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RESEARCH ARTICLE

Platelet Lymphocyte Ratio is Associated with Carotid Atherosclerosis in Hemodialysis Patients

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Abstract

Objective: We aimed to demonstrate whether there is a correlation between Platelet Lymphocyte Ratio (PLR) and carotid intima-media thickness (CIMT) which is an early marker of atherosclerosis in patients receiving dialysis where there is a chronic inflammatory process in the body.

Methods: 53 patients receiving dialysis 3 days a week and 54 persons as the control group were included. The exclusion criteria were determined as infection, using drugs that increase or decrease the number of leukocytes such as steroids, antithyroid, chronic liver diseases, rheumatic disease, maling disease and prior cardiovascular or cerebrovascular diseases. Patients' age, gender, body mass index, hemogram and biochemical parameters were recorded. CIMT values were measured by Carotid Doppler examination.

Results: When the two groups were compared; there was no significant difference between them in terms of age, gender, blood pressures, DM, ejection fractions, lipid levels. PLR, neutrophil-to-lymphocyte ratio (NLR) and CIMT were significantly higher ($p=0.009$, $p<0.001$, $p<0.001$; respectively) in the dialysis patients group. A positive correlation was found between CIMT and PLR, NLR ($r=0.59$ $p<0.001$, $r=0.38$, $p=0.004$). As a result of the linear regression analysis, PLR (B:0.714, 95%CI:3.425/14.393, $p=0.002$) and NLR were found as independent predictors in showing CIMT.

Conclusion: PLR is independently associated with subclinical atherosclerosis assessed by CIMT in people with dialysis patients

Key words: Platelet Lymphocyte Ratio is Associated with Carotid Atherosclerosis in Hemodialysis Patients

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Introduction

The prevalence of chronic kidney disease (CKD) in the world is constantly increasing. This increase is caused by the increasing number of obese, hypertensive and diabetic patients (Wróbel et al., 2016). CKD patients are at a high risk for the development of cardiovascular disease. Cardiovascular events are an important cause of morbidity and mortality in patients with end stage renal disease (ESRD). The risk of mortality from cardiovascular disease is 30 times higher in CKD

patients compared to normal population (Yilmaz et al., 2017; Yaprak et al., 2016; Bal et al., 2015).

Atherosclerosis and chronic inflammation are a component defined in malnutrition-inflammation-atherosclerosis syndrome in ESRD patients. This syndrome is associated with negative cardiovascular events in CKD patients (Yaprak et al., 2016; Bal et al., 2015) Atherosclerosis is not only a simple vascular damage occurring with lipid infiltration, but rather is an active event with inflammatory process also involved (Horne et al., 2005). Inflammation has an important role in both beginning, and development and progression of atherosclerosis (Corriere et al., 2018; Uçar et al., 2016). Chronic inflammation which is involved in the pathogenesis of atherosclerosis is more commonly seen in ESRD patients compared to population (Ikeda 2003).

Recent studies have demonstrated that PLR shows severity of coronary artery disease, predicted major cardiovascular events and mortality, and is a significant independent predictor of major cardiovascular events. Again, studies have reported that PLR is a new inflammatory marker (Wang et al., 2017; Uzun et al., 2017; Sambel et al., 2017).

CIMT is a well-defined early marker of atherosclerosis, and has a strong correlation with the severity of coronary atherosclerosis and the risk factors of cardiovascular disease (Corriere et al., 2016) CIMT measurement is a practical and easy to apply method (Yurtdaş et al., 2014). Briefly, CIMT is a marker of subclinical atherosclerosis, and is used in prediction of cardiovascular events (O'Leary et al., 1999).

In this study, we aimed to the relationship between PLR and subclinical atherosclerosis in Hemodialysis Patients.

Methods

Patients between the ages of 18-70 were taken into the study. Our study population consisted of 53 patients with end stage renal desease who dialyzed 3 days a week and 54 control patients who visited cardiology clinic. The exclusion criteria were determined as infection, using drugs that increase or decrease the number of leukocytes such as steroids, antithyroid, chronic liver diseases, rheumatic disease (such as rheumatoid arthritis), maling disease, prior cardiovascular or cerebrovascular diseases were also excluded. Approval was obtained from the ethics committee of Ordu University.

