

A Correlative Study of Platelet Indices in Different Stages of Chronic Kidney Disease Patients in A Tertiary Care Centre

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Abstract

Introduction: In the modern world, there is a rising trend of diabetes mellitus and hypertension in developing countries like India, which is favouring a rise in complications like Chronic kidney disease. Thrombotic complications are a high possibility in chronic kidney disease (CKD). In recent days, abnormalities in platelet parameters are found to be an effective tool in risk stratification of CKD patients to develop venous thromboembolism and vascular disease. Our study was conducted to assess relation of platelets indices, platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) in CKD patients. **Material and methods:** A retrospective evaluation was conducted on the blood biochemical data and hematological data obtained from the records of patients diagnosed with chronic kidney disease for over 5 months (January 2021- May 2021). The demographic data, urea, creatinine values and hematological findings were collected from the patient lab reports from the Department of Biochemistry and Pathology of Saveetha medical college and hospital. Platelet indices were obtained using Sysmex -XN 1000 automated analyser. 131 cases of known CKD was collected and correlated with Platelet indices values. **Results:** On gender and age distribution, male patients were predominant and age group between 41 to 60 were commonly affected. In CKD stage 2-39 patients, stage 3-32 patients, stage 4-28 patients, stage 5-14 patients were categorized according to their clinical findings and laboratory investigations. On correlation, there were no statistically significant differences in any PLT indices (platelet count, mean platelet volume, platelet distribution width and plateletcrit). However, Platelet count lower as the stage increases and MPV, PDW and plateletcrit were slightly higher in stage 5 CKD when compared with other stages of CKD. **Conclusion:** Platelet indices plays major mechanism in pathological processes of vascular thrombosis. The efficacies of platelet indices associated with CKD patients remain unknown. Prospective randomized controlled trials involving larger numbers of CKD patients are needed to determine the associations with platelet indices.

Keywords: Chronic kidney disease (CKD), platelet count, mean platelet volume, platelet distribution width and plateletcrit.

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INTRODUCTION

Chronic kidney disease is defined as a change in the renal function or its structure for more than 3 months that affects the health of an individual irrespective of the cause. Based on the glomerular filtration rate and albuminuria content, it is classified into five stages [1]. Kidney Disease Improving Global Outcomes (KDIGO) guidelines suggest that people with GFR ≥ 90 ml/min/1.73 m² are categorized into CKD -first stage where the kidney functions normally, 60–89 ml/min/1.73 m² falls in CKD -second stage with mildly decreased function. The CKD- third stage is subdivided into two; Individuals with 45–59 ml/min/1.73 m² and 30–44 ml/min/1.73 m², where the

GFR is mild to severely decreased. In CKD-stage 4, the GFR decreases to 15–29 ml/min/1.73 m² and in CKD-fifth stage <15 ml/min/1.73 m², kidney fails to function [1-3]. The early stages are usually asymptomatic and the end-stage is treated by dialysis or renal transplantation. Multifactorial pathological insults that affects the renal function and destroys the structure of nephrons. As a result, the other nephrons compensate the function of injured nephrons by hyper-filtration [5]. Over a longer period of time, it develops glomerular hypertension which leads to proteinuria, and eventually loss of renal function. Meta-analytical studies have proven that platelets play a major mechanism in thromboembolic activity, and are essential triggers for coronary diseases. Platelet activation is the initiating

factor for thrombosis mainly through inflammatory reactions(11). Previous research studies indicate that alterations in platelet indices can also be related to increased incidence of venous thromboembolism and vascular disease. Mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) parameters are generated using automated cell counters are proved to be cost effective and but not routinely ordered by clinicians during clinical practice [3]. These markers are mostly underutilized or ignored though it is easily available [7, 8]. To the best of our knowledge there are few studies available relating CKD and platelet parameters especially concentrated on platelet parameters such as MPV. However, the role of platelet indices in the CKD patients to develop complications is till unknown. Therefore this study was conducted to determine the correlation of platelet indices in different stages of chronic kidney disease patients in a tertiary care centre [4].

Inclusion Criteria: Includes age group of above 20 years and patients with hemodialysis.

