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Research Article

A Study of Lipid Profile and Staging in Non-Diabetic Chronic Kidney Disease

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Abstract
Background: *Patients with chronic kidney disease (CKD) are prone to develop diseases related to the cardiovascular system owing to the accelerated rate of atherosclerosis due to a multitude of factors, one of them being the characteristic "atherogenic" lipid profile abnormality that they exhibit.*
Aims and Objectives: *To study the pattern and correlation between lipid profile and staging in non-diabetic Chronic Kidney Disease patients.*
Materials and Methods: *A total 100 CKD patients (Case group) were studied and compared with 100 age and sex matched healthy subjects (Control Group) in the Department of Medicine, G.R. Medical College and J.A. Group of Hospitals, Gwalior between February 2014 to November 2015. Detailed history followed by blood urea, serum creatinine, serum albumin, albumin to creatinine Ratio (ACR), albumin excretion ratio (AER) was recorded. Plasma lipids concentration was also measured after a 12-h overnight fast.*
Results: *Male preponderance (56%) was observed. Value of triglyceride (166.3±51.8 vs. 109.9±26.86; p<0.0001 respectively) and VLDL (31.2±12.32 vs. 23.01±5.46; p<0.0001 respectively) were increased in cases as compared to control. HDL (30.44±7.06 vs. 46.98±10.67; p<0.0001 respectively) was lower in cases in comparison to controls. Comparing lipid profile with GFR categories showed that TG, LDL and VLDL were progressively increasing with successive categories while HDL value was progressively decreasing. TG, HDL, LDL and VLDL value were more deranged in A3 category in comparison to A2 while cholesterol value was rather decreased in A3(p >0.05). Negative correlation was obtained between GFR and triglycerides (r=-0.543, p=0.001), total cholesterol (r=-0.275, p=0.001), LDL (r=-0.427, p=0.001) and VLDL (r=-0.476, p=0.001) while positive correlation was recorded with HDL (r=0.268, p=0.001).*
Conclusion: *The high prevalence of lipid abnormalities in CKD may accelerate the progression of CVD and increase the mortality of patients. Hence it is important to test and detect patients at high risk early on and manage accordingly.*
Keywords: *Lipid abnormality, chronic kidney disease, non-diabetic CKD.*

Introduction

Cardiovascular disease (CVD) is one of the major cause of mortality and morbidity in patients with chronic kidney disease (CKD). The prevalence of hyperlipidemia or dyslipidemia is much higher compared to the general population. The majority of patients with CKD die of CVD rather than of end stage renal disease (ESRD).[1]

The KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines on dyslipidemias in CKD suggest that all patients should therefore be evaluated for dyslipidemias. They should have a complete fasting lipid profile with total, low density lipoprotein (LDL) and high-density lipoprotein (HDL), and triglycerides measured to identify those at risk and those who require treatment.[2]

Patients with CKD should be considered a "very high risk" category and aggressive therapeutic intervention initiated to reduce the risk of cardiovascular events. In addition to its effect on the cardiovascular system studies in a variety of animal models have shown that hypercholeste-rolemia accelerates the rate of progression of kidney disease.[1] All patients with chronic kidney disease experience a secondary form of dyslipidemia that mimics the atherogenic dyslipidemia of insulinresistant patients. This is characterized by an increase in serum triglycerides with elevated VLDL, small dense LDL particles, and low HDL cholesterol.[3]

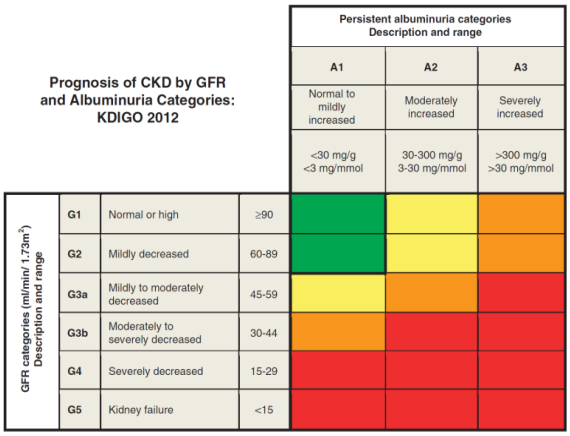
Hence in present study we tried to evaluate pattern and correlation between lipid profile and staging in non-diabetic Chronic Kidney Disease patients.

Material and Methods

The present study was performed on 100 patients (Case group) in the Department of Medicine, G.R. Medical College and J.A. Group of Hospitals, Gwalior from February 2014 to November 2015. Hundred age and sex matched healthy subjects were included for comparison (Control group).

All cases of chronic kidney disease as defined in the criteria were included. Patients with diabetes mellitus, dyslipidemia/already on lipid lowering drug therapy, chronic liver disease and hypothyroidism were excluded from the study.

