

Importance of Platelet Markers for Demonstrating the Presence of Inflammation in the Different Stages of Chronic Renal Diseases

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ABSTRACT

There is no consensus about association between platelet markers and atherosclerosis in chronic renal diseases. In our study, we aimed to show the effects of platelet markers, in the patient with different stages of chronic renal diseases. Four groups as control, chronic renal diseases, hemodialysis and peritoneal dialysis groups were included; in the study. Venous blood samples were taken from all of the patients following a 12-hour fasting period and anemia and biochemical parameters were measured. Known as atherosclerotic risk factors the levels of C-reactive protein, HOMA-IR, C-peptide with platelet markers (mean platelet volum, plateletcrit, platelet distribution width) were measured and their's correlations were evaluated. The values of C-reactive protein, HOMA-IR, C-peptide and mean platelet volum in the patient groups were found higher than in the control grup. The positive correlation was determined the between levels of mean platelet volum with C-reactive protein, HOMA-IR, C-peptide, in the patient groups. Plateletcrit levels of the cases in chronic renal disease group were found to be significantly higher than the cases in other groups. No different was shown to the values of platelet distribution width, between the patients with different stages of chronic renal disease. We found that mean platelet volume was increased in the patients with chronic kidney diseases and they might associated the increased risks of inflammation and atherosclerosis. It is possible to use platelet markers as a biomarker to estimate atherosclerosis risk; in chronic kidney diseases.

Key Words: Chronic renal disease, dialysis, inflammation, platelet markers

Kronik Böbrek Hastalıklarının Farklı Evrelerinde İnflamasyon Varlığını Göstermede Platelet Markırlarının Önemi

ÖZET

Bir çok hastalıkta platelet markırlarının aterosklerosis ve inflamasyon ile ilişkisi olduğu gösterilmiştir. Ancak, kronik böbrek hastalıklarının farklı evrelerinde platelet markırlarının aterosklerosis ve inflamasyon ile ilişkisi konusunda fikir birliğine varılamamıştır. Çalışmamızda; kronik böbrek hastalıklarının farklı evrelerinde platelet markırlarının etkilerini göstermeyi hedefledik. Kontrol grubu, kronik böbrek hastalığı, hemodiyaliz ve periton diyalizi olmak üzere dört grup çalışmaya dahil edildi. Tüm hastalardan, 12 saatlik açlığı takiben eş zamanlı venöz kanlar alınarak anemi ve biyokimyasal parametreler ölçüldü. Aterosklerotik risk faktörü olarak bilinen C-reactive protein, HOMA-

IR, C-peptide ile platelet markirları ((mean platelet volum, plateletcrit, platelet distribution width) seviyeleri ölçülerek; aralarındaki ilişki değerlendirildi. Hasta gruplarında, C-reactive protein, HOMA-IR, C-peptide ve mean platelet volüm değerleri kontrol grubuna kıyasla anlamlı düzeyde yüksek saptanmıştır. Hasta grubunda mean platelet volüm ile C-reactive protein, HOMA-IR, C-peptide değerleri arasında pozitif korelasyon bulunmuştur. Kronik böbrek hastalıklı gruptaki olgularda plateletcrit değerleri, diğer gruplara kıyasla anlamlı yüksek bulunmuştur. Kronik böbrek hastalığının farklı evrelerindeki hastalar arasında platelet distribution width değerleri açısından farklılık saptanmamıştır. Sürekli inflamasyon varlığı ve artmış aterosklerosis riski olan kronik böbrek hastalarında; mean platelet volümün değerlerinin arttığını bulduk. Kronik böbrek hastalığının farklı evrelerinde inflamasyon ve aterosklerosis riskini tahmin etmek amacıyla, platelet markirlarının biyomarkir olarak kullanımı mümkün olabilir.

