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**ORIGINAL PAPER**

# Chronic Kidney Disease with Special Reference to Dyslipidemia

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**ABSTRACT**

*Background**:** Lipid abnormalities in chronic kidney disease (CKD) are significant, because atherosclerotic heart disease is the foremost cause of morbidity and mortality in patients with end stage renal disease. The growing recognition that dyslipidemia is a major risk factor for coronary heart disease has prompted interest in the identification and management of abnormalities in plasma lipids and lipoproteins. Method: It was hospital based observational study conducted from January 2014 to January 2015 in Department of Medicine and Nephrology, Gauhati Medical College, where 50 patients of chronic kidney disease were included and evaluated for dyslipidemia. Results**:** Most common presenting symptoms were swelling of legs (80%), followed by anorexia, nausea, vomiting (72%), puffiness of face ( 64%), decrease urine output (60%). 100% patients presented with anemia, 80 % with edema and 76% with hypertension. 24 (48%) patients had normal ECG, 13 (26%) patients had left ventricular hypertrophy ( LVH). 13 patients (26%) had hyperkalemia. Mean total cholesterol (TC) was 189±43.3mg/dl, triglyceride 174±60.7, high density lipoprotein (HDL) 36.51 ±5.1, very low density lipoprotein (VLDL) 34.88±12.15, low density lipoprotein (LDL) 116.49±38.34 and HDL/ TC ratio 0.2002±0.0478. Conclusion: Dyslipidemias are the important predictive indices for the risk of developing coronary artery disease in chronic kidney disease patients, and so early evaluation and treatment of dyslipidemia may improve the cardiovascular outcome.*

***Keywords:** Chronic kidney disease, dyslipidemia*

**INTRODUCTION**

Lipid abnormalities in chronic kidney disease (**CKD**) are significant, because atherosclerotic heart disease is the foremost cause of morbidity and mortality in patients with end stage renal disease. Cardiovascular disease is a major cause of morbidity and mortality among patients with chronic kidney disease.[1-3] The growing recognition that dyslipidemia is a major risk factor for coronary heart disease has prompted interest in the identification and management of abnormalities in plasma lipids and lipoproteins. In CKD the most prevalent lipid disorders are hypertriglyceridemia and decrease in high density lipoprotein (**HDL**) concentration. Low density lipoprotein (**LDL**) levels are usually normal or marginally increased.[4-6]Also there are reports available regarding accelerated atherosclerosis in chronic kidney disease due to altered lipid metabolism. In recent years, the levels of high density lipoproteins have gained importance in view of the fact that increasing reports are available incriminating decreased high density lipoprotein (HDL) levels as one of risk factors for cardiovascular disease. So, the analysis

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of lipoprotein subclass in chronic kidney disease patients is very much essential to assess the clinical outcome.

**Aims: (i)** To identify the different lipoprotein fractions in patients with chronic kidney disease and **(ii)** To identify the pattern of dyslipidemias in conservatively treated patients and in patients managed with hemodialysis.

## MATERIALS AND METHODS

The present study was a hospital based observational study conducted from January 2014 to January 2015 in Department of Medicine and Department of Nephrology (both OPD and Indoor), Gauhati Medical College and Hospital, where 50 patients of chronic kidney disease were included. Chronic kidney disease (CKD) is defined as kidney damage or glomerular filtration rate (**GFR**) below 60 ml/min per 1.73 $m^2$ for 3 months or more irrespective of the cause. CKD patients are divided into 5 stages according to GFR as shown in **Table 1**.