Figure 1: KDIGO Classification of CKD



In all the cases written inform consent was obtained from each subjects and detailed clinical history including complaints, past history, personal history, family history was taken. All the selected patients were subjected to relevant investigations like CBC, blood urea, serum creatinine, serum albumin, albumin to creatinine Ratio (ACR), albumin excretion ratio (AER) was performed.

Patient was considered as anemic if facial pallor was associated with conjunctival and buccal mucous membrane pallor and nail pallor. It was later confirmed by hemoglobin estimation. Anemia was defined as hemoglobin level of < 13 gm/dl in males and < 12 gm/dl in females. Edema was considered as present when the pitting was demonstrated which persisted for more than 30 seconds. Hypertension was defined as blood pressure > 140 mmHg systolic and/or > 90 mmHg diastolic. Oliguria was defined as urine output < 400 ml/24 hrs or <0.5 ml/kg/hr in study population. GFR was calculated on the basis of CKD- EPI equation. Plasma lipid concentration was also measured after a 12-h overnight fast.

All the data was analyzed using IBM SPSS ver. 20 software. Cross tabulation and frequency distribution was used to prepare table. Microsoft excel 2017 was used to prepare graphs. Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in Number (%). Quantitative and Categorical data was analyzed using student t test

and Chi square test respectively. Level of significance was assessed at 5% level.

Results

Most of the patients in cases (23%) belong to age group of 51-60 years and in control group 34% belonged to age group of 40-51 years. Among cases 56% were male whereas in control 59% were males.

Table 1: Comparing mean lipid levels between both the groups

Parameters	Cases		Control		P value
	Range	Mean±SD	Range	Mean±SD	
TC	92-236	158.8±38.8	67-268	153±41.53	NS
TG	44-184	166.3±51.8	38-328	109.9±26.86	<0.0001
HDL	23-84	30.44±7.06	16-53	46.98±10.67	<0.0001
LDL	47-171	109.2±39.6	39-190	97.97±30.77	NS
VLDL	8.9-36	31.2±12.32	11-65	23.01±5.46	<0.0001

Data is expressed as Mean±SD, TC; total cholesterol, TG; triglyceride, HDL; high density lipoprotein, LDL; low density lipoprotein, VLDL; very low density lipoprotein, NS; not significant, p value <0.05 is considered as significant

Table 2: GFR category wise lipid profile distribution

Category	N (n=100)	TC	TG	HDL	LDL	VLDL
G1	01	150	87	36	60	17.4
G2	02	113±9.89	89±29.69	38±2.82	72±22.62	17.8±5.93
G3a	08	119±32.82	87.75±35.85	46.11±11.96	65.25±22.12	16.92±5.59
G3b	09	154.48±41.4	136.02±35.37	32.75±6.86	94.15±39.05	21.44±7.72
G4	11	174.27±45.33	163.72±25.56	31.45±6.89	104±27.54	29.1±8.81
G5	69	162.97±36.03	183.1±46.45	29.24±6.31	118.84±39.05	35.05±11.85

Data is expressed as Mean ± SD, TC; total cholesterol, TG; triglyceride, HDL; high density lipoprotein, LDL; low density lipoprotein, VLDL; very low density lipoprotein, NS; not significant, p value <0.05 is considered as significant, GFR; glomerular filtration rate

Table 3: Albuminuria category wise lipid profile distribution

Category	N (n=100)	TC	TG	HDL	LDL	VLDL
A1	2	135±21.21	98.5±16.26	38±2.82	74±19.79	19.7±3.25
A2	22	161±43.64	155.18±54.2	31.05±8.26	103.39±35.39	27.19±11.89
A3	76	158.79±38.2	171.25±50.67	30.06±6.74	111.77±41.05	32.66±12.33

Data is expressed as Mean ± SD, TC; total cholesterol, TG; triglyceride, HDL; high density lipoprotein, LDL; low density lipoprotein, VLDL; very low density lipoprotein, NS; not significant, p value <0.05 is considered as significant

The strongest correlation was with triglycerides (r=-0.543, p=0.001). With decreasing GFR, triglyceride level increases. Apart from this total cholesterol (r=-0.275, p=0.001), LDL (r=-0.427, p=0.001) and VLDL (r=-0.476, p=0.001) have negative correlation with GFR while HDL (r=0.268, p=0.001) showed positive correlation i.e. with decreasing GFR, HDL level also fell.

Discussion

In present study lipid profile in patients with chronic kidney disease showeda significant deviations in the lipid parameters as compared to controls.

According to CKD fact sheet,[4] incidence of chronic kidney disease increases with age because risk factors for CKD also increase with age. In present study majority of patients were in age group 51-60 yrs. (23%), with a mean age of 47±16 yrs. (range 14-81 yrs). Kayima et al[5], had similar age distribution of patients in their study. In the study conducted by Avasthi et al[6], mean age of patients and controls was 51.17±13.53 (range 22-70 years) and 49.80±15.20 (range 21-75 years) respectively. Rajapurkar et al., found that mean age for CKD in western zone of India is 50.2 ± 14.9 years with male: female ratio of 69:31.[7]

In the present study, male outnumbered females in sex distribution; out of 100 patients, 56% were male. Lim et al[8] studied, 46 patients of CKD, out of which 56.22% were male and 43.48% were female and maximum patients were of age group 29-59 years with a mean age of 42.8±6 years.

