RESEARCH ARTICLE

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Can the Triglyceride/HDL Ratio in Chronic Kidney Disease be Predictive of Cardiac Risk?

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Objective: Chronic Kidney Failure is one of the important causes of increased morbidity and mortality recently. Cardiovascular mortality is an important cause of mortality in patients with chronic kidney failure. It has been reported that triglyceride/high density lipoprotein ratio (TG/HDL) cholesterol ratio shows cardiac risk in previous studies. In our study, we aimed to show whether there is a relationship between TG/HDL cholesterol ratio and cardiovascular risk in patients with chronic renal failure receiving dialysis treatment and not.

Materials and Methods: A single-center retrospective study. In our study, 40 healthy, 50 dialysed patients with chronic renal failure and 50 patients without receiving dialysis (predialysis) who applied to internal medicine outpatient clinic were included. Patients' files were scanned retrospectively. TG/HDL ratios were recorded and calculated.

Patients who use lipid-lowering drugs and patients with diabetes were not included in our study.

Results: TG/HDL cholesterol ratio was found to be statistically significantly higher in predialysis patients and patients receiving dialysis due to chronic renal failure compared to healthy controls. TG/HDL cholesterol ratio was higher in patients with chronic renal failure that did not undergo dialysis compared to patients with chronic renal failure that were dialysed, but it was not statistically significant.

Conclusion: As an indicator of cardiovascular mortality due to chronic kidney disease, the TG/HDL-C ratio can be an inexpensive, reproducible predictor. TG/HDL-C ratio was found to be higher in patients with chronic kidney disease that did not undergo dialysis, compared to chronic kidney patients undergoing dialysis and the healthy control group.

Key Words: *Chronic renal failure, trigliserid/HDL cholesterol ratio, cardiac risk*

Kronik Böbrek Hastalığında Trigliserit/HDL Oranı Kardiyak Riskinin Öngördürücüsü Olabilir mi?

Amaç: Kronik Böbrek Yetmezliği, son zamanlarda artan morbidite ve mortalitenin önemli nedenlerinden biridir. Kardiyovasküler mortalite, kronik böbrek yetmezliği olan hastalarda önemli bir ölüm nedenidir. Önceki çalışmalarda trigliserid/HDL (TG/HDL) kolesterol oranının kardiyak riski gösterdiği bildirilmiştir. Çalışmada, diyalize girmeyen kronik böbrek yetmezliği ve diyalize giren kronik böbrek yetmezliği hastalarında TG/HDL kolesterol oranı ile kardiyovasküler risk arasında bir ilişki olup olmadığını göstermeyi amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmaya Dahiliye Polikliniği'ne başvuran 40 sağlıklı, 50 diyalizli kronik böbrek yetmezliği hastası ve diyalize girmeyen 50 kronik böbrek hastası dahil edildi. Hastaların dosyaları geriye dönük olarak tarandı. TG/HDL oranları kaydedildi ve hesaplandı.

Çalışmada lipid düşürücü ilaç kullanan hastalar ve diyabetli hastalar dahil edilmedi.

Bulgular: TG/HDL kolesterol oranı diyaliz öncesi ve kronik böbrek yetmezliği olan hastalarda sağlıklı kontrollere göre istatistiksel olarak anlamlı yüksek bulundu. TG/HDL kolesterol oranı, diyaliz uygulanmayan kronik böbrek yetmezliği olan hastalarda, diyaliz yapılan kronik böbrek yetmezliği hastalarına göre daha yüksekti, ancak istatistiksel olarak anlamlı değildi.

Sonuç: Kronik böbrek hastalığına bağlı kardiyovasküler mortalitenin bir göstergesi olarak, TG/HDL-C oranı ucuz, tekrarlanabilir bir prediktör olabilir. Diyalize giren kronik böbrek hastaları ve sağlıklı kontrol grubuna göre diyalize girmeyen kronik böbrek hastalığı olanlarda TG/HDL-C oranı daha yüksek bulundu.

Anahtar Kelimeler: *Kronik böbrek yetmezliği, trigliserid/HDL kolesterol oranı, kardiyak risk*

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Introduction

Kidney injury is considered as renal dysfunction or structural damage to the kidney according to the 2012 Kidney Disease Improving Global Outcomes (KDIGO), Kidney Disease Outcomes and Quality Initiative (KDOQI), and National Kidney Foundation (NKF) guidelines. Indicators of this damage are proteinuria, albuminuria (>30 mg/day), abnormal urine deposits, histological disorders detected by biopsy, history of kidney transplantation, and radiologically detected renal parenchymal damage (1).

