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Evaluation of platelet indices in chronic kidney disease

Mahmut Egemen Senel[1], Ertugrul Erken[2], Ilyas Ozturk[3], Neziha Erken[4], Orcun Altunoren[2]

[1] Necip Fazil City Hospital, Department of Internal Medicine, Kahramanmaras, Türkiye
[2] Kahramanmaras Sutcu Imam University, Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Kahramanmaras, Türkiye
[3] Necip Fazil City Hospital, Department of Internal Medicine, Division of Nephrology, Kahramanmaras, Türkiye
[4] Necip Fazil City Hospital, Department of Internal Medicine, Division of Geriatrics Medicine, Kahramanmaras, Türkiye

Abstract

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Objective: Chronic kidney disease (CKD) is characterized by an irreversible decrease in kidney functions and accumulation of uremic toxins in the body. Platelet indices have the potential to predict the inflammatory status and disease progression in patients with CKD. In this study it was aimed to investigate platelet indices and their relations with renal function and comorbid conditions in CKD patients.
Method: In this study it was included 411 CKD patients. We looked for associations between platelet indices and estimated glomerular filtration rate (eGFR). We generated linear regression models for platelet indices that may be associated with eGFR. We evaluated CKD patients for possible associations between platelet indices and comorbid conditions such as diabetes, hypertension, and cardiovascular diseases.
Results: The mean age of CKD patients was 60.5 and the GFR value was 40.1+24.8 mL/min/1.73m2. While the mean platelet count, MPV, PCT, PDW, P-LCR values were lower in the advanced CKD group, hematocrit adjusted platelet count (HAPC), MPV/Lymphocyte ratio and SII parameters were higher in the advanced CKD group ($p<0.05$ for all). In analyzes a positive correlation was detected between eGFR and HAPC, and a negative correlation was detected between MPV/Lymphocyte ratio and eGFR ($p<0.001$ and $p=0.036$). MPV, PCT, PDW, P-LCR and SII index were observed to be higher in diabetic CKD patients ($p<0.05$ for all).
Conclusion: Platelet indices have the potential to provide valuable data about chronic diseases and their complications. MPV/Lymphocyte ratio and HAPC can give an idea about CKD progression. Our findings suggest that elevations in platelet volume indices could be indicative of diabetic nephropathy and increased inflammatory status.
Keywords: Chronic kidney disease, Glomerular filtration rate, Hematocrit-adjusted platelet count, Mean platelet volume, Platelet indices, Systemic immune-inflammation index

INTRODUCTION

Chronic Kidney Disease (CKD) is characterized by an irreversible decline in renal functions, leading to metabolic and hormonal disturbances alongside chronic systemic inflammation. Atherosclerotic heart disease emerges as the principal cause of mortality and morbidity in CKD (1). In advanced stages of CKD, there is an increased risk of bleeding and thrombosis (2). This hemostatic imbalance in CKD patients can be attributed to significant coagulation cascade abnormalities and platelet dysfunction (3). Factors such as elevated inflammation, accumulation of uremic toxins, and impaired signaling molecules are known to adversely affect platelet morphology and functionality (4).

Platelets are disc-shaped elements produced in the bone marrow by megakaryocytes, playing a crucial role in hemostasis. They are involved in plug formation via adhesion and aggregation, as well as in the orchestration of the fibrin meshwork, which is essential for blood clotting (5). Recent research has also highlighted the significant role of platelets in both innate and adaptive immune responses. (6). With the introduction of fully automated hematological analyzers, routine assessments now extend beyond platelet count and plateletcrit (PCT) to include platelet volume indices (7). While these indices were initially used primarily for diagnosing primary thrombocytosis, recent studies have begun investigating their connections to chronic systemic

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Corresponding Author: İlyas Öztürk, Necip Fazil City Hospital, Department of Internal Medicine, Kahramanmaras, Turkey
Email: dregemensenel@gmail.com
ORCID iD: 0000-0003-2829-5050

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diseases. Studies involving platelet indices and specific metrics from blood tests have explored their association with cardiovascular disease (CVD), diabetes mellitus (DM), hypertension (HT), and a range of chronic conditions (8,9,10). The increased risks of systemic inflammation and thrombotic disease in advanced CKD may necessitate to examine the potential links between platelet indices and CKD progression. Although studies evaluating platelet indices in CKD patients have provided some valuable data, there is room for further investigation (6,11,12).

