

Mean Platelet Volume as a Prognostic Factor in Acute Kidney Injury

Venu Gopala D MD¹, Shyamala KV MD² Rashmi K S³

¹Department of medicine, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India

²Department of Physiology, Father Muller Medical College, Mangalore, Rajiv Gandhi Health University, -575002, India

³ Department of Physiology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education University, -575001, India

E-mail of Corresponding Author: drshyamala@live.com

Abstract:

Introduction: Acute kidney injury is a global health burden that is associated with high incidence of morbidity and mortality. There are not much studies about the already available parameters of complete blood count. Mean Platelet Volume can be an investigation that can be put for in-depth study to know the prognosis of acute kidney injury. Methods: This cross sectional study was carried out in acute kidney injury patients for a period of 2 years from September 2016 to September 2018. Blood report of mean platelet volume including red blood cell distribution width were collected. Result: It was seen that patients belonging to middle age between 31-50 years constituted the majority of the cases of acute kidney injury. It was shown that patients having a lower values of Mean Platelet Volume are more prone for the requirement of dialysis when the two groups were compared to look for significance in predicting the requirement of dialysis (P=0.03) Improvement after dialysis was better in patients with higher values of Mean Platelet Volume than patients with lower values of Mean Platelet Volume even though the difference between the values of Mean Platelet Volume were not significant. (P=0.568) There is a negative correlation between values of creatinine and Mean Platelet Volume (P <0.001). Conclusion: Mean Platelet Volume could be inexpensive and superior investigation to creatinine in early detection of acute kidney injury which needs to be studied further with larger sample size .

Key words: Acute kidney injury creatinine dialysis mean platelet volume

Introduction:

Acute kidney injury is a global health burden that is associated with high incidence of morbidity and mortality. United states has seen a 30% increase in prevalence of chronic kidney disease in the last decade. Unfortunately from India there is no longitudinal study and limited data are available on the prevalence of chronic kidney diseases.¹The etiology is also diverse and results

from various conditions including infections, shock, obstructive uropathies etc. Platelets have been proved to be an inflammatory marker in various studies. Platelets serve as an important marker of inflammation since the platelet turn over in the marrow increases with inflammation. As the turnover of the platelets increases more immature platelets are released into circulation. The further maturation of platelets depend upon various factors. MPV is the average volume of all the platelets counted in the coulter machine. Normal volume is 7.2-11.2 fL.² We feel 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. Association between platelet count and platelet volume can be affected by while megakaryopoiesis is flawed in setting of heightened damage and growing size of platelets in an atmosphere rich in triggering cytokines can affect connection amid platelet count and platelet volume. Platelet granules can offer tool for self-directive by altering the form and discharge of granule substance. MPV can stand distinct here because whatever the pathology is involved there will be high platelet turn over secondary to inflammation. High MPV with low platelet count was seen in immune thrombocytopenia and preeclamsia^{3,4}

Acute kidney injury from all the causes were considered together in this study. This is the limitation of this study. The degree of inflammation and subsequent bone marrow stimulation from different cause will be different. So the platelet volume changes cannot be applied uniformly to acute kidney injury from all cases. Cut off value for Mean platelet volume should be determined for each aetiology separately.

There is an urgent need to have appropriate social and political strategy for prevention of chronic kidney diseases. ¹Creatinine has been always the standard baseline investigation to gauge acute renal injury in the initial workup of a patient and still being commonly used as a cheap investigation. There are not much studies about the already available parameters in the complete blood count. Mean Platelet Volume can be an investigation that can be put for in-depth study to know the prognosis of various diseases. It is to be noted that MPV is part of the complete blood count that will be done in all modern hematology analyses. Once it is proven that MPV can predict the patient outcomes in acute kidney injury, then it will definitely be a better marker than serum creatinine since this is a separate investigation asked. None of the newer biomarkers used regularly in medical practice for treating acute kidney injury have proved to be an inexpensive one. So this study on MPV as a prognostic factor in acute kidney injury patients was taken up.

Materials & methods:

This cross sectional study was carried out for a period of 2 years from September 2016 to September 2018.

