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EVALUATION OF PLATELET PARAMETERS IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS- A TERTIARY CARE CENTRE EXPERIENCE

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Abstract

Background: Chronic Kidney Disease (CKD) is a global issue, with cardiovascular complications as a common cause of mortality in CKD patients on hemodialysis (HD). Platelet indices play major mechanism in pathological processes of vascular thrombosis.

Aim: The aim of the study was to assess platelet parameters including count and platelet indices namely Mean platelet volume (MPV), Platelet large cell ratio (P-LCR), Platelet distribution width (PDW) and Plateletcrit (PCT) in CKD patients undergoing hemodialysis.

Methods: A retrospective evaluation was conducted on the biochemical and hematological parameters accessed from the hospital records of hemodialysis patients who have chronic kidney disease for a period of one year. Platelet indices were obtained using Sysmex-XN 1000 automated six part hematology analyzer.

Statistical Analysis: The data was entered into Excel spreadsheet (Microsoft, Redmond, Washington) version SPSS 20.0 for data analysis.

Results: The results showed male predominance (73.33%) with 45 to 65 years age group commonly affected by CKD. The Mean platelet volume, Platelet distribution width and Plateletcrit were found to be elevated in CKD patients in comparison to controls. However only Mean platelet volume and Platelet distribution width were found statistically significant and Platelet counts were lower among the study population.

Conclusion: Early screening of alterations in platelet parameters may prove to be an efficient factor in risk stratification of CKD patients prone to develop venous thromboembolism and cardiovascular diseases.

Keywords: Chronic kidney disease (CKD), Hemodialysis, Platelet parameters.

Introduction:

In the present world, there is an increasing tendency of diabetes mellitus and hypertension in Asian countries like India, which is favoring a rise in its complications like chronic kidney disease. 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. Thrombotic complications are a high possibility in these patients.[1]

CKD affects 10%–16% of the adults worldwide, with United States alone being affected with 14 million individuals.[2]The existence of CKD increases risk for hospitalizations, cardiovascular events and mortality because of the disturbed internal physiologic milieu from failing kidneys, resulting in increased inflammation, platelet dysfunction, bone and mineral disorder and other effects.[3]In correlation with the general population, CKD patients tend to have 16% greater risk of thrombotic cardiovascular events, such as acute myocardial infarction or ischemic stroke.[4,5] Furthermore, in comparison to individuals with normal kidney function, those with CKD have a 38% higher risk of mortality after a cardiac event or stroke.[4]

Currently, it is known that morbidity and mortality risk increase in patients with hemodialysis and peritoneal dialysis treatment compared to general population. Additionally, vascular calcification, inflammation causes the development of atherosclerosis and thereby; they contribute to the increased morbidity; in every stage of chronic renal disease.[6,7]

In some meta-analytical studies it is seen 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.[8] Research studies in past have illustrated that alterations in platelet indices can also be related to increased incidence of venous thromboembolism and vascular disease. Mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), Platelet large cell ratio (P-LCR) parameters generated using automated cell counters although cost effective are not routinely used by clinicians during clinical practice.[9]These markers are mostly underutilized or ignored though easily available. The platelet indices in the CKD patients prone to develop complications is still largely unknown. Hence this study was done to determine the correlation of platelet indices on hemodialysis patients diagnosed with chronic kidney disease in our hospital setting.

Material and methods:

A retrospective study was done on CKD patients undergoing hemodialysis in our hospital during a duration of one year. The patients were diagnosed with CKD on the basis of clinical history, radiological diagnosis, biochemical investigations and hematological parameters. Platelet parameters were obtained from Sysmex-XN 1000 autoanalyzer. These platelet parameters (Mean platelet volume, platelet distribution width, plateletcrit and large platelet cell ratio) including Platelet count were standardized by routine external and internal quality control checks.

The study population was divided into two groups A and B. Group A (cases) included 30 patients with CKD undergoing intermittent hemodialysis at our institute. All cases underwent three sessions of hemodialysis per week with each session lasting for 4 hours. A blood flow of 250 ml/min using bicarbonate bufferand dialysate flow of 500ml/min was used in hemodialysis.

Group B (controls) included 30 apparently healthy adult volunteers with normal renal function who were either employees of our institute or individuals who attended health checkups.

Patients with comorbidities including septicemia, past history of coronary artery disease/cerebrovascular disease and those on antiplatelet medications were excluded from the study.

Statistical Analysis:

The results were presented as mean ± SD. Microsoft word and Excel was used to generate graphs and tables. Appropriate statistical tests were used to evaluate the platelet parameters in CKD patients undergoing hemodialysis. P-value <0.05 was considered statistically significant.