The patients were rested for 15 minutes and their blood pressures were measured. The average of 3 measurements was taken. The weights and heights of the patients were measured with standard measurement techniques while they were hungry and standing. Body mass index (BMI) (kg/m2) was calculated using the formulas “weight (kg)/height (m)2 (Nimitphong et al., 2018).

Blood samples were taken from the patients after 8-12 hours of fasting. Biochemical parameters were studied from these blood samples and were measured cholorometrically using an Abbott original reagent on Abbott Architect 8000 auto analyzer. Beckman-Coulter Gen-S system device (Beckman-Coulter Inc., USA) was used for the complete blood count. NLR was calculated by the ratio of neutrophil count to lymphocyte count and PLR was calculated by the platelet count to lymphocyte count.

Carotid artery was performed with doppler device with 13-MHz probe. The brand of the device was Hitachi Preirus, Tokyo, Japan. The patients were lying on their back and right and left CCA imaging were performed.

Statistical analysis

The Kolmogorov–Smirnov normality test was used to evaluate the distribution of all quantitative data. Statistical Package for Social Sciences (SPSS) Version 22.0 (SPSS Inc., Chicago, Illinois. USA) was used for statistical analysis. Independent sample T test was used for continuous variables, and chi-square test for categorical variables. Non-parametric statistics was used if data were not normally distributed. Correlations were assessed using Pearson test. Lineer regression analysis was used to identify the independent predictors of KIMK. Continuous variables were defined as mean ± standard deviation, and categorical variables were given as percentages. Any P value <0.05 was considered as statistically significant.

Results

107 patients were included in the study. Control group (n=54) had normal renal function and mean age was 53,07±14,47. Patient group (n=53) had end-stage renal disease (dialyzed patients) and mean age was 54,33±7,32. 45% of the dialysis patient group and 53% of the controls were male. The clinical characteristics and the hematological and biochemical parameters of both patient groups are presented in Table 1. When the two groups were compared; there was no significant difference between them in terms of age, gender, systolic and diastolic blood pressures, presence of DM, ejection fractions, cholesterol and triglycerides levels. PLR (Figure 1), NLR and CIMT (Figure 2) were

significantly higher (p=0.009, p<0.001, p=0.003; respectively), and hemoglobin and albumin values were significantly lower (p<0.001, p<0.001; respectively) in the dialysis patient group (Table 1).

A positive correlation was found between CIMT and PLR, NLR (r=0.59 p<0.001, r=0.38, p=0.004).

As a result of the linear regression we performed to determine the independent predictors showing CIMT, PLR (Beta [B]: 0,714, 95% confidence interval [CI]: 3,425 to 14,39, P=0.002) and NLR (B: -1,218, 95%CI: -0.898 to -0.411, P<0.001) were found as the independent predictors (Table 2).

Table 1. Comparison of Dialysis Patient Group And Control Group

	In Hemodialysis Patients Group N=53	**Control Group N=54**	**P**
Age (year)	*54,33±7,32*	53,07±14,47	0,57
Gender			
Male (%)	*45*	53	0,41
BMI (kg/m^2)	*24,19±4,42*	24,80±4,10	0,45
Diabetes Mellitus (%)	*21,31*	14,03	0,34
SBP (mmHg)	*120,13±19,27*	117,83±27,12	0,60
DBP (mmHg)	*77,26±15,88*	77,51±15,19	0,90
Hemoglobin (g/dl)	*11,44±1,39*	14,12±1,94	***<0,001***
WBC (x10^3/µL)	*6,77±1,72*	6,61±1,65	0,60
PLR	*153,69±4,02*	141,43±27,68	***0,009***
NLR	*3,01±0,45*	1,87±0,36	***<0,001***
Creatinin (mg/dl)	*9,5±4,2*	0,72±0,33	***<0,001***
Total-Cholesterol (mg/dl)	*185,30±35,65*	180,2±31,20	0,43
Triglycerides (mg/dl)	*144,58±66,34*	136,62±54,6	0,50
HDL-Cholesterol (mg/dl)	*43,03±5,80*	44,8±7,12	0,14
LDL-Cholesterol (mg/dl)	*113,57±26,69*	110,55±21,8	0,55
Albumin (mg/dl)	*3,6±0,30*	4,5±,037	***<0,001***
Ejection Fraction (%)	*63,80±4,02*	64,28±3,32	0,50
CIMT	*0,73±0,23*	0,61±0,21	***0,003***
HsCRP	*3,42±1,92*	1,18±0,60	***<0,001***

