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A Comparative Study of Platelet Parameters in Chronic Kidney Disease, End Stage Renal Disease Patients Undergoing Hemodialysis and Healthy Individuals

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ABSTRACT

Background: With the rising trend of diabetes mellitus and hypertension, there is also a rise in chronic complications like chronic kidney disease (CKD) and end stage renal disease (ESRD).

Cardiovascular complications remain the most common cause of death among ESRD patients and those on hemodialysis (HD). Hemodialysis patients behave in a distinct way that they are relatively more prone for bleeding than thrombotic manifestations. In recent days, abnormalities in platelet parameters are found to be an effective tool in risk stratification of patients with chronic kidney disease (CKD) to develop coronary artery disease. Platelet parameters are considered as inflammatory markers. The present study was taken to find the association of various platelet parameters among hemodialysis patients and CKD patients.

Objectives: The aim was to study the platelet distribution width (PDW), mean platelet volume (MPV), plateletcrit (PCT) and platelet large cell ratio (PLCR) among ESRD patients undergoing maintenance hemodialysis and compare with CKD patients and healthy age and sex matched controls.

Methods: The present study was done on three groups. Group 1 included 20 healthy individuals from hospital staffs and healthy volunteers matched for age and sex, Group2 included 60 CKD patients and Group 3 included 40 ESRD patients on maintenance HD. **Results:** The mean values of platelet distribution width (PDW), mean platelet volume (MPV), platelet count, plateletcrit ratio (PCT) and platelet large cell ratio (P-LCR) were found to be higher in CKD and ESRD patients when compared to healthy controls. PDW, PCT and L-PCR attained statistical significance, while MPV did not. **Conclusions:** Abnormality in platelet parameters can be used as a predictor of underlying inflammation and severity of atherosclerosis as all these parameters are lesser than that observed in control population.

Keywords: Chronic kidney disease, Hemodialysis, Cerebrovascular disease, Platelet distribution width, Mean platelet volume, Platelet large cell ratio and plateletcrit ratio.

INTRODUCTION

Chronic kidney disease (CKD) and end stage renal disease (ESRD) are considered inflammatory processes as there are many inflammatory stimuli as uremia, anemia, and malnutrition **(1).**

In (CKD) both bleeding and thrombotic complications are observed. Early stages

of chronic kidney disease are typically associated with a pro thrombotic tendency.

Whereas, in its more advanced stages and ESRD patients also suffer from a bleeding diathesis **(2).**

platelet parameters were found to be correlated with inflammation as they are inflammatory markers whereas platelets have been identified as being effector cells that enhance inflammatory responses, with the ability to 'cross-talk' with endothelial cells and leukocytes **(3).**

Interest has also been given to platelet size, which has been found to be linked with platelet activity. MPV has been found to be associated with cardiovascular risk and, due to the relative ease of measuring (available with routine blood counts), it has been proposed as a potential tool for identifying high-risk patients **(4).**

As well as platelet size, the ratio of platelets to other circulating cells (PCT) has been used as tool for identifying inflamed and subsequently high-risk patients **(5).**

The present work aimed to compare mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit ratio (PCT) and platelet large cell ratio (L-PCR) in normal individuals, chronic kidney disease patients and end stage renal disease patients on maintenance hemodialysis.

PATIENTS AND METHODS

This is descriptive cross sectional study conducted from March 2017 to march 2018. At AL-Hussein University Hospital Internal Medicine Department, Clinical Hematology and Nephrology Units and AL-Qabbary Hospital, Nephrology Department.

The study included 20 normal subjects, 60 CKD patients (stage 2, 3 and 4) and 40 ESRD patients on maintenance hemodialysis.

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Adults aged patients above 18 years old with CKD and ESRD on maintenance hemodialysis were included in the study.

Patients with sepsis, active malignancy, HCV positive, abnormal platelet disorders as ITP and patients with acute stroke and DKA were excluded from the study.

Data including name, age, sex, past medical history, and data obtained from clinical examination were recorded at enrollment.

The study was approved at AL-Azhar University ethical committee; all persons enrolled to the study signed informed consents. The study was conducted at level of declaration of Helsinki.

Statistical analysis of the data: Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Chi-square test for categorical variables, to compare between different groups. And F-test (ANOVA) for normally distributed quantitative variables, to compare between more than two groups, and Post Hoc test (Turkey) for pairwise comparisons Significance of the obtained results was judged at the 5% level. Pearson coefficient to correlate between two normally distributed quantitative variables

