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ORIGINAL ARTICLE

Frequency of Dyslipidemia among End-Stage Renal Disease Patients on Thrice Weekly Maintenance Hemodialysis

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ABSTRACT

Background: Serum lipid abnormalities are strongly related to cardiovascular as well as all-cause mortality. The most common dyslipidemia among dialysis patients is low HDL followed by hypertriglyceridemia. Total cholesterol and LDL levels are normal. Dyslipidaemia in end-stage renal disease is multifactorial in addition to abnormalities in lipid metabolism, malnutrition, inflammation, low albumin, and inadequate hemodialysis also contribute to premature atherosclerosis. That's why treatment of dyslipidemia in hemodialysis patients should be individualized.

Objective: To determine the frequency of dyslipidemia among patients of end-stage renal disease on thrice-weekly hemodialysis.

Study Design: Cross-sectional study

Place and Duration of Study: Dialysis Unit, Department of Nephrology Sir Ganga Ram Hospital, Lahore from 1s9th March 2021, to 18th September 2021

Methodology: Seventy two patients having maintenance HD at our center were enrolled. The data included the patient's name, age, gender, duration of maintenance hemodialysis, BMI, HTN, DM, IHD, and smoking status. Fasting lipid samples of patients were collected in serum vials and samples were analyzed in the major laboratory for any lipid abnormality.

Results: Forty four (61.1%) patients have dyslipidemia among which 27 (61.4%) were males and 17 (38.6%) were females. The mean age was 47.5±11.5 years. The most common lipid abnormality in our patients was low HDL levels i.e., 56.8% followed by hypertriglyceridemia 6.9%. Total cholesterol and LDL levels are normal in 98% and 100% respectively.

Conclusion: The frequency of dyslipidemia among patients of thrice-weekly maintenance hemodialysis is 61.1%. Low HDL is the most common lipid abnormality followed by hypertriglyceridemia 56.8% and 6.9% respectively.

Key words: Dyslipidemia, End-stage renal disease (ESRD), Hemodialysis

INTRODUCTION

Chronic kidney disease (CKD) is a global health burden exhibiting rising frequency and prevalence, having a negative impact on the economy and a significant surge in morbidity and mortality.[1,2] Irreversible deterioration in renal structural or functional capability persisting for more than 3 months is termed as CKD.[3] As per the latest National Health and Nutrition Examination Survey (NHANES) report and estimating the latest trends in the prevalence of CKD in the USA, it is revealed that the prevalence trend is static around 15%.[4] In Asian countries large-scaled data is sparse, however available data revealed 10-18% prevalence, while in Pakistan reported prevalence of CKD is 12.6% where GFR was measured using CKD EPI equation.[5] Globally over 2.6 million patients as of now get dialysis treatment.[6] Cardiovascular events and sepsis are two major factors having the highest contribution in mortality among hemodialysis (HD) patients.[7] The extraordinarily high death rate in end-stage renal disease (ESRD) patients going through HD is recorded, at 15%-20% per year in the USA. When compared to the general population, Cardiovascular mortality is 10 to 30 times higher in CKD patients.[8] Among HD patients enhanced cardiovascular mortality is linked to left ventricular hypertrophy, inadequate HD, oxidative stress, hyperphosphatemia, hypoalbuminemia, low hemoglobin levels, and advanced atherosclerosis.[9]

Dyslipidaemia, characterized by high triglyceride (TRIG) levels, high total cholesterol (TC, high low-density lipoproteins (LDL), and low levels of high-density lipoproteins (HDL)[10], is a key factor for the development of atherosclerosis subsequently leading to high cardiovascular mortality in the general population and CKD patients. In CKD patients delayed breakdown, increased production by the liver and inhibition of lipoprotein lipase leads to increased triglycerides levels. Oxidation of LDL is enhanced, although the absolute levels of LDL sometimes remain normal in CKD patients. The oxidized form of LDL is considered more atherogenic. HDL which in general term regarded as good cholesterol, mobilizes cholesterol from vessels back to the liver. In the uremic milieu, lecithin acyltransferase enzymatic activity is reduced, cholesterol ester transfer protein activity is increased and apolipoproteins 1 and 2 levels are reduced, ultimately leading to reduced HDL levels and blocking its functionality.[11]

