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Lipid Profile, Oxidative Stress and Homocysteine in Chronic Renal Failure

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ABSTRACT
Patients with chronic renal failure CRF suffer from lipid abnormalities, changes in the level of oxidative stress status and hyperhomocysteine, and these accelerate the development of atherosclerosis. Hence this study was undertaken to know the risk of cardiovascular morbidity in CRF patients. A case-control study was carried out in department of Nephrology, NIMS, Jaipur with 50 patients and 50 healthy volunteers of both sexes aged 20-59 years. Test for serum lipid profile, urea creatinine, FBS, PPBS, total protein and albumin were carried out in all the cases and controls. The results were analyzed and compared with the controls using Microsoft Excel software. The levels of serum TG, TC, LDL-C, VLDL-C, TC/HDL-C and LDL-C/HDL-C ratio were significantly increased and HDL-C was significantly decreased in cases when compared to controls. Serum TG, TC, VLDL-C and HDL-C are significantly increased in conservatively managed patients than hemodialysis patients. Serum MDA was significantly increased and SOD was significantly decreased in cases when compared to controls. These changes were more pronounced in hemodialysis patients when compared to conservatively managed patients. We conclude that lipid abnormalities in CRF accelerates the progression of the renal failure and predisposes to atherosclerosis, hence it is worthwhile detecting and treating hyperlipidemia in CRF patients early on. Chronic kidney disease, hemodialysis and lipid prole.

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Key Words
Chronic kidney disease, hemodialysis and lipid prole

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INTRODUCTION

Reduced effective functioning of renal tissue leads to an irreversible decline in renal function, known as chronic kidney disease (CKD) or chronic renal failure (CRF)[1]. The ensuing weakening of the kidney's excretory, metabolic, and endocrine activities causes the clinical syndrome of uremia to emerge[2,3]. However, since the introduction of dialysis, the severity of the effects of CKD has changed significantly[4]. In Brazil, the condition is becoming more common and has a poor prognosis despite the expensive nature of treatment[5]. The Brazilian Society of Nephrology conducted a census in 2010 that assessed the number of dialysis patients in Brazil to be 92-091 individuals. Of those who started treatment in that year 18-972 were considered to be HD[6,7]. Hyperhomocysteinemia and dyslipidemia are significant risk factors linked to the early start of atherosclerosis. When dyslipidemia and high blood pressure are combined, renal function may be compromised. Dyslipidemia and abnormal lipid metabolism are widespread in renal illness, which has a higher mortality rate among obese individuals with renal failure. These conditions are known to contribute to glomerulosclerosis. Furthermore, there is a link between elevated lipid levels after transplant and a higher risk of heart disease and vessel wall disease. Serum triglycerides, total cholesterol, low-density lipoprotein (LDL) very low density lipoprotein (VLDL) cholesterol and significant oxidation of low-density lipoprotein (LDL) cholesterol are the main lipid profiles examined. They have all been linked to a higher risk of atherosclerosis in both genders experiencing renal failure[8,9]. The way that hyperlipidemia encourages kidney failure.

Step 1: Fatty acids, phospholipids and cholesterol are reabsorbed in the glomerulus
Step 2: Filtered material includes lipoproteins and albumin, among other proteins
Step 3: Tubule-interstitial inflammation caused by allumin and lipoproteins.
Step 4: Encourages tissue damage and foam cell production.
Step 5: The formation of matrix and glomerulosclerosis may be aided by lipoprotein accumulations in the glomerular mesangium.
Step 6: Cultured mesangial cells produce more matrix proteins in response to LDL.
Step 7: Boosts the production of cytokines that promote inflammation.
Step 8: Assist in enlisting and triggering the activity of circulating macrophages.
Step 9: eventually raises the amount of fat that is deposited in adipose tissue.

In accordance with the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKFK/DOQI) guidelines, the current study aims to investigate the altered lipid and lipoprotein abnormalities in CKD from stage III to stage V. These abnormalities are critical in the development of atherosclerotic cardiovascular disease.

MATERIALS AND METHODS

This study was conducted in 50 patients with chronic kidney disease and 50 normal people taken as controls. All the patients in this study group were selected from those who were admitted to department of Nephrology, NIMS, Jaipur.

