DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE

Manish Kumar Singh1, V.D. Charan2, Ishan Parasher3, Pranjal Pankaj4, Shrawan Kumar5, Kusum Gupta6, Vindhyawasini Prasad Singh7

ABSTRACT: INTRODUCTION: Chronic kidney disease encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Chronic kidney disease is a universal medical problem across the globe. Unless treated, it may lead to grave consequences. Chronic kidney disease leads to impairment of excretory, metabolic and endocrine functions of the kidney. As other complications of CKD occur, likewise it also results in profound lipid disorders In view of the effect of dyslipidemia on cardiovascular risk and possibly on the progression of renal disease, treatment seems sensible, although evidence is not abundant. AIMS AND OBJECTIVES: 1. Study the lipid profile in the cases of chronic kidney disease. 2. Study the significance of dyslipidemia in chronic kidney disease.

MATERIAL AND METHODS: The study was carried out in a group of patients who were admitted and patients visiting the outpatient department of the Department of Medicine at Rama Medical College, Kanpur, Patients were selected by adhering strictly to certain inclusion (Patients of chronic kidney disease on conservative treatment and on haemodialysis or peritoneal dialysis) and exclusion criteria (renal failure other than CKD or on hypolipidemic drugs). RESULTS: In our study 30% of the cases, the cholesterol value is within normal limits. 18% cases its level is high i.e. above 240 and in rest 52 % of cases it is within the borderline high range. The mean triglyceride is 218.74 mg/dl in patients of CKD and is 87.04 mg/dl in control subjects which is statistically very significant. The mean VLDL is 43.78 mg/dl in patients of CKD and is 17.41 mg/dl in control subjects which is statistically very significant. 90% cases had HDL <40 mg/dl. 6% of the patients had serum LDL value within normal range. 32% of the patients had optimal serum LDL cholesterol value near or above normal range. 36 % of the patient had serum LDL value in borderline high range. 12% of the patient had serum LDL cholesterol value in high range. 14% of the patient had serum LDL cholesterol value in very high range. The mean LDL/HDL ratio is 4.44 in patients of CKD and is 2.66 in control subjects. The mean TG/HDL ratio is 7.02 in patients of CKD and is 1.88 in control subjects. Mean TG/LDL ratio is 1.66 in patients of CKD and is 0.71 in control subjects. CONCLUSION: In the cases of chronic kidney disease there is dyslipidemia with maximum impact on level of triglycerides with a very significant increase. The level of total cholesterol is increased, that of HDL is decreased and level of VLDL is increased. These changes are occurring independently in chronic kidney disease.

KEY WORDS: Chronic kidney disease, dyslipidemia, Cholesterol, LDL, HDL, VLDL

INTRODUCTION: Chronic kidney disease encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Chronic kidney disease is a universal medical problem across the globe. Unless treated, it may lead to grave consequences, chronic kidney disease leads to impairment of excretory,
metabolic and endocrine functions of the kidney that leads to development of clinical syndrome of uratemia which includes features like anaemia, metabolic bone disease, neuropathy, myopathy, endocrine abnormalities, hypertension, dyslipidemia, acidosis and susceptibility to infections. As other complications of CKD occur, likewise it also results in profound lipid disorders, which stem largely from dysregulation of high density lipoproteins (HDL) and triglyceride rich lipoprotein metabolism. Specifically, maturation of HDL is impaired and its composition is altered in CKD. In addition, clearance of triglyceriderich lipoproteins and their atherogenic remnants is impaired, their composition is altered, and their plasma concentrations are elevated in CKD. Impaired maturation of HDL in CKD is primarily due to down regulation of lecithin-cholesterol-acyltransferase and, to a lesser extent, increased plasma cholesteryl ester transfer protein (CETP). Triglyceride enrichment of HDL in CKD is primarily due to hepatic lipase deficiency and elevated CETP activity. The CKD induced hypertriglyceridemia, abnormal composition, and impaired clearance of triglyceride-rich lipoproteins and their remnants are primarily due to down regulation of lipoprotein lipase, hepatic lipase, and the very low density lipoprotein receptor, as well as, up regulation of hepatic acyl-CoA cholesterol acyltransferase (ACAT).These abnormalities are compounded by down regulation of apolipoproteins apoA-I, apoA-II and apoC-II in CKD. Together, these abnormalities may contribute to the risk of atherosclerotic cardiovascular disease and may adversely affect progression of renal disease and energy metabolism in CKD. Plasma triglyceride concentration is frequently elevated in patients and experimental animals with CKD. However, plasma cholesterol concentration is usually normal, even reduced, and only occasionally elevated in patients with end-stage renal disease (ESRD). Elevation of plasma triglycerides in ESRD patients is accompanied by increased plasma concentration and impaired clearance of VLDL. This is associated with the accumulation of atherogenic VLDL remnants, commonly known as IDL. Similarly, clearance of chylomicrons is impaired and plasma concentration of chylomicron remnants is elevated in CKD patients. In contrast, plasma concentration of LDL is usually normal and only occasionally elevated in ESRD patients. Plasma HDL concentration is consistently reduced, and maturation of cholesterol ester-poor HDL-3 to cholesterol ester-rich cardio protective HDL-2 is impaired in CKD. As noted earlier, CKD is consistently associated with reduced plasma HDL cholesterol concentration, impaired maturation of cholesterol ester-poor HDL-3 to cholesterol ester-rich HDL-2, increased HDL triglycerides, and depressed plasma apoA-I. In view of the effect of dyslipidemia on cardiovascular risk and possibly on the progression of renal disease, treatment seems sensible, although evidence is not abundant. There is some role for non-pharmacological intervention, although treatment with statins and fibrates in most cases are acceptable. Keeping in view of the importance of lipid profile in chronic kidney disease, we opted the study on the dyslipidemia in the cases of chronic kidney disease.