In this study, it was aimed to investigate the potential relationships between the stage of CKD, various clinical indicators, and a broad spectrum of platelet indices. Platelet indices such as platelet count, PCT, mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR), hematocrit-adjusted platelet count (HAPC), MPV/Platelet count, MPV/Lymphocyte count, systemic immune-inflammation index (SII) were shown to be associated with various chronic diseases. (10,12,13). We believe that these indices could serve as promising markers for the progression and inflammation related complications of CKD.

METHOD

Case Selection and Data Collection

In this study, it was included that patients over the age of 18, diagnosed with CKD and followed up at the Nephrology Department of Kahramanmaras Sutcu Imam University between 2010 and 2020. Patients with malignancy, cirrhosis, heart failure, thyroid dysfunction, active infection, hematological diseases, severe anemia, and those with systemic inflammatory disease and severe immunosuppression were excluded. All laboratory values were obtained from the health record data bank. The estimated glomerular filtration rate (eGFR, mL/min/1.73 m^2) was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (14). Participants were categorized into CKD stages based on their eGFR values. The formula for the HAPC was platelet count x (1/1–Hematocrit), and the formula for the SII was (neutrophil count x platelet count)/lymphocyte count (12). Laboratory values for patients undergoing hemodialysis (HD) were obtained from midweek pre-dialysis blood results. Approval for the study was obtained from the Institutional Medical Research Ethics Committee (Date: 26.08.2020, Session No: 2020/16, Decision No: 09). The study was conducted in accordance with the Declaration of Helsinki.

Data Evaluation

Patients were divided into two subgroups. Patients with eGFR ≥30 mL/min/1.73 m^2 constituted the early-stage CKD group (stages 1, 2, 3a, 3b), and those with eGFR<30 mL/min/1.73 m^2 were placed into the advanced CKD group (stages 4, 5). Demographic data (age, gender, etc.), clinical features (history of chronic diseases, blood pressure, etc.), and platelet indices (platelet count, MPV, plateletcrit, PDW, P-LCR, HAPC, MPV/Platelet count, MPV/Lymphocyte count, SII) were compared between the groups. The effects of comorbid diseases on platelet indices were examined. Correlation analysis was conducted between eGFR and platelet indices. Regression models were generated for the relations between various variables and platelet indices that showed worthy associations with eGFR.

Table 1. Demographics, Clinical Features, and Laboratory Values in CKD Patients

Variable	CKD Patients (n = 411)
Age, *years*	60.5 ± 14.7
Sex, *M/F*; ***n* (%)**	208 (51) / 203 (49)
CKD stage 1/2/3/4/5; *n* (%)	14 (3) / 75 (18) / 171 (41) / 62 (15) / 89 (21)
HD Cases, *n (%)*	47 (11.4)
eGFR, *mL/min/1.73 m^2*	40.1 ± 24.8
DM; *n* (%)	169 (41.1)
HT; *n* (%)	312 (75.9)
CVD; *n* (%)	128 (31.1)
Systolic Blood Pressure, *mmHg*	133 ± 18
Diastolic Blood Pressure, *mmHg*	81 ± 11
Creatinine, *mg/dL*	2.61 ± 2.37
Albumin, *g/dL*	4.16 ± 0.44
Ca x P product, *mg^2/dL^2*	34.1 ± 9.1
Uric Acid, *mg/dL*	6.7 ± 1.9
Hemoglobin, *g/Dl*	12.3 ± 1.9
Platelet Count mean/median, *$x10^6$/ mm^3*	255 ± 75 / 248
MPV mean/median, *fL*	10.4 ± 0.9 / 10.4
Platelecrit mean/median, *%*	0.26 ± 0.07 / 0.26
PDW mean/median, *fL*	12.4 ± 3.6 / 12
P-LCR mean median, *%*	28.4 ± 7.3 / 28.2
HAPC, *$x10^3/mm^3$*	409 ± 120 / 396
MPV/Platelet Count mean/median, *$fL/10^8$ platelet/ cm^3*	4.48 ± 1.62 / 4.15
MPV/Lymphocyte Count mean/ median, *fL/ 10^6 lenfosit / cc blood*	6.33 ± 3.48 / 5.54
SII mean/median, *$x10^6$ cell/mm^3*	800 ± 655 / 641

