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Original Articles

Lipid abnormalities in patients with chronic kidney disease

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Abstract

Background: The burden of Chronic Kidney Disease (CKD) is increasing rapidly worldwide and has become a major health problem. Patients with CKD are at higher risk for cardiovascular disease (CVD) than patients in the general population. Lipid disorders are recognized risk factors for CVD. **Objectives:** To observe the pattern of lipid profile in non-dialyzed CKD patients. **Methods:** This comparative study was carried out in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period of July 2013 to June 2014. A total number of 100 subjects of both sexes were selected with age ranging from 18 to 60 years according to selection criteria. Among them, 50 CKD patients were included in group I and 50 health subjects in group II. Serum lipid profile among the groups were assessed and statistically compared. For statistical analysis Student t-test was performed using SPSS for windows version 16. **Results:** The mean (±SD) of serum TG level was significantly higher in CKD patients (209.12 ± 38.20) than healthy control group (140.44 ± 37.99) and the mean (±SD) of serum HDL level was significantly lower in CKD patients (30.50 ± 10.77) than healthy control group (39.94 ± 9.26). **Conclusion:** Dyslipidemia is more common in non-dialyzed CKD patients.

Key words: Chronic kidney disease, Dyslipidemia.

Introduction

Chronic kidney disease (CKD) is a major public health problem worldwide[1]. According to Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF), CKD is either kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR) or GFR < 60 ml/min/1.73 m^2 for ≥ 3 months, with or without kidney damage[2]. The incidence and prevalence of chronic kidney disease (CKD) are increasing worldwide. According to the 1999 – 2004 National Health and Nutritional Survey (NHANES), the prevalence of CKD in the US population is 15.3%[3]. In the developing countries, the awareness and burden of CKD on society has been high lightened during last decade. Incidence of CKD in Bangladesh is 19%[4]. The prevalence of CKD is increasing worldwide as a consequence of hypertension and diabetes mellitus[5]. Increase in prevalence of CKD is an alarming condition. Because it is an irreversible condition and is associated with increased health hazards[6]. A patient with CKD leads to many complications over a period of time, the most common include cardiovascular, cerebrovascular and peripheral vascular disease[7]. The incidence of cardiovascular disease (CVD) is also high in patients with CKD. CVD is the leading cause of death among the patients with chronic kidney disease[8]. There is growing evidence that cardiovascular damage begins as soon as the kidney loses function and increases in severity during the progression of kidney disease[9]. Dyslipidemia independently or in combination with elevated blood pressure can cause deterioration in renal function. Abnormalities in lipid metabolism and dyslipidemia are known to contribute to glomerulo-sclerosis and are common in renal disease. The impact of lipid abnormalities

on renal function has been evaluated in various studies[10]. Abnormal lipid profiles start to appear soon after renal function begins to deteriorate[11]. Dyslipidemia has been established as a well known traditional risk factor for CVD in the general population as well as in CKD patient. CKD patients usually display elevated triglyceride (TG) and reduced serum high density lipoprotein-cholesterol (HDL-C). Serum total cholesterol and low density lipoprotein-cholesterol (LDL-C) levels usually remain within normal limits[12]. The National Kidney Foundation (NFK), Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines on the management of dyslipidemia in CKD patients with 1) Fasting triglycerides >500mg/dl (5.65 mmol/L); 2) LDL-C>100mg/dl (2.59 mmol/L) and 3) non-HDL cholesterol >130mg/dl (3.36 mmol/L) should be considered for treatment to reduce the cardiovascular complications in these patients[13]. Keeping in view, the mortality associated with CVD and the association of lipid profile levels with CVD in CKD patients, we have planned to study the serum lipid profile of CKD patients.