Anahtar kelimeler: Kronik renal hastalık, diyaliz, inflamasyon, platelet markir

INTRODUCTION

The most important cause of morbidity and mortality is the cardiovascular disease and inflammation in every stage of chronic kidney disease (1,2). The effect of chronic vascular inflammation in the pathophysiology of cardiovascular diseases has been accepted. Therefore, atherosclerosis is considered among main factors playing role in the development of cardiovascular diseases. Currently, the opinion of vascular inflammation and oxidative stress with known association with development of atherosclerosis providing also important contribution to development of cardiovascular disease and therefore it can be important cause of morbidity and mortality in the dialysis patients remains at the forefront (3). In the study results, it was shown that the risk for development of insulin resistance, hyperinsulinism and platelet function disorders increased in the presence of chronic kidney disease, in every stages of chronic kidney disease and they were important risk factors for atherosclerosis and atherothrombotic complications (4).

The prothrombotic effect of platelet function disorders and their contributions to the development of atherosclerosis in the presence of many diseases (such as diabetes mellitus, obesity, ischemic heart diseases) were investigated and it was found that there might be an important association between the value of serum mean platelet volume showing platelet functions and atherothrombotic complications (4,5).

The association between increased platelet volume and increased atherothrombotic risk has been tried to be demonstrated with in-vitro studies. It was determined in in-vitro studies that platelets became enzymatically and metabolically more active with increased platelet volume and they contained more prothrombotic materials such as; thromboxane A2 and B2 and glycoprotein IIB-IIIA (6).

Today, it is thought that mean platelet volum values might be biomarker for the estimation of atherosclerosis and atherothrombotic complication risks (4,5). However, there is no consensus about the effects of mean platelet volum values; in chronic kidney patients and dialysis patients (7).

Also, in our study, we aimed to show the effects of platelet markers values (mean platelet volum, plateletcrit, platelet distribution width) the patients with different stages of chronic renal diseases in whom the risk for observation of atherosclerosis complication increased by comparing the healthy population.

MATERIAL AND METHOD

The patients with chronic renal diseases and dialysis treatments who were followed-up and treated regularly in Nephrology Clinic of Istanbul Bakirkoy Dr Sadi Konuk Training and Research Hospital between 2012 and 2013 and healthy group visiting for control were included in the study. The study was approved by the Ethics Committee of Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital (Grand number: 538/2015). Each patient was informed about the study and the volunteer patients giving consent participated in the study. During study, no intervention was performed and no drug was administered and the available treatments of the patients were not changed.

The patients with dialysis adequacy receiving peritoneal dialysis, hemodialysis replacement therapy for at least one year and the patients with chronic renal diseases and healthy control group participated in the study. Our aim in our study was to demonstrate the effect of presence of chronic kidney disease on mean platelet volum values in the patients with various stages of chronic kidney disease and to demonstrate the association between mean platelet volum and atherosclerotic risk factors. Therefore, the patients with diagnosis of hypertension, previous myocar-

Table 1. Demographic and Clinical Features in All Groups.

	Minumum- Maximum	Mean±SD
Age (years)	18-77	46.69±16.13
Body mass index (kg/m ²)	16.16-32.90	23.60±3.95
Dialysis duration (years)	0.50-12.00	3.58±2.82

dial infarction and diabetes mellitus and iron deficiency anemia were excluded from the study. Since it would affect the levels of C- reactive proein, known to be acute phase reactant, the patients were excluded from the study in case of presence of acute inflammation (upper respiratory tract infection, lower respiratory tract infection etc.), exacerbation of chronic inflammatory disease (psoriatic arthritis, familial Mediterranean fever) and antiaggregant treatment or disease requiring antiaggregant treatment (peripheral vascular disease etc.).

Age, gender, height and weight of all patients were recorded. Venous blood samples were taken from all of the patients following a 12-hour fasting period under suitable conditions and sent to the laboratory without hemolysis. Assessment of hemoglobin, platelet, mean platelet volum, plateletcrit, platelet distribution width, iron, iron binding capacity, ferritin and biochemical parameters were measured by the same individual using the same device.