Abbreviations: CKD, Chronic Kidney Disease; HD, hemodialysis; DM, diabetes mellitus; HT, hypertension; CVD, cardiovascular disease; eGFR, estimated Glomerular Filtration Rate; MPV, Mean Platelet Volume; PDW, Platelet Distribution Width; P-LCR, Platelet Large Cell Ratio; HAPC, Hematocrit-adjusted Platelet Count; SII, Systemic Immune-Inflammation Index.

Table 2. Comparisons of platelet indices in early stage (1, 2, & 3) and advanced (4 & 5) CKD patients

Variable	CKD Patients (n=411)		
	Early Stage CKD (n=260)	Advanced CKD (n=151)	p
Age, *years*	61.6 ± 14.6	58.8 ± 14.8	**0.044**
Sex, *M/F*; ***n* (%)**	131 (50) / 129 (50)	77 (51) / 74 (49)	0.905
DM; *n* (%)	108 (42)	61 (41)	0.838
HT; *n* (%)	189 (73)	123 (82)	**0.039**
CVD; *n* (%)	84 (32)	44 (29)	0.515
Creatinine, *mg/dL*	1.36 ± 0,87	4.77 ± 2.59	**<0.001**
eGFR, *mL/min/1.73 m²*	55.0 ± 18.3	14.3 ± 7.6	**<0.001**
Hemoglobin, *g/dL*	12.88 ± 1.77	11.52 ± 1.89	**<0,001**
Albumin, *g/dL*	4.24 ± 0.40	4.03 ± 0.48	**<0.001**
Ca^{+2}, *mg/dL*	9.22 ± 0.65	8.93 ± 0.99	**<0.001**
P, *mg/dL*	3.36 ± 0.61	4.45 ± 1.22	**<0.001**
Ca^{+2} x P product, *mg^2/dL^2*	30.9 ± 5.8	39.6 ± 12.3	**<0.001**
Uric Acid, *mg/dL*	6.60 ± 1.74	6.93 ± 2.21	0.368
Platelet Count, *$x10^6/mm^3$*	261 ± 73	245 ± 76	**0.020**
MPV, *fl*	10.4 ± 0.8	10.2 ± 0.9	**0.031**
Plateletcrit, *%*	0.27 ± 0.07	0.25 ± 0.08	**0.002**
PDW, *%*	12,5 ± 3.0	12.3 ± 4,7	**0.010**
P-LCR, *%*	29.1 ± 7.0	27.3 ± 7.9	**0.031**
HAPC, *$x10^6/mm^3$*	427 ± 118	376 ± 115	**<0.001**
MPV/Platelet Count, *fL/ 10^8 platelet / cc kan*	4.36 ± 1.48	4.68 ± 1.82	0.145
MPV/Lymphocyte Count; *fL/ 10^6 lymphocyte / cc blood*	5.82 ± 2.34	7.22 ± 4.73	**0.007**
SII, *$x10^6$ cell/mm^3*	712 ± 424	951 ± 908	**0.027**

*All of the parameters were non-normally distributed. Abbreviations: CKD, Chronic Kidney Disease; DM, diabetes mellitus; HT, hypertension; CVD, cardiovascular disease; eGFR, estimated Glomerular Filtration Rate; MPV, Mean Platelet Volume; PDW, Platelet Distribution Width; P-LCR, Platelet Large Cell Ratio; HAPC, Hematocrit-adjusted Platelet Count; SII, Systemic Immune-Inflammation Index.

