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Study of Lipid Profile in Chronic Kidney Disease: A Cross Sectional Study

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Abstract

Introduction: Lipid abnormalities are very common in chronic kidney disease contributing to high incidence of premature atherosclerosis and cardiovascular diseases in such patients. Deaths due to cardiovascular complications are 4-20 fold higher in CKD patients than any other cause in general population. In the course of CKD, lipoprotein disturbances vary significantly depending on the stage of the disease. So, the present study is undertaken to study lipid profile of cases of in chronic kidney disease.

Material and method: This cross-sectional study was conducted in Indira Gandhi Government Medical College and Hospital, Nagpur. 100 diagnosed chronic kidney disease patients attending medicine outpatient department (OPD) and/or admitted in ward/kidney unit in this institute were enrolled for the study. Cases were divided in five stages of disease based on the Glomerular Filtration Rate. All the cases were investigated for kidney function test and lipid profile.

Result: Mean age of study subject was 47.49 ± 11.70 years, ranging from 21 to 65 years. Male study subjects were 59 %. Diabetes Mellitus was the main aetiology of CKD followed by Hypertension. Mean triglyceride was 217.4 ± 44.11 and mean VLDL cholesterol was 44.37 ± 8.99.

Conclusion: Mean serum creatinine and blood urea values increases as the stage of CKD increases in study subjects (p=0.000). Mean triglyceride and VLDL cholesterol level increases as the stage of CKD increases from stage I to stage V (p=0.000).

Key words: Chronic Kidney Disease, Glomerular Filtration Rate, Kidney function test, Lipid profile, Stages of CKD.

Introduction: In the year 1836, hyperlipidemia was first recognized when Richard Bright commented on the "milky serum" of patients with end stage renal disease.[1] Lipid abnormalities are very common in chronic kidney disease contributing to high incidence of premature atherosclerosis and cardiovascular diseases in such patients. This is of particular interest since the prevalence of coronary atheroma in uremic patients was shown to be approximately 30% by autopsy and coronary angiography

studies.[2] As well as deaths due to cardiovascular complications are 4-20 fold higher in CKD patients than any other cause in general population.[3]

Relatively few studies have evaluated the estimated GFR and the risk of outcomes in the general population. In the Second National Health and Nutrition Examination Survey (NHANES II), an estimated GFR of < 70 ml/min/per1.73 m^2 was associated with a 68 % increase in the risk of death from any cause and a 51 % increase in the risk of death from cardiovascular causes, as compared with an estimated GFR of at least 90 ml/min/per1.73 m^2. In the Atherosclerosis Risk in Communities Study[4], an estimated GFR of 15 to 59 ml/min/per 1.73 m^2 at baseline was associated with a 38 % increase in the risk of cardiovascular disease, as compared with an estimated GFR of 90 to 150 ml/ min/ per 1.73 m^2.

Chronic kidney disease results in profound lipid disorders, which are largely due to dysregulation of high-density lipoprotein (HDL) and triglyceride-rich lipoprotein metabolism. Specifically, HDL maturation is impaired and its composition is also altered in CKD. In addition, clearance of triglyceride-rich lipoproteins and their atherogenic remnants is impaired, their composition is altered so that the most common quantitative lipid abnormalities in predialysis CKD patients are hypertriglyceridemia, increased concentrations of triglyceride-rich lipoprotein remnants, reduced high-density lipoprotein cholesterol levels as well as increased concentrations of lipoprotein (a). Notably, total and LDL-cholesterol levels are usually within normal limits or slightly reduced in these individuals. [5, 6]

In the course of CKD, lipoprotein disturbances vary significantly depending on the stage of the disease and method of treatment. Abnormal lipid metabolism is frequently observed in dialysis patients and is characterised by increased plasma triglycerides and reduced plasma high density lipoprotein cholesterol. [7, 8]

Considering the above facts, estimation of serum biochemical parameters such as total cholesterol, triglyceride, VLDL cholesterol, HDL cholesterol and LDL cholesterol may prove beneficial in assessing cardiovascular risk in patients of chronic kidney disease. So, the present study is undertaken to study lipid profile in chronic kidney disease.

Material and Methods

Study design and setting

This cross-sectional study was conducted in Indira Gandhi Government Medical College and Hospital, Nagpur, from February 2014 to August 2014.

Selection of study subjects

100 diagnosed chronic kidney disease patients attending medicine outpatient department (OPD) and/or admitted in ward/kidney unit in this institute and who were willing to participate in the study were selected for the present study. Cases were divided in five stages of disease based on the level of kidney function[9] as follows,

Stage I- GFR (Glomerular Filtration rate) more than or equal to 90 ml/min/1.73m^2.

Stage II- GFR 60-89 ml/min/1.73m^2,

Stage III - GFR 30-59 ml/min/1.73m^2,

Stage IV - GFR 15-29 ml/min/1.73m^2 and

Stage V - GFR less than 15 ml/min/1.73m^2.

