acute kidney injury (AKI) who were receiving continuous renal replacement therapy, it was found that a mean MPV greater than 10.2fL was associated with 28-day all-cause mortality.[6] This finding is consistent with the results of our own study. While, another study by Yousefichaijanet al. observed that MPV less than 8.2fL was linked to a poor outcome.[14] In contrast, an Indian study by Gopala et al. found no significant association between MPV and the need for dialysis or patient outcome.[15]

The previous studies, including our own, have all been limited in sample size, with less than 400 participants and have been conducted at a single center. The inconsistent results from these studies suggest that more research is needed, specifically large-scale, multicenter studies with larger sample sizes to further investigate the association between MPV and outcomes in AKI patients.

It is believed that low MPV values observed in inflammatory conditions could be due to the fact that large platelets are being consumed at the site of inflammation. However, the association between platelet count and platelet volume can be affected by different factors all linked to megakaryopoesis, which can be hindered during inflammation. Additionally, platelet granules can act as a form of self-regulation by altering the form and release of granule substances. Conditions such as immune thrombocytopenia and preeclampsia have been linked to high MPV and low platelet count.[16,17]Therefore, it is important to determine a separate cut-off value for MPV for each cause of acute kidney injury.

We found that the maximum mean MPV was seen in cases of contrast nephropathy (11.3 ±1.39), followed by toxin (10.33 ± 1.19) and sepsis (10.04 ± 1.22) whereas the minimum was seen in cases of malaria (8.3 ± 1.20), burns (8.8 ± 0.01) and post-renal obstruction (8.9 ± 0.14). An etiology-wise MPV assessment has been reported only sparsely in the literature. In fact, to date, no study from India has analyzed this platelet parameter's variation with different inflammatory etiology.

A recent study on the correlation between mean platelet volume (MPV) and the severity of inflammation in acute pancreatitis patients found that a lower MPV was associated with more

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

severe pancreatitis.[18] This finding is consistent with other studies that have found a negative correlation between MPV and various inflammatory disorders.[19]

Studies have also described a relationship between platelet count and MPV in both pathological and physiological conditions, suggesting that the body tends to maintain haemostasis by regulating the platelet mass.[20] In inflammatory conditions, a high rate of platelet production combined with a lack of time for growth can lead to the accumulation of large platelets at sites of inflammation, which are rapidly used up.[21] These rapid changes in platelet size and number may be due to the actions of prothrombotic and pro-inflammatory mediators in platelets and the role of platelet granules in sympathetic activation and stress of exercise.[22,23]

Our study had various limitations like small sample size, single-center analysis, lack of control group, lack of long-term follow-up, lack of analysis of confounding factors, and no assessment of the underlying mechanisms. However, the inclusion of etiologies was one major strength of our study. This is especially important in the Indian context where the etiologies vastly differ from developed countries. Therefore, to gain a better understanding of AKI, we suggest conducting large-scale, multi-centric studies focused on the etiology of AKI.

## Conclusion

In conclusion, our study found that patients with AKI who required dialysis had lower MPV values compared to those who did not require dialysis. Additionally, patients who expired in the hospital after acute kidney injury were found to have lower MPV values than those who survived. Furthermore, patients with lower MPV values had a prolonged stay in the hospital. These findings suggest that MPV may be a valuable marker in predicting the outcomes of acute kidney injury patients and may have potential clinical applications in the management of these patients. However, further research is needed to confirm these findings and to investigate the underlying mechanisms linking MPV to acute kidney injury.

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