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Research Article

Hypertriglyceridemia in Reference to Chronic Kidney Disease

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Abstract
Introduction: *Chronic kidney disease is in increasing trend due to increase inprevalence of Diabetes mellitus and Hypertension. Dyslipidemia is most common entity seen in chronic kidney disease patients and is responsible for Cardiovascular Disease (coronary artery disease). Hypertriglyceridemia is most common form of deranged lipid profile seen in them. So its utmost importance to identify dyslipidemia and treatment of the same to prevent morbidity and mortality related to it.*
Methods: *It is a case control study conducted in NSCB MCH JBP, MP after ethical committee clearance. Where, Subjects of 50 in number who are healthy people placed in Group-1, CKD patients who never underwent hemodialysis of 50 in number are in Group-2 and CKD patients who are on maintenance hemodialysis of 50 in number in Group-3. The baseline characteristics were noted and baseline investigations are done and after 12 hours of fasting, blood is collected for lipid profile, the values are tabulated and compared with each group.*
Results: *In our study we found that, there is increase in Tryglycerides (TG) in CKD patients with and without hemodialysis. The values are more consistent with increase in stages of CKD. TG values are more high in group 3 compared to group 2. Also TG values are higher in CKD patients with Diabetes Mellitus compared to CKD patients without DM. The values were statistically significant in each comparison (p-value <0.05). Along with Triglycerides (TG), Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL) and Total Cholesterol increased in group 2 and 3 compare to group 1. High Density Lipoprotein (HDL) is decreased in group 2 and 3 compare to healthy patients.*
Conclusion: *Present study demonstrated that there is dyslipidemia with predominant hypertriglyceridemia in CKD patients irrespective of mode of management, but the derangement is much more common and significant in CKD with hemodialysis group and they are at high risk of cardiovascular disease. So one should consider to start lipid lowering drugs which decreases disease progression and dyslipidemia and its related morbidity and mortality.*
Keywords: *Chronic Kidney Disease (CKD), Hypertriglyceridemia, Hemodialysis, Cardiovascular disease.*

Introduction

Chronic kidney disease (CKD) is an irreversible final event of the long lasting renal parenchymal disease, because of various causes which are known more for its morbidity than for its mortality. Since the advent of various medical therapy and invasive therapies like hemodialysis and peritoneal dialysis the severity of the CKD and its consequences have undergone tremendous changes. Cardiovascular disease (CVD) especially coronary artery disease is a most important and most common cause of morbidity and mortality in patients with CKD[1].

Irrespective of the causes of CKD, it leads to structural and functional hypertrophy of surviving nephrons in initial stages and atrophy in advanced stages. Clinically the patients are asymptomatic in early disease, with progression of disease process the increasing amount of nephron losses leads to the end stage of renal disease (ESRD) which then manifest with prolonged signs and symptoms of uremia.

The traditional risk factors for CVD include old age, male gender, smoking, hypertension, diabetes, and hyperlipidemia and non traditional risk factors such as anemia, inflammation and oxidative stress, and mineral and bone abnormalities in CKD have an undeniable effect on the increased prevalence of CVD seen in CKD patients. One of the most important pathophysiological mechanisms for CVD in patients with CKD is the widespread and accelerated rate of formation of atherosclerotic plaques due to hyperlipidemia and other causes being uremic toxins, inflammation, oxidative stress, and endothelial dysfunction[2].

In a retrospective cohort study only a minority of patients (0.5–1%) with mild to moderate CKD developed ESRD over a 5-year follow up, while as many as 19 and 24% of these patients with mild and moderate renal insufficiency, respectively, died mostly of cardiovascular complications in the same period[3]

Indian studies on lipid profile abnormalities in chronic Kidney Disease (CKD) have varied from no abnormalities at all to significant abnormality (Hypertriglyceridemia and reduced HDL) as described in the Western literature. In, Atherosclerosis Risk in Communities (ARIC) cohort study. A serum triglyceride level of ≥182 mg/dL was found to be significantly associated with an increased risk for cardiovascular disease among CKD participants[4], but in analysis of the Modified Diet in Renal Disease (MDRD) study showed there is no association between serum triglycerides and CVD, the progression of CKD or death among non-diabetic CKD patients[5]

The study done by B Shah, S Nair, which shows that CKD is predominantly accompanied by lipid abnormality in the form of Hypertriglyceridemia[6], Various studies conducted in CKD have confirmed that dyslipidemia leads to progression of renal disease other than complications. The American Heart Association (AHA) has issued guidelines for the management of hypertriglyceridemia in the general population, which implies the fact that serum triglyceride is also an important risk factor for cardiovascular disease and death[7].

