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Study of Mean Platelet Volume and Platelet Distribution Width in Patients with Chronic Kidney Disease Attending A Tertiary Care Hospital

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Abstract

Chronic kidney disease, an important cause of morbidity and mortality across the world is associated with qualitative platelet dysfunction which leads to a thrombotic milieu leading to various cardiovascular complications. However, there are only a few studies regarding the relationship of platelet indiceswith progression of chronic kidney disease.In this hospital based cross sectional study of 1 year duration among 100 chronic kidney disease patients seeking inpatient and outpatient care from departments of General Medicine and Nephrology in Government Medical College, Ernakulam, the primary objective was to estimate mean platelet volume and platelet distribution width of the study participants.The secondary objective was to find the correlation between the mean platelet volume and estimated GFR in chronic kidney disease patients. The data for the study was collected from the routine investigations done for the patients. The data were entered into Microsoft excel sheet and analysed using R software version 4.2.0. Qualitative variables were expressed as proportions and quantitative variables were expressed as mean and standard deviation. Association between qualitative variables were tested

using Chi square test. Association between quantitative variables were done by Independent sample t test. Significance level was fixed at a p value ≤ 0.05. The correlation between mean platelet volume and estimated glomerular filtration rate was estimated using correlation coefficient.The estimated mean MPV (mean platelet volume) was 8.4±1.4 fL in chronic kidney disease patients. The estimated mean PDW (platelet distribution width) was 15.8±0.6. A statistically significant negative correlation was seen between eGFR and mean platelet volume (MPV). A statistically significant negative correlation was seen between eGFR and platelet distribution width(PDW). Thus, platelet indices like mean platelet volume and platelet distribution width)can be utilised as predictive markers for follow-up of chronic renal disease patients and early management of athero-thrombotic complications, thereby minimising morbidity, since the platelet indices are simple to measure in most primary health facilities and in resource-poor settings.

Keywords: Chronic kidney disease,Mean platelet volume, Platelet distribution width.

Introduction

Chronic kidney disease is one of the most important cause of morbidity and mortality across the world. The global burden of chronic kidney disease was estimated to be 9.1% in 2017 roughly amounting to 700 million cases.(1) The prevalence of chronic kidney disease among general population in India is 16% (2)(3). Being implicated in the development of coronary plaques and the thrombotic problems that result in acute cardiovascular events, platelets represent a crucial stage in atherogenesis. In actuality, cardiovascular events continue to be a major factor in both morbidity and mortality of chronic kidney disease patients. Numerous researches have been conducted to determine the factors that predict increased platelet reactivity and to enhance antithrombotic methods in high-risk patients, such as those with chronic kidney disease (4). The Platelet indices, which are inexpensively and routinely measured by automated cell counters, is a readily available indicator of platelet activation and function. The association of increased MPV and PDW in relation to progression of kidney disease have been shown in many studies. It is associated with a variety of prothrombotic and proinflammatory diseases. In this study, I aim to study platelet parameters in chronic kidney disease and its correlation with severity of chronic kidney disease.

Materials and Methods

Study design: Hospital based cross sectional study.

Study Setting: Government Medical College Hospital, Ernakulam.

Study Duration: - The study was conducted over duration of one year.

Study Subjects: - Patients admitted in Internal Medicine wards and Medical Intensive Care units, those undergoing dialysis in Nephrology department and attending Nephrology OP in Government Medical College Hospital, Ernakulam with a diagnosis of chronic kidney disease. The diagnosis of chronic kidney disease being made by considering eGFR (calculated by Cockroft Gault equation for creatinine clearance), the renal biochemical parameters and duration of illness. Chronic kidney disease will be staged according to KDIGO guidelines.

Inclusion criteria

Patients above the age of 18 years with a diagnosis of chronic kidney disease according to Cockroft Gault equation. (5)

Exclusion criteria

The following patients were excluded from the study

- Patients with history of malignancy.
- Patients with congestive heart failure.
- Patients with history of chronic liver disease.
- Patients with hepatitis B or hepatitis C infection.
- Patients having haematological disease (e.g., immune thrombocytopenia or myelodysplastic syndrome).
- Those who were not willing to give consent.

Sample size

According to the previous study conducted by Monica Vedoria et al,titled "Impact of renal function on mean platelet volume and its relationship with coronary artery disease:A single centre cohort study",(49) the mean platelet volume in chronic kidney disease patients was found to be 11 with a standard deviation of 1.Based on this data and using the formula $4SD^2/D^2$, where SD is the standard deviation and D is the absolute precision ,the minimum sample size for the present study was estimated to be 100 with an absolute precision of 0.2 and at 95% significance levels.