**Table 1** Stages of Chronic kidney disease

| Stages | GFR (ml/min) |
|---|---|
| 1 | ≥ 90 |
| 2 | 60- 89 |
| 3 | 30- 59 |
| 4 | 15- 29 |
| 5 | < 15 |

Chronic kidney disease was diagnosed by clinical, biochemical and ultrasonographic evidence. Patients of chronic kidney disease age more than 12 years were included. Patients with diabetes mellitus, thyroid and liver disease, history of alcohol consumption and smoking, lipid lowering drugs and patient on CAPD (continous ambulatory peritoneal dialysis) were excluded. The patients included in the study were subjected to a detailed history, physical examination and laboratory tests. Study of lipid profile was done by enzymatic method by using autoanalyser.

## RESULTS

In the present study, 50 patients of CKD were included, out of which 31 patients (62%) were male and 19 patients (38%) were female. On decade wise grouping, maximum numbers of patients were in the age group 41-50 years (30%). Mean age for male was 46.6 years and that for female was 45.4 years. Male to female ratio in the study group was 1.6:1. The age and sex distribution of the patients were shown in **Table 2.**

**Table 2** Showing the age and sex distribution of the patients

| Age Group | Total No Of Cases | Percentage | Male | Percentage | Female | Percentage |
|---|---|---|---|---|---|---|
| <20 | 2 | 4 | 1 | 50 | 1 | 50 |
| 21-30 | 8 | 16 | 4 | 50 | 4 | 50 |
| 31-40 | 5 | 10 | 5 | 100 | 0 | 0 |
| 41-50 | 15 | 30 | 9 | 60 | 6 | 40 |
| 51-60 | 10 | 20 | 5 | 50 | 5 | 50 |
| 61-70 | 9 | 18 | 6 | 66.66 | 3 | 33.34 |
| >70 | 1 | 2 | 1 | 100 | 0 | 0 |
| Total | 50 | 100 | 31 | | 19 | |

Most common presenting symptom was swelling of legs (80%). Anorexia, nausea, vomiting was present in 72% of patient, puffiness of face was present in 64 % of patients, decreased urine output was present in 60 % of patients, and breathing difficulty was present in 32% of patients. All the patients (100%) included in the study had anemia,80 % of patient had edema, 76% of patient had hypertension, 36% of patient had ascites, 32% of patient had pleural effusion, 32% of patients had acidotic breathing, 20% of patient had raised JVP and 16% of patient had altered sensorium. The presenting symptoms and the clinical signs are shown in **Table 3** and **Table 4** respectively.

**Table 3** Showing the presenting symptoms among CKD patients

| | Swelling of legs | Puffiness of face | Decrease urine output | Anorexia nausea vomiting | Breathing difficulty |
|---|---|---|---|---|---|
| Patients | 40 | 32 | 30 | 36 | 16 |
| Percentage | 80% | 64% | 60% | 72% | 32% |

**Table 4** Showing the clinical signs in CKD patients

| | Anemia | Hypertension | Edema | Raised JVP | Ascites | Pleural effusion | Acidotic breathing | Altered sensorium |
|---|---|---|---|---|---|---|---|---|
| Patients | 50 | 36 | 40 | 10 | 18 | 16 | 16 | 8 |
| Percentage | 100% | 72% | 80% | 20% | 36% | 32% | 32% | 16% |

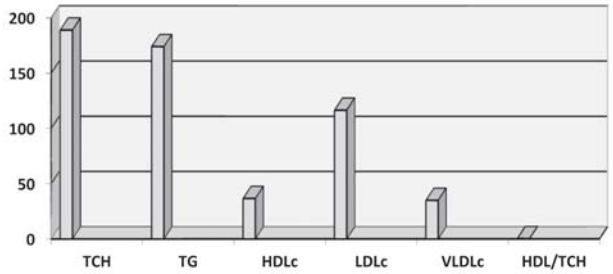
Nine (9) patients were in stage 3, 18 patients were in stage 4 and 23 patients were in stage 5. Stage 3 and stage 4 patients were treated conservatively and stage 5 patients were on renal replacement therapy (hemodialysis). Mean values for urea was 135.26±41.99 mg/dl and creatinine 11.12±5.09 mg/dl.

