# **Original Article**



# Comparison of different lipid abnormalities between hemodialysis and peritoneal dialysis in patients with ESRD

Naimeh Mesri Alamdari<sup>®</sup>, Sahar Allahverdikhan-Vaziri, Mehran Rahimi, Vahideh Sadra<sup>•®</sup>

Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

\*Corresponding Author: Vahideh Sadra, Email: sadra.vahideh@gmail.com

## Summary

**Background:** cardiovascular disease is the most common cause of death in patients with chronic kidney disease. Abnormalities of plasma lipids and lipoproteins are the underling cause in chronic kidney disease (CKD) patients. This study aimed to determine the prevalence of lipid disorders in end-stage renal disease (ESRD) patients undergoing hemodialysis (HD) and peritoneal dialysis and compare them between two groups.

**Methods:** This cross-sectional study evaluated the lipid profile of 300 ESRD patients (150 HD and 150 PD) at baseline and one year after dialysis using the patients' documents.

**Findings:** One year after dialysis, serum total cholesterol, triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels were significantly higher in patients undergoing PD in comparison with HD groups ( $195.57 \pm 47.61 \text{ mg}$ /dL vs.  $157.89 \pm 44.04 \text{ mg}$ /dL (P < 0.001),  $197.18 \pm 18.70 \text{ mg}$ /dL vs  $152.68 \pm 75.84 \text{ mg}$ /dL (P < 0.001), and  $105.87 \pm 35.45 \text{ mg}$ /dL vs  $87.69 \pm 15.91 \text{ mg}$ /dL (P = 0.002). Serum high-density lipoprotein cholesterol (HDL-C) levels were lower in HD patients relative to PD ( $39.33 \pm 13.86 \text{ mg}$ /dL vs.  $51.92 \pm 20.11 \text{ mg}$ /dL (P < 0.001)). We observed a significantly higher frequency of serum TG > 200 mg/dL and LDL-C > 130 mg/dL in patients undergoing PD relative to HD. Serum HDL-C levels less than 40 mg/dL in men and less than 50 mg/dL in women were significantly more frequent in HD patients.

**Conclusion:** The results of our study showed that dyslipidemia is more prevalent in ESRD patients undergoing PD which may cause cardiovascular events.

Keywords: End-stage renal disease, Chronic kidney disease, Dyslipidemia, Cardiovascular disease

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# Introduction

End-stage renal disease is one of the most common public health problems globally. It is estimated that the prevalence of end-stage renal disease (ESRD) is about 29%-68% globally.<sup>1,2</sup> With a glomerular filtration rate (GFR) less than 15 mL/min, ESRD patients fall into the GFR category G5. Therefore, this amount of renal function is insufficient to filter the body's blood and survive; they need replacement treatments, including hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation. The most common type is HD treatment.<sup>3</sup>

The risk of cardiovascular disease, the leading cause of death in ESRD patients, is 5-10 times higher than the general population. The leading causes of cardiovascular disease in these patients are mostly diabetes, hypertension (HTN), albuminuria, dyslipidemia, and smoking.<sup>4</sup>

Abnormalities of plasma lipids and lipoproteins are prevalent in chronic kidney disease (CKD) patients. The concentration of triglyceride (TG) in triglyceride-rich lipoproteins, very low-density lipoproteins (VLDLs) and chylomicron is increased due to the decreased lipoprotein lipase activity, and the decreased hepatic lipase activity which results in an increased concentration of the atherogenic remnants of VLDLs and chylomicrons. The concentration of high-density lipoprotein cholesterol (HDL-C) is increased with reduced lecithin-cholesterol acyltransferase activity and increased activity of cholesteryl ester transfer protein. These changes in lipoproteins contribute to the increased risk of cardiovascular disease in ESRD patients.<sup>5,6</sup>

Differences in lipid metabolism and profile have been observed between HD and PD. Some studies have reported more atherogenic lipid profiles in patients on PD. Plasma lipoprotein (a) (LP(a)) levels are increased in PD patients compared to patients receiving HD, probably due to enhanced synthesis in the liver secondary to protein loss.<sup>7,8</sup> Moreover, cardiovascular death has been seen with an increased hazard in PD patients one year after initiation of dialysis.<sup>9</sup> However, some studies have reported no significant difference in de novo major ischemic heart disease risk between the two modalities.<sup>10,11</sup>

Although statins in the early stages of CKD effectively reduces the risk of atherosclerosis in HD patients, but do not affect the survival of patients.<sup>12,13</sup>

Given the importance of timely intervention in lipid disorders to reduce the risk of cardiovascular disease, increase the lifespan and prognosis of ESRD, this study aimed to comparison of the lipid profile and the dyslipidemia frequency in ESRD patients undergoing HD and PD.