BMI: Body Mass Index SBP: Systolic Blood Pressure DBP: Diastolic Blood Pressure WBC: White Blood Cell PLR: Platelet Lymphocyte Rate NLR: Neutrophil Lymphocyte Ratio CIMT: Cathodic İntima Media Thickness

Table 2. Evaluation of Independent Predictors of Carotid İntima Median

	r	**p**	**B**	**%CI**	**p**
Platelet Lymphocyte Ratio	0.59	<0.001	0,714-	3,425/14,39	0,002
Neutrophil Lymphocyte Ratio	0.38	0.004	-1,218	-0,898/-0,411	<0,001
HsCRP	0,83	<0.001	-0,828	-0,189/-0,024	0,012

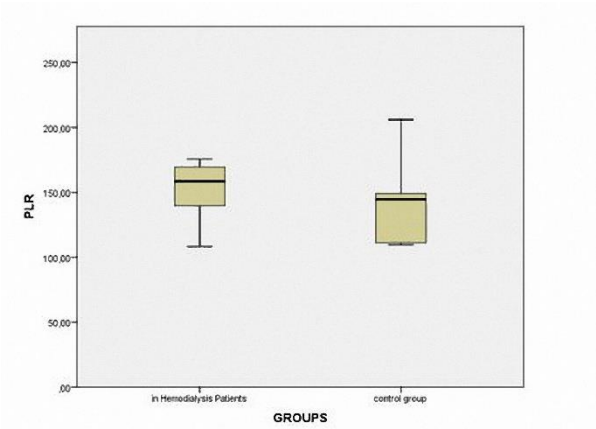

Figure 1. Comparison of mean PLR Between Control Group and in Hemodialysis Patients Group

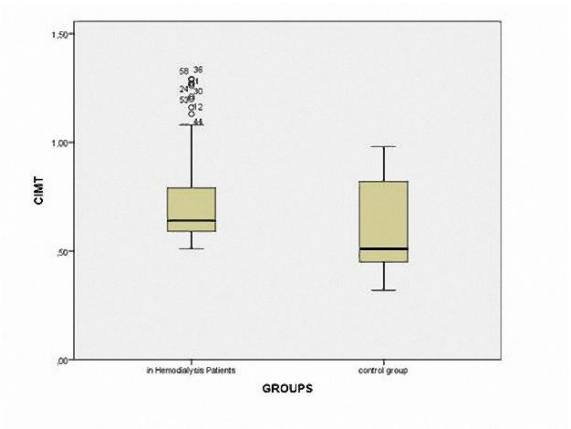

Figure 2. Comparison of mean CIMT Between Control Group and in Hemodialysis Patients Group

Discussion

In this study, we showed the relationship between PLR and CIMT as a marker of subclinical atherosclerosis in hemodialysis patients without a history of cardiovascular or cerebrovascular diseases.

Studies have reported a close association between PLR and inflammation (Samlet et al., 2017; Tola 2018; Fukuda et al., 2018). Severe and prolonged inflammation as in atherosclerosis leads to increased proliferation in megakaryocyte series, which in turn cause to an increase in platelet count (Uzun et al., 2017; Samlet et al., 2017). The bone marrow increases neutrophil count and decreases lymphocyte count during chronic stres (Yüksel et al., 2015). In addition, neutrophil count increases secondary to inflammation in cases of chronic severe continuous inflammation, and re-distribution of lymphocytes to the lymphocytic organs due to induction by stress and severe apoptosis contribute to a decrease in lymphocyte count (Corriere et al., 2018; Uzun et al., 2017).