Dyslipidemia spectrum is almost similar in HD as compared to CKD patients without HD support. Raised TRIG and low HDL are like CKD patients, but TC and LDL levels are generally normal in the HD population. Various studies have reported > 100mg/dl LDL levels in 57% HD patients linked to more than 50% cardiovascular mortality.[12] Reduced activity of lipoprotein and hepatic lipases, anticoagulants especially heparin, and use of low flux dialyzers are linked to increased TRIG levels. Low HDL levels in HD patients are mainly because of increased cholesterol ester transfer protein actions, use of acetate dialysate, and low flux dialyzers.[13] Recent KDIGO guidelines recommend the regular monitoring of dyslipidemia keeping in mind its strong association with mortality rates.

The purpose of this study is to check the frequency of dyslipidemia in patients of end-stage renal disease on thrice-weekly hemodialysis

MATERIALS AND METHODS

This single-center cross-sectionalobservational study was conducted at the Dialysis unit of Sir Ganga Ram Hospital, Lahore, from 18-3-2021 to 18-9-2021. Non-probability, convenient sampling technique was used and all the patients (72) who were receiving thrice-weekly hemodialysis were enrolled. Patients on hemodialysis for acute kidney disease were excluded from the study. After approval from the institutional ethical review board, 72 patients which fulfilled the inclusion criteria and those patients who have given consent were registered in this study from the dialysis unit of Sir Ganga Ram Hospital, Lahore. Fasting blood samples were collected and a lipid profile was done. Patients were evaluated for age, gender, body mass index, presence of hypertension (blood pressure >130/90), diabetes *HbA1c>6.5%), ischemic heart disease (history), smoking status, and duration of maintenance hemodialysis were registered. Dyslipidaemia was recorded as per operational definition (TRIG: elevated >200 mg/dl, HDL: reduced <35 mg/dl, Total cholesterol: elevated >240 mg/dl, LDL cholesterol: elevated >130 mg/dl). Data were analyzed in the

statistical package for social sciences v. 25. Qualitative variables (gender, dyslipidemia, diabetes, hypertension, and smoking) were measured in frequency and percentage. Quantitative variables i.e., age, body mass index, total cholesterol triglycerides, HDL were measured as mean and standard deviation. Effect modifiers like age, gender body mass index, diabetes, hypertension, smoker, maintenance hemodialysis duration were controlled through stratification. Post-stratification, the chi-square test was with a p-value equal to or less than 0.05 considered as statistically significant.