Out of 50 patients, 24 (48%) patients had normal electrocardiogram (ECG). 13 (26%) patients had left ventricular hypertrophy (LVH) of which 9 (69.23%) were male and 4 (30.77%) were female. 13 patients (26%) had changes of hyperkalemia of which 8 (61.54%) were male and 5 (38.46%) were female.

The mean total cholesterol (TC) was 189±43.3mg/dl, mean triglyceride was 174±60.7 mg/dl, mean HDL was 36.51 ±5.1 mg/dl, mean very low density lipoprotein (VLDL)was 34.88±12.15 mg/dl, mean low density lipoprotein (LDL) was 116.49±38.34 mg/dl and HDL/ TC ratio 0.2002±0.0478. The mean values of the lipid profiles are shown in the **Table 5** and **Graph 1** below:

**Table 5** Showing the biochemical (lipid profile) data in CKD patients (Mean ± SD) mg/dl

| | |
|---|---|
| Total cholesterol | 189±43.3 |
| Triglyceride | 174±60.7 |
| HDLc | 36.51±5.1 |
| LDLc | 116.49±38.34 |
| VLDLc | 34.88±12.15 |
| HDL/TC | 0.2002±0.0478 |

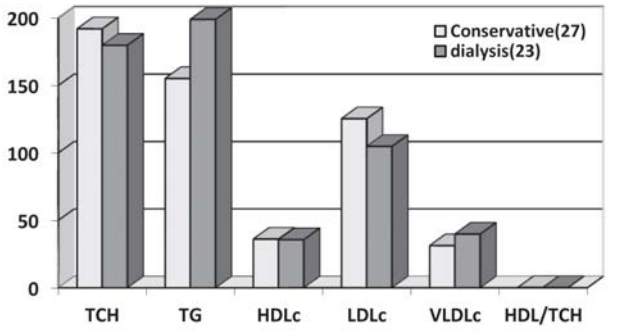



**Graph 1** Lipid profile in CKD patients

The lipid profile of the patients in the conservative group and in the hemodialysis group are shown in **Table 6** and **Graph 2** below

**Table 6** Showing lipid profile in the conservative and hemodialysis group

| Group | Conservative Treatment (N=27) | Dialysis (n=23) | t-value | p- value |
|---|---|---|---|---|
| Total Cholesterol | 191.990 ±50.73 | 179.826 ±31.66 | 0.7595 | ns |
| Triglyceride | 155.176±47 | 199.01±70 | 2.052 | Sig p<0.05 |
| HDLc | 36.1±5.76 | 35.7±5.20 | 0.1964 | ns |
| LDLc | 125.38±44.3 | 104.87 ±25.10 | 1.492 | ns |
| VLDLc | 31.27±9.525 | 39.82±14 | 1.991 | ns |
| HDL/TC | 0.20±0.053 | 0.202 ±0.0405 | 0.1130 | ns |




**Graph 2** Comparison of lipid profile between conservative and dialysis group

The above table 6 and graph 2 shows comparison of biochemical mean values of TC, TG, HDL, and HDL/TC between patients managed conservatively and patients managed with hemodialysis. Mean total cholesterol in patients on conservative treatment was 191.99 ± 50.73 mg/dl and for patients on hemodialysis it was 179.826±31.66 mg/dl and this difference was statistically not significant (P>0.05). The mean triglycerides in patients of CKD on conservative treatment was 155.1764±7 mg/dl and the mean triglycerides in hemodialysis group was 199.01±70mg/dl. This difference was statistically significant (P<0.05). The mean HDL value in conservative treatment group was 36.1±5.76 mg/dl and the mean HDL value in hemodialysis group was 35.7±5.20mg/dl and this difference was statistically not significant. The mean LDL value in CKD patients on conservative group was 125.38±44.3mg/dl and the mean LDL value in hemodialysis

group was 104.87±25.10mg/dl and this difference was statistically not significant. The mean VLDL values for patients in conservative group and hemodialysis group was 31.27±9.525 mg/dl and 39.82±14mg/dl respectively and this difference was statistically not significant. The difference in mean values of HDL/TC in both conservative treatment group and hemodialysis group was also statistically not significant.