Glomerular filtration rate was measured with MDRD formula; in the chronic renal disease group. MDRD was calculated by using $186 * \text{Serum Creatinine}^{-1.154} * \text{Age}^{-0.203} * \text{Gender} * \text{Race}$ formula. It was determined that urine outputs of hemodialysis and peritoneal dialysis patient groups were equal and less than 100-300 ml/day and therefore the presence of proteinuria, microalbuminuria and residual renal function was not assessed. Hemodialysis patients were receiving hemodialysis replacement therapy three times a week for 4 hours. The patients receiving continuous ambulatory peritoneal dialysis therapy made changes with CAPD 2 stay safe peritoneal dialysis solutions four times a day. CAPD 2 stay safe peritoneal dialysis solutions of 2000/2500 ml were used in these patients. According to clinical and labora-

tory assessment of the patients, glucose calcium content was changing (1.5% glucose, 2.3% glucose and calcium content; 1.25 mmol/l, 1.75 mmol/l). Kt/V >1.40 and URR>70.00% in hemodialysis patients and Kt/V >1.70 in peritoneal dialysis patients were considered as dialysis adequacy.

Patients' data were evaluated according to ADA (American Diabetes Association) criteria to exclude the diagnosis of Diabetes Mellitus (8). The patients with HbA1c value of >6% and fasting blood glucose level of >110 mg/dl were excluded from the study.

The following formula was used to calculate the body mass index (BMI): $(\text{body weight})/(\text{height})^2$. Dry weight was calculated in the dialysis patients during measurement of body weight.

Iron and iron capacity were analyzed with Abbott Architect 1600 device by using Ferene method (normal range; iron: 40-150 mg/dl; iron binding capacity: 225-480 mg/dl). Serum ferritin levels were measured with Abbott Architect 1200 device by using CMIA method (normal range:13-150 µg/l). Hemoglobin, hematocrit, platelet, mean platelet volum, plateletcrit, platelet distribution width values were studied with Beckman Coulter device using Beckman method. Normal range of platelet, mean platelet volum, plateletcrit and platelet distribution width values was accepted; 100.000 mm³/l- 300. 000

Table 2. The Evaluation of Renal Functions in the Patients with Chronic Renal Disease.

Chronic Renal Disease Group	
Creatinine (mg/dl)	Glomerular Filtration Rate (ml/dk)Age (Years)
2.45	35.28
1.98	78.52
3.72	22.10
2.47	27.66
1.99	35.49
2.35	29.29
3.03	21.85
3.52	22.10
2.04	18.38
2.81	17.68
2.09	24.88
2.74	18.21
2.50	20.24
2.20	23.45

Table 3. Comparison of Biochemical Parameters in All Groups.