Sampling Method

Consecutive cases of patients satisfying inclusion criteria were included in the study till the required sample size was met.

Study variables

- Sociodemographic variables.
- Platelet volume indices- mean platelet volume (MPV), platelet distribution width (PDW).
- eGFR (estimated glomerular filtration rate).

Data collection tools

1. A structured questionnaire was used to collect information on sociodemographic characteristics and the medical history of the participant.

Study Procedure

Institutional Ethics Committee clearance was obtained for the study. All consecutive cases of chronic kidney disease who satisfy the inclusion criteria were included in the study. After obtaining informed written consent from the study participants, a detailed history taking and physical examination including general examination and systemic examination were done and the findings were recorded. Chronic kidney disease was graded using KDIGO guidelines. (6)

Stage	Description	GFR(ml/min/1.73m2)
1	Kidney disease with normal or high GFR	>90
2	Kidney damage with mild reduction in GFR	60-89
3	Moderate reduction in GFR	30-59
4	Severe reduction in GFR	15-29
5	Kidney failure (ESRD)	<15

Table 1: Staging of CKD

A minimum quantity of blood ~ 4 ml was taken from a peripheral vein under aseptic precautions. The sample was used to do blood routine examination using BC-6800 Auto hematology analyser in the hematology lab of Medical College Hospital, Ernakulam. The platelet indices were obtained along with the blood routine examination. Renal function tests, liver function tests and serum electrolytes estimation were done in the biochemistry lab of Medical College Hospital, Ernakulam. Urine samples were collected, and urine routine examination was done in pathology lab and Urine P:C ratio was estimated in the biochemistry lab. The results were entered in the proforma. The Platelet indices of the participants were studied**.** The creatinine clearance(CCr) or eGFR was calculated using Cockroft Gault equation. (9)

$$CCr = \frac{\{((140 - age) x weight)\}}{72 x SCr}$$

Multiplying this formula by 0.85 gives creatinine clearance in females.

Data analysis

- Data were entered into Excel sheet. Data was analysed using R statistical software version 4.2.0
- Qualitative variables were expressed as proportions and quantitative variables were expressed as mean and standard deviation.
- Association between qualitative variables was tested using Chi square test. Association between quantitative variables was done by Independent sample t test.
- Significance level was fixed at a p value ≤ 0.05. The correlation between Mean platelet volume and estimated glomerular filtration rate was estimated using correlation coefficient.

Ethical considerations

- Institutional ethical committee clearance was obtained
- Written Informed consent was obtained from the participants
- Confidentiality was ensured and maintained throughout the study.

Budget

No additional expenses were incurred by participants during the study.

Observation and Results

Data was entered in Microsoft Excel 365 Software and analysed using R software version 4.2.0.

The continuous variables like age, body weight, haemodynamic parameters, haematological parameters, and biochemical parameters were summarised as mean and standard deviation. Urine protein creatinine ratio and eGFR were summarised as median and IQR. Categorical variables like sex, district, education level, socioeconomic status, residential status, comorbidity status, type of dialysis, frequency of haemodialysis, CVS, CNS, GIT and respiratory system findings, urine albumin level, stage of chronic kidney disease, and prevalence of kidney failure were summarised as frequency and proportions. Age was also categorised into intervals of 10.

Association between eGFR and MPV was assessed using Pearson correlation analysis. ROC analysis was done to find a cut-off of MPV to diagnose kidney failure.

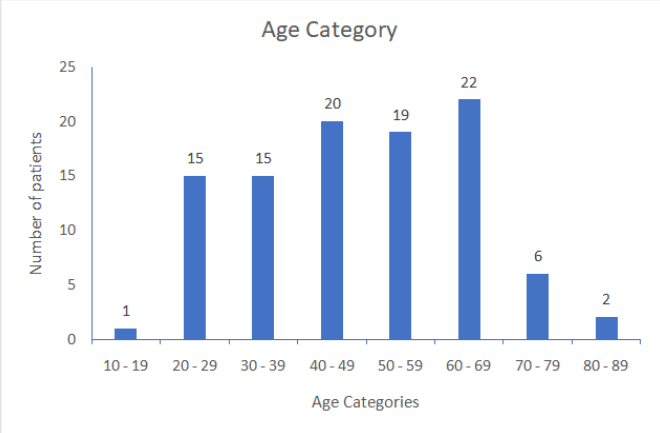

Fig.1: Age distribution of study participants

The mean age of the study participants was 48.6 (16.1) years.

