Volume : 3 | Issue : 5 | May 2014 • ISSN No 2277 - 8179

Research Paper

Dyslipidemia and Chronic Kidney Disease

Medical Science

KEYWORDS : CKD, CVD, Dyslipidemia

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ABSTRACT

Chronic Kidney Disease (CKD) is becoming a worldwide health problem due to increasing incidence and prevalence, high cost and poor outcomes. It is a pathophysiological process with multiple etiologies resulting in the inevitable attrition of functional nephrons and frequently leading to End Stage Renal Disease (ESRD). Lipid abnormalities are commonly found in patients with chronic renal failure and recognized as risk factors for atherosclerosis. There is a significant increase of serum triglycerides and Very Low Density Lipoprotein (VLDL) with a decrease in serum High Density Lipoprotein–Cholesterol (HDL-C) in CKD patients when compared with control. But there is no alteration in serum total cholesterol and Low Density Lipoprotein Cholesterol (LDL-C) in both groups. All these factors are suggestive of abnormal lipid profile. This study would be beneficial for patients with CKD for aggressive therapeutic intervention initiated to reduce the risk of cardiovascular events, which will improve the quality of their lives.

INTRODUCTION

Chronic kidney disease (CKD) is a major health problem due to increasing incidence and prevalence, high cost and poor outcomes. Globally, CKD is the 12th cause of death and the 17th cause of disability, respectively (Grassmann A et al 2005). In India, it has been recently estimated that the age-adjusted incidence rate of ESRD to be 229 per million population (pmp). Lipid abnormalities are commonly found in patients with chronic renal failure and recognized as risk factors for atherosclerosis (Singh AK et al 2013).

The Kidney Disease Outcomes Quality Initiative defines chronic kidney disease as either kidney damage or a decreased kidney Glomerular Filtration Rate (GFR) of less than 60 ml/min/1.73m2 for 3 or more months (Levey AS et al 2005) The Chronic Kidney Disease is characterized by specific metabolic abnormalities of plasma lipids both qualitatively and quantitatively. This may be a significant risk factor for vascular complications leading to increased morbidity and mortality in CKD patients.

On the other hand, it is well documented that cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with CKD. Thus, although some patients with CKD will ultimately develop end stage renal disease (ESRD), most patients with CKD will die of CVD before dialysis becomes necessary. Mild chronic impaired renal function contributes actively to the development of CVD, so the American Heart Association has recommended that these patients should be classified in the highest risk group for developing cardiovascular events. In patients who finally advance to ESRD and especially dialysis patients, the prevalence of clinical coronary heart disease is 40% and CVD mortality is 10 to 30 times higher than in the general population of the same gender, age and race (Sarnak MJ et al 2003). Therefore this study was undertaken to assess the lipid profile in CKD patients.

MATERIAL AND METHODS

The study comprised of a total of 50 patients with evidence of CKD. The patients were admitted into Nephrology unit of IKD hospital, Ahmedabad. They were included in the study on the basis of clinical signs and symptoms of kidney disease along with an elevated serum urea and serum creatinine level and a lowered eGFR (estimated Glomerular Filtration Rate). Patients with eGFR values of less than 15 ml/min were included under stage V (ESRD) and rest of the others whose eGFR ranged from 90 ml/min to 15 ml/min were grouped under stages I to IV. The control group comprised of 50, age and sex matched healthy subjects who were free of features of kidney disease and having a normal serum urea and serum creatinine level. Informed consent was taken from the patients and subjects who participated in the present study. In all these group serum urea, creatinine and lipid profile were estimated. The serum urea was estimated by GLDH–Urease method, serum creatinine was estimated by Jaffe's method. The serum total cholesterol and High Density Lipoprotein Cholesterol (HDL-C) were analyzed using cholesterol oxidase method, triglyceride assessment was carried out by glycerol kinase method while Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C) were calculated by using Frieldwald's formula. The eGFR was computed by MDRD formula. All the data are expressed in mean and standard deviation. For the statistical significance, student 't' test was performed using Graph pad software.