Exclusion Criteria: Includes pediatric age groups, malignancy, surgery, major trauma within the previous six months, pregnant women and history of bleeding disorders.

MATERIALS AND METHODS

A retrospective study was carried out in line with research regulations, including the approval of the Ethical committee. In total, 113 CKD patients of age group of above 20 years who were admitted in Saveetha Medical College and Hospital, Thandalam under various clinical departments, from January 2021 to May 2021 were taken up for this study. The diagnosis of CKD was based on clinical history, radiological diagnosis, biochemical investigation (urea and creatinine etc.) and hematological parameters. Total platelet parameters were generated from Sysmex XN 1000 autoanalyser. These parameters (Platelet count, Mean platelet volume, platelet distribution width and plateletcrit) were standardized by routine external and internal quality control checks.

Statistical Analysis

The results were expressed as mean ± SD. Microsoft word and Excel were used to generate graphs, and tables. Statistical methodology were used to evaluate the significance of differences between stages of CKD patients. The study was approved by the Saveetha institutional ethical committee.

RESULTS

In our study, on gender comparison, out of 113 patients, male patients were 66 and female patients were 47, male population was predominant. On age distribution, 17 patients belonged to the age group of 21 to 40 years, 72 patients belonged to the age group of 41

to 60 years and 24 patients were above 60 years of age. Patients of the age group 41 to 60 years were predominantly affected (Fig 1 & 2).

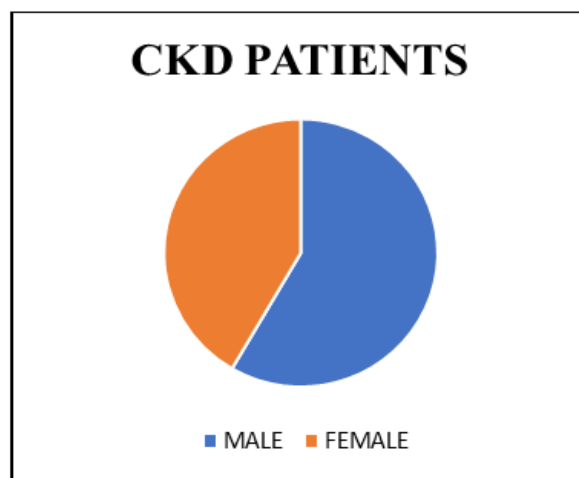


Fig 1: Gender distribution of CKD patients

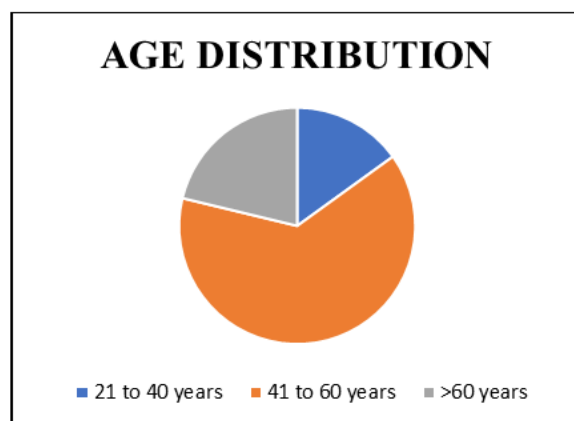


Fig 2: Age distribution of CKD patients

Stages of CKD patients were categorized by clinical history, hematological parameters, radiological diagnosis, biochemical investigation such as urea, creatinine 39 patients were diagnosed as Stage 2 of CKD, 32 patients diagnosed as Stage 3 of CKD, 28 patients diagnosed as Stage 4 of CKD and 14 patients diagnosed as Stage 5 of CKD irrespective of age and gender (Fig 3).