Inclusion criteria:

- Patients between age group of 18-59 years with established chronic Kidney disease[2]. Patients who were on conservative treatment[3]. Established renal failure was ensured by radiological evidence

Exclusion criteria:

- Patients with Acute renal failure, nephrotic syndrome[2]. Who are on drugs β blockers, statins and oral contraceptive pills[3]. Pregnant female patients

History regarding symptoms and duration of the kidney disease, hypertension, diabetes, smoking, alcoholism, drug intake and treatment were elicited. A detailed clinical examination was performed in all patients including Height and Weight, Blood Pressure, renal function tests, abdominal ultra-sonogram and Electrocardiogram were done for all patients. After 12 hours of overnight fasting blood sample was taken for lipid profile from patients and controls and for TSH levels from patients. Evaluation of lipid profile The lipid profile evaluation was carried out based on the classification of the values obtained for LDL cholesterol, HDL cholesterol and triglycerides, according to reference values of V Brazilian Guideline on Dyslipidemias and Atherosclerosis prevention (2013). The results of lipidogram were obtained from the database of the own clinic, directly from the electronic patient data file. Biochemical dosages were gotten in the clinical laboratory, which uses enzymatic colorimetric method. Statistical analysis data obtained were processed in Excel for Windows and statistical package for the social science (SPSS) version 18.0. It was performed an exploratory and descriptive analysis in the variables. For continuous variables, data werepresented as mean and standard de viation and for categorical variables with measures of absolute and relative frequencies. For the comparisons in relation to quantitative variables between the groups, it has been used the parametric, since such variables followed the normal distribution, according assessment through

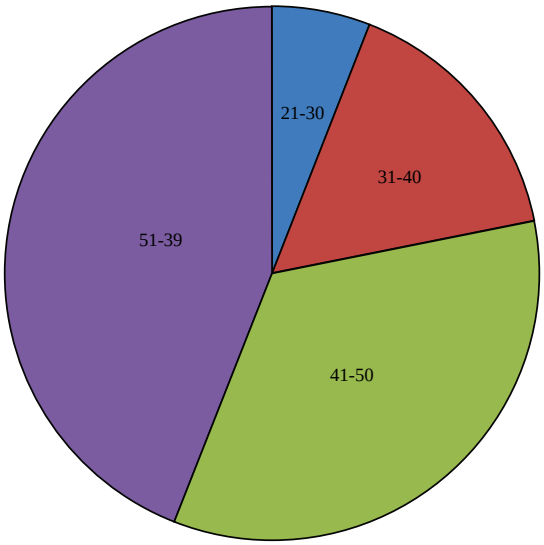

Fig 1: Age wise distribution of patients

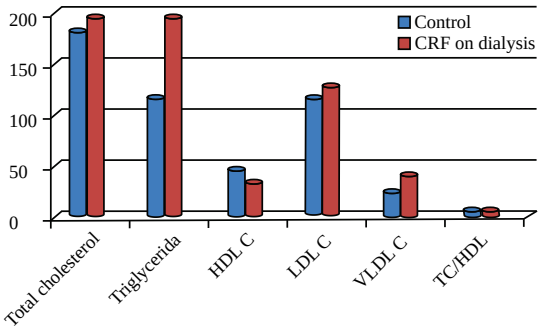

Fig 2: Complete lipid profile of CKD patients

Table2: Lipid profile in CKD patients

Lipid profile measured	Control	CKD
Total cholesterol	171.78±35.73	168.54±3.82#
TG	129.12±34.43	171.43±2.98#
HDL cholesterol	37.12±8.34	29.92±1.89#
LDL cholesterol	119.32±8.74	109.72±7.32#
VLDL cholesterol	21.32±9.01	33.91±3.28#

the kolmogorov-smirnov test. The associations between variables were tested by applying the chi-square test. In addition, Pearson's correlation analysis was applied to find out the correlation. A significance level of $p<0.05$ was used in all analyses.

RESULTS

The patients ranged in age from 20-59 years old. The majority of patients are in the 50-59 age range. Table 1 illustrates that, in comparison to the control group, CKD patients had lower levels of total cholesterol, HDL cholesterol and LDL cholesterol as well as higher levels of triglycerides and VLDL cholesterol. However, there was no statistical significance seen in the values. $p>0.05$) Fig 1 and 2.

DISCUSSION

One of the main factors contributing to higher rates of morbidity and death in the general population is chronic renal failure. According to estimates, it affects 785 people per million. Compared to other causes, cardiovascular problems accounted for 20 times more deaths in people with CRF. A clinical picture of early atherosclerosis is seen in CRF patients. Key pathways of atherogenesis in CRF[10] are disorders of lipoprotein metabolism during uremia and dialysis. Fifty patients with chronic renal disease who received inpatient or outpatient care were included in this cross-sectional descriptive research. Over the course of 1.5 years, the instances were gathered. Among the patients were those receiving hemodialysis and conservative care. The study's findings indicate that these CKD patient's lipid profiles have undergone significant changes. Other studies on the lipid profile in individuals with chronic kidney disease (CKD) found elevated LDL and decreased HDL[11,16] as well as hypertriglyceridemia and hypercholesterolemia. Contrarily, in the current investigation, we have seen decreased blood cholesterol and LDL, increased VLDL, decreased HDL, and hypertriglyceridemia.

