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Original Article

Study of Lipid Profile in Patients with Chronic Kidney Disease on Conservative Management and Hemodialysis

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Abstract

Background: Chronic renal failure results in profound lipid disorders which stem largely from the deregulation of high-density lipoproteins (HDL) and triglyceride-rich lipoprotein metabolism which increases the risk of arteriosclerotic cardiovascular disease which is the leading cause of mortality among chronic kidney disease (CKD) patients.

Materials and Methods: This is a cross-sectional observational study conducted after ethical committee approval about lipid profile on CKD patients on conservative management and hemodialysis compared with normal healthy controls at our hospital and movement for global mental health between June 2015 and June 2016, after considering inclusion and exclusion criteria. Lipid profile was collected from eligible patients and controls.

Results: There were a statistically significant decrease in HDL and increase in thyroglobulin, low-density lipoprotein (LDL), and total cholesterol levels when compared with normal healthy controls. There was a negative correlation between serum creatinine and HDL levels. Among CKD patients, there was a significant decrease in HDL and increase in LDL level in both conservative and hemodialysis groups.

Conclusion: Treatment of dyslipidemia helps to decrease mortality in CKD patients.

Key words: Chronic kidney disease, Hypertriglyceridemia, Lipid profile

INTRODUCTION

Chronic kidney disease (CKD) has become a public health problem with a global prevalence of around 8–16%[1,2] and with an estimate of >10% (i.e., >20 million) prevalence in the adult United States population.[3] Data from National Health and Nutrition Examination Survey showed that CKD prevalence among ages 60 and above increased from 18.8% in 1988-1994 to 24.5% in 2003-2006.[4]

Cardiovascular diseases (CVD) remain the number one cause of death among patients with kidney diseases.[5,6] The United States Renal Data System 2013 annual data report indicates that CKD patients not only have higher rates of congestive heart failure, acute myocardial infarction, and cerebral vascular accident compared to non-CKD patients but they also have lower survival rates compared to non-CKD patients. This survival further decreases with severity of CKD.[7]

Dyslipidemia is a well-established risk factor for CVD in the general population but this relationship is not straightforward in CKD population. While dyslipidemia is associated with CVD in pre-dialysis CKD and hemodialysis population, data regarding its association in peritoneal dialysis patients is lacking. With an ever increasing CKD burden worldwide, providing treatments for modifiable risk factors, like dyslipidemia, becomes an essential component for improving outcomes.

Since hyperlipidemia can be modulated by therapeutic intervention, it is worthwhile to study and compare lipid profile abnormalities in CKD patients. Indian studies on lipid abnormalities in CKD have not been

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consistent. Sharma *et al.*[10] and Kunde *et al.*[11] found no hyperlipidemia, whereas Gupta *et al.*[12] and Das *et al.*[13] observed hypertriglyceridemia and reduced high-density lipoprotein (HDL) levels in CKD patients as in western countries. In view of inconsistency and limited evidence in the southern part of this country, it was decided to study the lipid profile in our patients with CKD patients.

Aims of the Study

The aims of this study are as follows:

1. To estimate various lipid profile abnormalities in CKD patients and normal healthy controls.
2. To study the correlation between the serum creatinine levels and lipid profile abnormalities in CKD.
3. To compare lipid profile in patients with CKD on conservative management and hemodialysis.

MATERIALS AND METHODS

This study was conducted in 50 patients with CKD and 50 normal healthy persons.

All the patients in this study group were selected from the Department of Medicine, MGM Hospital, Warangal, during June 2015–June 2016. The controls were selected from those who were accompanying the patients.

Study Design

This was a cross-sectional observational study.

Inclusion Criteria for Patients

The following criteria were included as patients in the study:

1. Patients between the age group of 15 and 85 years with established CKD.
2. Patients who were on conservative or dialysis treatment for CKD.
3. Established renal failure was ensured by radiological evidence or biochemical evidence for >3 months.

Inclusion Criteria for Controls

Normal healthy patients who were age and sex related to patients were included as controls.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients with acute renal failure and nephrotic syndrome.
2. Patients having diabetes, liver disease, Cushing's, or other metabolic disorder.
3. Those who are on drugs affecting lipid metabolism such as β-blockers, statins, and oral contraceptive pills.
4. Female patients who were pregnant.

Patients with CKD and controls included in the study were matched according to age and the results were analyzed.