In present study triglycerides were markedly elevated compared to control group. Attman et al [9]stated that hypertriglyceridemia is the most common plasma lipid abnormality in adult patients and children with renal failure. Mohanraj et al[10] also had similar findings.

The precise cause for hypertriglyceridemia in CKD patients has not been delineated. Available data derived from kinetic studies with intra lipid administration have demonstrated that reduced catabolism of triglyceride is the predominant defect due to deficiency of lipoprotein lipaseor hepatic triglyceride lipaseor both.[11,12] These enzymes are the primary mediation of the process, reason for decrease in activity of these enzymes is not clear.

In present study TC values were raised in patients as compared to controls but this value was statistically not significant. Appel et al[13] found decreased values of cholesterol in CKD patients in comparison to normal healthy control. Increase in TC was found in studies conducted by Anderson et al[21]and Mohanraj et al[10], whereas there was no significant change in cholesterol level in study conducted by Shah et al.[14]

In present study there was decrease in HDL cholesterol seen in patients compared to controls. Goldberg et al[15] and Fuh et al.,[16] also found decrease in HDL concentration in CKDpatients compared to controls. Contrary to present study Rapoport et al [17]showed that there was no decrease in HDL concentration in chronic kidney disease patients.

Studies have shown that low HDL is associated with decrease in both the fractional catabolic rate and the total synthetic rate of Apo AI/HDL. The worse the renal function slower is the fractional catabolic rate and the lower the Apo AI/HDL.[18]

The changes in lipoprotein lipase activity, the enzyme that are responsible for VLDL-triglyceride hydrolysis, may play a major role in this regard. For example lipoprotein lipase activity is decreased in patients with CKD.[19] The lower the lipoprotein lipase activity is, the lower the plasma HDL concentration. There is also evidence that patients with CKD have a factor in the plasma which inhibits lipoprotein lipase. Thus there are several possible mechanisms involving an abnormality in VLDL - triglyceride hydrolysis which could result in abnormal HDL metabolism and HDL concentration in patients with chronic renal failure.[18]

There is significant rise in VLDL levels in CKD patients compared to controls (P<0.001). Cheung et al.[20]showed increase in very low density lipoproteins. The LDL levels were marginally raised in patients as compared to controls and this was not statistically significant (P=0.0811). Anderson et al.,[21] showed increase in LDL levels. Appel et al[13]showed normal or decrease in LDL levels. Mohanraj et al[10]stated that in the absence of heavy proteinuria CKD does not significantly affect gene expressions of either hydroxyl-3-methylglutaryl-CoA reductase (HMG-CoA reductase) which is the rate-limiting enzyme for cholesterol biosynthesis, or that of cholesterol 7α-hydroxylase which is the rate-limiting enzyme for cholesterol catabolism and conversion to bile acids. So when there is absence of heavy proteinuria hepatic LDL receptor gene expression is not altered, thereby LDL levels are not elevated.[10]

In correlating lipid profile with GFR categories, value of TG, LDL and VLDL showed progressively increasing trend with successive categories while HDL value was progressively decreasing and HDL was lowest in G5. Total cholesterol value showed increasing trend from G2 to G4 but in G5 value was lower than G4.In correlating lipid profile with albuminuria categories; TG, HDL, LDL and VLDL value were more deranged in A3 category in comparison to A2 while cholesterol value was rather decreased

in A3. There was no statistical difference in lipid profile between A2 and A3 staging. (p value>0.05) Similar reports were revealed by Gantaet al.[22]

Present study showed positive correlation of lipid profile with HDL i.e. with decreasing GFR, HDL level was falling while total cholesterol, triglyceride, LDL and VLDL were showing nega-tive correlation with decreasing GFR, their value increased. Similar results were shown by Appel et al[13], Anderson et al.,[21] and Mohanraj et al [10].

However, there is need of further large studies to strengthen the data and give further recommendation for early detection of lipid abnormalities and cardiovascular abnormalities. As a limitation; effect of lipid lowering drug therapy on lipid profile was not studied as duration of study was short.

Conclusion

Study showed that there was significant increase in TG and VLDL in comparison to controls and there was significant decrease in HDL in comparison to control. While TC and LDL were raised in comparison to control but were found non-significant. Significant correlation between lipid profile parameters and GFR was found (most significant was of TG). It proves that as GFR decreases (or stage increases), dyslipidemia worsens. As most of the patients present in stage 4 or 5, there is need of screening program to detect patients at earlier stage. The rise in triglyceride and VLDL concentrations and reduction in HDL is the cause for increase cardiovascular abnormalities in CKD patients and CVD is the most common cause of mortality in CKD patients, it can be concluded that it is worthwhile detecting and treating dyslipidemia in these patients.

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