Statistical Analysis

All analyses were performed using SPSS version 23.0 (SPSS Inc, Chicago, IL, USA) software. Data were presented as mean and standard deviation (mean ± SD) or percentage (%). The Shapiro-Wilk test was used to evaluate the distribution of the data. Parametric data between two groups were compared using Student's t-test and the Mann-Whitney U test. For non-parametric data comparison, the Chi-square (X^2) test and Fisher's exact tests were utilized. Correlation analysis were conducted using Spearman test. We generated linear regression models for potential influences on the platelet indices. Platelet indices were selected as dependent variable when their correlation coefficients are not very weak.

RESULTS

Demographic Data and Clinical Features in CKD Patients

In this study, it was included that 411 patients diagnosed with CKD. The mean age of the patients was 60.5 ± 14.7. There were 208 women (50.6%) and 203 men (49.4%). DM was present in 169 patients (41.1%). HT and CVD were present in 312 (75.9%) and 128 (31.1) CKD patients. The mean systolic blood pressure (SBP) was 133 ± 18 mmHg, and diastolic blood pressure (DBP) was 81 ± 11 mmHg. The mean creatinine level was 2.61 ± 2.37 mg/dL, and the mean eGFR was 40.1 ± 24.8 mL/min/1.73 m2. Based on eGFR values, 14 patients were classified as stage 1 (3.4%), 75 as stage 2 (18.2%), 171 as stage 3 (41.6%), 62 as stage 4 (15.0%), and 89 as stage 5 (21.6%) CKD. Forty-seven stage 5 CKD patients were receiving HD. When examining hematological parameters of the patients, the mean values for hemoglobin, platelet count and MPV were 12.3 ± 1.9 g/dL, 255 ± 75 $10^3/mm^3$, and 10.4 ± 0.9 fL respectively. The mean PDW and P-LCR were 12.4 ± 3.6 fL, and 28.4 ± 7.3%. The mean HAPC was 409 ± 120 $x10^6$ hc/mm^3, mean value for MPV/Platelet count ratio was 4.45 ± 1.63 fL/10^8 platelets/cc blood, mean MPV/Lymphocyte count ratio was 6.33 ± 3.48 fL/10^6 platelets/cc blood, and the mean SII was 800 ± 655 $x10^6$ hc/mm^3. The demographic characteristics and laboratory results of the patients are presented in **(Table 1)**.

We also evaluated CKD cases in terms of gender and comorbid conditions. The eGFR level was similar between female and male cases (F/M; 40.8±25.9 vs 39.5±23.9 mL/min; p=0.876). The mean hemoglobin level was lower in female cases than in males (F/M; 11.6±1.6 vs 13.1±2.0 g/dL;

p<0.001). Platelet indices such as platelet count, MPV, P-LCR, and SII were found to be higher in women (p<0.001, p=0.01, p=0.024, and p=0.003 respectively). The presence of HT and CAD did not make a difference in terms of platelet indices (p>0.05 for all). In CKD patients with DM (n=169), mean MPV, PCT, PDW, P-LCR, and SII levels were higher compared to those without the dignosis of DM (n=242) (p=0.011, p=0.035, p=0.010, p=0.011, and p=0.006 respectively).

Comparison between Early-Stage CKD and Advanced CKD Groups

Early-stage and advanced CKD groups were compared. Of the total 411 patients, 260 were early-stage and 151 were advanced CKD patients. The mean age of advanced CKD patients was lower, and the frequency of HT was higher in this group (respectively p=0.044 and p=0.039). There was no difference between the groups in terms of the presence of DM and CVD.