		Control Group (n=16)	Hemodialysis Group (n=42)	Peritoneal Dialysis Group (n=30)	Chronic Renal Diseases Group (n=15)	p
Body mass index (kg/m ²)	Mean±Sd	21.03±1.47	22.43±2.86	23.53±3.81	29.77±2.27	ª0.001 **
	Median	20.65	22.17	21.20	29.30	
Fasting blood glucose (mg/dl)	Mean±Sd	92.63±7.67	92.21±10.81	91.40±10.10	99.60±13.54	ª0.089
	Median	93.50	95.50	92.50	99.00	
C- peptide (µmol/l)	Mean±Sd	1.30±0.34	7.64±4.37	7.09±3.86	6.97±9.04	ª0.001 **
	Median	1.24	6.80	6.77	4.19	
HOMA-IR (mmol/l)	Mean± Sd	0.73± 0.49	1.66 ± 1.62	1.94±2.19	1.70± 2.20	ª0.001 **
	Median	0.77	1.76	2.07	1.67	
LDL- cholesterol (mg/dl)	Mean±Sd	106.44±16.11	95.14±39.06	123.00±36.26	120.13±50.66	ª0.012 *
	Median	107.00	91.50	122.50	105.00	
HDL-cholesterol (mg/dl)	Mean±Sd	45.69±7.91	35.98±10.72	38.40±9.32	45.47±12.47	ª0.002 **
	Median	46.50	36.00	36.50	42.00	
C-reactive protein (mg/dl)	Mean± Sd	0.18± 0.24	1.04± 0.91	1.18± 1.60	0.51± 0.48	ª0.001 **
	Median	0.23	0.98	1.34	0.66	
Hemoglobin (gr/dl)	Mean±Sd	13.09±1.21	10.40±1.52	10.62±1.33	10.79±1.88	ª0.001 **
	Median	12.90	10.10	10.50	10.50	
Platelet (µ/l)	Mean±Sd	137.00±24.95	190.55±68.27	266.27±93.04	300.80±103.08	ª0.001 **
	Median	133.00	189.00	265.50	275.00	
Mean platelet volume (femtolitre)	Mean±Sd	7.36±0.53	8.23±1.39	8.59±1.03	8.69±1.50	ª0.002 **
	Median	7.15	8.10	8.40	8.90	
Plateletcrit (ng/ml)	Mean±Sd	0.21±0.04	0.20±0.06	0.23±0.07	0.27±0.07	ª0.007 **
	Median	0.23	0.21	0.21	0.23	

ªMann Whitney U Test, ºStudent-t Test, ¸Kruskal Wallis Test, ¸p<0,01**

mm³/l, <0.1 ng/ml and 7.4-12 femtolitre and 9-14 femtolitre; respectively.

Abbott Architect 1600 device was used to measure fasting serum glucose levels. HbA1c level was analyzed with Premier Hb9210-Primus ultra II device by using HPLC (high performance liquid chromatography) method. Insulin level was analyzed with Siemens Immulite 2000 device by using enzyme-linked Chemiluminometric Immunoassay method. C-peptide level was studied with Siemens Immulite 2000 device by using two-way Chemiluminometric Immunoassay method. HOMA-IR index was calculated by using fasting blood glucose (mg/dl) x fasting insulin level (µU/ml)/405 formula. Plasma C- reactive protein levels were measured by using Chemiluminometric Immunoassay method.

Statistical Evaluations

NCSS (Number Cruncher Statistical System) 2007 Statistical Software (NCSS, LLC Kaysville, Utah, USA) program was used for the statistical analysis. During the evaluation of the study data, regarding the comparisons of quantitative data as well as descriptive statistical methods (mean, standard deviation, median, frequency and ratio), One-way Anova test was used for the intergroup comparisons of parameters with normal distribution and Tukey HDS test and Games Howell test were used for the determination of the group causing difference. Student t test was used for assessments according to two groups. Kruskal Wallis test was used for the intergroup comparisons of parameters without normal distribution and Mann Whitney U test was used for the determination

Table 4. Comparison of Anemia Parameters in the Patients with Chronic Renal Disease and Dialysis Treatments.

		Hemodialysis Patients Group	Peritoneal Patients Group	Chronic Renal Diseases Group	p
Iron (mg/dl)	Mean±Sd	105.44±115.34	50.21±21.79	75.52±22.59	0,004
	Median	63 (45.50-80)	50 (37-62)	61 (48. 46 - 77)	
Iron binding capacity (mg/dl)	Mean±Sd	240.31±121.87	210.05±46.02	180.65±55.76	0,095
	Median	206.50 (186-247)	206 (183-229)	190.75 (170-190)	
Ferritin (µg/l)	Mean±Sd	514.97±418.89	283.41±215.52	250.89±110.76	0.007
	Median	394.5 (206-717)	207 (141-390)	190.89 (121- 290)	
Platelet distribution width (fl)		9,40	10,20	10,65	0.095

Mann Whitney U Test, Student-t Test, p< 0,05

of the group causing difference and for the comparison of two groups. The results were evaluated in 95% confidence interval and at a significance level of p<0,05.