Table 1: Age distribution in patients

Age in years	Number of patients (%)
15–25	2 (4)
26–35	14 (28)
36–45	11 (22)
46–55	11 (22
56–65	10 (20)
66–75	1 (2)
>75	1 (2)
Total	50 (100)

Table 2: Sex distribution

Gender	Total (%)
Male	34 (68)
Female	16 (32)

Table 3: Comparison of lipid profile between other studies and our study

Studies	TGL	LDL	HDL	TC
Shah *et al.*				
Study group	222.78	109.63	52.69	211.33
Control group	121.78	140.33	44.22	184.11
Diana *et al.*				
Study group	194.051	170.148	38.6	239.75
Control group	06.28	131.47	2.53	189.14
Our study				
Study group	186.86	131.57	42.82	209.29
Control group	102.18	112.26	54.14	184.89

TGL: Triglyceride, LDL: Low-density lipoprotein, HDL: High density lipoprotein, TC: Total cholesterol

Written consent was obtained from both patients and controls. A detailed history regarding symptoms and duration of the kidney disease, hypertension, diabetes, smoking, alcoholism, drug intake, and treatment was elicited.

A detailed clinical examination was performed in all patients. Blood pressure, renal function tests, and abdominal ultrasonogram were done for all patients. Blood sample was taken for lipid profile from patients and controls.

ATP-III NCEP guidelines were applied to the lipid profile.

Glomerular filtration rate (GFR) was calculated using modification of diet in renal disease (MDRD) formula:

$$GFR\ (mL/min/1.73\ m^2) = 175 \times (S_{cr})^{-r^5}\ mL/\times (Age)^{-} \times (Ag \times (0.742 \text{ if female}) \times (1.212 \text{ if African American}).$$

Table 4: Various studies on progression of kidney disease and associated plasma lipid abnormalities

Study	Patients	Number of patients	Follow up	Lipid
MDRD	CKD	840	2.2 years	↓HDL
Samuelsson *et al*.	CKD	73	3.2 years	↑TCh,↑LDL,↑ApoB
Locatelli *et al*.	CKD	456	2 years	No relationship
Massy *et al*.	CKD	138	12 years	↑TG,↓HDL
Our study	CKD	50	-	↓HDL,↑TG↑TC,↑ LDL

TGL: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TC: Total cholesterol, CKD: Chronic kidney disease

All individuals with eGFR <60 ml/min/1.73 m^2 are taken into the study.

Ultrasonogram showing reduced kidney size (<9 cm) was taken as radiological evidence of CKD.

RESULTS AND OBSERVATIONS

Age Distribution

Age of the patients varied from 17 years to 82 years. Majority of patients fall in the age group between 26 and 55 years. The mean age in this study was 45.28 years.

Sex Distribution

Males constitute 34 (68%) and females constitute 16 (32%) in this study.

Occupation

Patients in this study belonged to low socioeconomical status which is being reflected by their occupations. A quarter of the patients were doing agriculture or agriculture-related profession. Most women were homemakers.

Blood Pressure Readings

Patients with blood pressure of >140/90 mmHg were considered hypertensives. Most patients (39 patients) were hypertensives at the time of presentation. Only 11 patients had blood pressure <140/90 mmHg.

Personal Habits

In this study, 38% (19 patients) were smokers and 50% (25 patients) were alcoholics.

Renal Parameters

Lowest urea value found in these patients was 17 mg/dl and the highest was 230 mg/dl. Mean value of blood urea was 121.22. Creatinine values ranged between 0.5 mg/dl and 22.6 mg/dl. Mean values of creatinine was 6.74 mg/dl.

Radiological Examination

Radiological examination was done by abdominal ultrasonogram. In 37 patients (74%), the right kidney was <9 cm; in 34 patients (68%), the left kidney was <9 cm; and both kidneys were <9 cm in 30 patients (60%). Both kidneys were normal in 9 patients.

Treatment Scenario

Among the 50 patients, 33 patients (66%) were on conservative treatment only and 17 patients (34%) received hemodialysis. 66% of patients were treated with drugs only. During our study, no patients were admitted with a history of previous transplantation [Table 1].

Lipid Pattern in Our Study

HDL PATTERN Serum HDL values ranged between 30mg/dl to 80mg/dl. Patients showed abnormal HDL levels (<40 mg/dl) were 25 (50%). Its mean value was 42.82 and standard deviation was 12.37 [Table 2]. Its mean value was 42.82 and standard deviation was 12.37. Among the control groups, the lowest value of HDL was 46 mg/dl and the highest was 65 mg/dl. Their mean was 54.14 and standard deviation was 4.06.

Mean deviation and standard error of the difference between two means were calculated. The standard error of the difference between two means was 1.841. This was statistically significant since the actual difference was 2 times higher than the standard error of difference between two means. $P < 0.05$ was statistically significant. It showed that there was a significant reduction in HDL-C levels in patients with CKD than that of controls.

LDL PATTERN Lowest value of LDL 65 mg/dl and the highest value was 173mg/dl. Abnormally high LDL levels (>130mg/dl) were found in 23 patients and they constitute 46%. Their mean value was 131.57 mg/dl and standard deviation was 26.44.