The mean hemoglobin value and platelet count were lower in the advanced CKD group (11.52±1.89 g/dL / 12.88±1.77 g/dL) (p<0.001 and p=0.002 respectively). The mean MPV was significantly lower in the advanced-stage CKD group (10.2±0.9 fL / 10.4±0.8 fL) (p=0.031). The mean PCT, PDW, and P-LCR values were also lower in the advanced CKD group (p=0.002, p=0.001, and p=0.031 respectively). While HAPC was lower in the advanced CKD group, the MPV/Lymphocyte count ratio and SII parameter were higher (p=0.001, p=0.007, and p=0.027 respectively). There was no difference in MPV/Platelet count ratio between the groups. Comparisons of clinical data and platelet indices between early-stage and advanced CKD groups are presented in **(Table 2)**.

Correlations Between Platelet Indices and eGFR

When a correlation analysis was conducted between the clinical data and eGFR values, no significant relationship was found between patient age and eGFR. Hemoglobin and albumin values demonstrated a positive correlation with eGFR, whereas the calcium-phosphorus product showed a significant negative correlation. When possible correlations between eGFR and platelet were investigated, weak correlations were observed between eGFR and platelet indices such as platelet count, MPV, PCT, PDW, P-LCR, and SII. Besides, a positive correlation was found between HAPC and eGFR (r=0.253 and p<0.001). More than that, there was a negative correlation between the MPV/Lymphocyte count and eGFR (r=-0.191 and p<0.001). Correlation analysis of eGFR with clinical data and platelet indices in CKD patients is presented in **(Table 3)**.

Evaluation of Clinical Variables That Could Affect Platelet Indices

After examining the data, it was appropriate to conduct multiple linear regression models for possible confounders that could affect HAPC and MPV/Lymphocyte count. In an analysis that was controlled for multiple potential confounders, the positive correlation between HAPC and eGFR persisted **(Table 4)**. According to a similar multiple regression model, we demonstrated that, eGFR decreases significantly along with increasing MPV/Lymphocyte count values **(Table 5)**.

Table 3. Correlation Analysis of eGFR with Clinical Data and Platelet indices in CKD Patients

Variable	eGFR (n=411)	
	R	p
Age	-0.008	0.872
Creatinine	-0.949	**<0.001**
Hemoglobin	0.414	**<0.001**
Albumin	0.276	**<0.001**
Ca^{+2}xP Product	-0.429	**<0.001**
Uric Acid	-0.117	**0.017**
Platelet Count	0.124	**0.012**
MPV	0.108	**0.029**
Plateletcrit	0.157	**0.001**
PDW	0.150	**0.002**
P-LCR	0.120	**0.015**
HAPC	0,253	**<0.001**
MPV/Platelet Count	-0,82	0,099
MPV/Lymphocyte Count	-0.191	**<0.001**
SII	-0.125	**0.011**

*Spearman's rank correlation was used for the non-normal distribution of variables
Abbreviations used: eGFR for estimated Glomerular Filtration Rate, CKD for Chronic Kidney Disease, MPV for Mean Platelet Volume, PDW for Platelet Distribution Width, P-LCR for Platelet Large Cell Ratio, HAPC for Hematocrit-adjusted Platelet Count, SII for Systemic Immune-Inflammation Index.

Table 4. Linear Regression Model Generated for Potential Influences on HAPC in CKD Patients

Variable	B	95% CI	β	p
Age	0.218	-0.568:1.005	0.027	0.585
Gender	20.195	-2,411:42.802	0.086	0.080
DM	-5.941	-29.05:17.17	-0.025	0.613
HD	-47.164	-86.92:-7.41	-0.128	**0.020**
eGFR	1.092	0.55:1.64	0.231	**<0.001**
Albumin	-12.687	-39.07:13.70	-0.048	0.345
Ca^{+2}x P Product	0.917	-0.38:2.22	0.076	0.166

Abbreviations used: HAPC for Hematocrit-adjusted Platelet Count, CKD for Chronic Kidney Disease, CI for Confidence Interval, DM, diabetes mellitus; HD, hemodialysis; eGFR for estimated Glomerular Filtration Rate