# Methods

This is the cross-sectional study which was conducted on ESRD patients who went under HD or PD at the Imam Reza hospital, Tabriz, Iran on May to August 2020. Each group consist of 150 individuals which were selected using random sampling method and the random number table.

The inclusion criteria were patients over 18-year-old under HD or PD, receiving dialysis for at least one year, not changed their dialysis methods over the past year, have no familial lipid disorders. The exclusion criteria were as follows; patients with a history of kidney transplant, receiving immunosuppressive drugs, active liver disease, diagnosed with malignancy. Medical records of the patients were used to collect the data needed for the study.

Hypertension was defined as systolic blood pressure higher than 140 mm Hg and/or diastolic blood pressure higher than 90 mm Hg. According to the American Diabetes Association, diabetes mellitus (DM) criteria is a fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, or a 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT), or a random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, or a hemoglobin A1c (HbA1c) level of 6.5% (48 mmol/mol) or higher.<sup>14</sup>

According to the US National Cholesterol Education Program guidelines, total cholesterol levels more than 240, low-density lipoproteins cholesterol (LDL-C) levels more than 130, and TG levels more than 200 were defined as high, and HDL-C levels less than 40 were considered as low.<sup>15</sup>

#### Statistical analysis

The Kolmogorov-Smirnov test was used to check the normal distribution of the data. Mean and standard deviation were used for the quantitative variables. Also, percentages and frequency were used to measure qualitative variables. Independent t test and chi-square test was used for the comparison between two groups. Analysis of covariate (ANCOVA) was applied to adjust age, weight, body mass index (BMI), sex, DM, HTN, and infection. Data were analyzed through the SPSS Statistics software version 26. *P* value less than 0.05 was assumed as statistically significant.

## Results

About 300 ESRD patients (150 patients on HD, group and 150 patients on PD group) were evaluated in this study. mean age of participants were  $57.28 \pm 16.71$  years, 53.3% were men, and the most common comorbidity was HTN. The patients' baseline characteristics are shown in Table 1. The studied groups are different in terms of age, weight, height, BMI, sex, HTN and DM (*P*<0.05).

The lipid profile comparisons at baseline and one year

Table 1. Baseline characteristics of the study population

Variable		Hemodialysis group (n=150)	Peritoneal dialysis group (n=150)	P value
Age (y)		$63.72 \pm 13.57$	50.7±17.10	< 0.001
Weight (kg)		71.80±13.31	$63.14 \pm 14.27$	< 0.001
Height (m)		$1.66 \pm 0.10$	$1.63\pm0.09$	0.032
BMI (kg/m <sup>2</sup> )		$25.7 \pm 5.02$	$23.55 \pm 4.52$	< 0.001
Gender	Male	97 (64.7%)	63 (42%)	< 0.001
	Female	53 (35.3%)	33 (58)	
Diabetes mellitus		81 (54%)	33 (22%)	0.001
Hypertension		114 (76%)	49 (32.7%)	0.001
Glomerulonephritis		3 (2%)	4 (2.7%)	0.702
Renovascular disease		2 (1.3%)	2 (1.3%)	1.000
Infection		1 (0.7%)	8 (5.3%)	0.018
Nephrolithiasis		7 (4.7%)	11 (7.3%)	0.331
Polycystic kidney disease		9 (6%)	5 (5.3%)	0.274
Statin use		37 (24.7%)	26 (14.3%)	0.119
Fibrate use		1 (0.7%)	5 (3.3%)	0.099
Corticosteroid use		1 (0.7%)	6 (4%)	0.056

after dialysis are manifested in Table 2. All lipid profile components differed significantly between two groups at baseline and one year after dialysis, except LDL-C at baseline. Lipid profile changes after one year of dialysis were only significant for LDL-C levels (P=0.03).

The frequency of dyslipidemia at baseline and one year after dialysis is shown in Table 3. The analysis was adjusted for age, BMI, gender, DM, and HTN. One year after initiation of dialysis, the number of patients with low serum HDL-C levels was significantly higher in HD patients (P=0.004). Furthermore, one year after dialysis, the frequency of high serum TG and LDL-C levels was higher in the PD group (P=0.003, P=0.045).