Results:

After considering inclusion criteria, 30 CKD patients on hemodialysis and 30 healthy voluntaries were enrolled in our study. The gender distribution was predominantly male in both groups with mean age of 45.56±12.43 in cases and 46.21±12.78 in controls. The mean Basal Metabolic Index was 24.91±5.23 for cases and 25.48±4.71 for controls, showing no significant difference. However, hypertension was notably more prevalent in cases (28 cases) compared to controls (2 cases) which was reflected in significantly higher mean systolic (153.24±21.34 mmHg) and diastolic (94.56±14.65 mmHg) blood pressure levels in Group A (cases) compared to Group B (controls) (systolic: 123.27±6.98 mmHg, diastolic: 76.21±4.36 mmHg). Similarly, diabetes was more prevalent in Group A (25 cases) compared to Group B (3 cases) [Table 1].

The hemodynamic characteristics revealed notable differences between Group A (cases) and Group B (controls).Group A exhibited lower hemoglobin levels (10.35±2.11 g/dL) compared to Group B (13.75±2.05 g/dL), indicative of anemia commonly associated with CKD. Conversely, Group A showed significantly elevated levels of blood urea nitrogen (49.87±14.65 mg/dL) and serum creatinine (9.89±3.21 mg/dL) compared to Group B (blood urea nitrogen: 13.22±2.98 mg/dL, serum creatinine: 0.98±0.14 mg/dL), reflecting impaired kidney function in CKD patients. Additionally, Group A exhibited a higher levels of serum uric acid (5.80±3.58 mg/dL) compared to Group B (3.48±0.98 mg/dL), which could be attributed to decreased renal excretion in CKD. These findings highlight the distinct hemodynamic profiles between CKD patients on hemodialysis and healthy individuals [Table 2].

On comparing the platelet parameters between the cases and controls, mean platelet count in control and chronic kidney disease patients were 2.31 ± 1.29 $x10^3$/µL and 1.76 ±0.9$x10^3$/µLrespectively which was statistically significant. Mean value of MPV in control and chronic kidney disease patients was 9.86 ± 1.2fL and 11.98 ± 1.9fL and mean PDW in control and chronic kidney disease patients was 11.99 ± 2.21fL and 13.89± 2.3fL respectively. A statistically significant difference was observed in values of MPV and PDW. However comparison of the mean value of Plateletcrit and Platelet large cell ratio between cases and controls yielded no significant difference [Table 3].

Table 1: Demographic profile and co-morbidities of the study population

Variables	Group A Mean ± SD (n=30)	Group B Mean ± SD (n=30)
Sex (M/F)	22/8	21/9
Age (years)	45.56±12.43	46.21±12.78
BMI (kg/m^2)	24.91 ± 5.23	25.48 ± 4.71
Diabetes	25	03
Hypertension	28	02
Systolic blood pressure (mmHg)	153.24±21.34	123.27±6.98
Diastolic blood pressure (mmHg)	94.56±14.65	76.21±4.36

Table 2: Hematological and Biochemical characteristics among the study population

Variables	Group A Mean ± SD (n=30)	Group B Mean ± SD (n=30)
Hemoglobin (g/dL)	10.35±2.11	13.75±2.05
Blood urea nitrogen (mg/dL)	49.87±14.65	13.22±2.98
Serum creatinine (mg/dL)	9.89±3.21	0.98±0.14
Serum uric acid(mg/dL)	5.80±3.58	3.48±0.98

Table 3: Comparison of platelet parameters in cases and control

Parameters	Group A (cases) n =30	Group B (control) n=30	P value
Platelet count (x10^3/uL)	**1.76±0.9**	**2.31±1.29**	**0.0021**
Mean platelet volume (fL)	**11.98±1.9**	**9.86.46±1.2**	**0.0014**
Plateletcrit (%)	**0.19±0.09**	**0.19±0.04**	**0.5**
Platelet Distribution Width (fL)	**13.89±2.3**	**11.99±2.21**	**0.0001**
P-LCR (%)	**35.60±7.35**	**37.85±7.53**	**0.178**

Discussion:

The correlation between platelet activity and adverse clinical outcomes has been recently investigated in the literature. The findings suggested the importance of monitoring platelet function and potentially targeting platelet activity as part of the therapeutic approach to reduce adverse clinical outcomes in CKD patients. In our study, we aimed to demonstrate changes in platelet parameters in patients with CKD. Monitoring these parameters could be crucial for managing and mitigating adverse clinical outcomes in CKD patients.

The demographic data of study population showed that sex distribution, age and BMI was almost similar amongst cases and control. However, the study cases showed a markedly higher prevalence of diabetes and hypertension, with 25 out of 30 participants having diabetes and 28 having hypertension as compared to control population. Correspondingly, Group A comprising of cases exhibited higher mean systolic and diastolic blood pressures (153.24/94.56 mmHg) than controls (123.27/76.21 mmHg).