RESULTS

The studied variables are summarized in table (1). The demographic data in table (1) showed age, sex and body mass index (BMI) distribution between the three studied groups where group 1 included 20 normal individuals, five were males (25%) and fifteen were females (75%). The mean age of the group was 46.35 ± 9.05 years old, and the mean BMI was 27.83 ± 4.28 kg/m2. Group 2 included 60 subjects, 33 were females (55%) and 27 were males (45%). The mean age of the group was 51.32 ± 12.79 years old and the mean BMI was 27.67 ± 3.42 kg/m2. Group 3 included 40 subjects, 28 were females (70%) and 12 were males (30%). The mean age of the group was 49.88 ± 13.03 years old and the mean BMI was 26.74 ± 3.59 kg/m2. In addition, the clinical data include SBP and DBP. In group 1 the mean SBP was 126.50 ± 8.75 mmHg, the mean DBP was 81.50 ± 9.33mmHg. In group 2 the mean SBP was 130.16 ± 15.30 mmHg, the mean DBP was 83.72 ± 11.16 mmHg and the mean of MBP was 99.11 ± 12.09 mmHg. In group 3 the mean SBP was 124.25 ± 22.52 mmHg, the mean DBP was 81.0 ± 14.11mmHg and the mean of MBP was 94.99 ± 16.88 mmHg.

The mean serum calcium level was significantly lower in group 3 (8.06 ± 0.62 mg/dl) in comparison with group 2 (9.24 ± 1.13 mg/dl) and group 1 (9.02 ± 0.35 mg/dl) with a p -value < 0.001. While, there was no significant difference between group 1 and 2. The mean serum phosphorus level was significantly higher in group3 (5.74 ± 1.28 mg/dl) as compared to group 2 (4.61 ± 0.67 mg/dl) and group 1 (4.50 ± 0.28 mg/dl) with a p- value < 0.001, but there was no significant difference between group 1 and 2.

The mean urea level was significantly higher in group 3 (163.4 ± 46.03 mg/dl) in comparison with group 2 (89.90 ± 50.47 mg/dl) and group 1 (25.05 ± 6.96 mg/dl). In addition, urea was significantly higher in group 2 as compared to group 1 with a p value < 0.001. The mean creatinine level was significantly higher in group 3 (11.12 ± 2.74 mg/dl) in comparison with group 2 (2.17 ± 1.50 mg/dl) and group 1 (0.66 ± 0.11 mg/dl). In addition, urea was significantly higher in group 2 as compared to group 1 with a p value < 0.001.

HB was significantly higher in group 1(12.90 ± 1.70 g/dl) in comparison with group 2 (10.41 ± 2.03 g/dl) and group 3 (10.54 ± 1.31 g/dl) with P-value <0.001, but the difference between group 2 and 3 was not significant.

The platelet count ($x10^3/mm^3$) was significantly higher in group 1 (295.3 ± 70.30) in comparison to group 2 (138.43 ± 85.19) and group 3 (112.7 ± 53.46) with P-value <0.001, but there was no significant difference between group 2 and 3.

MPV was lower in group 1 (8.65 ± 0.72 fl) in comparison with group 2 (9.11 ± 0.98 fl) and group 3 (9.01 ± 1.01 fl), but the difference was not significant with P-value 0.187.

PDW was significantly lower in group 1 (11.85 ± 0.98 fl) in comparison with group 2 (12.81 ± 1.49 fl) with P-value 0.026, but as compared to group 3 (12.33 ± 1.52 fl) the difference was not significant as well as between group 2 and 3. PCT was significantly lower in group 1 (0.19 ± 0.05 %) in comparison with group 2 (0.25 ± 0.10%) with P-value 0.003. In addition, PCT was significantly lower in group 1 in comparison to group 3 (0.28 ± 0.04 %) with P-value 0.001, but the difference between group 2 and 3 was not significant.

L-PCR was significantly lower in group 1 (18.81 ± 5.31 %) as compared to group 2 (23.42 ± 7.27 %) with P-value 0.012, but in comparison with group 3 (21.66 ± 7.18 %) the difference was not significant and also between group 2 and 3.

Table (1): comparison between the three studied groups according to demographic, clinical, laboratory data, platelet and platelet parameters.

Groups / parameters	Group 1 (n=20)	Group 2 (n=60)	Group 3 (n=40)	value
Gender				
Females [n (%)]	15 (75%)	33(55%)	28(70%)	
Males [n (%)]	5 (25%)	27 (45%)	12(30%)	0.155
Age	46.35 ± 9.05	51.32 ± 12.79	49.88 ± 13.03	0.300
SBP	126.50 ± 8.75	130.16 ± 15.30	124.25 ± 22.52	0.240
DBP	81.50 ± 9.33	83.72 ± 11.16	81.0 ± 14.11	0.502
BMI	27.83 ± 4.28	27.67 ± 3.42	26.74 ± 3.59	0.384
calcium (mg/dl)	9.02 ± 0.35	9.24 ± 1.13	8.06 ± 0.62	<0.001*
Phosphorous (mg/dl)	4.50 ± 0.28	4.61 ± 0.67	5.74 ± 1.28	<0.001*
urea (mg/dl)	25.05 ± 6.96	89.90 ± 50.47	163.4 ± 46.03	<0.001*
creatinine (mg/dl)	0.66 ± 0.11	2.17 ± 1.50	11.12 ± 2.74	<0.001*
Hb	12.90 ±1.70	10.41 ± 2.03	10.54 ±1.31	<0.001*
Platelets ($x10^3/mm^3$)	295.3 ± 70.30	138.43 ± 85.19	112.7 ± 53.46	<0.001*
MPV (fl)	8.65 ± 0.72	9.11 ± 0.98	9.01 ± 1.01	0.187
PDW (fl)	11.85 ± 0.98	12.81 ± 1.49	12.33 ± 1.52	0.026*
PCT (%)	0.25 ± 0.05	0.21 ± 0.10	0.19 ± 0.04	0.001*
L-PCR (%)	18.81 ± 5.31	23.42 ± 7.27	21.66 ± 7.18	0.037*