Hence it is important to study the lipid profile changes in CKD patients which may help in proper evaluation of disease pathogenesis, pathogenesis of dyslipidemia and in prevention of disease progression, application of therapeutics and prevention of CVD related incidences.

Methodology

This is a case control study which is conducted in Chronic Kidney Disease Patients of age group 18 to 80 years who presented in NSCB MCH Jabalpur (MP) between March 2017 to August 2018. Study is done after getting Ethical clearance from institutional ethical committee. The Informed consent is taken from all subjects participating in this study. Total 150 candidates are divided in to three groups. Group1: Healthy Control patient (n=50), Group 2: CKD patients on conservative management (that is without hemodialysis) (n=50) and Group 3: CKD patients on hemodialysis (n=50).

Inclusion Criteria

Patients with established chronic kidney disease are included in study irrespective of the etiology, as evidenced radiologically (bilateral shrunken kidney/ loss of corticomedullary differentiation) or biochemically (elevated blood urea, serum creatinine for more than 3 months.)

Exclusion Criteria

Those with Acute Kidney Injury, Renal transplant patients, Nephrotic syndrome, patients who are on drugs affecting lipid metabolism such as beta blockers, statins and oral contraceptive pills and Female patients who are pregnant are excluded from study.

The baseline details like duration of symptoms of CKD, associated comorbidities like diabetes, hypertension and drug history, habits, anthropometry, vitals measurement and brief systemic examination was done and findings were recorded.

After overnight fasting of 12 hours, venous blood is collected for lipid profile and Renal function tests Along with complete blood count, Liver function tests, urine examination, USG abdomen and pelvis were collected. The serum total cholesterol(TC), high density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and very low density lipoprotein (VLDL) are measured using commercially available RANDOX autoanalyzer and low density lipoprotein cholesterol (LDL-C) calculated using Friedewald`s Formula (LDL=TC-HDL-TG\5)[8].

Non numerical entries were coded numerically into nominal/ordinal distribution before analysis. Continuous variables were analyzed using Mean± standard deviation. Mean difference between two independent groups was analyzed using student t-test. This was analyzed using Epi Info^{tm} 7.1.5 and SPSS for windows version 20.0 (Trial version).

eGFR[9] calculation is done by Equation from the Modification of Diet in Renal Disease (MDRD), Estimated GFR (ml/min per 1.73 m2) = $1.86 \times (SCr)^{-1.154} \times (age)^{0.203}$ Multiply by 0.742 for women, Multiply by 1.21 for black-African ancestry, 0.763 for Japanese, 1.233 for Chinese.

Patients are grouped based on eGFR values in to stages according Kidney Disease Improving Global Outcome (KDIGO) Classification[10]. GFR (ml/min/1.73m^2) categories, Stage-1:>90, Stage-2:60-89, Stage-3A: 45-59, Stage-3B:30-44, stage-4:15-29, Stage-5: <15.

Results

The basic characteristic features of candidates have been shown in table-1. Majority of people (42%) were belong to 25-49 years in group-2, 52% in 50-74 years in group-3. Males were higher in number in group 2 and 3 (72% and 56% respectively). Most of the subjects were having BMI 17.5-22.99 (46% and 48% in group 2 and 3 respectively). CKD patients with DM were 40% and 56% in group 2 and 3 respectively. In this study, in group-2: 6,15,29 candidates were in stages 3b, 4 and 5 and in group-3: 2 and 48 candidates were in stage 4 and 5 respectively, which has been tabulated in second table.

The fasting lipid profile pattern between healthy controls and CKD patients is depicted in table-3 and in graph-1. There is increase in TC,LDL,TG and VLDL and decrease in HDL in CKD patients compare to healthy controls and comparison is statistically significant for each parameter ($p<.05$). The stage wise distribution of TG is shown in table-4 and graph-2, in which There is increase in triglyceride with increase in stages of CKD. In our study the TG values in stages 3B and 4 in groups 2 and 3 was not significant and comparison could not be done as sample size in these groups was small, but it is found that the values were significant ($p<.05$) as sample size was adequate in stage 5 in each group. The TG was increased in 68% people in group-2 and 73% in group-3 people of stage-5 and the maximum values were 216.56 and 263.45 in groups 2 and 3 respectively. We also found significant increment in TG values diabetic CKD patients compare to non diabetic CKD patients ($p<.05$) as depicted in table-5.There is increase in TG values in males and females of CKD patients compare to healthy counterpart ($p<.05$) as shown in table-6.