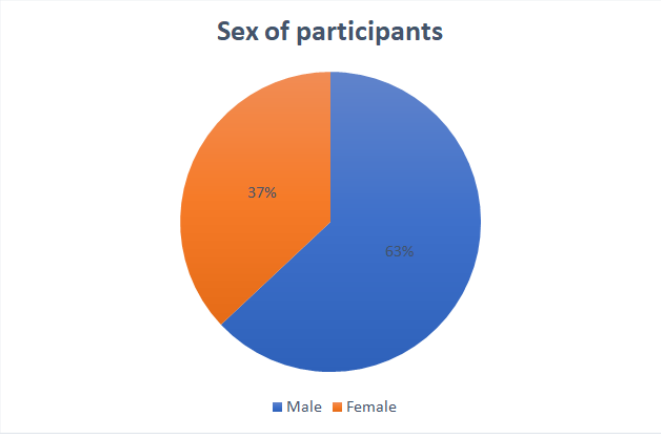

Fig. 2: Sex distribution of study participants

Out of the 100 participants, 63 (63%) were males.

Table 2: Body weight of the participants

	Mean	SD
Body weight (kg)	60.6	7.1

Table 3: Comorbidity status of the patients

Comorbidity	n	%
Diabetes Mellitus	55	55.0
Hypertension	56	56.0
Coronary Artery Disease	27	27.0
Thyroid dysfunction	15	15.0

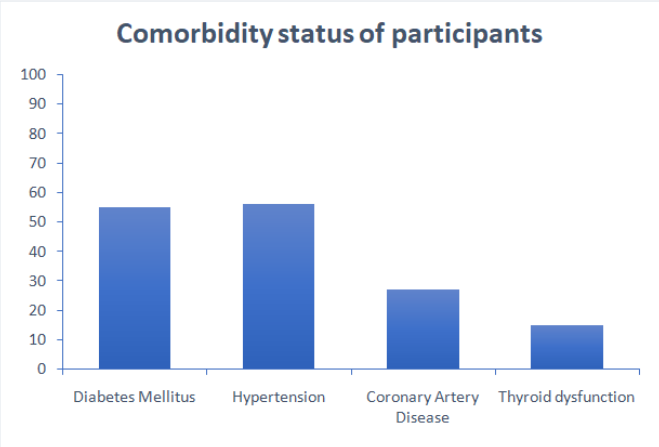

Fig. 3 : Comorbidity status of study participants

The majority of participants were suffering from hypertension (56%) and diabetes mellitus (55%).

Table 4: Type of dialysis of the patients

Type of dialysis	n	%
Peritoneal Dialysis	1	1.0
Haemodialysis	46	46.0

Only one (1%) patient was undergoing peritoneal dialysis and 46 (46%) were undergoing haemodialysis among the participants.

Table 5: Haematological parameters of the patients

Haematological parameters	Mean	SD
Haemoglobin (mg/dl)	10.4	2.0
PCV	32.9	7.6
Total Count	7350.4	2054.5
Differential count (%) – Polymorphs	60.0	9.2
Differential count (%) – Lymphocytes	25.5	7.3
Absolute Neutrophil Count	4468.8	1640.4
Absolute Lymphocyte Count	1872.5	715.5
ESR (mm in first hour)	39.0	22.8
Platelet count (in Lakhs)	2.4	0.8
MPV	8.4	1.4
PDW	15.8	0.6
Platelet – Large Cell Ratio	22.8	4.3

Table 6: Biochemical parameters of the participants

Biochemical parameters	Mean	SD
Urea	82.0	47.6
Creatinine	6.6	4.6
Total Protein	6.9	0.5
Albumin	3.6	0.5
Serum Sodium	136.4	5.0
Serum Potassium	4.4	0.8
Random Blood Sugar	185.4	83.8

Table 7: Urine albumin of the participants

Urine Albumin	n	%
Nil	18	18.0
Trace	5	5.0
1+	33	33.0
2+	31	31.0
3+	7	7.0
4+	6	6.0

Table 8: Urine protein creatinine ratio of the participants

	Median	IQR
Urine protein creatinine Ratio	1.4	0.7, 2.4

Table 9: Stage of CKD of the participants

Stage of CKD	n	%
2	8	8.0
3	25	25.0
4	12	12.0
5	55	55.0

Majority of the participants (55%) in the study had stage 5 CKD.