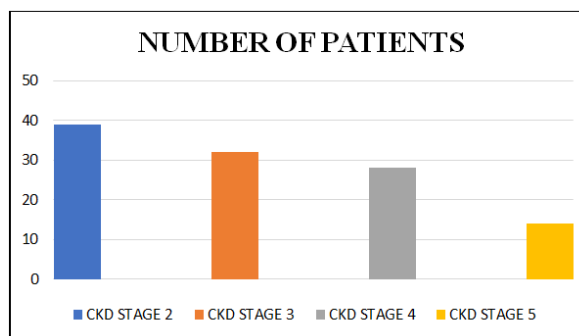


Fig 3: Stages of CKD patients

Table 1: Correlation of platelet indices in different stages of CKD patients

| PARAMETERS | CKD STAGE 2 (Mean ±SD) | CKD STAGE 3 (Mean ± SD) | CKD STAGE 4 (Mean ± SD) | CKD STAGE 5 (Mean ± SD) |
|----------------|---------------------------|----------------------------|----------------------------|----------------------------|
| PLATELET COUNT | 2.35±0.96 | 2.09±0.85 | 2.02±1.3 | 1.77±1.1 |
| MPV | 9.08±0.81 | 10.21±0.64 | 9.08±0.91 | 11.28±2.08 |
| PDW | 13.32±2.14 | 13.98±3.02 | 12.30±0.87 | 15.04±1.09 |
| PLATELETCRIT | 0.22±0.20 | 0.21±0.71 | 0.21±0.27 | 0.23±0.92 |

On correlation of platelet count with stages of CKD patients, stage 2 was 2.35 ±0.96, stage 3 was 2.09±0.85, stage 4 was 2.02±1.3 and stage 5 was 1.77±1.1. As the stage increases, there is a mild decrease in platelet count (Fig 4). On correlation with Mean platelet volume (MPV), stage 2 was 9.08±0.81, stage 3 was 10.21±0.64, stage 4 was 9.08±0.91 and stage 5 was 11.28±2.08. MPV was not correlated with stages of CKD (Fig 5). On correlation with platelet distribution width (PDW), stage 2 was 13.32±2.14, stage 3 was 13.98±3.02, stage 4 was 12.30±0.87 and stage 5 was 15.04±1.09. PDW was not correlated with stages of CKD (Fig 6). On correlation with plateletcrit (PCT), stage 2 was 0.22±0.20, stage 3 was 0.21±0.71, stage 4 was 0.21±0.27 and stage 5 was 0.23±0.92 (Fig 7). PCT was not correlated with stages of CKD. However, Platelet count lower as the stage increases and MPV, PDW and plateletcrit were significantly slightly higher in stage 5 CKD patients when compared with other stages of CKD (Table 1).