Table-1: Baseline features of study group.

Characteristics	Group-1	Group-2	Group-3
No of Candidates	50	50	50
Age(years) (mean±SD)	39.92±16.59	42.02±14.30	48.08±13.15
Sex(male/Female)	22/28	36/14	28/22
BMI(kg/m^2)	22.43±2.14	22.99±1.90	22.86±2.11
No of Diabetes patients	00	20	28

Table-2: Stage wise Distribution of CKD patients.

CKD Stage	CKD patients without HD	CKD patients with HD
3B	6	--
4	15	2
5	29	48

HD -Hemodialysis

Table-3 Fasting lipid profile of healthy controls and CKD patients

Parameter (mg/dl)	Healthy controls (mean±sd)	CKD patients (mean±sd)	p-value
Total cholesterol	130.59±16.12	195.21±24.64	<0.05
HDL-cholesterol	54.21±3.94	38.35±4.01	<0.05
LDL-cholesterol	94.96±18.83	153.07±23.84	<0.05
Triglycerides	94.02±19.92	205.75±53.40	<0.05
VLDL	13.96±3.78	29.14±16.33	<0.05

Table-4: Stage wise distribution of Triglyceride in CKD patients.

Stage	CKD patients without HD	CKD patients with HD	p-value
3B	165.43±17.18	-------	-------
4	174.54±5.78	182±2.1	>0.05
5	189.15±24.26	225.41±36.64	<0.05

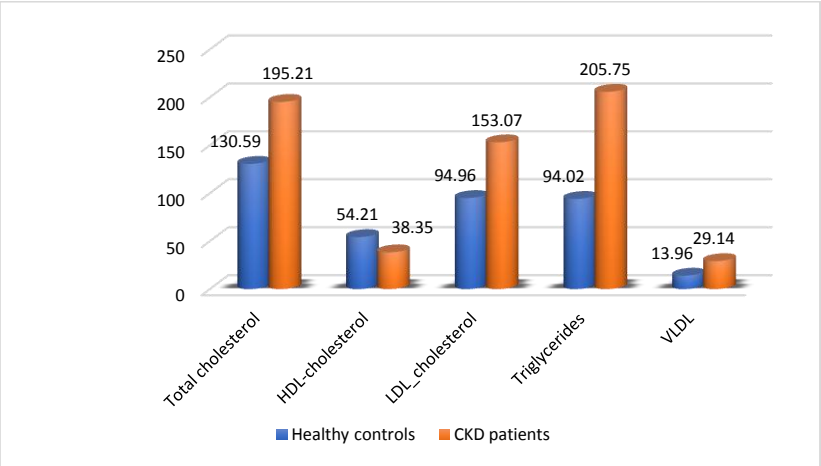
Table-5: Triglyceride value in diabetic and non-diabetic CKD patients.

CKD patients without Diabetes	CKD patients with Diabetes	p-value
184.78 ±48.33	228.56 ±49.55	<0.05

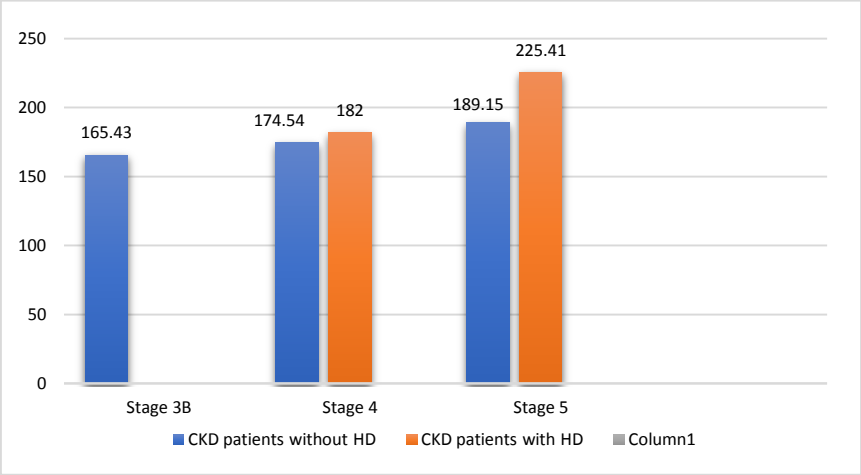
Table-6: Triglyceride values in male and female patients.