In controls, the mean and SD were 112.26 and 13.69 (range 85–150 mg) respectively. Standard error of difference between two means was 4.21. Actual difference between two means was 2 times greater than the standard error o3 difference between two means. Student *t* value was calculated and $P < 0.05$ was considered as statistically significant.

Triglyceride (TGL) pattern TGL value in our study group ranged between 95 mg/dl and 350 mg/dl. Range of TGL value in control group was 90–122 mg/dl. TGL levels were abnormal in 24 patients which constitute 48%. Mean and standard deviation of the study group were 186.86 and 49.94, respectively. In controls, the mean and standard

deviation were 102.18 and 7.84. Standard error of the difference between two means was 7.140. $P < 0.05$ was considered as statistically significant.

Total cholesterol (TC) The range of TC levels in the study group was 120–258 mg/dl. The lowest value in the control group was 119 and the highest value was 222 mg/dl. TC was >240 mg/dl in 8 patients (16%).

The mean values of the study group and control group were 209.29 and 184.89 mg/dl, respectively. Their standard deviations were 36.9 and 15.31, respectively. Standard error of the difference between two means was obtained. It was 5.706, but the actual difference was >2 times higher than that of standard error of difference between the two means. $P < 0.05$ was considered to be statistically significant.

DISCUSSION

This study was conducted to determine the lipid profile changes in CKD patients on conservative management and regular hemodialysis and to compare them with normal healthy controls [Table 3].

The study population was 100, of which 50 were patients and 50 were controls. They were selected as per the inclusion criteria. Serum TC, HDL cholesterol (HDL-C), LDL-C, and TGLs were measured using autoanalyzer. The results were statistically analyzed.

In our study, most common lipid abnormalities found were low HDL levels (50%) and hypertriglyceridemia (48%) along with a modest increase in LDL and TC.

Decreased HDL Levels

The low HDL levels in patients with CKD in our study were consistent with Lee *et al.* who studied the lipid profile in CRF patients. This low HDLC levels were also an independent risk factor for the development of CKD in the Framingham offspring study.

Several mechanisms may underlie these reductions in HDLC levels, which is usually an indication of impaired reverse cholesterol transport. Thus, uremic patients usually exhibit decreased levels of apolipoprotein AI and AII (the main protein constituent of HDL). Diminished activity of LCAT (the enzyme responsible for the esterification of free cholesterol in HDL particles) as well as increased activity of cholesterol ester transfers protein that facilitates the transfer of cholesterol esters from

HDL to TGL-rich lipoproteins that reduce serum concentrations of HDL cholesterol. In MDRD study, low HDL levels in CKD patients were one of the independent risk factors for the progression of kidney disease. Although, in our study, the mean value was 42.82, it is significantly less than the age-matched healthy controls.

Elevated TGLs

Hypertriglyceridemia was observed in 48% of patients. TGLs were significantly elevated in our study than control group. Abnormal TGL values were found in 48% of patients in our study. Shah *et al.* most western studies demonstrated that hypertriglyceridemia was theabnormality found in CKD patients. Gupta *et al.*, Das *et al.*, Bagdade, and Chan *et al.* also found that hypertriglyceridemia was the major abnormality in their studies.

Hypertriglyceridemia represents an early feature of renal failure. Indeed, previous studies have shown that patients with impaired renal function exhibit increased concentrations of TGLs even though serum creatinine levels were within normal limits.

In addition, individuals with renal insufficiency usually display abnormal increase in serum TGLs after a fat meal (postprandial lipemia). Experimental studies revealed that accumulation of TGL-rich lipoprotein (very LDL [VLDL], chylomicrons, and their remnants) in individuals with predialysis CKD is mainly due to their decreased catabolism. The downregulation of the expression of several genes along with the changes in the composition of lipoprotein particles and the direct inhibitory effect of various uremic toxins on the enzymes involved in lipid metabolism represents the most important pathophysiological mechanism underlying the development of hypertriglyceridemia in renal failure. Interestingly, it has been proposed that secondary hyperparathyroidism may also contribute to the impaired catabolism of TGL-rich lipoproteins and that parathyroidectomy or the administration of calcium channel blocker Verapamil may partially ameliorate the hypertriglyceridemia of CKD. It is well known that impaired insulin sensitivity represents an early feature of CKD. Thus, it could be due to insulin resistance driven over production of VLDL may significantly contribute to the development of hypertriglyceridemia in CKD patients.