# Discussion

Cardiovascular disease is the leading cause of death in patients with CKD. Dyslipidemia is accused for the cardiovascular disease. It should be noted that even a mild reduction in kidney function is a significant risk factor for atherosclerotic cardiovascular disease.

The present study results showed that the serum total cholesterol, TG, and LDL-C levels were significantly higher in patients undergoing PD. Serum HDL-C levels were significantly lower in HD patients one year after dialysis.

HDL-C dysfunction is recognized as a hallmark in ESRD patients. In HD patients, HDL's anti-inflammatory and anti-apoptotic functions are suppressed. Nevertheless, in PD patients, paraoxonase activity associated with HDL-C is low.<sup>16</sup> The main lipid abnormality in ESRD associated with atherogenesis is the LDL-C and HDL-C subclass pattern changes toward smaller sub fractions. HDL-C sub fractions are influenced in ESRD; HD patients have

Table 2. Comparison of	ipid profile at baseline and	one year after dialysis
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Variable		Hemodialysis (n=150)	Peritoneal Dialysis (n=150)	P value
Total cholesterol (mg /dL)	Baseline	$161.02 \pm 44.19$	$189.19 \pm 46.56$	< 0.001
	OYAD	$157.89 \pm 44.04$	$195.57 \pm 47.61$	< 0.001
	Difference	$-3.13 \pm 46.35$	$7.13 \pm 43.72$	0.092
Triglyceride (mg /dL)	Baseline	158.3±4 80.72	$190.27 \pm 114.07$	0.010
	OYAD	$152.68 \pm 75.84$	$197.18 \pm 118.70$	< 0.001
	Difference	$-6.05 \pm 74.74$	$6.90 \pm 117.75$	0.165
LDL-C (mg /dL)	Baseline	$91.89 \pm 37.27$	$100.45 \pm 35.30$	0.651
	OYAD	$87.69 \pm 35.91$	$105.87 \pm 35.45$	0.002
	Difference	$-4.19 \pm 40.51$	$5.41 \pm 41.34$	0.034
HDL-C (mg /dL)	Baseline	$37.73 \pm 13.42$	$50.32 \pm 17.78$	< 0.001
	OYAD	$39.33 \pm 13.86$	$51.92 \pm 20.11$	< 0.001
	Difference	$1.60 \pm 17.16$	$1.60 \pm 21.34$	0.691

OYAD, One-year after dialysis; TG, Triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

more large HDL-C subfractions compared to healthy individuals. Thus, the quality may be more important than the serum levels.<sup>17,18</sup> The study conducted by Moradi et al. studied the lipid profile of 33 109 chronic HD patients and the relationship between lipid profile and mortality. They reported that as the level of HDL-C in plasma increases, the mortality rate decreases. However, when plasma HDL-C levels approach 50 mg /dL, this trend is reversed, and HDL-C greater than 60 mg /dL increases mortality. Therefore, the relationship between HDL-C and mortality was shown as a U-shaped pattern.<sup>19</sup> In our study, serum HDL-C levels were significantly lower in HD patients at baseline and one year after dialysis, and the prevalence of low serum HDL-C levels was higher in patients on HD at baseline and one year after dialysis. While several studies have reported no significant difference between the two groups,<sup>20-22</sup> the study conducted by Kadiroğlu et al reported that HDL-C levels were significantly higher in icodextrin based PD patients after at least three months of dialysis.<sup>23</sup>

LDL-C levels are a known risk factor for cardiovascular disease. Lowering LDH-C levels is an accepted treatment to reduce cardiovascular disease risk, but many ESRD patients experience cardiovascular events, even with normal LDL-C serum levels. Some articles have reported that LDL-C particle number has a stronger association with the disease than LDL-C or HDL-C.24 Due to daily losses of protein, PD creates a condition in the human body that resembles nephrotic syndrome and heavy proteinuria. Thus, PD patients develop hypercholesterolemia and elevated serum levels of LDL-C ascribed to mechanisms that also happen in nephrotic syndrome.<sup>6,25</sup> As earlier noted, LP(a) levels are higher in patients on PD due to protein loss. This pro-inflammatory and atherogenic lipoprotein is a fraction of the reported LDL-C levels, and laboratory methods do not distinguish LDL-C cholesterol from LP(a). This makes serum LDL-C levels