RESULTS

There were 46(63.9%) male patients and 26(36.1%) female patients. Among these patients 8.3% were from the age group 18-30 years, 54.2% were from the age group 31-50 years, 37.5% were from the age group above 51 years. Among them, most males were of age group 31-50 years (53.1%) whereas the mean age of the study population was 47.5 ± 11.5. Among these patients, 5(6.9%) have BMI <18, 47(65.3%) have BMI between 18 -25 and 20(27.8%) have BMI >25.Among these patients 25(34.7%) were diabetic, 69(95.8%) were hypertensive, 18 (25%) had ischemic heart disease and 7(9.7%) were smokers. Out of these 72 patients, 52(72.2%) were on dialysis for > than 3years, 15(18.1%) were on dialysis for 1-3 years, 1(1.4%) were on dialysis for 1year and 6(8.3%) were on dialysis for < 12months. Dyslipidaemia was observed in 61.1% of the study population. Among these patients 5(6.9%) has > 240mg/dl of triglyceride and 67(93.1%) has < 240mg/dl of triglyceride. There were 71(98.6%) patients with cholesterol <200mg/dl and 1(1.4%) with cholesterol > 200mg/dl. All patients 72(100%) have LDL Cholesterol < 130mg/d. HDL Cholesterol >30mg/dl was present in 31(43.1%) and <30mg/dl was present in 41(56.9%). Among a total of 46 male patients, 2(4.3%) were in the age group 18-30, 26(56.5%) were in the age group 31-50 and 18(39.1%) were in the age group 51 and above. Among a total of 26 female patients, 4(15.4%) were in the age group 18-30, 13(50%) were in the age group 31-50 and 9(34.6%) were of age group 51 and above.Among the total of 25 diabetic patients, 12(16.6%) were in the age group 31-50, 13(18.1%) were above 50 but no patient was in the age group 18-30. Total 69 patients were hypertensive among which 5(7.8%) were of age group 18-30, 38(51.5%) were of age group 31-50 and 26(35.9%) were above 50. 18 patients had IHD among which 18(18.1%) were in the age group 31-50 and 5(6.9%) were above 50. 7 patients were smokers among which 6(8.3%) were in the age group 30-50 and 1(1.4%) were above 51. Among diabetic patients, 89.5% were male whereas 10.5% were females. Hypertensive males were 67.2% whereas females were 32.8%. IHD was present in 84.6% of males and 15.4% of females. All smokers were males.On stratification of BMI with Gender 3.1% males and 4.7% females had BMI <18, 42% males and 23.4% females had BMI 18-25 and 18.7% males, and 7.8% females had BMI >25. Among diabetics 10.5% have BMI <18, 63.5% have BMI 18-25 and 23.6% have >25 BMI. Thus, most diabetics on MHD have normal BMI. Among hypertensive patients, 5(8.2%) has BMI<18 whereas 40(65.6%) has BMI between 18-25 and 16(26.2%) had >25 BMI.Among hypertensive patients, the most common dyslipidemia is low HDL that was 55.1% however triglycerides, total cholesterol, and LDL cholesterol were normal in the majority of the population i.e. 94.2%, 98.6%, and 100% respectively. Among diabetic patients, the most common dyslipidemia is low HDL that was 68% however triglycerides, total cholesterol, and LDL cholesterol was normal in the majority of the population i.e. 84%, 100%, and 100% respectively.In patients, IHD with the most common dyslipidemia is low HDL that was 66.7% however triglycerides, total cholesterol, and LDL cholesterol were normal in most of the population i.e., 83.3.3%, 100%, and 100% respectively.In smokers with the most common dyslipidemia is low HDL was 71.4% however triglycerides, total cholesterol, and LDL cholesterol were normal in the whole of the population i.e., 100%, 100%, and 100% respectively. In this study, dyslipidemia is more prevalent in the male population as compared to the female population, but it is statistically insignificant. Among diabetics, hypertriglyceridemia was statistically significant (p=0.03). No statistically significant association was found among dyslipidemia and gender, BMI and comorbidities such as HTN, IHD, and smoking. LDL levels were statistically significant in all variables<0.0001, as 100% of cases showed normal LDL levels (Table 1).

Table 1: Descriptive statistics of the patients

Variable	TRIG (mg/dl)		T. CHOL (mg/dl)		HDL (mg/dl)		LDL (mg/dl)	
	<200	>200	<240	>240	<30	>30	<130	>130
Gender								
Male	42 (58.3%)	4 (5.6%)	45 (62.5%)	1 (1.4%)	25 (34.7%)	21 (29.1%)	46 (63.9%)	-
Female	25 (34.7%)	1 (1.4%)	26 (36.1%)		16 (22.2%)	10 (13.8%)	23 (31.9%)	-
P value	0.44		0.45		0.55		< 0.0001	
Age (years)								
18-30	6 (9%)	-	6 (8.5%)	-	3 (7.3%)	3 (9.7%)	6 (8.3%)	-
31-50	37 (55.2%)	2 (40%)	38 (53.5%)	1 (100%)	21 (51.2%)	18 (58.1%)	39 (54.2%)	-
≥51	24 (35.8%)	3 (60%)	27 (38%)	-	17 (41.5%)	10 (32.3%)	27 (37.5%)	-
p-value	0.504		0.651		0.715		< 0.0001	
Body mass index (kg/m^2)								
Normal	5 (6.9%)	-	5 (6.9%)	-	3 (4.2%)	2 (2.8%)	5 (6.9%)	-
Overweight	44 (61.1%)	2 (2.8%)	45 (62.5%)	1 (1.4%)	23 (31.9%)	23 (31.9%)	42 (58.3%)	-
obese	18 (25%)	3 (4.2%)	21 (29.2%)	-	15 (20.8%)	6 (8.3%)	17 (23.6%)	-
p-value	0.27		0.75		0.26		< 0.0001	
HD duration								
3-6 months	6 (9%)	-	6 (8.5%)	-	5 (12.2%)	1 (3.2%)	6 (8.3%)	-
6-12months	1 (1.5%)	-	1 (1.4%)	-	1 (2.4%)	-	1 (1.4%)	-
1-3 year	13 (19.4%)	-	13 (18.3%)	-	9 (22%)	4 (12.9%)	13 (18.1%)	-
>3 years	47 (70.1)	5 (100%)	51 (71.8%)	1 (100%)	26 (63.4%)	26 (83.9%)	52 (72.2%)	-
p-value	0.599		0.942		0.232		< 0.0001	
IHD								
Yes	52 (77.6%)	2 (40%)	53 (74.6%)	1 (100%)	29 (70.7%)	25 (80.6%)	54 (75%)	-
No	15 (22.4%)	3 (60%)	18 (25.4%)	-	12 (29.3%)	6 (19.4%)	18 (25%)	-
p-value	0.061		0.561		0.336		< 0.0001	