RESULTS

The study was performed in Nephrology Clinic of Istanbul Bakirkoy Dr Sadi Konuk Training and Research Hospital between 2012 and 2013 in total 103 patients including healthy subjects visiting for control and the patients with chronic renal disease. peritoneal and hemodialysis patients who were followed-up and treated regularly. When the distribution of the patients according to presence of chronic kidney disease was evaluated, it was determined that 15.50% (n=16) of the patients were healthy subjects. 14.60% (n=15) of them were the patients with chronic renal disease and 40.80% (n=42) of them were receiving hemodialysis therapy and 29.10% (n=30) of them were receiving peritoneal dialysis replacement therapy. Considering to the chronic renal disease stage was found that 6.66% (n=1) of patient had stage 2 chronic renal disease and %13.33 (n=2) and 80.01% (n=12) of patients had stage 3 and stage 4 chronic renal diseases; respectively.

When demographic characteristics and biochemical parameters of all groups were compared, the body mass index value of the patients in the peritoneal dialysis and chronic renal diseases groups was determined to be sta-

tistically significantly higher in the patients in normal and dialysis groups (p=0.001; p=0.014; p<0.05).

It was seen that C-peptide levels were statistically significant according to groups (p=0.001; p<0.01). C-peptide values of the patients in the hemodialysis, peritoneal dialysis and chronic renal diseases groups were determined to be statistically significantly higher compared to C-peptide values of the healthy subjects (p=0.001; p<0.01). HOMA-IR values in the chronic renal diseases and dialysis patients groups were determined higher than in the control group (p=0.001; p<0.01). Serum C-reactive protein levels in the patients with dialysis and the chronic renal diseases were found higher than in healthy subjects (p=0.001; p<0.01) (Table 3).

According to the groups, platelet counts were found to be statistically significant (p=0.001; p<0.01). Platelet values of the patients in the hemodialysis, peritoneal dialysis and chronic renal diseases groups were determined to be statistically significantly higher compared to platelet values of the subjects in control group (p=0.005; p=0.001; p=0.001; p<0.01), platelet values of the patients in the peritoneal dialysis and chronic renal diseases groups were determined to be statistically significantly higher compared to platelet values of the patients in hemodialysis group (p=0.001; p<0.01) (Table 3).

According to the groups, mean platelet volum levels were found to be statistically significant (p=0.002; p<0.01). Mean platelet volum values of the patients in the hemodialysis, peritoneal dialysis and chronic renal diseases

Table 5. Considering to the All Groups Evaluations of Post Hoc for the Body Mass Index and Results of Biochemical Parameters.

	Control and Hemodialysis	Control and Peritoneal Dialysis	Control and Chronic Renal Diseases	Hemodialysis and Peritoneal Dialysis	Hemodialysis and Chronic Renal Diseases	Peritoneal Dialysis and Chronic Renal Diseases
Body mass index (kg/m ²)	0.079	0.014*	0.001**	0.550	0.001**	0.001**
C- peptide (µmol/l)	0.001**	0.001**	0.001**	0.810	0.093	0.100
HOMA-IR (mmol/l)	0.001**	0.001**	0.001**	0.039	0.234	0.332
LDL- cholesterol (mg/dl)	0.085	0.170	0.984	0.002**	0.069	0.470
HDL-cholesterol (mg/dl)	0.009**	0.104	1.000	0.754	0.014*	0.134
C-reactive protein (mg/dl)	0.001**	0.001**	0.001**	0.389	0.574	0.267
Hemoglobin (gr/dl)	0.001**	0.001**	0.001**	0.939	0.836	0.984
Platelet (mµ/l)	0.005**	0.001**	0.001**	0.001**	0.001**	0.373
Mean platelet volume (femtolitre)	0.024*	0.001**	0.003**	0.142	0.180	0.552
Plateletcrit (ng/ml)	0.271	0.915	0.017*	0.252	0.001**	0.011*

