Original Research Article

Study of dyslipidemia associated with chronic kidney disease

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Abstract

Background: Chronic Kidney Disease (CKD) hasan increased risk of cardiovascular diseases (CVD) prevalence and lethality. Dyslipidemia is mostly associated in these patient populations with abnormalities in lipid profile and is a principal risk factor for CVD development. Patients with CKD exhibithigh triglycerides, low high density lipoprotein-cholesterol,and altered lipoprotein composition. **Aims and objectives:** The study was undertaken to observe the lipid profile of healthy and diseased subjects to study its association with CKD. **Material and Methods:** A total of 100 subjects were included; of which 50 were the control group and 50 were thestudy (evidence of CKD) group. 5ml of venous blood was obtained from antecubital fossa from each subject and kept in a plain vial, after which serum separation was analyzed for biochemical parameters. **Results:** Among various parameters tested urea, creatinine, sugar, triglycerides, and very low-density lipoprotein levels were significantly higher in the study group as compared to the control group ($p<0.05$). Low-density and high-density lipoprotein levels were significantly lower in the study group as compared to the control group ($p<0.05$). There was no significant change observed in total lipids and phospholipids levels in between the healthy control and studygroup. **Conclusion:** It can be concluded that CKD patients are at higher risk of development of hypertriglyceridemia, dyslipidemia characterized with elevated urea and creatinine, and decreased HDL levels leading to more prevalence of CVD.

Keywords: Chronic kidney disease, lipid profile, cardiovascular disease

Introduction

CKD is a common health problem with increasing frequency and poor health outcomes among the population. On the other hand, it is well documented that CVD may be a major basis for prevalence and lethality[1]. Although some CKD patients eventually develop end-stage kidney disease (ESRD), most CKD patients die from CVD before dialysis is required[2,3].Impaired kidney function actively contributes to the development of cardiovascular disease, which is why the American Heart Association recommended that these patients be classified in the group with the highest risk of cardiovascular events[4].

There are several factors that contribute to the incidence of CVD among CKD patients. These threat elements may be each conventional ones consisting of age, male gender, diabetes, obesity, hypertension, and dyslipidemia and non-conventional uremia-associated threat elements consisting of anemia, hyperhomocysteinemia, mineral bone disease-CKD with hyperparathyroidism, oxidative stress, hypoalbuminemia, and persistent inflammation[5,6].

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In the overall population, excessive overall high low-density lipoprotein (LDL) cholesterol, excessive triglyceride (TG), and reduced levels of high-density lipoprotein (HDL) cholesterol are all well-known threat elements for CVD development[7,8]. The disturbance generated during lipoprotein synthesis and degradation leads to prolonged renal sickness developing a condition termed Dyslipidemia[6]. Dyslipidemia is a common problem in CKD and altered lipoprotein metabolism and is related to a decrease in glomerular filtration rate (GFR).

Lipid profile is related to the level of kidney function and degree of proteinuria[9,10,11]. This abnormality in lipoprotein degradation is due to inappropriate activity of metabolic pathways and enzymes, which leads to early-stage kidney failure and dyslipidemia, which is also a risk factor for the development of artherosclerosis[12]. These metabolic abnormalities contribute to CKD progression and also adversely affect renal function[6,13].This study aims to investigate the role of lipid profile, urea, and creatinine in progression to CKD.

Material and methods

Study design and location

This case-control study was conducted for six months in the Department of Biochemistry, SMS Medical College and Hospital, Jaipur for periodic check-up of their blood urea-creatinine and lipid profile. The basis of the study was biochemical in nature.

Inclusion Criteria

The subject of study was divided into two groups:- Control Group- This comprises of 50 healthy subjects (25 males and 25 females) of age group 18-76 years, who were free of features of kidney disease and dyslipidemia. Study groups- This comprises 50 subjects (27 males and 23 females) of age group 32-84 years clinically diagnosedCKD and having elevated serum urea-creatinine.

Exclusion criteria
Body Mass Index (BMI) more than 24.9 kg/ml, known case of acute renal failure, diabetes mellitus, hypertension, ischemic heart disease, and taking drugs that affect lipids and lipoprotein level.

Sampling procedure& Methodology
Blood was collected from Indoor patients. Five ml of venous blood was drawn aseptically from the antecubital fossa of every patient and control after an overnight fast for lipid profile determination. Blood was allowed to clot and serum was separated after centrifuging the samples at 3000 rpm for 10 minutes. Other biochemical parameters like serum sugar, urea, creatinine along with the lipid parameters like total cholesterol, TG, LDL, and HDL cholesterol were also analyzed using Beckman Coulter AU680 auto analyzer. The determination of serum creatinine, urea,total cholesterol, TG,and HDL concentration was performed by appropriate enzymatic methods**.** Serum LDL was estimated using Friedewald's Formula (LDL Cholesterol = Total cholesterol – (HDL cholesterol + TG/5 {VLDL-C}).

Statistical analysis
All the data are expressed in mean and standard deviation. For the statistical significance, p-value and student 't' test were performed using Microsoft Excel and Graph Pad Software along with Quick Calc. p-value < 0.05 was considered statistically significant.