Sex	Healthy Control	CKD patients	p-value
Male(28/64)	93.90±20.46	191.43±25.27	<0.05
Female(22/36)	94.17±29.69	203.55±32.14	<0.05

Graph-1: Lipid profile of Healthy controls and CKD patients



Graph-2: Stage wise distribution of Triglycerides in CKD patients.



Discussion

We conducted this study to determine the lipid profile changes in CKD patients on conservative management and on maintenance hemodialysis and to compare them with lipid profile of healthy controls. The study is conducted in 150 people, of which 50 were CKD patients on conservative management, 50 were CKD patients on maintenance hemodialysis and rest 50 were healthy controls. Study population were selected as per the inclusion and exclusion criteria. Serum TC, HDL cholesterol (HDL-C), LDL-C, and TGLs were measured using Randox autoanalyzer. The results were tabulated and statistically analyzed.

Lipid transport occurs by two pathways, (1) an exogenous pathway concerned with the absorption of dietary fat, its transport by chylomicrons, and the eventual breakdown of the derived triglyceride into glycerol and fatty acids, and (2) an endogenous pathway. In the endogenous pathway, the liver secretes triglyceride-rich VLDL particles, the triglycerides of which are cleaved into glycerol and fatty acids by the enzyme lipoprotein lipase (LPL) located in the endothelium of adipose and other tissues. This enzyme requires Apo CII as an activator. The VLDL particles are reduced in size and become remnants or intermediate-density lipoproteins (IDL). The IDL (that is, the VLDL remnants) normally are present only transiently in the plasma, and can either be taken up by the liver (via the same receptors as LDL) or lose ApoE and be converted to LDL particles. The LDL particles contain Apo Bl00 (which binds to the LDL receptor) as well as a considerable amount of cholesterol, but very little triglyceride. The LDL particles transport cholesterol to hepatocytes and peripheral tissues and are removed from the circulation both by the receptor-mediated action of hepatocytes and other cholesterol-requiring tissues and by nonspecific binding to hepatocytes and peripheral tissue. The HDL particles, secreted by the liver and other tissues, are transformed in the circulation from HDL3 to HDL2 particles bythe acquisition of additional protein moieties. The HDL particles readily take up free cholesterol and transport it between cells in the body; these particles are important in the removal of cholesterol from certain tissues. The major apoprotein associated with HDL, Apo Al is an activator of the enzyme lecithin cholesterol acyltransferase (LCAT). This enzyme esterifies free cholesterol in HDL, allowing HDL to transfer the cholesterol esters to other lipoprotein particles (VLDL and LDL) for transport to the liver and subsequent removal.

Triglyceride levels were significantly elevated in our study than control group. The present study demonstrates that CKD is commonly accompanied by lipid abnormality in the form of hypertriglyceridemia. Result of our studies were similar to the result of various studies conducted in Western countries and recent Indian studies like Gupta DK, Das BS[11,12]et al. The increase in

triglyceride levels is because of impaired activity of lipoprotein lipase (LPL)[13] and also by direct inhibitory effect of various uremia induced toxins on the enzymes involved in lipid metabolism[14] which represent the most prominent pathophysiological mechanisms of development of hypertriglyceridemia in chronic kidney disease patients.

In study U Sreenivasulu et al[15] the TG values in group-2 with comparison to group-3 were 181.6±15.8, 199.2±10.1 (<0.0001), In Lokesh Rao Magar et al[16] in group-2 and 3 TG- 206.7±15.3, 236.3±13.4($p<0.05$), In Hariom Sharma et al[17] In group-2 and 3 were TG- 209.0 (200.0, 216.0), 240.5 (206.0, 272.0) ($p<0.05$). These study results in reference to TG were comparable to our study. The increase in Triglycerides in hemodialysis patients is more compare to conservative CKD patients due to, heparin which is used in hemodialysis inhibits lipoprotein lipase (LPL), which is responsible for hydrolysis of triglycerides.

Conclusion

Dyslipidemia is most prominent change in CKD patients compare to healthy controls. There is increase in serum triglyceride level in patients with CKD with increase in stage but is statisticallys significant in ESRD. There is also significant increase in TG levels in males and females of CKD patients compare to healthy counterpart ($p<0.05$). Similarly predominant lipid abnormality in diabetic CKD patients was elevation in TG which is significantly increased in group 3 as compare to group-2.

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