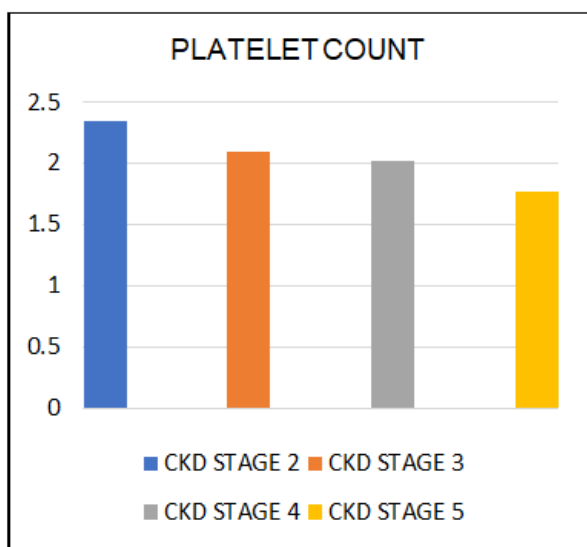


Fig 4: Correlation of platelet count with stages of CKD

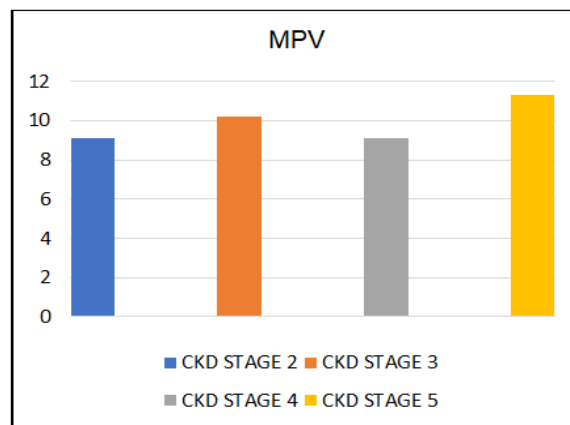


Fig 5: Correlation of MPV with stages of CKD

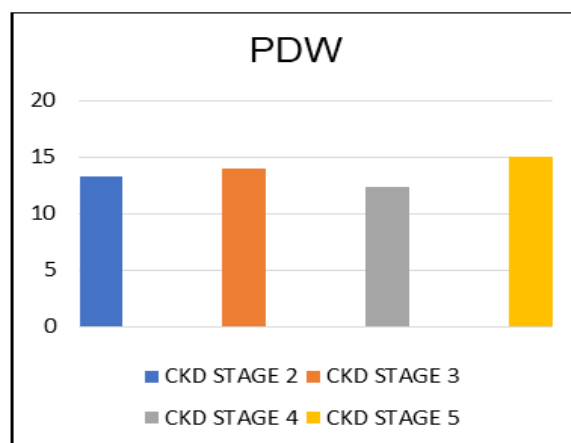


Fig 6: Correlation of PDW with stages of CKD

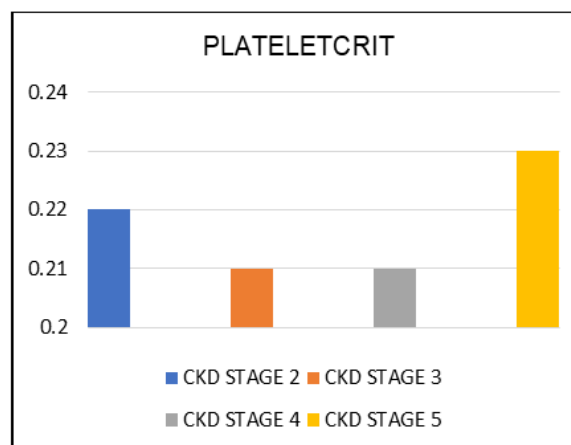


Fig 7: Correlation of plateletcrit with stages of CKD

DISCUSSION

Many meta analytical research studies indicate that with a decrease of glomerular filtration rate and increasing of proteinuria, the multifactorial causes lead to increase mortality and morbidity risk will dramatically increase. The pathogenesis of thrombovascular activity and chronic kidney disease has several overlapping mechanism [8]. Both thrombovascular activity and CKD promote each other in pathogenesis. Thus, understanding their relationship will greatly improve the prevention of chronic kidney disease and delay the disease progression. Megakaryocytic activity, platelet aggregation and adhesion contribute to the thrombovascular activity [9]. Impaired release of platelet granules also leads to a chronic inflammatory state which favours the development of foam cells, leukocyte infiltration and accelerates the process of atherosclerosis [6]. Larger platelets are likely to be more reactive, contain more granular particles and contribute greater amounts of vasoactive and prothrombotic factors. As mean platelet volume, platelet distribution width and plateletcrit can reflect the platelet activity, it is necessary to evaluate the value of these parameters in patients with chronic kidney disease. We thought analyzing the impact of CKD on platelet indices may be helpful in understanding the pathogenesis of coagulation abnormalities and thrombotic events occurring in these patients [5]. Our study was conducted with the aim of assessing the relationship between the effects of different stages of chronic kidney disease with platelet indices like platelet count, mean platelet volume, platelet distribution width and plateletcrit parameters in the patient. MPV is average size of the platelets in blood reported in femto litre (fL) and is available on most hematology auto analyzers. $MPV = (\text{mean} \pm \text{SD})$, $MPV = (9.7 \pm 1.48)$ fL. Variation in platelet size comprising of both small platelets and giant/ mega platelets is an indication of over production of platelets in bone marrow is calculated as PDW (Mean \pm SD), $PDW = (14.46 \pm 1.68)\%$. Plateletcrit is a measure of total platelet mass. Normal range of PCT is 0.1 - 0.31%. Benefits of platelet indices are that it is quick, simple and often requires no additional blood, it is an inexpensive test which also eliminates the observer bias [7].