Triglycerides: Triglycerides were somewhat higher in the current investigation and there was a statistically significant difference between the study group and the control group (p-values 0.001). Hypertriglyceridemia may result from decreased triglyceride clearance from the plasma as a result of inhibition of both hepatic and Lipoprotein Lipase (LPL)[17]. The decreased activity of hepatic triglyceride lipase (HTL) which cleaves triglycerides into free fatty acid (FFA) for energy synthesis or storage and LPL is probably the cause of the impaired catabolism. The following factors are most likely to blame for the decreased hepatic and LPL activity: 1) The hemodialyzed patients' frequent heparinization, 2) An elevated apo C-III/apo C-II ratio, 3) The presence of other lipase inhibitors in the plasma and 4) Reduced LPL synthesis as a result of hyperparathyroidism and suppressed insulin levels.

In comparison to apo C-II, the plasma apo C-III level is elevated disproportionately. LPL[19] is activated by apo C-II and inhibited by apo C-III. HDL and LDL alterations in size and content are caused by hypertriglyceridemia. Increased hepatic VLDL secretion due to hypertriglyceridemia triggers the activation of the Cholesteryl Ester Transfer Protein (CETP). Triglycerides are transferred from CETP to LDL and

HDL, resulting in the production of triglyceride-rich LDL and HDL. The triglyceride content of HDL and LDL particles is hydrolyzed by hepatic triglyceride lipase, resulting in the creation of a subfraction known as tiny dense LDL and HDL. Small dense LDL (SDLDL) is more prone to oxidation, has a lower affinity for the LDL receptor and can pass through artery walls more readily[20]. Due to its strong atherogenic properties, oxidised SDLDL raises the risk of cardiovascular illnesses. Hypertriglyceridemia, low HDLc and increased lipoprotein a have been observed by Maheshwari *et al*.[21]. These conditions may raise the risk of atherosclerosis and cardiovascular disease, which in turn may increase morbidity and mortality in patients on maintenance hemodialysis.

HDL cholesterol: In the current investigation, there was a statistically significant (p<0.001) drop in HDL cholesterol between the patient and control groups. The primary protein components of HDL, apolipoproteins A-I and A-II are found in lower concentrations in patients with compromised renal function[22]. LCAT (lecithin cholesterol acyl transferase) the enzyme that esterifies free cholesterol in HDL particles, has lower activity in CKD patients[23] whereas CETP (cholesteryl ester transfer protein) has higher activity[24]. CETP facilitates the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins, which lowers serum concentrations of HDL cholesterol. Storing the apo C and apo E needed for the metabolism of chylomicrons and VLDL[25] is one of HDL's primary roles. When compared to controls, DSSK Raju *et al*.'s study found that blood HDL-C was significantly lower in CKD patients in both the non-dialysis and hemodialysate groups[26].

Total cholesterol: Although total cholesterol levels were lower in CKD patients in the current investigation when compared to controls the differences were not statistically significant (p-value 0.09). Hypercholesterolemia was noted in CKD patients in a number of additional investigations. The racial variation of the study group and eating habits that vary based on geographic variation and culture could be the cause of the discrepancies in observations between the studies. Malnutrition and related infections, which are particularly prevalent in hospital patient populations, can also result in lower cholesterol levels. Significantly higher levels of cholesterol were seen in CKD patients than in controls, according to Balode *et al*. Sixty patients with chronic renal failure were investigated by Sumathi *et al*. for serum total cholesterol, TGL, HDLc, LDLc and VLDLc. When comparing the patient group to their controls, they found a significant decrease in HDLc and a significant increase in serum total cholesterol, LDLc and VLDLc.

VLDL: When CKD patients were compared to controls, their VLDL levels increased significantly (p<0.001). The overproduction of VLDL brought on by insulin resistance and decreased clearance of LDL cholesterol are the primary causes of the increase in VLDL cholesterol in CKD.

LDL: The value of LDL was found to be lower in the CKD group as compared to the controls, however there was no discernible difference in LDL levels between the patients and controls (p-value 0.059). Hepatic LDL receptor gene expression is not changed in patients with chronic kidney disease (CKD) until severe glomerulosclerosis or high proteinuria occurs. Patients with CKD have altered LDL particle metabolism, which results in the production of sdLDL. A subfraction of LDL called sdLDL is created when hypertriglyceridemia is present. It increases atherogenesis, becomes oxidised, and has an elevated atherogenic potential.

CONCLUSION

Most of the chronic renal failure patients are at high risk of prevalence of cardiovascular disease due to elevated serum lipid profile. Among the lipid profile parameters the decrease in HDL level and VLDL level favours the potential risk among renal failure patients. The under lying factor behind this is prolonged usage of heparin, low flux dialyzer and acetate usage in the dialyzer. Elevated lipid profile not only affects the cardiovascular system, it has decreases the quality of dialysis access. Regular screening of lipid profile may reduce the risk of several complications in the body not only in the renal failure patients and also in the healthy peoples.

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