Table 3. The frequency of dyslipidemia at baseline and one year after dialysis

Variable		Hemodialysis (n=150)	Peritoneal dialysis (n=150)	P value
Total cholesterol >240	Baseline	10 (6.7%)	22 (14.7%)	0.099
mg /dL	OYAD	7 (4.7%)	20 (13.3%)	0.166
TC > 200 mg /dl	Baseline	31 (20.7%)	50 (33.3%)	0.133
1G>200 mg/dL	OYAD	37 (24.8%)	54 (36%)	0.003*
IDI C> 120 mg /dl	Baseline	18 (12%)	27 (18%)	0.932
LDL-C > 150 Hig /dL	OYAD	15 (10%)	42 (28%)	0.045*
HDL-C<40 mg/dL in men	Baseline	113 (75.3%)	61 (40.7%)	< 0.001
HDL<50 mg /dL in Women	OYAD	108 (72%)	55 (36.7%)	0.004*

OYAD, One-year after dialysis; TG, Triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

\*P < 0.05 statistically significant.

much more critical in atherosclerosis risk assessment in these patients.<sup>7,8,26</sup>

The present study reports no difference in the prevalence of high serum cholesterol levels between the groups. The prevalence of high serum TG and LDL-C levels was significantly higher in the PD group. Serum total cholesterol, TG and LDL-C levels were significantly higher at baseline and one year after dialysis in PD patients. In contrast to our study, Kadiroğlu et al reported higher TG levels in HD patients.<sup>23</sup> In a study including 919 patients which compared patients on dialysis in Italy and China, after five years of follow-up, serum levels of total cholesterol, TG, and LDL-C were reported to be higher in the patients on PD. There was no difference at the baseline.<sup>27</sup>

Studies have shown, however, that treatment of dyslipidemia with statins in the early stages of CKD effectively reduces the risk of atherosclerosis, but in patients undergoing HD, it does not affect the survival of these patients. Vaziri and Norris, in their study, attributed this to the changes in ESRD that are unfixable by inhibiting cholesterol synthesis. These abnormalities include HDL-C deficiency and dysfunction, more abundant small subfractions of LDL, oxidative stress, and inflammation.<sup>28</sup> Treatment for lipid abnormalities in ESRD patients receiving dialysis should be personalized based on dialysis modality, patient-specific factors, and the nature of dyslipidemia observed in every patient.<sup>29</sup>

Although the pathophysiology of differences in patients' lipid profiles on different dialysis types has not yet been clearly explained, it is suggested that glucose uptake from dialysis fluid may play an influential role in increasing insulin levels and increase hepatic VLDL-C synthesis and secretion.<sup>30</sup> While there is no direct relationship between serum lipid levels and glucose uptake from peritoneum in patients on PD, recent studies have shown that low glucose utilization using Icodextrine or amino-acidbased solutions effectively improves the lipid profile of these patients.  $^{\rm 31-33}$ 

# Limitations

There were some limitations of this retrospective study that needs to be acknowledged. First, the baseline characteristics of the groups were not completely matched. We used ANCOVA and binary logistic regression to overcome this problem. Second, the sample size was not large enough to conclude confidently. Third, we did not measure apolipoproteins in patients. Aplolipoproteins play an essential role in lipid metabolism. Therefore, there is a need for large-scale studies investigating the role of apolipoproteins in dyslipidemia in dialysis patients.

# Conclusion

The results of our study showed that after one year of dialysis, the total cholesterol, TG, and LDL-C levels of ESRD patients undergoing PD were significantly higher than that of HD patients, which is similar to previous studies. Serum HDL-C levels were significantly lower in patients on HD.

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# **Authors' Contribution**

Conceptualization: Vahideh Sadra. Data curation: Naimeh Mesri Alamdari. Formal analysis: Naimeh Mesri Alamdari. Funding acquisition: Vahideh Sadra.

Investigation: Sahar Allahverdikhan-Vaziri.

Methodology: Sahar Allahverdikhan-Vaziri.

Project administration: Vahideh Sadra.

Resources: Vahideh Sadra.

Supervision: Vahideh Sadra.

Validation: Mehran Rahimi.

Visualization: Vahideh Sadra.

Writing-original draft: Naimeh Mesri Alamdari, Sahar Allahverdikhan-Vaziri, Mehran Rahimi.

Writing-review & editing: Naimeh Mesri Alamdari, Vahideh Sadra.

# **Competing Interests**

The authors declare no conflict of interest.

# **Ethical Approval**

The experimental protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences (Ethical code: IR.TBZMED.REC.1398.723). Informed consent was taken from all participants. The study was executed in agreement with the protocols of the Declaration of Helsinki and the Guideline for Good Clinical Practice.

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