RESULT AND DISCUSSION

Serum urea and serum creatinine registers an increase in their levels in patients with CKD when compared to those of controls ($p<0.001$, Table 1). The reason attributed to raised serum urea and creatinine in patients with CKD is the declining of glomerular filtration. CKD produces characteristic effects on major lipoprotein fractions. Hypertriglyceridemia is one of the most common lipid abnormalities in patients with CKD. In the present study the mean serum triglyceride was significantly elevated in CKD patients when compared with control ($p<0.0001$; Table 1). This observation is in agreement with Raju DSSK et al (2013).

The accumulation of triglycerides leading to triglyceridemia in CKD is the consequence of both a high production and a low catabolism of triglycerides (Prinsen BH et al 2003). Various factors contribute to this metabolic aberration in CKD, which includes: Reduced lipoprotein lipase (LPL) activity as a consequence of the down regulation of the enzyme gene (Vaziri ND et al 1999), a disproportionate increase in plasma apolipoprotein C-III which is a possible cause of lipoprotein lipase inactivation (Moberly JB et al 1999). All these factors result in a decreased catabolism of triglycerides in chylomicrons and VLDL.

CKD is usually associated with secondary hyperparathyroidism. The secondary hyperparathyroidism leads to the impaired catabolism of triglyceride-rich lipoproteins, which provide an additional mechanism for raised plasma triglyceride concentrations in CKD (Vaziri ND et al 1997).

In the present study, serum cholesterol is not altered in CKD patients when compared with control group. Our observation in the present study was in agreement with findings of Tsimihodimos V et al (2011).

Volume : 3 | Issue : 5 | May 2014 • ISSN No 2277 - 8179

The serum LDL-C is not altered in CKD patients in the present study 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. Our observation that serum LDL cholesterol level does not undergo any change in CKD patients is in agreement with Jain PK et al (1991).

In the present study, serum HDL-C is significantly decreased in CKD patients when compared with control. ($p<0.0001$; Table 1) This result is in agreement with Mordasini R et al (1977). The significant decrease of HDL-C in CKD can be attributed to diminished levels of apolipoproteins AI and AII; the main protein constituents of HDL (Vaziri ND et al 1999). Reduced activity of LCAT; the enzyme responsible for the esterification of free cholesterol in HDL particles (Guarnieri GF et al 1978), enhanced activity of Cholesteryl Ester Transfer Protein (CETP) that facilitates the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins (Kimura H et al 2003). All these factors collectively act to decrease the serum concentration of HDL-C.

Serum VLDL-C in the present study is significantly raised in CKD patients when compared with control group ($p<0.001$; Table 1). This result is in agreement with Bagdade J et al (1976). The factors which explain the increase in serum VLDL include, (i) the increased activity of CETP which increases transfer of cholesterol ester to VLDL and promotes more VLDL formation, increased apo C-III, which is an LPL inhibitor inhibitng the degradation of VLDL. These factors increase the level of serum VLDL-C in CKD patients.

Table: 1 Comparative study of Diagnostic and Lipid profile Parameter in control and CKD Patients.

Parameter (mg/dL)	Control (Mean±SD)	CKD Patients (Mean±SD)
Urea	29.5±7.35	128.73±39.54*
Creatinine	0.90±0.17	4.22±1.90*
Total Cholesterol	162.28±11.80	165.52±12.69
Triglyceride	127.84±19.57	187.24±30.68*
HDL-C	47.12±5.76	41.04±3.91*
LDL-C	89.59±13.97	87.03±14.87
VLDL-C	25.57±3.91	37.45±6.14*

***p<0.0001**

CONCLUSION

Cardiovascular disease is a major cause of mortality and morbidity in patients with CKD. 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 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. These alterations in serum lipid in CKD enhance the risk of atherosclerosis and favours 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. 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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