AIMS AND OBJECTIVES: 1. Study the lipid profile in the cases of chronic kidney disease. 2. Study the significance of dyslipidemia in chronic kidney disease

MATERIAL AND METHODS: The study was carried out in a group of patients who were admitted and patients visiting the outpatient department of the Department of Medicine at Rama Medical College, Kanpur. Patients were selected by adhering strictly to certain inclusion and exclusion criteria. Patients included in the study underwent a uniform process of evaluation. Age was self-
reported in most cases. Detailed history was taken including demographic data; medical history with special reference to symptoms attributable to kidney disease was recorded. Any history that would presumably associate with an acute deterioration of kidney function was recorded, and such patients were excluded from the study. The patients studied were from 20-70 years range and weighed between 40-70kgs. They were on low protein diet for last two weeks. A complete physical examination, including anthropometric data (weight and height), examination of blood pressure, general and systemic examination was done. Height and weight were recorded in centimeters and kilograms, respectively. After a detailed history, clinical examination and investigations, the 50 cases of chronic kidney disease were divided into 4 groups. 30 cases of chronic glomerulonephritis, 12 cases of Hypertensive nephrosclerosis, 6 cases of polycystic kidney disease, 2 cases of obstructive uropathy. Controls were randomly selected among hospital staffs, nurses and students as well as patients visiting the hospital for some other purpose. These controls were analysed according to the protocol mentioned earlier, with thorough general examination, recording the vitals plus various investigations including lipid profile.

INCLUSION CRITERIA:
2. Patients of chronic kidney disease on haemodialysis and peritoneal dialysis.
3. Males and females of 20-70 years age

EXCLUSION CRITERIA:
1. Patients of acute kidney injury.
2. Patients of diabetic nephropathy.
3. Obese patients, patients of nephrotic syndrome, patients on androgen therapy.
4. Patients with disorders of lipoprotein metabolism.
5. Patients on therapy with statins or fibrates or both.

RESULTS AND DISCUSSION: Out of all patients, 25 controls and 50 cases of chronic kidney disease selected randomly. These controls as well as cases were subjected to study protocol with parameters like physical examination with blood pressure, routine haematological examinations, fasting lipid profile, random blood sugar, blood urea, serum creatinine, USG whole abdomen, routine examination of urine, urine culture and sensitivity. These parameters were compared between the both groups and various observations were made, which are as follows;

<table>
<thead>
<tr>
<th>AGE GROUP</th>
<th>NO. OF CASES</th>
<th>%</th>
<th>SEX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MALE</td>
</tr>
<tr>
<td></td>
<td>NO.</td>
<td>%</td>
<td>NO.</td>
</tr>
<tr>
<td>20-29</td>
<td>4</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>30-39</td>
<td>12</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>40-49</td>
<td>14</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>50-59</td>
<td>8</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>60-70</td>
<td>12</td>
<td>24</td>
<td>8</td>
</tr>
</tbody>
</table>

Table-1: Age and Sex distribution of cases
Table 2: Final diagnosis in cases

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>FINAL DIAGNOSIS</th>
<th>NO OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHRONIC GLOMERULONEPHRITIS</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>HYPERTENSIVE NEPHROSCLEROSIS</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>POLYCYSTIC KIDNEY DISEASE</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>OBSTRUCTIVE UROPATHY</td>
<td>2</td>
</tr>
</tbody>
</table>

The mean value of serum creatinine value is 9.6 mg/dl in group 1 i.e. cases and is 0.91 in group 2 i.e. control subjects.

Table 3: Comparison of Mean Serum Creatinine values in both groups

The mean HB is 6.3 gm% in patients of CKD and is 13.6 gm% in control subjects.
The mean total cholesterol is 213.5 mg/dl in patients of CKD and is 186.7 mg/dl in control subjects.

Table 5: Comparison of Mean Total Cholesterol level in both groups

The mean triglyceride is 218.74 mg/dl in patients of CKD and is 87.04 mg/dl in control subjects.

Table 6: Comparison of Mean Triglyceride Level in both groups
The mean HDL is 31.5 mg/dl in patients of CKD and is 46.5 mg/dl in control subjects.