Recent studies have investigate the place of inflammation in the pathophysiology of cardiovascular diseases, and found significant correlations between various inflammatıory markers (such as fibrinogen, C-reactive protein [CRP], interleukin-18 and tumor necrosis, factor-α, neutrophil lymphocyte ratio) and cardiovascular diseases (Ucar et al., 2016; Uzun et al., 2017; Li et al., 2017; Damman et al., 2017; Sinning et al., 2006; Celik and Bugan 2011; Kaya et al., 2014). Furthermore, studies have demonstrated a strong correlation between the number of platelets in the circulation and major cardiovascular events regardless having a known coronary artery disease (Uzun et al., 2017). Increased platelet count or increased platelet activation plays an important role in the onset and progression of atherosclerosis. (Wang et al., 2017; Uzun et al., 2017; Trakarnwijitr et al., 2017; Zhou et al., 2017). In addition, decreased lymphocyte count in patients with coronary artery disease and heart failure is reported to be associated with major negative cardiovascular events (Uzun et al., 2017; Trakarnwijitr et al., 2017; Zhou et al., 2017).

CIMT is a well-known biomarker of subclinical atherosclerosis. In addition, CIMT is a risk factor for cardiovascular disease, and a marker used in predicting cardiovascular events (Li et al., 2017; O'Leary et al., 1999).

Studies have reported a close association between the worsened prognosis and complications of cardiovascular, metabolic, malignant, and inflammatory diseases and NLR (Corriere et al., 2018; Li et al., 2017; Akbas et al., 2014; Ulu et al., 2013; Jiang et al., 2018; Polat et al., 2017; Uysal et al., 2016; Kalay et al., 2012; Xiao et al., 2014; Wei et al., 2014). In addition, NLR is stated to be a new inflammatory marker for cardiovascular risk and cardiac mortality (Uysal et al., 2016; Tatar et al., 2016). It has reported that NLR can be used as a parameter predicting mortality in end stage renal failure (Tatar et al., 2016).

Studies have reported that PLR may be an important predictor showing the prognosis of coronary artery disease (CAD) and negative cardiovascular events such as acute coronary syndrome. In addition, a high PLR level is among the independent predictors, that are used in estimating the severity of CAD (Yuksel et al., 2015; Trakarnwijitr et al., 2017; Uysal et al., 2016; Ozcan et al., 2016; Gary et al., 2013). In their study, Yuksel et al. divided the patients who underwent coronary angiography into three groups as the controls, moderate and severe groups according to the Gensini score, investigated the association with PLR, and reported that PLR predicted the severity of atherosclerosis (Yuksel et al., 2015). The roles of leukocytes and platelets in atherosclerosis are well-known. PLR which is a new prognostic marker also gives information both about aggregation and inflammation (Davi et al., 2007; Zouridakis et al., 2000). Turkmen et al. reported that PLR was a strong marker showing inflammation is ESRD patients (Turkmen et al., 2013). In their study on hemodialysis patients, Yaprak et al. found that PLR better predicted mortality than NLR.3 Compared with the other inflammatory cytokines, PLR is an easy to apply and inexpensive biomarker (Trakarnwijitr et al., 2017; Zhou et al., 2017).

As the result of the present study, PLR and NLR that are known as inflammatory markers were found significantly higher in the dialysis patient groups as expected. CIMT which is an early marker of atherosclerosis was positively correlated with PLR and NLR. The analysis showed that PLR is one of the independent predictors of CIMT.

Study limitations

Sample size was small and it was a single center design. In this study there were no data on other inflammatory markers (interleukin 10 (IL-10), interlökin 18 (IL-18), tumor necrotizing factor alpha (TNF-α) etc.)

Conclusion

In this study, increased PLR, a simple non-specific inflammatory marker, was observed to be an independent predictor of subclinical atherosclerosis assessed by CIMT in people with dialysis patients. This finding is of clinical importance, since early initiation of preventive measures may prevent the progression of atherosclerosis.

Ethics Committee Approval: Ethics committee approval was received for this study from Clinical Research Ethics Committee of Ordu University.
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