Inclusion criteria: Adult patients aged more than 18 years admitted to the medical college hospitals with the diagnosis of acute kidney injury as per Kidney Disease : Improving Global Outcomes (KIDGO) guidelines

Exclusion criteria: Patients who are diagnosed as chronic kidney diseases and on chronic dialysis ,patients with associated hematological disorders, patients with terminal malignancy ,patients on chemotherapeutic agents or drugs causing bone marrow suppression, patients with a history of platelet transfusion within 24 hours and chronic smokers .

Sample size and calculation: 130 cases of acute kidney injury

Formula used to calculate sample size is:

$$n = (Z_{\alpha})^2 \times \sigma^2 / d^2$$

mean=123.5⁷ & Standard deviation σ =107.6

Z_{α} =1.96 at 95% confidence interval

Sample size⁷ calculated is 130

Methods:

Informed written consent was taken by all the patients after getting the approval by the institutional ethical committee. The patients admitted in the hospitals attached with a medical college were approached in the wards. The nature and objectives of the study were explained to them in a language they comprehend .A detailed history along with physical examination and laboratory investigations were taken. Venous blood samples were collected with 1.5 mg/ml of dry K₂EDTA in plastic topped vacutainers and analyzed within 2-6 hours using Beckman coulter hematology analyzer LH 480 .Blood report of mean platelet volume and red blood cell distribution width were collected .AKI was diagnosed as per KIDGO guidelines .All patients with confirmed diagnosis of AKI without any exclusion criteria were included .The data collected was entered and analyzed using SPSS version 17.0. Comparison between the two groups were done by students unpaired t test . Correlation between MPV ,RDW and other variables were done by Pearson coefficient of correlation. P <0.05 was considered significant.

Result: Table 1: Values of mean platelet volume in fL with age

	Age(in years)				Total
	30 &above	31-50	51-70	Above 70	
MPV≤8.8 n	13	34	18	4	69
%	18.8	49.3	26.1	5.8	100
MPV≥ 8.8 n	7	29	24	1	61
%	11.5	47.5	39.3	1.6	100
Total	20	63	42	5	130
	15.4	48.5	32.3	3.8	100

Table 2: Values of mean platelet volume with sex:

Values of mean platelet volume in fL	Male	Female	Total
≤8.8 n= %	44 63.8	25 36.2	69 100
≥8.8 n= %	45 73.8	16 26.2	61 100
Total n= %	89 68.5	41 31.5	130 100

Table 3: Values of mean platelet volume with number of dialysis required patients and their improvement

Values of mean platelet volume in fL	Dialysis required patients	Dialysis not required patients	No patients improved	No patients not improved
Mean ±Std	8.4717±1.19179	9.0986±1.31947	8.88±1.26	8.48±1.41
≤8.8 %	38 55.1	31 44.9	55	14
≥8.8 %	22 36.1	39 63.9	51	10

Table 4: Correlations of Values of mean platelet volume & other parameters:

Parameters	Pearson correlation	P
Age	0.124	0.159
Haemoglobin	0.056	0.531
RDW	-0.077	0.384
Urea	-0.103	0.241
Creatinine	-0.288	0.001*
Platelet	-0.193	0.028*
Hospital stay	-0.398	0.000*
PCT	-0.190	0.113

* Significant

Fischer's Exact test was used to compare MPV values between two groups. $P=0.240$ (not significant) It was seen that patients belonging to middle age between 31-50 years constituted the majority of the cases of AKI(table 1) So this age group constitutes nearly 50% of the sample size. Chi-square test was done to study MPV values with sex in two groups. $P=0.221$ (not significant) . It is proved that patients having a lower MPV are more prone for the requirement for dialysis. $P< 0.005$ It is proved that patients having a lower MPV are more prone for the requirement for dialysis when the two groups were compared to look for significance in predicting the requirement of dialysis($P=0.03$)(Table 3). Our study showed that mean value of MPV of those patients who underwent dialysis was 8.47fL and mean value of those who recovered without dialysis was 9.09.It is to be noted that the difference in the mean value of MPV between those who got dialyzed and those who did not ,is meagre(0.6269).Improvement after dialysis was better seen in patients with higher MPV values than patients with lower MPV values even though the difference between mean MPV values were not significant. It is observed that the MPV of patients who improved was 8.88 and who did not improve was 8.48 fL.The differences were not significant when mean MPV values were compared between two patients groups ($P=0.568$) When the creatinine values of all the patients were correlated with their MPV values using Pearson correlation (table 4)there is a negative correlation between creatinine value and MPV and it is statistically significant ($P <0.001$).