^{aa}Tukey HSD&Games-Howell, ^{cc}Mann Whitney U test, *p<0,05, **p<0,01

groups were determined to be statistically significantly higher compared to mean platelet volum values of the cases in control groups (p=0.024; p=0.001; p=0.002; p<0.05). According to the groups, plateletcrit levels were found to be statistically significant (p=0.007; p<0,01). Plateletcrit values of the patients in the chronic renal diseases group were determined to be statistically significantly higher compared to plateletcrit values of the cases in control, hemodialysis and peritoneal dialysis groups (p=0.017; p=0.001; p=0.011; p<0.05) (Table 3). No statistically significantly was found the between platelet distribution width values; between the dialysis and chronic renal disease groups (Table 4).

Serum iron levels in the peritoneal dialysis group were determined less than in the hemodialysis and chronic re-

nal diseases group (p= 0.004; p<0,01) (Table 4). The positive correlation was found the between mean platelet volum and platelet with C- reactive protein, C- peptide and HOMA-IR (p<0.05) (Table 5).

DISCUSSION

In the chronic kidney diseases, it is known that the risk for development of presence of persistent chronic inflammation and atherosclerosis even though in the early stages where the glomerular filtration rate is not reduced yet. It has been shown that coronary artery disease was a more serious problem among cardiovascular diseases

whose risk for development was increased in the patients with chronic kidney disease and the rate of incidence of coronary artery disease could increase threefold in dialysis patients (1,2,3).

In our study, we tried to demonstrate and compare the presence of chronic inflammation; in the patients. Additionally, we aimed to determine the role of platelet markers providing contribution to development of atherosclerosis complications in estimation of inflammation; in the patients with chronic renal diseases.

It has been demonstrated in the studies that glucose metabolism disorders were seen beginning from the early stages of chronic kidney diseases and the risk for development of insulin resistance was increased especially in end-stage kidney disease but the mechanism of development of glucose metabolism disorders could not be explained clearly (9,10). Many disorders such as uremic milieu, chronic inflammation, anemia, secondary hyperparathyroidism and chronic acidosis provide contribution to development of insulin resistance in the presence of chronic kidney disease. It has been supported by the studies that glucose metabolism disorders and insulin resistance developing might provide contribution to increase of risk for atherosclerosis; in every stage of chronic kidney diseases (11). Recently, at the end of studies related to C-peptide, it has been shown that C-peptide has important role in determination of beta-cell dysfunction in pancreas and impaired insulin secretion in early period. Additionally, it has been considered that increased C-peptide levels could show risk of subclinical atherosclerosis (12). In our study, we think that determination of fasting HOMA-IR and C-peptide levels to be higher in the chronic renal diseases and dialysis patient groups compared to control group can be evidence of chronic inflammation and subclinical atherosclerosis other than indicating development of impaired glucose metabolism in these patients. Also; we shown to be the presence of positive correlation between the values of HOMA-IR and C-peptide with C-reactive protein levels. It is known that C-reactive protein has been implicated in the initiation and progression of inflammation and atherosclerosis (13). This results might supported the increased risks of inflammation and atherosclerosis, in our patients.

We think that finding higher serum LDL-cholesterol levels in peritoneal dialysis patient group in our study can be due to glucose-based peritoneal dialysis solutions used in dialysis therapy. Presence of many glucose degrada-

tion products in peritoneal dialysis solutions is known. Glucose degradation products may cause development of various metabolic disorders by entering systemic circulation apart from injuring the membrane locally by causing formation of advanced glycation end-products (AGEs). It has been proven that metabolic disorders such as weight gain, lipid abnormalities and insulin resistance might develop due to glucose content of peritoneal dialysis solutions (14,15).