Materials and Methods

This comparative study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period of July 2013 to June 2014. A total number of 100 subjects of both sexes were selected purposively with age ranging from 18 to 60 years. Among them, 50 patients were CKD patients (Group I) and 50 were healthy comparison group (Group II). Patients were selected from Nephrology ward of Dhaka Medical College Hospital, Dhaka. Patients taking lipid lowering medications, hypothyroidism patients, chronic liver diseases patients, pregnancy, age <18 years and >/60 years and malignancy were excluded from the study. After selection of subjects, the objectives, nature, purpose and benefit of the study were explained in detail in each subject. Informed consent was taken. Data were collected in pre designed structured questionnaire form by the researcher herself. Age, sex, occupation, marital status was noted as per statement of the participants at the time of interview. History regarding smoking habit, hypertension, diabetes mellitus, pregnancy, history of any cardiovascular event, thyroid disorder, chronic liver disease, any malignancy was taken. Drug history regarding lipid-lowering drugs was noted. Then participants were examined for height, weight, blood pressure. The study parameter was serum lipid profile. Estimation of study parameter was done in the Department of Biochemistry, Dhaka Medical College. Serum total cholesterol (TC), triglyceride (TG) and high density lipoprotein-cholesterol (HDL-C) were assayed on semi automated biochemical analyzer. Low density lipoprotein-cholesterol (LDL-C) was calculated by Friedwald equation. LDL-C=Total Cholesterol – (HDL-C +/5).

Results

Table 1 shows demographic, clinical and laboratory parameters of the study subjects. The mean age of CKD patients was 41.26 ± 14.00. BMI of the patients was lower in CKD patients than that of the control (19.9 ± 3.5 vs 21.7 ± 2.9 and $p<0.05$). The mean values of urea (141.60 ± 56.44) and creatinine (6.62 ± 3.21) in CKD patients were found to be very high as compared to control (25.04 ± 5.59 and 0.99 ± 0.87 respectively). Both the systolic (182 ± 29) and diastolic (99 ± 16) blood pressure in patients were significantly higher when compared to that of the controls (117 ± 9and 77 ± 8) respectively ($p<0.05$).

Table II shows distribution of study subjects according to lipid profile in group I and group II. The mean of triglyceride (209.12 ± 38.20) was significantly higher and HDL-C (30.50 ± 10.77)

was significantly lower when compared with that of control (140.44 ± 37.99 and 39.94 ± 9.26) respectively ($p<0.05$).

Table III shows lipid profile in CKD patients according to presence or absence of diabetes mellitus. The mean (±SD) of serum total cholesterol level, HDL-C level, LDL-C level and triglyceride level in diabetic CKD patients were 184.25 ± 30.36, 28.25 ± 9.03, 120.50 ± 33.16, 198.41 ± 30.29, respectively; and non-diabetic CKD patients were 177.50 ± 43.54, 31.21 ± 11.28, 118.32 ± 28.57 and 212.50 ± 40.13, respectively. The difference of lipid profile between diabetic and non-diabetic CKD patients was non-significant ($p>0.05$).

Table I: Demographic, clinical and laboratory parameters of the study subjects

Variables	Group-I (CKD)	Group-II (Healthy control)	p-value
Age (Years) (mean ±SD)	41.26 ± 14.00	37.94± 12.26	0.210
Gender			
Male n (%)	22 (44.0)	26 (52.0)	0.428
Female n (%)	28 (56.0)	24 (48.0)	
BMI (kg/m^2) (mean ± SD)	19.9 ± 3.5	21.7 ± 2.9	0.009
Blood Urea (mg/dl)	141.60 ± 56.44	25.04 ± 5.59	0.0001
Serum Creatinine (mg/dl)	6.62 ± 3.21	0.99 ± 0.87	0.0001
Blood pressure (mmHg)			
Systolic BP	182 ± 29	117 ± 9	0.0001
Diastolic BP	99 ± 16	77 ± 8	

Unpaired Student t-test was done to compare the two groups. p value <0.05 was taken as level of significant. n = Number of subjects. Results are expressed as mean± SD.

Table II: Distribution of study subjects according to lipid profile in group I and group II

Lipid profile	Group		p-value
	Group-I (CKD) (n=50)	Group-II (Healthy) (n=50)	
TC (mg/dl)	179.12 ± 40.58	166.80 ± 35.89	0.111
HDL-C (mg/dl)	30.50 ± 10.77	39.94 ± 9.26	0.001
LDL-C (mg/dl)	118.84 ± 29.40	107.17 ± 28.30	0.053
TG (mg/dl)	209.12 ± 38.20	140.44 ± 37.99	0.001

Unpaired Student t-test was done to compare the two groups. p-value <0.05 was taken as level of significant. Results are expressed as mean±SD.