On comparing mean values of TC, TG, HDL, LDL, VLDL values between male and female patients, there was increase in TG and decrease in HDL in male patients and there was increase in TC and LDL in female patients. However these differences were statistically not significant (P >0.05)

33 patients (66%) had total cholesterol <200mg/dl (desirable range) and 17 patients (34%) had abnormal value, among them 12 (24%) patients had borderline high values (200- 239 mg/dl) and 5(10%) patients had high values (>240 mg/dl). 19 patients (38%) had normal TG values (<150mg/dl), 31 patients (62%) had elevated TG values, among them 16 patients (32%) had TG in borderline high (150-199 mg/dl) range and 15 patients (30%) had TG in high (200-499 mg/dl) range. This was statistically significant (P<0.05). 41 patients (82%) had HDL values <40mg/dl, 9patients (18%) had HDL>40mg/dl. 17 patients (34%) had normal LDL levels (<100 mg/dl), 17 patients (34%) had near optimal LDL levels (101-129 mg/dl), 8 (16 %) had borderline high LDL levels (130-159 mg/dl), 6 (12 %) had high LDL levels (160- 189 mg/dl) and 2 (4 %) patients had very high LDL levels (>130 mg/dl). This was statistically not significant (p> 0.05).

**DISCUSSION**

In the present study, out of 50 patients of CKD, 31 patients (62%) were male and 19 patients (38%) were female. Maximum number of patients was in the age group 41-50 years (30%) and the mean age for male was 46.6 years and that for female was 45.4 years.

In the study group of CKD patients 18% were in stage 3, 36% stage 4, 46% stage 5. Total 27 patients were treated conservatively (stage 3 & stage 4) and 23 patients (stage 5) were treated by hemodialysis.

In this study, triglyceride levels were markedly elevated**.** P.O Attmanet al.[7] stated that hypertriglyceridemia is the most common plasma lipid abnormality found in patients of chronic kidney disease.

The cause for hypertriglyceridemia in chronic kidney disease patients has not been clearly delineated. Available data derived from Kinetic studies have demonstrated that reduced catabolism of triglycerides is the predominant defect due to deficiency of lipoproten lipase [7- 9] or hepatic triglyceride lipase or both. Reasons for decrease in activity of these enzymes are not clear. It can be possibly due to:

- Presence of circulatory inhibitor of lipolytic enzymes in the serum[1].
- Changes in apoprotein concentrations which can effect lipoprotein lipase activity
- Insulin resistance seen in renal insufficiency[7]
- Alteration of lipoprotein substrate[10]

The relationship between hypertriglyceridmia and atherosclerotic heart disease is far less clear. Thomas Quaschning et al.[11] reported that combined hyperlipidemia (elevated cholesterol and triglycerides) with low HDL cholesterol reflects more atherogenic condition.

In the present study, there was decrease in high density lipoprotein (HDL) cholesterol seen in CKD patients. P.O. Attmanet al.[7] found decrease in plasma high density lipoprotein (HDL) cholesterol concentration in patients with chronic kidney disease. It was also reported that decreased HDL was associated with decrease in both the fractional catabolic rate and the total synthetic rate of ApoA1/HDL. The slow fractional catabolic rate of Apo A1 in patients with chronic kidney disease could be a primary event resulting from a decrease in synthesis or secretion of Apo A1. John D Bagdadeet al.[12] demonstrated that patients of renal failure treated by chronic dialysis have lower HDL levels compared to controls.

There was marginal increase of serum total cholesterol in chronic kidney disease patients. P.O. Attman et al.[7] in their study showed no significant change in levels of total cholesterol. Thomas Quasctininget al.[11] reported combined hyperlipidemia (elevated total cholesterol and triglycerides) in their study.