*: Statistically significant at $p \leq 0.05$
p values for ANOVA test, Sig. bet. grps was done using Post Hoc Test (LSD)

Statistical Correlations

Table (2) showed statistically significant negative correlation between MPV and platelet count in normal and ESRD groups. Also, showed statistically significant negative correlation between PDW and platelet count in normal and ESRD groups. In addition, statistically significant positive correlation between PCT and platelet count in the three studied groups and between PCT and WBCs in ESRD group. Besides, there was statistically significant negative correlation between L-PCR and platelet count in the three studied groups.

Table (2): correlation between platelet parameters and other different parameters in the three studied groups

groups / correlations	Group 1 (n=20)		Group2 (n=60)		Group 3 (n=40)	
	r_s	p	r_s	p	r_s	p
MPV versus platelets	-0.659*	0.002*	-0.425	0.001	-0.508*	0.001*
PDW versus platelets	-0.677*	0.001*	-0.425	0.001	-0.514*	0.001*
PCT versus platelets	0.932*	0.001*	0.638*	<0.001*	0.845	<0.001*
PCT versus WBCs	0.276	0.239	0.112	0.393	0.407*	0.009*
L-PCR versus platelets	-0.685*	0.001*	-0.478*	<0.001*	-0.554*	<0.001*

r: Pearson coefficient
*: Statistically significant at $p \leq 0.05$

DISCUSSION

Platelet parameters were found to be correlated with inflammation as they are inflammatory markers whereas platelets have been identified as being effector cells that enhance inflammatory responses, with the ability to 'cross-talk' with endothelial cells and leukocytes [(3)].

In this study, the platelet count was significantly higher in group 1 in comparison to group 2. It was significantly higher in group 1 in comparison to group 3, but there was no significant difference between group 2 and 3. This was in accordance with Schoorl et al. [(6)] 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% after the first passage of blood along the dialysis membrane at t=1 min after starting HD.

Abnormal platelet function is a major contributor of a low normal platelet count among CKD patients [(3)].

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 [(7)].

MPV, a readily available indicator of platelet activation and function, is a useful predictive and prognostic biomarker of cardiovascular and cerebrovascular disease in CKD. MPV is associated with a variety of pro thrombotic and pro inflammatory diseases. MPV reflects the average platelet size and it tends to be larger when body produces more numbers of platelets [(8, 13)]. In this study, there was insignificant difference in MPV between the studied groups.

In this study, there was statistically significant negative correlation between MPV and platelet count in normal and ESRD groups. Koroglu et al. [(9)] observed a high MPV in CKD patients and concluded that MPV can be used as a biomarker to estimate atherosclerosis risk in CKD patients and patients on hemodialysis [(10)]. PDW was significantly lower in group 1 in comparison with group 2, but in comparison with group 3, the difference was not significant and also between group 2 and 3. Schrool et al. [(6)] found that there was no significant variation in PDW between HD and CKD patients. PDW increased during platelet activation and thereby can predict activation of coagulation more efficiently in general population. There are limited data to support its role on HD patients. In our study, there was statistically significant negative correlation between PDW and platelet count in normal and ESRD groups.

PCT was significantly lower in group 1 in comparison with group 2. In addition, PCT was significantly lower in group 1 in comparison with group 3, but the difference between group 2 and 3 was not significant. A higher PCT in CKD patients was attributed to chronic inflammation, which probably might increase the risk of atherosclerosis. The use of PCT as a biomarker for atherosclerosis in hemodialysis patients remains controversial. In our study, there was statistically significant positive correlation between PCT and platelet count in the three studied groups and between PCT and WBCs in ESRD group.

L-PCR was significantly lower in group 1 in comparison with group 2, but in comparison to group 3 the difference was not significant as well as between group 2 and 3. Koroglu et al. [(9)] observed that PLCR falls significantly in thrombocytosis while it rises in thrombocytopenia. In our study, there was statistically significant negative correlation between L-PCR and platelet count in the three studied groups. There was no significant correlation between platelet parameters and urea and creatinine in the three studied groups.

Conclusion

The platelet parameters are extensively studied in association with coronary artery disease, cerebrovascular disease, chronic kidney disease and obesity. They were found to be a reliable predictor of underlying inflammation and severity of atherosclerosis as all these parameters are lesser than that observed in control population.

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