According to 2016 data of Turkish Society of Nephrology (TSN), source of the most accurate and accessible information on End-Stage Renal Disease (ESRD) in Turkey, the point prevalence of ESRD requiring renal replacement therapy in Turkey

was 933 per million population (this number includes pediatric patients). The incidence of renal replacement therapy (RRT) in Turkey was 140 per million population, including pediatric patients according to 2016 TSN data (2).

Patients with chronic kidney disease (CKD) appear to have a much higher risk of cardiovascular disease compared to the general population. For example, the prevalence of coronary artery disease is approximately 40% and the prevalence of left ventricular hypertrophy is approximately 75% among patients treated with hemodialysis or peritoneal dialysis. Cardiovascular mortality is estimated to be approximately 9% per year in patients with CKD. Annual cardiovascular mortality rate in patients with CKD is estimated to be about 9%. Cardiovascular mortality is 10 to 20 times higher in dialysis patients compared to the general population (3). Low HDL level and high triglyceride (TG) level are independent risk factors for the development of atherosclerosis and coronary artery disease in the general population (4).

Characteristic lipoprotein abnormalities in uremia contribute to the prevalence of cardiovascular mortality and CVD in patients with ESRD. More than 90% of patients in the hemodialysis (HD) population have dyslipidemia with increased concentration of TG-rich apo-B containing lipoproteins, VLDL and LDL, and low high density lipoprotein ratio (HDL) level. These lipoprotein changes promote atherosclerosis and represent risk factors for developing cardiovascular disease in the ESRD population (5).

The TG/HDL-cholesterol ratio is a good marker in the evaluation of insulin resistance and early CVD. A TG/HDL-C ratio of less than 0.87 is considered ideal in some studies. Triglyceride/HDL-cholesterol ratio above 1.74 is a very high risk for coronary artery disease (6).

In the present study we aimed to show the correlation between the Triglyceride/HDL ratio and cardiac risk, and the correlation between dialysis and CKD with increased cardiac risk by reviewing the archives of people with CKD disease who are on dialysis, people with CKD disease who are not on dialysis, and healthy people.

Materials and Methods

Ethic Committie Approval: The ethics committee and work permits from Cumhuriyet University Ethic Commitie were taken with 20.05.2020 date and number 2020-05/18.

40 healthy patients with normal kidney function tests, 50 patients with chronic renal failure but who has never undergone dialysis, and 50 patients with chronic renal failure undergoing dialysis, who were admitted to the Sivas Cumhuriyet University Internal Medicine Outpatient Clinic, were included in our study. A complete blood count, urea, creatinine, glucose, sodium, potassium, calcium, phosphorous, total cholesterol, LDL cholesterol, HDL cholesterol, TG levels of the patients recorded in our hospital system were scanned and recorded. Blood tests were not performed except for routine examinations. Patients using lipid-lowering agents were not included in our study.

Statistical Analysis: Statistical comparisons were made using the statistical software package SPSS 23.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnow test was used for data with normal distribution. The Student t-test was used to compare parameters without a normal distribution, and the Mann–Whitney U test for parameters with a normal distribution. A chi-squared test was used to compare categorical variables. The results of statistics were noted as “mean ± standard deviation (SD)” and “Median (interquartile, IQR)”. P value of 0.05 was considered as statistically significant.

Results

The mean age of 130 patients included in our study was 76.33±5.39, BMI 27.49±5.14, creatinine 3.04±2.72, calcium 9.03±0.62, haemoglobin 12.54±2.11, TG 1.51±0.75, HDL-cholesterol 1.18±0.34, and TG/HDL-cholesterol ratio 1.48±1.07 (Table 1).

Table 1. Demographic and laboratory data of the patients included in the study

	Mean±Standart Deviation
Age (year)	76.33±5.39
Weight (kg)	74.06±14.19
Length (cm)	164.18±8.40
Creatinin (mg/dL)	3.04±2.72
Total protein (mg/L)	69.97±5.16
Albumin (mg/L)	40.71±5.07
Calcium (mg/dL)	9.03±0.62
Phosphorus (mg/dL)	3.75±0.85
Parathormon (pg/mL)	161.13 (8.4-1434.3)
Hemoglobin (g/dL)	12.54±2.11
C reactive protein (mg/L)	0.75±1.12
CKD_EPI (mL/dk/1.73m^2)	38.0 (3.2-90)
Body mass index (kg/m^2)	27.49±5.14
Triglyceride (mmol/L)	1.51±0.75
HDL (mmol/L)	1.18±0.34
TG/HDL ratio	1.48±1.07