Inclusion Criteria: Diagnosed chronic kidney disease patients of either sex between 21 to 65 years, on control diet.

Exclusion Criteria: Patients with diagnosed cases of acute renal failure like pre-renal, renal and post-renal acute renal failure or azotemia, renal transplantation, abnormal cardiac function secondary to myocardial ischemic disease and/or left ventricular dysfunction,

nephritic syndrome, liver disease. Patients on drug therapy, that interferes with serum lipid levels. Patient on lipid lowering medications were excluded.

Methodology:

Ethical clearance from Institute Ethics Committee was obtained prior to the study. Informed written consent was obtained from all the study subjects enrolled in the study. Written permission to conduct the study was sought from Department of Medicine. All the study subjects were examined and information noted in predesigned and pretested proforma. All the cases were investigated for kidney function test and lipid profile and results were noted in proforma. Serum levels of creatinine, sodium, potassium, blood urea and serum lipid profile comprising of total cholesterol (TC), triglyceride (TG), very low density lipoprotein cholesterol (VLDL-C), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C) were measured.

For estimation of these parameters, 5 ml of fasting venous blood sample was withdrawn from the ante-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes without the aid of a tourniquet. Haemolysed samples were excluded from the study. 2 ml of blood sample was transfer to a heparinised tube for urea estimation and the remaining 3ml blood sample was allowed to coagulate for 30 minutes in a clean dry sterile plain bulb. Thereafter both the tubes were centrifuged to separate the plasma/ serum. Serum used for estimation of serum creatinine, sodium, potassium, lipid profile and plasma used for urea estimation. The blood samples were analyzed immediately.

For estimating these parameter following methods were used-

1. Serum Creatinine - Initial rate method using alkaline picrate[10]
2. Blood Urea - Enzymatic method UV-Kinetic initial rate method[11]
3. Total Cholesterol - Enzymatic method- cholesterol oxidase and peroxidise- End point[12]
4. Triglycerides- Enzymatic method- Glycerol phosphate oxidase and peroxidase, end point[13]
5. VLDL-C and LDL-C - Indirect method - Friedewald Equation[14]
6. HDL-C - Precipitation method - End point[15.]

Statistical analysis:

Data expressed in percentage, mean ± SD (standard deviation). Level of significance was calculated by applying chi square test and ANOVA test Bonferroni test (post hoc test)

Results: Present cross sectional study of lipid profile in CKD, includes 100 diagnosed patient of chronic kidney disease. These 100 cases divided in to 5 stages of disease depend on the Glomerular filtration rate. Table 1 shows the characteristics of study subjects.

Table 1 Characteristics of study subjects (CKD)

Characteristics		**Number (n=100)**	**percentage**
Stage of disease	Stage I	08	08
	Stage II	11	11
	Stage III	19	19
	Stage IV	23	23
	Stage V	39	39
Age in years	21-30	07	07
	31-40	20	20
	41-50	29	29
	51-60	28	28
	60 and Above	16	16

Sex	Male	59	59
	female	41	41
Etiological cause	Diabetes Mellitus	33	33
	Hypertension	19	19
	Diabetes + Hypertension	17	17
	Glomerular disease	11	11
	Tubulointerstitial disease	08	08
	Obstructive nephropathy	05	05
	Other	07	07

Most of the study subjects was in stage V followed by stage IV. Mean age of study subject was 47.49 ± 11.70 years, ranging from 21 to 65 years. Male study subjects were 59. Diabetes Mellitus was the main aetiology of CKD followed by Hypertension. Seven cases were due to other cause such as renovascular disease and iatrogenic.

Parameter	Stage I (n=8) Mean± SD	Stage II (n=11) Mean± SD	Stage III (n=19) Mean± SD	Stage IV (n=23) Mean± SD	Stage V (n=39) Mean± SD	Total (100) Mean± SD	P-Value
Sr. Creatinine (mg/dl)	0.87±0.10	1.11±0.14	1.90±0.27	3.28±0.60	8.29±4.54	4..55±4.20	**0.000**
Blood Urea (mg/dl)	36.75±6.73	40.18±8.82	63.05±17.56	92.96±32.29	161.54±61.44	103.72±64.96	**0.000**
Sr. Na^+ (mEq/L)	139.25±4.132	137.27±5.51	138.47±5.74	139.70±6.12	139.51±4.55	139.09±5.21	0.75
Sr. K^+ (mEq/L)	3.99±0.50	4.06±0.51	4.26±0.70	4.60±0.63	4.73±1.01	4.48±0.83	**0.024**

Table No. 2: Kidney function test in chronic kidney disease cases, stage wise

Table 2 shows the kidney function test in study subjects as per stage of the disease. Mean serum creatinine amongst study subject was 4.55 ± 4.2 mg/dl, its value increases as the stage of chronic kidney disease increases and it is statistically highly significant (p = 0.000). Mean blood urea was 103.72 ± 64.96 mg/dl. Blood urea reading increases as the stage of disease increases and it is statistically highly significant (p = 0.000). Mean serum sodium in study subject was 139.09 ± 5.21 mEq/L. Serum sodium difference as per stage of disease is not statistically significant (p = 0.75). Mean serum potassium was 4.48 ± 0.83 mEq/L. Serum potassium level increases as the stage of disease increases, and is statistically significant (p = 0.024)

Table 3: Serum lipid profile of chronic kidney disease cases, stage wise.