Table III: Lipid profile in CKD patients according to presence or absence of diabetes mellitus

Lipid profile	Diabetes n =12 (mean ±SD)	Non-diabetes n =38 (mean ±SD)	P value
TC (mg/dl)	184.25 ± 30.36	177.50 ± 43.54	0.620
HDL-C (mg/dl)	28.25 ± 9.03	31.21 ± 11.28	0.412
LDL-C (mg/dl)	120.50 ± 33.16	118.32 ± 28.57	0.826
TG (mg/dl)	198.41 ± 30.29	212.50 ± 40.13	0.270

Two groups were compared by Unpaired Student't' test. P value < 0.05 was considered as significant. Results are expressed as mean±SD.

Discussion

CKD is a worldwide health problem and is the leading cause of morbidity and mortality in the developed world. Patients with CKD are at greater risk for cardiovascular disease (CVD) and cerebrovascular disease and they are more likely to die of CVD than to develop ESRD.

In this study, blood urea and serum creatinine in CKD patients were found to be very high as compared to control. The reason attributed to raised blood urea and serum creatinine in patients with CKD is the declining of glomerular filtration[14]. In this study these test were done for diagnosis of CKD patients.

The result of the current study showed that mean±SD of serum triglyceride, HDL-C, TC and LDL-C were 209.12 ± 38.20, 30.50 ± 10.77, 179.12 ± 40.58 and 118.84 ± 29.40 in CKD patients and 140.44 ± 37.99, 39.94 ± 9.26, 166.80 ± 35.89 and 107.17 ± 28.30 in healthy controls respectively.

In this study, serum triglyceride was significantly higher and HDL-C was significantly lower in CKD patients when compared with that of control but there was no statistically significant difference found between LDL-C and total cholesterol ($p>0.05$). This observation is in agreement with Baria et al.[15]

The accumulation of triglycerides leading to triglyceridemia in CKD is the consequence of both a high production and a low catabolism of triglycerides. But the predominant mechanism which is attributed for triglyceridemia in CKD is decreased catabolism of triglycerides[16]. Various factors contribute to this metabolic aberration in CKD, which includes- i) reduced activity of lipoprotein lipase (LPL)[17] ii) a disproportionate increase in plasma apolipoprotein C-III which is a possible cause of lipoprotein lipase inactivation in uremia[18] iii) The presence of inhibitors of lipase in CKD patients[19].All these factors result in a decrease catabolism of triglycerides in chylomicrons and VLDL thus increased serum triglyceride level.

In the present study, serum cholesterol is not altered in CKD patients when compared with control group. Tsumura et al.[20] observed hypercholesterolemia in their study of patients with CKD. Hypercholesterolemia in their cases was attributed to heavy proteinuria. The mechanism attributed to hypercholesterolemia due

to heavy proteinuria in CKD involves altered gene expression of HMG-COA reductase, 7 alpha hydroxylase and hepatic LDL receptor[21]. In the present study, proteinuria was minimal and hence no change in serum cholesterol level was observed. Vasilis et al.[22] reported that there is no significant change in serum cholesterol level in CKD patients, as these patients were not having any significant degree of proteinuria. Our observation in the present study was in agreement with findings of Vasilis et al.[22] and was characterized by a normal serum cholesterol level due to minimal proteinuria.

In the present study, the serum LDL-C is not altered in CKD patients when compared with control group. Elevated plasma LDL cholesterol is common in nephrotic syndrome but it is not a typical feature of patients with advanced CKD.

In the present study, serum HDL-C is significantly decreased in CKD patients when compared with control ($p<0.001$; Table 2). The significant decrease of HDL-C in CKD can be attributed to- i) decreased levels of apolipoproteins AI and AII; the main protein constituents of HDL[23] ii) diminished activity of LCAT; the enzyme responsible for the esterification of free cholesterol in HDL particles[24] iii) increased activity of Cholesteryl Ester Transfer Protein (CETP) that facilitates the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins[25].

All these factors combinedly act to reduce the serum concentration of HDL-C.

In this study, the difference of lipid profile between diabetic and non-diabetic CKD patients with and without dialysis was non-significant. Similar type of observation was made by Shilpa (2010)[26].

Conclusion

In our study dyslipidemia was observed in CKD patients characterized by a statistically significant increase of serum triglycerides with a decrease in serum HDL-C when compared with the controls. However there was no hypercholesterolemia and serum LDL-C was not significantly altered in CKD patients when compared with controls. The accompanying serum lipid alteration i.e. hypertriglyceridemia and decreased serum HDL in CKD enhance the risk of atherosclerosis and favors higher incidence of cardiovascular complications. Therefore lipid regulation must be instituted to decrease the risk of complications in CKD patients.

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