Table 10: Prevalence of ESRD (Stage 5 CKD)

ESRD	n	%
Yes	55	55.0
No	45	45.0

The majority of the participants (55%) in the study were suffering from End stage renal disease.

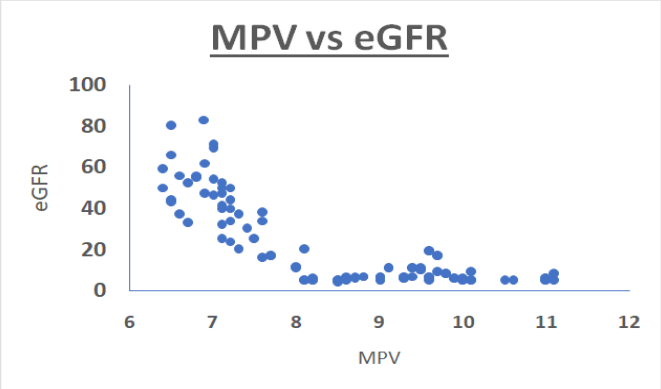

Fig. 4: eGFR with Mean Platelet Volume

Pearson correlation coefficient of eGFR with MPV is -0.80. There was a significant correlation between eGFR and MPV with a p-value <0.001.

Table 11: MPV (Mean Platelet Volume) of the participants with stages of CKD

	Early CKD (Stage 1,2 & 3)	Late CKD (Stage 4&5)	p-value
MPV Mean (SD)	6.9(0.3)	9.2 (5.5)	<.001

MPV was significantly higher in those with late CKD with p-value <0.001.

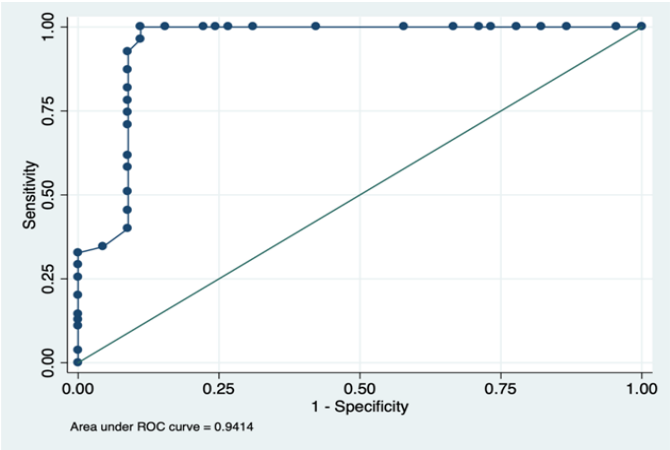

Fig. 5: ROC curve of MPV for diagnosing kidney failure

ROC analysis revealed an area under the curve of 0.94 [95% CI 0.89 - 1.0], with a cut-off of mean platelet volume ≥ 8.0 diagnosing End stage renal disease(ESRD) with a sensitivity of 100.0% and specificity of 88.9%.

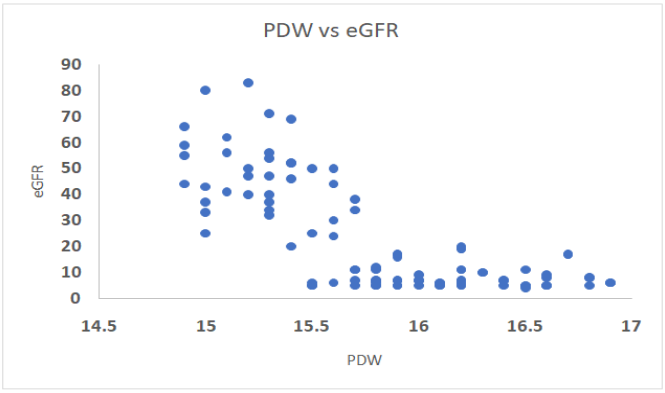

Fig. 6: eGFR with Platelet Distribution Width

Pearson correlation coefficient of eGFR with PDW is -0.74. The correlation was statistically significant with a p-value <0.001.

Discussion

In the present hospital based cross sectional study conducted among patients of General Medicine and Nephrology department of Government Medical College Ernakulam during March 2021- February 2022, the total number of cases was 100 out of which 63 were males

and 37 were females with a male to female ratio 1.7:1. The mean age of the study participants was 48.6 ±16.1 years**.** Similar male preponderance was observed in study conducted by Kumar et al at Allahabad where male to female ratio was 1.8:1 and mean age was 51.5±18.3 years.(7)

In this study, hypertension was the most common comorbidity seen in 56% of patients followed by Diabetes mellitus(55%) which is similar to that of study conducted by van Bladel et al.(8)

46% of patients underwent hemodialysis of which 80.4% patients had twice weekly dialysis. 1 patient underwent peritoneal dialysis and rest was managed conservatively without dialysis.