HDL: High density lipoprotein; TG/HDL: Trigliyceride/high density lipoprotein ratio

In our control group, CKD group not undergoing dialysis, and CKD group undergoing dialysis, the mean age was 75±5, 77±6, and 76±5; creatinine level was 0.89±0.14, 1.41±0.33, and 5.97±2.24; calcium level was 9.37±0.52, 9.18±0.44, and 8.67±0.66; TG level was 1.25±0.49, 1.67±0.87, and 1.51±0.73; HDL-cholesterol level was 1.29±0.31, 1.12±0.36, and 1.17±0.32; TG/HDL-cholesterol ratio was 1.04±0.51, 1.74±1.27, and 1.48±1.02, respectively (Table 2).

Levene’s test was performed to determine the homogeneity of the variance between the groups before the ANOVA test. It was determined as a result of this test that the variance between the groups was not homogeneous (P<0.05).

Table 2. Evaluation of laboratory and demographic data of predialysis and dialysis groups by control group

	Control	Predialysis	Dialysis
Age (year)	75±5	77±6	76±5
Weight (kg)	77±11	80±13	67±14
Length (cm)	164±6	166±11	162±6
Creatinin (mg/dL)	0.89±.0.14	1.41±0.33	5.97±2.24
Total protein (mg/L)	70.1±3.6	70.3±5.2	69.6±5.9
Albumin (mg/L)	44.1±2.7	42.2±3.7	37.2±5.3
Calcium (mg/dL)	9.37±0.52	9.18±0.44	8.67±0.66
Phosphorus (mg/dL)	3.37±0.43	3.37±0.55	4.35±0.94
Parathormon (pg/mL)	50.3±22.8	68.8±32.3	320.0±293.4
Hemoglobin (g/dL)	14.07±1.52	13.33±1.72	10.84±1.53
C reactive protein (mg/L)	0.467±0.890	0.575±0.934	1.094±1.332
CKD_EPI (mL/dk/1.73m^2)	75.88±9.33	43.67±8.51	9.84±6.70
BMI (kg/m^2)	28.36±4.16	29.18±4.83	25.29±5.26
Triglyceride (mmol/L)	1.25±0.49	1.67±0.87	1.51±0.73
HDL (mmol/L)	1.29±0.31	1.12±0.36	1.17±0.32
TG/HDL ratio	1.04±0.51	1.74±1.27	1.48±1.02

HDL: High density lipoprotein; TG/HDL: Trigliyceride/high density lipoprotein ratio

Table 3. Evaluation of triglyceride/HDL cholesterol ratio and control group and CKD patients who are on dialysis and not on dialysis

Group		Mean±Standart Deviation	P
Control	Predialysis	0.706±0.20	0.003
	Dialysis	0.439±0.17	0.037
Predialysis	Control	0.706±0.20	0.003
	Dialysis	0.266±0.23	0.579
Dialysis	Control	0.439±0.17	0.037
	Predialysis	0.266±0.23	0.579

F-test was performed to determine whether the TG/HDL ratio between the groups was different. It was concluded as a result of this test that the ratio differed between the groups ($F=4.303$, $P<0.05$).

As a result of the Tamhane Post-Hoc test, which was conducted because the variance structure between groups was not homogeneous, while the mean TG/HDL ratio of the control group was lower than the predialysis and dialysis patients, with a statistically significant difference, the predialysis patients had a higher rate than dialysis patients, however this rate was not statistically significant. TG/HDL-cholesterol ratio was also statistically significantly higher in CKD patients not undergoing dialysis compared to the control group (1.04±0.51, 1.74±1.27 P=0.003). TG/HDL-cholesterol ratio was also found to be statistically significantly higher in CKD patients undergoing dialysis compared to the control group (1.04±0.51, 1.48±1.02 P=0.037). TG/HDL-cholesterol ratio was found to be higher in CKD patients not undergoing dialysis compared to CKD patients undergoing dialysis, with no statistically significant difference between these two groups (1.74±1.27, 1.48±1.02 P=0.579) (Table 3).

Discussion

The necessary significance of abnormal lipoprotein values in uremia and associated coronary heart disease in patients with ESRD cannot be demonstrated by regular cholesterol measurement. Therefore, it was stated that a specific method based on LDL cholesterol, HDL-cholesterol, and triglycerides should be developed to identify kidney patients with high cardiovascular risk requiring lipid-lowering treatment (7).