In our study, platelet count was decreased as the stage increases. Although, platelet counts did not show that our patients were not in a potential bleeding risk, thrombocytopenia was an important risk factor for occurrence of bleeding among a minority of CKD study patients. Gafter U *et al.*, conducted a study in 1987 was done on the platelet count in 55 patients with end-stage renal failure on maintenance hemodialysis and in 19 predialysis patients with CRF before hemodialysis. This study showed the decrease of platelet count and mild thrombocytopenia in patients in CKD patients with renal failure are at high risk of bleeding due to

thrombocytopenia and platelet dysfunctions [11]. In our present study we also found a mild thrombocytopenia among CKD patients but only in a minority population. Correlation of Mean platelet volume with stages of CKD was not significant. However, mean platelet volume was raised in stage 5 CKD, when compared with other stages. Koroglu M *et al.*, observed a high MPV in CKD patients and concluded that MPV can be used as a biomarker to estimate thromboembolic risk in CKD patients and patients on hemodialysis. Berssman JD *et al.*, in their study observed hyper destructive causes to be the major pathogenesis for the cause of high MPV with low platelet count, in hematological disorders like thalassemia to be the commonest cause of high MPV with normal platelet count, myeloproliferative disorders and inflammation to be the commonest cause of high MPV with increased platelet count [5]. They also observed that MPV was low in patients with chronic renal failure independent of platelet count, an observation similar to our study. Previous meta analytical research study suggests MPV can be used as predictor of thromboembolism in CKD patients. CKD is associated with impaired haemostasis manifest in decreased platelet aggregation and prolonged bleeding times. Because larger platelets are more reactive and have been reported to be associated with myocardial infarction [10, 17]. The increase in MPV shown in this study may be one factor in the correction of the homeostatic defect of CKD and the increased risk of thrombosis which is now recognised as a side effect of r-HuEPO. Platelet volume is seen as a variable that relates to homeostatic function and larger platelets are known to produce more thromboxane A₂, contain denser granules, and secrete more serotonin and thromboglobulin compared with those of smaller size, while larger platelets are known to aggregate preferentially in the presence of adenosine diphosphate [13, 15]. In our present study, Platelet distribution width in CKD patients was not significant enough, but PDW in stage 5 patients was elevated, when compared with other stages of CKD. Mehmet Koroglu *et al.*, in their study found that there was no significant variation in PDW between dialysis and CKD patients. PDW increase during platelet activation and thereby can predict activation of coagulation more efficiently in general population. The increase of PDW can be used as one of the indicators to judge platelet activation. A study conducted in Chinese population, cohort study involving 31,751 participants without coronary heart disease at baseline, after 5 year follow-up, the result indicated that the lower level of PDW was significantly related to lower risks of CVD was observed. Another study also confirmed that higher PDW values on admission could predict 90 day mortality and shortened survival rate [17]. Taken together, PDW may be regarded as a more specific marker of platelet reactivity and can predict thrombovascular events in CKD patients. Correlation of plateletcrit with various stages of CKD patients was non-significant. However,

plateletcrit was raised in stage 5 CKD, when compared with other stages. A higher PCT in CKD patients was attributed to chronic inflammation, which probably might increase the risk of thrombotic activity [20]. Usefulness of PCT can be used as a biomarker for thrombovascular event in CKD patients remains controversial. Some limitations of our study are we done in small sample size. At last, we did not take the drugs into account, which may cause bias in our results. However, we excluded the antiplatelet drugs, whether the other drugs influence the platelet indices that needs further exploration.

CONCLUSION

In our study, we found platelet count decreased as the stage of CKD increased. Secondly MPV, PDW and PCT were mildly elevated in stage 5 CKD patients when compared with other stages. The platelet indices are extensively studied in association with chronic kidney disease patients of different stages and it is found to be a reliable predictor of underlying inflammation and severity of thrombovascular activity. However efficacies of indices associated with platelet function in determining the prognosis of renal failure in patients remains unknown. Larger numbers of randomized controlled trials study involving of CKD patients are needed to determine the mechanism of associations.

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Statement of Ethics:

This study was approved by Ethics Committee of Saveetha Medical and Hospital. As this study was a retrospective study, there was no patient's privacy data such as patient name, ID number, telephone and address were involved. Only demographic information and laboratory testing data of patients were collected and analyzed in this study.

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