Discussion: since MPV value does not change with age, ($P>0.05$) it can be applied to patients of any age group as a prognostic factor. Similar to this study done by David Bessman et al in which they evaluated the platelet size in health and diseases, there was no correlation of the platelet size with regards to the age of the patients.⁵ .MPV values do not change with sex(table 2) . It is also shown by Butkiewicz et al even though women have higher platelet count due to different hormonal profiles.⁶ Since the difference in the mean value of MPV between those who got dialyzed and those who did not is very less(0.6269))it is not logical to apply it directly on AKI patients to determine their requirement for dialysis .Our suggestion is to study platelet indices in a large sample of AKI patients and determine the cut off value from it. In a study done by JS Han et al in 349 patients with AKI for continuous renal replacement therapy, they predicted mean MPV >10.2 fL was associated with 28 -day all cause mortality⁷ .This is in contradiction with our study because we have a negative correlation of MPV with requirement of dialysis .In another study done by P Yousef et al they found that MPV <8.2 fL was associated with poor outcome.⁸.So we are getting mixed results from the previous studies. All the previous studies including ours were on a sample <400 and were a single centered study .Our suggestion to get a clear picture is to do large scale multi centric study on AKI patients and to narrow down to etiology -based AKI study. A study on MPV with severity of inflammation in acute pancreatitis patients it was found out that a lower MPV was correlated with severity of pancreatitis.⁹ In some other studies also when MPV was correlated with various inflammatory disorders negative correlation was found out^{9,10}. MPV is an indicator measures the bone marrow activity and problems in platelet structure. Preeclampsia, septic conditions, consumption of cytotoxic drugs, aplastic anemia, Bernard-Soulier syndrome and Wiskott- Aldrich syndrome

are some conditions where MPV gets affected¹¹. Studies have described an counter relationship among platelet count and MPV in both pathological and physiological conditions suggesting a tendency to maintain haemostasis by maintaining the platelet mass.¹² This type of relationships are mainly seen in inflammatory conditions. Huge quantity of platelet fabrication with inadequate time for growth, results in stock of great sized platelets at the sites of swelling which are used up closely in the practice of swelling¹³. Quick changes within minutes to hours in the platelet size and number may take place due to group of prothrombotic and pro inflammatory mediators in platelets. The role of platelet granules are limited to the sympathetic activation and stress of exercise¹⁴

A significant negative correlation was seen between MPV values and serum creatinine levels of AKI patients. ($P < 0.001$). Previous research reports suggest the rapport amid MPV and serum creatinine¹⁵⁻¹⁷. In Kidney disease patients; when the relationship between changes in MPV and serum creatinine levels were evaluated, no significant changes were seen. However, in patients with high blood pressure relationship of serum creatinine levels with MPV was inversely significant.¹⁸ It was reported that creatinine and proteinuria has direct relationship with MPV.¹⁷ MPV with GFR have reverse relationship¹⁷. There was a finding that, in patients with CKD, GFR has inverse association with MPV.¹⁵ Adding, it was suggestively amplified with the advancement of CKD with GFR in patients.^{15,19}

A change in MPV occurs before creatinine elevation in patients with AKI. Creatinine is not diagnostic test for early stage of kidney failure. Serum creatinine level increases in significant damage of²⁰ diagnosis of CKD in early stage can drastically decrease health costs.¹⁸ MPV could be inexpensive and superior investigation to creatinine when compared to the timing of detection of AKI which needs to be studied further with larger sample size and timely blood sample analysis.