Uremia is considered to be an indicator of the activated acute phase response. Increased levels of IL-6 and CRP in serum are thought to be predictors of cardiovascular mortality in hemodialysis patients. Some acute phase proteins such as fibrinogen and lipoprotein a, known determinants of coronary artery diseases, are elevated in plasma in hemodialysis patients in this current inflammatory condition (8).

Serum TG levels increase due to the production and storage of TG-rich lipoproteins such as VLDL in ESRD. In parallel with this, components of high-TG lipoproteins, such as apoB, apoC-III and apo-E, are found at a high concentration in ESRD. On the other hand, levels of a number of antiatherogenic markers are reduced, especially where low HDL-cholesterol and apoA-I levels are most noticeable (9).

Combined hyperlipidemia (high cholesterol and triglycerides) with low HDL-cholesterol levels reflects a higher atherogenic event than isolated LDL cholesterol elevation. Studies have shown that cholesterol ester transfer from HDL decreases in hemodialysis patients, resulting in impaired reverse cholesterol transport. Individuals with high TG levels appear to have high-risk lipoprotein subclass profiles that worsen if they have underlying diabetes mellitus. Oxidized lipoproteins can affect endothelial vasodilation and vascular apoptotic cell death through stimulation of O_2 formation (10).

Patients with ESRD are at high risk not only for decreased renal function but also for the development of atherosclerosis due to changes in lipid metabolism. Therefore, these high-risk patients should be identified, and their cardiovascular mortality should be reduced with adequate lipid-lowering treatment as there is evidence of the effectiveness of lipid reduction in reducing cardiovascular mortality (11).

Small dense LDL-cholesterol (sdLDL-C) levels were monitored for four years and fifty-four cardiovascular events were detected in a retrospective study including one hundred and forty-five patients with ESRD. A strong correlation was found between sdLDL-C and cardiovascular disease risk in patients with ESRD as a result of this study (12).

77.762 (85.6%) of the patients were grouped as having myocardial infarction without coronary artery disease and 13.033 (14.4%) as having myocardial infarction due to coronary artery disease in a study involving 90.795 hemodialysis patients. Hypercholesterolemia was shown to be closely associated with increased mortality in the myocardial infarction group without coronary artery disease according to this study (13).

The causes of increased serum TG/HDL-C ratio and its association with cardiovascular mortality were investigated in a study including approximately 50.000 hemodialysis patients with ESRD. This study showed that increased TG/HDL-C ratios predicted negative cardiovascular disease outcomes in individuals with chronic renal failure (14).

TG/HDL-C ratio is a reliable and easily accessible marker to evaluate cardiovascular mortality and survival in patients without diabetes (15). 60% of deaths occurred during the 4-year follow-up period due to cardiovascular disease, and high serum TG/HDL-C ratios have been shown to be associated with increased risk of cardiovascular disease mortality and all mortality causes in peritoneal dialysis patients in a study on 1.170 patients with CKD undergoing peritoneal dialysis (16).

In a study involving 7.000 patients diagnosed with acute myocardial infarction, the TG/HDL-C ratio was compared, and the patients were divided into three groups according to glomerular filtration rate (GFR). Major cardiovascular events were recorded in 593 patients during the one-year follow-up. A significant correlation was found between TG/HDL-C ratio and major cardiovascular diseases (such as cardiac death, myocardial infarction, repeated percutaneous coronary intervention) in the entire study group. When kidney functions were examined afterwards, renal function was found to be significantly correlated with high TG/HDL-C ratio and cardiovascular events in patients with normal renal function and mild renal dysfunction. TG/HDL-C ratio has been reported to be an easy-to-use and independent predictor for one-year follow-up in patients with acute myocardial infarction (17).

As a result, chronic renal failure is a very common condition worldwide. It is thought that it will be the main cause of morbidity and mortality in subsequent decades. TG/HDL-cholesterol ratio can be used as a cheap, reproducible predictor of cardiovascular mortality, particularly due to CKD. TG/HDL-cholesterol ratio was found to be higher especially in patients with CKD not undergoing dialysis compared to chronic kidney patients undergoing dialysis and healthy control group. In conclusion, it can be said that dialysis in CKD leads to a decrease in cardiovascular mortality even though the mechanism is not clear according to these results, and we need a large number of clinical studies on this subject that cover a wide range of patients.

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