Parameter (mg/dl)	Stage I (n=8) Mean± SD	Stage II (n=11) Mean± SD	Stage III (n=19) Mean± SD	Stage IV (n=23) Mean± SD	Stage V (n=39) Mean± SD	Total (100) Mean± SD	P-Value
Total Cholesterol	177.00±35.57	179.64±45.56	178.89±35.16	181.70±38.62	182.21±42.63	180.76±39.44	0.996
Triglycerides	176.13±27.21	193.91±35.51	206.21±35.24	218.57±42.24	237.26±44.64	217.40±44.11	**0.000**
VLDL Cholesterol	33.38±6.00	38.91±7.04	41.21±7.04	43.91±8.80	47.41±8.97	43.37±8.99	**0.000**
HDL Cholesterol	37.75±4.20	35.73±5.73	34.05±6.17	32.48±7.10	31.79±6.73	33.29±6.60	0.097
LDL Cholesterol	105.88±32.69	105.00±39.72	103.63±32.08	105.30±35.08	103.00±38.34	104.10±35.51	0.999
LDL:HDL Ratio	2.87±1.08	2.98±1.12	3.18±1.30	3.44±1.66	3.49±1.85	3.31±1.58	0.765
TC:HDL-C Ratio	4.76±1.22	5.10±1.32	5.44±1.61	5.91±2.14	6.05±2.19	5.69±1.95	0.319

Table 3 shows the lipid profile of study subjects as per stage of disease. Mean triglycerides of study subject was 217.4 ± 44.11 mg/dl and VLDL cholesterol was 43.37 ± 8.99 mg/dl. The reading of triglycerides and VLDL cholesterol increases as the stage of chronic kidney disease increases and it is statistically highly significant (p = 0.000). Total cholesterol, LDL cholesterol, reading not varies as per stage of disease and it is statistically not significant. HDL cholesterol decreases as the stage of CKD increases but it is not statistically significant. LDL: HDL ratio and TC: HDL ratio increases as the stage of CKD increases but this increase is not statistically significant.

Discussion: The incidence and prevalence of chronic kidney disease (CKD) are increasing worldwide and are associated with poor outcomes.[6] CKD is a global threat to health in general and for developing countries in particular, because therapy is expensive and life-long.[16] Cardiovascular disease is the leading cause of death in patients with chronic kidney disease.[17] Serum total cholesterol, triglyceride, VLDL cholesterol, HDL cholesterol, LDL cholesterol have roles in the

pathophysiology of cardiovascular disease.[18, 19] It has also been suggested that dyslipidemia could cause renal injury and may contribute to accelerate development of renal insufficiency.[20, 21] The characterization of the degree and type of lipid abnormalities therefore should be considered important in the management of patients to prevent CVD.[20]

Blood urea and serum creatinine are well-established biomarkers of renal function as both urea and creatinine are products of protein metabolism which are cleared almost entirely by the kidneys.[22] A reduced GFR leads to retention of nitrogenous waste products (azotemia) such as urea and creatinine.

In this study the lipid pattern and its relation with stage of the disease, it was found that, the mean levels of serum triglyceride and VLDL cholesterol was statistically highly significant ($p < 0.0001$). As the stage of disease increases these value increases. **Tsimihodimos V et al (2008)[6]** in their study reported that, in CKD lipid abnormality was present as increased concentrations of triglyceride, triglyceride-rich lipoprotein remnants, reduced (HDL)-cholesterol. And such type of dyslipidemia was evident even at the early stages of CKD and such disturbances increased as the renal function declined. **Piecha G et al (2009)[1]** also reported similar findings of dyslipidemia in the form of hypertriglyceridemia.

Important pathophysiological mechanisms underlying the development of hypertriglyceridemia in CKD was accumulation of triglyceride-rich lipoproteins (very-low-density lipoprotein (VLDL), chylomicrons and their remnants) either due to increase synthesis or decreased catabolism. But the decrease catabolism was found to be main mechanism.[7, 23, 24]

Conclusion: In this cross sectional study of lipid profile in chronic kidney disease. Mean serum creatinine, serum potassium and blood urea values increases as the stage of CKD increases in study subjects. Mean triglyceride and VLDL cholesterol level increases as the stage of CKD increases from stage I to stage V. Indicating the higher risk of Coronary heart disease in higher stage of CKD.

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