Table 5. Linear Regression Model Generated for Potential Influences on MPV/Lymphocyte Ratio in CKD Patients

Variable	B	95% CI	β	p
Age	0.001	-0.019:0.022	0.007	0.891
Gender	-0.279	-0.914:0.356	-0.047	0.389
DM	0.341	-0.257:0.939	0.056	0.263
HD	0.615	-0.411:1.642	0.066	0.239
eGFR	-0.016	-0,031:-0.001	-0.133	**0.036**
Albumin	0.081	-0.639:0.800	0.012	0.825
Ca^{+2}xP Product	-0.025	-0.059:0.008	-0.082	0.142
Hemoglobin	-0.277	-0.471:-0.082	-0.179	**0.005**

Abbreviations: MPV, Mean Platelet Volume; CKD, Chronic Kidney Disease; CI, Confidence Interval; DM, diabetes mellitus; HD, hemodialysis; eGFR, estimated Glomerular Filtration Rate

DISCUSSION

The progression of CKD is interrelated with accelerated atherosclerosis, metabolic abnormalities, and chronic inflammation. In the advanced stages of CKD, the hemostatic balance is adversely affected, increasing the risk for both bleeding and thrombosis. Chronic inflammation and elevated levels of uremic toxins in CKD are well-documented disruptors of platelet functionality. This indicates that platelet index parameters might change as CKD progresses. Although there are studies evaluating platelet characteristics in CKD, very few studies have assessed all platelet indices together (12,16,17). While platelet indices are cost-effective parameters that can be easily measured with automatic hematological analyzers, which platelet index is more beneficial for which chronic disease still remains unclear.

In this study, it was compared that early-stage and advanced CKD patients for all platelet indices. In advanced CKD patients, while platelet count, MPV, PDW, PCT, P-LCR, and HAPC were decreased, the MPV/Lymphocyte ratio and SII were increased. While evaluating the relationships of platelet indices with eGFR, HAPC had a positive relationship with eGFR, yet the MPV/Lymphocyte ratio had a negative one. Additionally, we noted higher platelet volume indices in female patients and those diagnosed with DM.

Although the platelet count is an indicator of the megakaryocyte reserve in the bone marrow the numbers in the peripheral blood are influenced by many factors, including splenic elimination, inflammatory conditions, and anemia (2,18). In this study, even if the platelet counts of our advanced CKD group were lower than those in early CKD stages, both groups had a sufficient number of platelets for hemostatic purposes. It is known that in advanced CKD, it is the functionality of platelets that is affected rather than numbers in the peripheral blood. In line with our findings, there are studies in the literature that reported lower platelet counts in advanced CKD and HD patients (16,19,20). It may be feasible to correct the impact of anemia on platelet number by adjusting the counts with the hematocrit level. HAPC is a parameter acquired by this way. In our CKD patients, HAPC value had a positive correlation with eGFR, even after adjustments for many variables. This correction with hematocrit value might provide a more accurate evaluation of the platelet counts. Hence, we believe that HAPC could be the measure that has the potential to reveal a relationship between eGFR and platelet counts.

MPV represents the mean volumetric measurement of platelets circulating within the bloodstream. While studies examining the relationship between eGFR and MPV have observed increased MPV values in advanced stages of CKD, some studies demonstrated opposite results (17,21,22). Our findings reveal a decrease in MPV values among advanced CKD patients; however, the correlation of MPV with eGFR was weak. PDW, another platelet volume index, indicates platelet anisocytosis. P-LCR quantifies the proportion of platelets larger than 12 fL, offering insights into platelet heterogeneity. In this study, it was observed that a decrease in PDW and P-LCR values in advanced CKD patients. Yu et al. also observed a decrease in PDW and P-LCR values in patients with advanced CKD. Furthermore, they demonstrated that these parameters might also be associated with CVD (12). We believe that a study with a larger sample size could more clearly elucidate the relationship between platelet volume indices and inflammation related clinical implications.