Elevated LDL

LDL was significantly elevated than that of controls in our study. We found that 44% of patients showed elevated LDL levels. This observation is similar to the studies of Lee *et al.* In an article published in archives of internal medicine, 32 patients were studied and compared the lipid profile on CKD and non-CKD patients. It was found that 60.5% of patients have elevated LDL-C than non-CKD patients ($P = 0.06$). However, most studies

find that uremic patients usually have normal or slightly reduced concentrations of LDL-C levels, and they exhibit important disturbance in the density distribution of LDL subfraction that is characterized by a predominance of small-dense LDL particles.

In our study, this elevated LDL-C may be due to the inaccuracy of Friedewald formula in estimating LDL-C.

Elevated TC

TC levels were significantly elevated in our study group. We observed the same findings in the study by Lee *et al.* However, most of the studies did not observe hypercholesterolemia. The possible reason for the hypercholesterolemia in our study is significant elevation of cholesterol-containing lipid fractions (IDL and LDL).

Correlation Studies

It was found that serum TGLs, TC, and LDL were not correlated significantly, whereas serum HDL levels had a significant negative correlation with serum creatinine. It means that when serum creatinine level rises, serum HDL level falls. This was the observation found in MDRD study.

Lipid Profile in CKD Patients on Conservative Management: Reported Studies

1. The characteristic plasma lipid abnormality is moderate hypertriglyceridemia - this is due to impaired carbohydrate tolerance leading to the increased hepatic synthesis of VLDL and decreased activity of lipoprotein lipase and hepatic TGL lipase leading to decreased fractional catabolic rate of TGLs.
2. Decrease in HDLC - this is due to the deficiency of LCAT which is essential for the esterification of cholesterol. LCAT plays an important role in HDL-mediated cholesterol uptake from the extrahepatic tissues and serves as a main determinant of HDL maturation and plasma HDLC level. Decrease in HDL level is also contributed by elevation of CETP.
3. Normal or slightly increased LDLC level.
4. Normal or slightly increased TC level.

Observation on Lipid Profile Changes on Conservative Management Showed the Following Results

The final results in our study revealed are as follows:

1. Significant decrease in HDLC.
2. Significant increase in TGL.
3. Non-significant changes in serum LDL and TC. According to Bagdade *et al.* there was moderate hypertriglyceridemia and decrease in HDL levels in CKD patients. Indian studies on lipid profile abnormalities in chronic renal failure have varied from no abnormalities at all to significant abnormality Hypertriglycerdemia and reduced HDL as described in Western literature. Sharma *et al.* and Kunde *et al.* observed no hyperlipidemia in patients of CKD. On the other hand, Gupta *et al.* and Das *et al.* observed lipid abnormalities similar to those reported in Western studies.

Lipid Profile in CKD Patients on Hemodialysis: Reported Studies

1. Moderate increase in TGL levels.
2. Decrease in HDL levels.
3. Normal/slightly elevated TC and LDLC.
4. Increased Lp(a), increased apoB and apoA IV, and decreased apoA I.

In addition to factors responsible for renal dyslipoproteinemia, the other contributing factors in a CKD-HD patient are as follows:

1. Reduced lipolytic activity following repeated heparinization. The exact reason is not understood but may be due to functional insulin deficiency or insulin resistance and also due to the presence of non-dialyzable factor of lipolytic enzyme (lipoprotein lipase), in the plasma of CKD-HD patients. The changes are more pronounced with the use of conventional heparin than low molecular weight heparin.
2. The presence of acetate in the dialysate which gets converted to long chain fatty acids and later to cholesterol in the liver.
3. Carnitine deficiency where carnitine is necessary for fatty acid oxidation.

Observation on lipid profile changes on hemodialysis showed the following results:

The final results revealed are:

1. Significant decrease in HDLC.
2. Significant increase in triglyceride levels.
3. Non-significant changes in serum TC and LDL-C.

Variation in lipid profile in hemodialysis patients in previous studies has not been consistent. Shah *et al.* noticed hypertriglyceridemia in 11% of patients on hemodialysis. Zolezzi *et al.* noticed raised TC in 20%, decreased HDL in 50% and raised TGLs in 45% of their patients on hemodialysis. Ibels *et al.* noticed a decrease in TGL levels after dialysis.

Limitations of the Study

1. Most studies showed low or normal LDL-C levels, whereas this study observed significantly elevated LDL-C levels for reasons little known.
2. Smoking, alcoholism and may alter the lipid pattern in the body which were not excluded due to lack of cumulative dose criteria Their influences in the study group also have to be considered.

CONCLUSION

1. L-C levels were lower and TGLs, TC, and LDL-C levels were higher in the study group compared to controls. All were statistically significant.
2. There was a negative correlation exists between serum HDL-C level and serum creatinine levels which were statistically significant.
3. There was a significant decrease in HDL-C and increase in TGLs in both conservative and hemodialysis groups. Decrease in HDL is more in conservative management and increase in TGLs is more in hemodialysis group.

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