Table-6: Comparison of Mean HDL Level in both groups

Table-7: Comparison of Mean LDL level in both groups

The mean LDL is 138.20 mg/dl in patients of CKD and is 122.7 mg/dl in control subjects.
The mean VLDL is 43.78 mg/dl in patients of CKD and is 17.41 mg/dl in control subjects.

Table 8: Comparison of Mean VLDL level in both groups

The mean LDL/HDL ratio is 4.44 in patients of CKD and is 2.66 in control subjects.

Table 9: Comparison of Mean LDL/HDL ratio in both groups
The mean TG/HDL ratio is 7.02 in patients of CKD and is 1.88 in control subjects.

The mean TG/LDL ratio is 1.66 in patients of CKD and is 0.71 in control subjects.
### Table-12: Comparison of all Variants of Lipid Profile in both groups

<table>
<thead>
<tr>
<th></th>
<th>MEAN</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL CHOLESTEROL</td>
<td>213.5</td>
<td>186.7</td>
<td></td>
</tr>
<tr>
<td>TRIGLYCERIDES</td>
<td>218.74</td>
<td>87.04</td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>31.5</td>
<td>46.5</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>138.2</td>
<td>122.7</td>
<td></td>
</tr>
<tr>
<td>VLDL</td>
<td>43.78</td>
<td>17.41</td>
<td></td>
</tr>
</tbody>
</table>

Above table is showing significant alteration in fasting lipid profile in chronic kidney disease patients.

**A. Observations in control;**
- Out of 25 controls, 15 were males and 10 were females.
- Mean HB% value was 13.61 g/dL.
- Mean serum creatinine value was 0.91 mg/dL.
- Mean total cholesterol value was 186.76 mg/dL.
- Mean serum triglyceride value was 87.04 mg/dL.
- Mean serum HDL value was 46.52 mg/dL.
- Mean serum LDL value was 127.74 mg/dL.
- Mean serum VLDL value was 17.41 mg/dL.
- Mean serum TG/HDL ratio was 1.88.
- Mean serum TG/LDL was 0.71.
- Mean serum LDL/HDL was 2.66.
- USG was normal in all subjects.

**B. Observations in cases of chronic kidney disease;**
- 50 cases were selected out of which 30 were males and 20 were females.
- Out of 50 cases, 30 were of chronic glomerulonephritis, 12 of hypertensive nephrosclerosis, 6 of polycystic kidney disease and 2 were cases of obstructive uropathy.
- Mean HB% value was 6.31 g/dL.
- Mean serum creatinine value was 9.63 mg/dL.
Mean total cholesterol value was 213.56 mg/dL.
Mean serum triglyceride value was 218.74 mg/dL.
Mean serum HDL value was 31.56 mg/dL.
Mean serum LDL value was 138.20 mg/dL.
Mean serum VLDL value was 43.78 mg/dL.
Mean serum TG/HDL ratio was 7.02.
Mean serum TG/LDL was 1.66.
Mean serum LDL/HDL was 4.44.

Mean total cholesterol value was 213.56 mg/dL in cases and 186.76 mg/dL in control, similar study was done by Oliver and Boyd\textsuperscript{13} determined the level of total cholesterol between 100-250 mg%. Soperry\textsuperscript{120} reported the range of 192-382 mg% in normal individuals, Naht, Gupta and Iyer\textsuperscript{14} reported the level between 177-215 mg/100 ml. Mean triglyceride is 218.74 mg/dl in patients of CKD and is 87.04 mg/dl in control, similar elevated TG levels were observed by Novarini & Zuliani et al\textsuperscript{15} and Roovoets et al\textsuperscript{16}. Mean serum HDL value was 31.56 mg/dL in CKD patients and 46.52 mg/dL in control similar results were observed by Cassader M et al with significant increase in the levels of triglycerides and lipid components of VLDL and a significant reduction in HDL in patients of CKD.

CONCLUSION: Chronic kidney disease encompasses a spectrum of different pathophysiological process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Chronic kidney disease leads to impairment of excretory, metabolic and endocrine functions of the kidney that leads to development of clinical syndrome of uraemia which includes features like anaemia, metabolic bone disease, neuropathy, myopathy, endocrine abnormalities, hypertension, dyslipidemia, acidosis and susceptibility to infections. Lipid parameters were compared between the both groups and various conclusions were made, which are as follows; in the cases of chronic kidney disease there is dyslipidemia with maximum impact on level of triglycerides with a very significant increase. The level of total cholesterol is increased, that of HDL is decreased and level of VLDL is increased. These changes are occurring independently in chronic kidney disease, as I had excluded the cases of diabetic nephropathy and the patients who are already on statin therapy or any other drug which alters the level of lipids in body. Cardiovascular complications are rampant in general population and these complications are very common as well as the leading cause of morbidity and mortality in CKD patients. Considering this fact dyslipidemia which is occurring in these patients may accelerate the cardiovascular complications via various processes like atherosclerosis, hypertension and also by further accelerating the progression of CKD.

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