DISCUSSION

HDL levels tend to decrease at the early stages of CKD, and as kidney functions decline further impairment in HDL levels is observed. This finding has raised questions regarding the dual relationship between CKD and HDL levels. Whether lower HDL is causing progression of CKD, or it is just an aftereffect of CKD is still a matter of debate. However, regardless of its dual

relationship, lower HDL levels are strongly related to cardiovascular mortality in HD patients.[14] The most common lipid abnormality in our patients was low HDL levels i.e. less than 30mg/dl seen in 56.8% of patients, it was comparable with Pennell P's review that showed 51 % low HDL levels.[15] HDL has against atherosclerosis impacts and its low levels are related to incremental cardiovascular events.[16] Lipid management guidelines recommend the use of statins to bring HDL levels above 45 mg/dl.[17]

Serum total cholesterol (TC) hasa complex relationship with all-cause mortality. It has been observed that high TC levels (250 - 300 mg/dl or more) have led to increasing all cause mortality modestly, while on the other hand low TC levels (less than 100mg/dl) showed 3 times greater risk of death as compared to its high levels. Low levels of TC directly depict low muscle mass and proinflammatory states which has a strong association with low serum albumin levels, high CRP levels, and all-cause mortality. In developing stages of kidney disease, TC levels are high, and the use of statins significantly reduces cardiovascular events. In HD patients TC are generally high as reported by various studies but the treatment of dyslipidemias with statins improved serum levels but failed to reduce cardiovascular mortality.[18] Normal TC levels have been reported in other studies as well.[11,19] In our study 98.6% of patients have normal TC levels and 100% showed normal LDL levels.

In our study hypertriglyceridemia was present in 6.9% of patients, in contrast to other studies that showedhigh TRIG levels up to 33%in HD patients.[19,11] The serum TRIG levelsare profoundly reliant upon the non-fasting condition of the patient, so they showed high changeability in various investigations. Moreover, the use of erythropoietin and high flux dialyzer tend to lower TRIG levels even without statins use.[20]

In this study, dyslipidemia is more prevalent in the male population as compared to the female population, but it is statistically insignificant. Among diabetics, hypertriglyceridemia was statistically significant (p=0.03). No statistically significant association was found among dyslipidemia and gender, BMI and comorbidities such as HTN, IHD, and smoking.

As per KDIGO recommendation, lipid-lowering treatment ought not to be begun in patients on dialysis however ought to proceed in patients currently on it.[21] Because of the complexity in dyslipidemia pathophysiology in HD patients, simply lowering lipids levels doesn't bring any benefits which were normally seen in the general population. Researchers relate this non-beneficial statins therapy effect to the presence of non-atherosclerotic cardiovascular disease in HD patients.[22]

CONCLUSION

We concluded that the frequency of dyslipidemia among patients of thrice-weekly maintenance hemodialysis is 61.1%. Low HDL is the most common lipid abnormality followed by hypertriglyceridemia 56.8% and 6.9% respectively. Total cholesterol and LDL levels are normal in 98% and 100% respectively.

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