The MPV/Lymphocyte ratio has recently gained attention as an inflammatory marker. Increases in the MPV/Lymphocyte ratio have been shown in acute appendicitis and contrast-associated nephropathy (23,24). A recent study by Bei Xu et al. on pre-dialysis CKD patients indicates that the MPV/Lymphocyte ratio increases with the deterioration of kidney function (25). In this tudy, It was showed that the MPV/Lymphocyte ratio has a negative correlation with eGFR independently of many variables. We interpret this result as a reflection of inflammation

in CKD. We believe that the increase in the MPV/Lymphocyte ratio might be related to CKD progression and thrombotic activity in advanced-stage CKD.

The presence of DM is characterized by hyperglycemia, insulin resistance, increased inflammation, and oxidative stress. These conditions lead to increased platelet production and consumption (13,26). In this study, it was found that CKD patients with DM had significantly higher values of MPV and other platelet volume indices along with PCT and SII levels compared to those without a diagnosis of DM. Previous research indicates that in CKD and DM, the number of activated platelets increase due to chronic inflammation and amplified adhesion molecules (27). A study by Haile et al. suggests that MPV and PDW could be indicators of DM complications (13). Based on these findings, we believe that rises in PCT and platelet volume indices may refer to CKD progression in the presence of diabetic nephropathy.

The relationship between inflammation and CKD has been clearly demonstrated. Therefore, the SII might be useful in monitoring CKD patients. There are studies showing that SII can be associated with albuminuria, CVD, and the presence of CKD (28,29). In this study, it was observed that a significant elevation in the mean SII values among advanced CKD cases when compared to those in the early stages of the disease. We believe that the SII could serve as an indicator of chronic inflammation and its influence on the progression of CKD. Similarly, SII levels were negatively correlated with eGFR, but the strength of the correlation did not reach the level we expected. Therefore, we did not include SII index in our regression models. We believe that further research into the SII index's role in CKD could provide deeper insights into its predictive and diagnostic capabilities.

In this study, it was found that platelet count and some platelet volume indices were increased in females compared to males. These results seem to be consistent with general literature data. In female gender, anemia and hormonal status can also create changes in platelet indices (30,31). With this study, we examined the platelet indices of 411 CKD patients alongside clinical features. We believe our results are valuable due to our good sample size, our assessment of all platelet indices together, and our ability to account for many factors that could affect these parameters. We think that the MPV/Lymphocyte ratio and HAPC can reflect changes in eGFR. Meanwhile, SII index is a promising marker for CKD progression, and the platelet volume indices can reveal subclinical inflammation in CKD patients diagnosed with DM. All these results can be explained by increased platelet destruction, cytokine load, and inadequate thrombopoietin response in advanced-stage CKD (32).

Limitations of the study

The retrospective nature of our study, the absence of a healthy control group, and the inability to evaluate classic inflammatory markers can be considered as limitations of our study.

CONCLUSION

Platelet indices have the potential to provide valuable data about chronic diseases and their complications. MPV/Lymphocyte ratio and HAPC can give an idea about CKD progression. Our findings suggest that elevations in platelet volume indices could be indicative of diabetic nephropathy and increased inflammatory status. Future research will ascertain the importance of platelet indices for CKD and other related chronic conditions.

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Peer-Review

Both externally and internally peer reviewed.

Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Thesis

This study was prepared by rearrangement of the doctoral thesis by Mahmut Egemen Senel, entitled as "Evaluation of platelet indices in chronic kidney disease" and the supervisor of the relevant thesis is Ertugrul Erken.

Ethical Declaration

Ethical permission was obtained from the Kahramanmaras Sutcu Imam University, Medical Faculty Clinical Ethics Committee for this study with date 26.08.2020 and number 16/09, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: MES, EE, Design: MES, EE, Supervising: MES, EE, Financing and equipment: IO, NE, Data collection and entry: MES, IO, NE, Analysis and interpretation: EE, OA, Literature

search: MES, EE, IO, NE, Writing: MES, EE, Critical review: EE, IO, NE, OA.

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