The mean Haemoglobin was 10.4 ±2 with a PCV of 32.9± 7.6.

Platelet indices of the patients were studied and analysed. The current study found that the mean platelet count among the study participants was 2.4 ± 0.8 lakhs which was similar in the study done by Lokesh et al in 2016.(9). The mean MPV (mean platelet volume) was 8.4±1.4 fL. This was similar to various studies conducted by Tamadon et al in 2017(7) and Ata et al in 2019(10). The mean PDW (platelet distribution width) was 15.8±0.6 and mean P-LCR (platelet large cell ratio) was 22.8±4.3. Similar results were seen in study conducted by Varsha Kumar et al (7).

In this study, 55% of participants had stage 5 CKD; 25% had stage 3 CKD, 12% had stage 4 CKD and 8% had stage 2 CKD.

Mean platelet volume (MPV) is an indicator of average size and activity of platelets(11).In the present study the mean value of mean platelet volume was significantly higher in late CKD(i.e., stage 4 and stage 5 CKD).

There was a negative correlation between eGFR and MPV. Pearson correlation coefficient of eGFR with MPV was -0.08 with a p value of less than 0.001. This was similar to that of the findings in various studies conducted by Hu et al, Yu et al and Saad et al. (12)(13)(14)Young et al. showed statistically significant differences in MPV with progressive stages of chronic kidney disease.(14) Thus MPV can be considered a promising biomarker of progression of chronic kidney disease. (12)

MPV also can be considered as a herald to complications of chronic kidney disease mainly cardiovascular complications due to the qualitative platelet dysfunction as revealed by various studies conducted by Joki et al in 1997, Henning et al in 2002 and Khandekar et al in 2006 ; which has not been included in the present study. (15)(16)(17)

In the present study, ROC analysis revealed an area under the curve of 0.94 [95% CI 0.89 - 1.0], with a cut-off of mean platelet volume $\geq$ 8.0 diagnosing end stage renal disease with a sensitivity of 100.0% and specificity of 88.9%. Studies with similar observation are scarce.

Platelet distribution width (PDW) directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology. There was a negative correlation between eGFR and platelet distribution width. Pearson correlation coefficient of eGFR with PDW was -0.74. The correlation was statistically significant with a p-value <.001. This observation was similar to that of study conducted by Kumar et al. (7)

As renal function declines, athero-thrombotic risk gradually rises, according to numerous previous researches (18)(19)(20).Thus, platelet indices can be utilised as predictive markers for follow-up of chronic

renal disease patients and to initiate early management of athero-thrombotic complications, thereby minimizing morbidity, since the platelet indices are simple to measure in the majority of primary health facilities and in resource-poor settings.

Conclusion

In this study of 100 patients with chronic kidney disease, a statistically significant negative correlation was observed between eGFR and mean platelet volume (MPV).

A statistically significant negative correlation was observed between eGFR and platelet distribution width (PDW) in patients with chronic kidney disease.

Thus, platelet indices like mean platelet volume and platelet distribution width can be utilised as predictive markers for follow-up of chronic renal disease patients and to initiate early management of athero-thrombotic complications, thereby minimising morbidity, since the platelet indices are simple to measure in the majority of primary health facilities and in resource-poor settings.

Limitations

Since this was a hospital based cross sectional study, further studies will be necessary to determine the correlation between platelet indices and progression of chronic kidney disease.

Further studies are needed so as to find a diagnostic cut off value of Mean Platelet Volume to diagnose End Stage Renal Disease.

List of Abbreviations

CKD - Chronic Kidney Disease.

CNS - Central Nervous System.

Cr - Creatinine.

CCr - Creatinine clearance.

CVS - Cardiovascular System.

Egfr - Estimated Glomerular filtration rate.

ESR- Erythrocyte Sedimentation Rate.

ESRD - End Stage Renal Disease.

GFR- Glomerular filtration rate.

GIT - Gastrointestinal system.

IQR - Interquartile range.

KDIGO - Kidney Disease Improving Global Outcomes.

MPV - Mean Platelet Volume.

PCV - Packed Cell Volume.

PDW - Platelet Distribution Width.

RFT - Renal Function Tests.

ROC - Receiver Operating Characteristic.

SD - Standard deviation.

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