Results
Table 1 shows the Diagnostic and Lipid Profile parameters of 50 study subjects and 50 controls.The mean values of urea (183.80 ± 89.98mg/dL) and creatinine (6.48 ± 2.25mg/dL) in CKD patients were found to be very high as compared controls (25.68 ± 11.29mg/dL and 0.98 ± 0.24mg/dL). The lipid profile pattern in the CKD patients and the controls were compared. The mean ofTG (201.42 ± 70.29 mg/ dL) was higher when compared with that of controls(148.06 ± 31.58 mg/dL) respectively. Similarly, an elevation was observed in VLDL Cholesterol level in CKD patients (36.24 ± 15.69 mg/dL) as compared to control (34.18 ± 18.95 mg/dL). There was a reduction in the level of LDL Cholesterol observed in CKD patients as compared to controls (69.66 ± 33.27 mg/dL versus 109 ± 32.44 mg/dL). There was a slightreduction in HDL Cholesterol in study patients (29.70 ± 7.98 mg/dL) when compared with controls (39.5 ± 8.06 mg/dL). There is no significant increase in the level of total lipids and phospholipids. The difference between lipid profile values were statistically significant.

TABLE 1: Comparative study of Diagnostic and Lipid Profile Parameter in Control and CKD Patients

PARAMETERS	CONTROL PATIENTS (MEAN±SD) (N= 50)	CKD PATIENTS (MEAN±SD) (N=50)	P value
Age (yrs)	41.9 ± 14.52	52.84 ± 14.54	0.09006
Urea (mg/dl)	25.68 ± 11.29	183.80 ± 89.98	0.00001*
Creatinine (mg/dl)	0.98 ± 0.24	6.48 ± 2.25	0.005*
Sugar (F) (mg/dl)	92.84 ± 23.54	112.32 ± 75.56	> 0.05
Triglyceride (mg/dl)	148.06 ± 31.58	201.42 ± 70.29	0.00024*
Total Cholesterol (mg/dl)	170.64 ± 44.84	138.42 ± 40.27	> 0.05
HDL-C (mg/dl)	39.5 ± 8.06	29.70 ± 7.98	0.03581*
LDL-C (mg/dl)	109 ± 32.44	69.66 ± 33.27	0.00097*
VLDL-C (mg/dl)	34.18 ± 18.95	36.24 ± 15.69	> 0.05
Total lipid (mg/dl)	557.4 ± 119.21	562.22 ± 157.99	> 0.05
Phospholipids (mg/dl)	216.24 ± 68.23	203.76 ± 74.69	> 0.05
*P value = ≤ 0.05 is significant			

Discussion
Our study revealed that CKD patients have hypertriglyceridemia. It underlines the importance of lipid profile for CKD patients with dyslipidemia as lipids contribute directly to glomerulosclerosis and tubulointerstitial injury and the treatment of lipid abnormalities associated with the renal disease will slow down the progression of CKD[14].
This elevated TG level is due to a decline in the functioning of lipoprotein lipase (LPL) which breaks down TG and also increasesTG synthesis in the liver from free fatty acids liberated from fatty tissue and muscles[15]. Dyslipidemia emerges early in kidney failure and it becomes more evident as the kidney disease advances because of disturbance between lipoprotein synthesis and metabolism due to decline in activity of lipoprotein lipase and direct inhibitory effect of many uremic toxins on the enzymes involved in lipid metabolism[16].
As described in most of the Indian studies, there is no such confirmation of hypercholesteremia inthe initial stages of CKD but in ESRD cholesterol level is either normal or reduced whereas hypercholesteremia has been studied in some of the western studies. In the present study, we did not find hypercholesteremia instead the levels remain normal or minimally reduced in CKD patients. CKD results in extreme dysregulation of many key enzymes and receptors associated withthe degradation of lipoproteins, especially those of HDL and TG-rich lipoproteins. Reduction in the amount of LCAT (Lecithin–cholesterol acyltransferase), apoA-1, and hepatic lipase together with an increase in the amount of cholesterol ester transfer protein (CETP) are mainly responsible for the decrease in HDL cholesterol and increase of TG in CKD patients. In our study, we found increased levels of VLDL cholesterol and a reduction in levels of HDL cholesterol in CKD patients[15,17].
The level of LDL cholesterol is reduced in CKD patients as there is a disturbance in the density distribution of this lipoprotein characterized by the increased level of small, dense particles prone to oxidation i.e. oxidized LDL[18,19]. In our study, we did not find raised levels of LDL cholesterol instead the levels remain decreased in CKD patients.
In our study dyslipidemia was observed in CKD patients characterized by a statistically significant increase of serum triglycerides and VLDL with a decrease in serum HDL-C and LDL-C when compared with the controls. These alterations in serum lipid in CKD enhance the risk of atherosclerosis and favors higher incidence of cardiovascular complications. The majority of patients with CKD do not develop renal failure; indeed, most of them die of cardiovascular causes before the development of renal failure.

Conclusion
CKD patients are at high risk of the development of dyslipidemias, characterized by hypertriglyceridemia, increased VLDL-C levels, and reduced HDL-C levels. Total cholesterol and LDL cholesterol levels remain normal or reduced in these patients. These lipid and lipoprotein malfunctioning together increases the risk of developing CVD in these patients. Further research has to be done to ensure whether early detection and treatment (diet /drug therapy) of this Dyslipidemia is quite promising, in the prevention of severe clinical outcomes in CKD patients. This states the need for early evaluation of

these patients for lipid abnormalities as better treatment may prevent CVD and stop the progression of CKD.On the basis of the findings of the present study, it is suggested all CKD patients should be evaluated for dyslipidemia to decrease the risk of complications in CKD patients. Patients with CKD should be considered a "very high risk" category and aggressive therapeutic intervention initiated to reduce the risk of cardiovascular events. Planning for the preventive health policies and allocation of more resources for the treatment of CKD patients are essential in India.

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