References:

1. P.P Verma. Prevalence of chronic kidney diseases in India-Where are we heading? Indian J Nephrol 2015; 25(3):133-135
2. Dermirin H, Ozhan H, Ucun T, Celer A, Bulur S, Cil H, Gunes C, Yildirim H.A. Normal range of mean platelet volume in healthy subjects :insight from a large epidemiologic study. Thromb Res. 2011;128(4):358-60.
3. Alsheeha MA, Alaboudi RS, Alghasham MA, Iqbal J, Adanil. Platelet count and platelet indices in women with preeclampsia. Vascular health & risk management J. 2016;12:477-480.
4. D Schwartz, L Shorkey, PJ Armstrong, C Knudson and J Kelley. Platelet volume and plateletcrit in dogs with presumed primary immune-mediated thrombocytopenia. J Vet Intern Med 2014; 28(5):1575-79.
5. Bessman JD, Williams LJ, Gilmer Jr PR. Platelet size in health and hematologic disease. American J of Clinical Pathology. 1982;78(2):150-3

6. Butkiewicz AM, Kemoni H, Dymicka-Piekarska V, Matowicka-Karna J, Radziwon P, Lipska A. Platelet count, mean platelet volume and thrombocytopoietic indices in healthy women and men. *Thrombosis Research*. 2006;118(2):199-204.
7. Han JS, Park KS, Lee MJ, Kim CH, Koo HM, Doh FM. Mean platelet volume is a prognostic factor in patients with acute kidney injury requiring continuous renal replacement therapy. *Journal of Critical Care*. 2014;29(6):1016-21
8. Yousefichaijan P, Eghbali A, Rafiei M, Taherahmadi H, Shariatmadari F, Alinejad S. Mean platelet volume as a predictive marker for poor prognosis of acute renal failure in children. *Journal of Pediatric Nephrology*. 2015;3(3):92-4.
9. Beyazit Y, Sayilir A, Torun S, Suvak B, Yesil Y, Purnak T. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. *Clinics and research in hepatology and gastroenterology*. 2012;36(2):162-8.
10. Safak S, Uslu AU, Serdal K, Turker T, Sonar S, Lutfil A. Association between mean platelet volume levels and inflammation in SLE patients presented with arthritis. *African health sciences*. 2014;14(4):919-24.
11. Liu S, Ren J, Han G, Wang G, Gu G, Xia Q. Mean platelet volume: a controversial marker of disease activity in Crohn's disease. *Eur J Med Res*. 2012;17-27.
12. Thompson C. From precursor to product how do megakaryocytes produce platelets? *Progress in clinical and biological research*. 1986;215:361-71.
13. Thompson CB, Jakubowski JA. The pathophysiological and clinical relevance of platelet heterogeneity. *Blood*. 1988;72(1):1-8.
14. Yilmaz MB, Saricam E, Biyikoglu SF, Guray Y, Guray U, Sasmaz H. Mean platelet volume and exercise stress test. *Journal of thrombosis and thrombolysis*. 2004;17(2):115-20.
15. Ju HY, Kim JK, Hur SM, Woo SA, Park KA, Park MY. Could mean platelet volume be a promising biomarker of progression of chronic kidney disease? *Platelets*. 2015;26:143-7.
16. Yenigun EC, Aypak C, Turgut D, Piskinpaşa SV, Cevher SK, Koc E. Is there a relation between mean platelet volume and chronic kidney disease stages in diabetic patients? *Int J Clin Exp Med* 2016;9:330-5.
17. Turgutalp K, Ozhan O, Akbay E, Tombak A, Tiftik N, Ozcan T. Mean platelet volume and related factors in patients at different stages of diabetic nephropathy: a preliminary study. *Clin Appl Thromb Hemost*. 2014;20:190-5.
18. Mohammad Reza Tamadon, Sayed Mohammad-Ali Torabi, Jamileh Moghimi, Majid Mirmohammadkhani, Farahnaz Ghahremanfard. Serum creatinine levels in relationship with mean platelet volume in patients with chronic kidney disease *J Renal Inj Prev* 2018;7(1):38-41.
19. Sharpe PC, Dessai ZR, Morris T C. Increase in mean platelet volume in patients with chronic failure treated with erythropoietin. *J Clin Pathol* 1994;47:159-161.
20. Taylor EH. *Clinical Chemistry*. New York: John Wiley and Sons; 1989:58-62.