The present study showed no significant increase in LDL levels in CKD patients. In uremia LDL lipoproteins are qualitatively altered. Marion Morenaet al.[13] reported that there was increase in small, dense LDL sub-fractions in hemodialysis patients.

Hypertriglyceridemia observed in hemodialysis patients results from a reduced lipolysis of TG rich VLDL that leads to the accumulation of partially metabolized remnant lipoproteins (IDL and TG rich LDL). This lipoprotein catabolism impairment is usually associated with reduced

levels of HDL affecting reverse cholesterol transport. Such defect in atherogenic lipoprotein catabolism may predispose to the formation of small dense LDL particles, which appear to be more sensitive to ex vivo oxidation.

On comparing the lipid profile values between dialysis and conservatively managed patient it was seen that total cholesterol levels were decreased in patients on hemodialysis (HD) as compared to patients treated by conservative line but this difference was statistically not significant (P>0.05). HDL levels were marginally low in patients of HD compared to conservatively treated patients but this was also statistically not significant. VLDL in HD group was modestly increased compared to conservative group but this was also statistically not significant (P>0.05). LDL values were modestly low in patient treated with hemodialysis as compared to patients treated conservatively however this difference was statistically not significant. There was significant increase in triglycerides in patients treated with hemodialysis compared to patients on conservative treatment (P<0.05**).**

John D. Bagdade et al.[12] studied lipid profile in 27 patients of CKD of which 13 patients were on conservative treatment and 14 patients were on dialysis and they found that triglycerides were found to be elevated in both non dialysed and dialysed CKD patients.

Morena Marion et al.[13] in their study on hemodialysis patients stated that hemodialysis patients are exposed to several atherogenic factors resulting from qualitative and functional lipid abnormalities, including triglyceride rich particles, increased susceptibility to LDL oxidation and impairment of HDL protective effects.

S.M. Alamet al.[14] studied serum lipoprotein fractions in patients of CKD of conservatively managed group and those on maintenance hemodialysis **(HD)**. The total cholesterol in the conservative group was 232.3±56 and in HD group was 160.8±56.4, triglycerides in the conservative group was 243.7±119 and in HD group was 145.4±24.3, HDL in the conservative group was 19.0±6.1 and in HD group was 12.17±5.1. LS Ibels et al.[15] also studied serum lipoprotein fractions in patients of CKD of conservatively managed group and those on maintenance hemodialysis **(HD)**. The total cholesterol in the conservative group was 236±24 and in HD group was 216±57, triglycerides in the conservative group was 273±57 and in HD group was 237±112, HDL in the conservative group was 22±6 and in HD group was 24±9, LDL in the conservative group was 131±42 and in HD group was 116±34 and VLDL in the conservative group was 55±40 and in HD group was 47±28. In the present study total cholesterol in the conservative group was 191.99±50.73 and in HD group was 179.826±31.66, triglycerides in the conservative group was 155.176±47 and in HD group was 199.01±70, HDL in the conservative group was 36.1±5.76 and in HD group was 35.7±5.20, LDL in the conservative group was 125.38±44.3 and in HD group was 104.87±25.10 and VLDL in the conservative group was 31.27±9.525 and in HD group was 39.82±14. The important finding in the present study was significant increase in triglycerides in the patients on hemodialysis.

## CONCLUSION

One of the known metabolic changes associated with CKD is lipid disorders. Significant increase in TG, VLDL and reduction in HDL and HDL/total cholesterol ratio have been reported in various previous studies and the present study too has observed the same results. Dyslipidemias are the important predictive indices for the risk of developing coronary artery disease in chronic kidney disease patients, and so early evaluation and treatment of dyslipidemia may improve the cardiovascular outcome.

**Conflict of interest**: None declared.

**Ethical clearance**: Taken.

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