In our study, while we determined lower levels of hemoglobin levels in the chronic renal diseases and dialysis patient groups who were followed-up and treated regularly compared to control group, we found that there was no difference between hemoglobin levels in the chronic renal diseases and dialysis patient groups. In every stage of chronic kidney diseases, it is known that many factors like decreased erythrocyte production from the bone marrow with the effect of uremic toxins, increased bleeding diathesis due to platelet dysfunctions developed. Apart from that, anemia developed is an important risk factor for development of chronic inflammation and atherosclerosis. Therefore, determination of anemia in the patients with chronic renal diseases and dialysis treatments in our study is an expected result. Similar hemoglobin levels in the chronic renal diseases and dialysis patient groups can be explained by receiving regular treatment of the patients in the same clinic.

Platelet functions are an important risk factor for the development of mechanical and functional endothelial injury and therefore they can cause to the development of inflammation. Recently, it has been supported that increased numbers of platelets and cell-cell interaction between platelets and endothelial cells were important in development of atherosclerosis (16,17). In our study, we found that platelet levels in patient groups were significantly higher compared to control group. This results supported to the existence of positive correlation between platelets with inflammation, in the patient groups.

In our study, we observed that mean platelet volume levels in the patient groups were significantly higher compared to control group. It has been considered that mean platelet volume levels were associated with proinflammatory diseases as a matter of fact they could be prognostic biomarker in cardiovascular and atherosclerotic diseases. The results of relevant studies did not lead to any consensus on change of mean platelet volume levels in chronic kidney diseases. There are also studies indicat-

ing that mean platelet volume levels in dialysis patient do not change in addition to the studies indicating presence of a negative correlation between reduced glomerular filtration rate and mean platelet volume (18,19). We think that higher mean platelet volume levels in patient groups compared to control group in our study can be associated with increased risks of inflammation and atherosclerosis. Additionally, we observed that plateletcrit values were significantly higher in the chronic renal diseases patient group. It has been observed that plateletcrit values could provide information about thrombopoiesis apart from being associated with platelet function and reactivation similar to mean platelet volume. It has been considered that there was a positive correlation between increased production of platelet and plateletcrit during thrombopoiesis. Therefore, determination of higher levels of plateletcrit in the chronic renal diseases patient group of our study can be associated with increased platelet production rather than increased chronic inflammation. Higher levels of platelet in the chronic renal diseases patient group support our idea. Platelet distribution width associated with platelet activation. Also; platelet distribution width is a more specific marker of reactive thrombocytosis and thrombocytosis associated with myeloproliferative disorders (20). No different was found platelet distribution width values; between the patient groups and control group, in our study. This results suggested that the relationship between was found thrombocytosis with inflammation and were not the reactive thrombocytosis related diseases; in the patient groups.

In summary, known as atherosclerotic risk factors C- reactive protein, HOMA-IR, C- peptide and mean platelet volum values in the patients with different stages of chronic renal disease were determined higher than in healthy subjects, in our study. However; the positive correlation was found the between levels of mean platelet volum and platelet with C- reactive protein, HOMA-IR, C- peptide values. We thought that our study may support that increased levels of mean platelet volume in chronic kidney patients and dialysis patients can have a prognostic meaning in estimation of development of risk for chronic inflammation.

Conclusion

The association of platelet function disorder with inflammation and atherothrombotic complications is a special and different condition apart from causing development

of bleeding diathesis and anemia in chronic kidney diseases. Knowing the effects of mean platelet volume levels which indicate the platelet functions in chronic kidney diseases may provide favorable contribution to survival by causing prediction and treatment of development of inflammation and atherosclerosis which is the most important cause of morbidity and mortality.

Potential Financial Conflicts of interest

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Conflict of Interests

The authors have declared that no conflict of interest exists.