In our study, hematological and biochemical characteristics showed significant differences between cases and controls. Cases showed lower hemoglobin levels, higher blood urea nitrogen, serum creatinine and uric acid levels as compared to controls indicating compromised renal function and hematological profile in chronic kidney disease patients.

The platelet count in our study was significantly lower in cases (group A) in comparison to control (group B). This was in accordance with Schoorl et al who observed that CKD patients and ESRD patients on maintenance HD had lower range of platelet count within the reference limits. CKD patients also witnessed a drop of 13% in platelet count after the first passage of blood along the dialysis membrane at t=1 min after starting HD.[10] Abnormal platelet function is a major contributor of a low normal platelet count among CKD patients.[11]The probable cause for a low normal platelet count among chronic HD patients is likely to be due to platelet degranulation and adherence in the dialyzer.

Studies comparing CKD patients with healthy individuals have revealed larger platelet volumes in patients with CKD.[12,13] Thus, large and reactive platelets might contribute to the increased incidence of vascular disease. In fact, some studies have demonstrated an association between increased platelet size and cerebrovascular disease in CKDpatients.[13,14] On the other hand, as CKD progresses to end stage renal disease (ESRD), the presence of uremictoxins may lead to a qualitative decrease in platelet functions.[15] Therefore, we might assume that the size and reactivity of the platelets in patients with CKD might differ according to the CKD stage and inflammatorystatus.

In our study the average platelet count was found to be 1.76 ±0.9x10^3/µL among cases as compared to 2.31± 1.29x10^3/µL among controls, which was found to be statistically significant ($p<0.05$). Alghythan AK et al observed that the mean platelet count in pre hemodialysis patients was 199.19±56.74x10^3/µLas compared to controls with a platelet count of 262.32±48.00x10^3/µL which was statistically significant ($p < 0.001$).[16]

MPV is a hematologic parameter that has been proposed as a prognostic factor in tissue viability, and for guiding the appropriate management.[17] MPV is one of the important independent risk factors of thromboembolism and cardiovascular diseases.[18] Besides, MPV level usually increases in chronic inflammatory states and malnutrition.[19,20] Previous studies have shown that MPV is higher in patients with CKD.[21,22] Inflammatory markers and various cytokines have key roles in the early stage and

continuation of renal disease.[23,24] Mean platelet volume (MPV) is an indicator of the average size and activity of platelets.[25] The platelet volume is found to be associated with cytokines (thrombopoietin, interleukin-6 and interleukin-6 andinterleukin-3) that regulate megakaryocyte ploidy, number and result in the production of platelets.[26,27] When platelet production isdecreased, young platelets become bigger and more active and MPV levels increase. Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation. During activation, platelets shapes change from biconcave discs to spherical and a pronounced pseudopod formation occurs that leads to increased MPV.

In our study, the mean values of Plateletcrit (PCT) in cases and controls were 0.19±0.09% and 0.19±0.04%, respectively, and showed no statistically significant difference. Korogluet al.[28] demonstrated that the plateletcrit levels of the chronic renal disease group were significantly higher than the controls and dialysis group. Lokesh et al[29] demonstrated that the mean value of plateletcrit among cases of CKD receiving hemodialysis for more than 6 months was lower than that of healthy controls and the findings were statistically significant. Our findings were consistent with the results of Young et al wherein no statistically significant difference among the groups of CKD with respect to plateletcrit was observed.[15]

Platelet distribution width (PDW) directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology. In our study, mean PDW was higher in CKD patients than control and the difference was statistically significant. Lokesh et al[29] demonstrated significantly lower levels of PDW among cases of ESRD receiving haemodialysis for 6 months compared to healthy control. Koroglu et al in their study found no significant variation in PDW values between CKD patients and other groups comprising of controls and dialysis group.[28] Mean value of PDW increased significantly in group B compared to group A. Our finding was consistent with Young et al. who demonstrated that mean PDW increased with decrease in the eGFR from stage 1 to 4 of CKD.[15]

In our study the average values of mean platelet large cell ratio (P-LCR) among cases and controls was found to be 35.60±7.35% vs 37.85±7.53% (p=0.178), which was not found to be statistically significant. Schoorl M et al, in his study observed a similar lower mean P-LCR of 29.0±7.4% and further a 6% decline from the baseline value at t=150 min of hemodialysis.[10]

Conclusion:

The present study lays emphasis on the role of platelet parameters especially MPV and PDW in assessing the risk of thrombosis in patients with renal dysfunction. Since platelet indices can be easily assessed in most primary health centers in resource poor settings, it can be used as a prognostic marker for follow up and an adequate management in patients with end stage renal disease thereby reducing morbidity. However long term studies with larger sample size are required to conclusively establish the relationship between platelet indices and risk of progression of cardiovascular complications in CKD patients on hemodialysis.

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