REFERENCES

1. Allon M. Evidence-based cardiology in hemodialysis patients. *Am Soc Nephrol.* 2013;24(12):1934-1943.
2. Rosner MH, Ronco C, Okusa MD. The role of inflammation in the cardio-renal syndrome: a focus on cytokines and inflammatory mediators. *Semin Nephrol.* 2012; 32 (1):70-78.
3. Siti HN, Kamisah Y, Kamsiah J. The role of oxidative stress, antioxidants and vascular inflammation in cardiovascular disease. *Vascul Pharmacol.* 2015;71: 40-56.
4. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets.* 2004; 15(8):475-478.
5. Coban E, Ozdogan M, Yazicioglu G, Akcıt F. The mean platelet volume in patients with obesity. *Int J Clin Pract.* 2005; 59:981-982.
6. S. G. Chu, R. C. Becker, P. B. Berger, D. L. Bhatt, J. W. Eikelboom, B. Konkle, E. R., Mohler, M. P. Reilly, and J. S. Berger. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost.* 2010 ; 8(1): 148-156.

7. Casserly LF, Dember LM. Thrombosis in end-stage renal disease. *Semin Dial.* 2003; 16(3): 245-56.
8. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010; 33(4): 62-69.
9. Atamer A, Alisir Ecder S, Akkuş Z, Kocyigit Y, Atamer Y, İlhan N et al. Relationship between leptin, insulin resistance, insulin-like growth factor-1 and insulin-like growth factor binding protein-3 in patients with chronic kidney disease. *J Int Med Res*, 2008; 36(3): 522-28.
10. Sit D, Kadiroglu AK, Kayabasi H, Yılmaz ME. The prevalence of insulin resistance in nondiabetic nonobese patients with chronic kidney disease. *Adv Ther*, 2006; 23(6): 988-98 .
11. Hung AM, Ikizler TA: Factors determining insulin resistance in chronic hemodialysis patients. *Contrib Nephrol*, 2011; 171: 127-34.
12. Shpakov AO, Granstrem OK., Fiziol Zh Im I M Sechenova. C-peptide physiological effects 2013 ;99(2):196-211.
13. Frostegard J. Immunity, atherosclerosis and cardiovascular disease. *BMC Medicine*. 2013;11; 117.
14. Anjali B. Saxena, MD. Recent advances in the management of peritoneal dialysis patients. 2015, 1; 7:57.
15. Skubala A, Zywiec J, Zelobowska K, Gumprecht J, Grzeszczak W. Continuous glucose monitoring system in 72-hour glucose profile assessment in patients with end-stage renal disease on maintenance continuous ambulatory peritoneal dialysis. *Med Sci Monit* 2010, 16 (2):75-83.
16. Siegel-Axel DI, Gawaz M. Platelets and endothelial cells. *Semin Thromb Hemost.* 2007 ;33(2):128-35.
17. Badimón L, Vilahur G, Padro T. Lipoproteins, platelets and atherothrombosis. *Rev Esp Cardiol.* 2009 ;62(10):1161-78.
18. Ju HY, Kim JK, Hur SM, Woo SA, Park KA, Park MY, Choi SJ, Hwang SD. Could mean platelet volume be a promising biomarker of progression of chronic kidney disease? *Platelets.* 2015;26(2):143-7.
19. Hale Sakallı, Esra Baskın, Umut Selda Bayrakçı, Kaan Savaş Gülleroğlu, Gökhan Moray, Mehmet Haberal. Mean Platelet Volume as a Potential Predictor of Renovascular Thrombosis After Renal Transplant. *Experimental and Clinical Transplantation.* 2011; 27-31: 11(1).
20. Park MJ, Park PW, Seo YH, Kim KH, Park SH, Jeong JH, et al. The relationship between iron parameters and platelet parameters in women with iron deficiency anemia and thrombocytosis. *Platelets.* 2013;24(5):348-51.