

## Original Research Article

# A study of lipid profile in non-diabetic chronic kidney disease

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### ABSTRACT

**Background:** The present study focused on finding an approximate prevalence of dyslipidemia in the target reference population and the association with staging and management strategy used. An effort was also made to know the alteration in different lipoprotein fractions in chronic kidney disease. The objective of the study was to study the lipid profile in non-diabetic patients with chronic kidney disease.

**Methods:** The study was conducted in Ispat general hospital, Rourkela and data was collected from January 2014 to September 2015. Patients who were diagnosed with Chronic Kidney Disease admitted into the medical ward and dialysis unit of Ispat General Hospital, Rourkela, Odisha, who had willingly given their informed written consent for this study were the source of data. For diagnosis of CKD, history and clinical features with supportive biochemical and radiological evidence were taken as criteria. Patients with already known diabetes mellitus were excluded.

**Results:** The prevalence of dyslipidemia in CKD was found to be about 65%. And the prevalence was increasing with the increase in severity of the disease. There was a significant rise in the serum triglyceride concentration in the study population. This abnormality was followed by a fall in HDL cholesterol and rise in the total Serum cholesterol in patients suffering from CKD. On comparing patients with CKD on hemodialysis with that on conservative management there is a significant prevalence of dyslipidemia in the Hemodialysis group. There is a significantly higher level of triglycerides and Serum cholesterol and a significantly lower level of HDL cholesterol in the hemodialysis group.

**Conclusions:** The high prevalence of lipid abnormalities in CKD may accelerate the progression of CVD and increase the mortality of patients. Hence it is worthwhile to test and detect patients at high risk early on and manage accordingly.

**Keywords:** CKD, Lipid profile, Non diabetic

### INTRODUCTION

Chronic Kidney Disease (CKD) is a worldwide health problem. Prevalence of CKD in the United States is increasing and affects about 19 million Americans.<sup>1</sup> The United States has seen a 30% increase in patients suffering from CKD in the last decade.<sup>2</sup> Over the last

decade, it was established that CKD is associated with a very high mortality rate and accelerated Cardio-Vascular (CV) disease.<sup>3</sup> Recent studies suggest that the risk for death is increased in individuals with less severe impairment of kidney function that does not require dialysis when compared to those who have preserved kidney function. In patients who finally advance to ESRD

and especially dialysis patients, the prevalence of clinical coronary heart disease is 40% and CVD mortality is 10 to 30 times higher than in the general population of the same gender, age and race.<sup>3,4</sup>

Dyslipidemia may be worsened by dialysis, especially continuous ambulatory peritoneal dialysis (CAPD). Dyslipidemia among HD patients negatively impacts cardiovascular profiles, which in turn influence the frequency and/or duration of hospitalizations.<sup>5</sup> Patients on CAPD exhibit high levels of total cholesterol (TC) and low density lipoprotein (LDL).<sup>6</sup> After CAPD treatment for more than 12 months, these patients may reveal higher serum triglyceride and total serum cholesterol levels compared to their values before commencing CAPD. This phenomenon is not observed in HD patients, and it should be considered when selecting a dialysis modality given the risk of cardiovascular disease (CVD) in the dialysis population.<sup>7</sup> In addition, cross-sectional studies have found that variable results of lipid levels are related to their duration on dialysis.<sup>8</sup>

Although hemodialysis patients have excessive risk of morbidity and mortality from CVD, the evidence concerning treatment of hemodialysis patients with lipid lowering drugs is equivocal. Several multicentre international trials have been conducted but the results were inconclusive and further studies were recommended for answering the questions of the reasons for dyslipidemia and ideal lipid lowering strategy to be used in hemodialysis patients.<sup>9</sup> However, the relationship between dyslipidemia and CV risk in patients with renal disease is less clear than in those with normal renal function, as is the efficacy of statins for preventing CV risk. A lack of evidence exists since patients with CKD were excluded from the major trials that target dyslipidemia treatment in primary and secondary prevention of CV disease. In this study we tried to highlight the prevalence and type of dyslipidemia present in CKD patients in the Indian reference population.

There is lack of evidence when it comes to the prevalence of dyslipidemia in patients suffering from CKD in the Indian subcontinent and the subgroup of cholesterol that is majorly affected owing to the variations in the dietary habits and lifestyle differences from the western counterparts. An emphasis must also be laid on the derangement of lipid profile in patients with CKD in Indian reference population and the severity of dyslipidemia in relation to the severity of CKD. Major studies must be planned in the Indian sub-continent so that a better emphasis can be laid on the rising problem of dyslipidemia in CKD patients keeping in view the rising number of patients suffering from advanced CKD and ESRD. This study is mainly aimed at knowing the overall prevalence of dyslipidemia in hospitalized CKD patients and assess the derangement in lipid profile based on the severity of CKD.

## **METHODS**

### ***Study site***

Patients who were diagnosed with chronic kidney disease admitted into the medical ward and dialysis unit of Ispat general hospital, Rourkela, Odisha, who had willingly given their informed written consent for this study were the source of data.

### ***Study population***

Patients who met all the inclusion criteria were selected randomly. No distinction is made between males and females.

### ***Time frame***

January 2014 to September 2015.

### ***Inclusion criteria***

- Patients with history and physical findings of kidney disease for a duration of more than 6 months and Biochemical evidence of CKD. Sonological evidence with a radiological opinion suggesting CKD
- Patients within the age range of 20-80 years
- All patients who have given consent for enrolling into the study.

### ***Exclusion criteria***

- All patients who have refused to give consent for the study
- Patients with already diagnosed diabetes mellitus
- Patients with already diagnosed dyslipidemia and on medical management
- Patients with associated acute severe medical conditions requiring intensive care unit admissions.

### ***Study design***

It's an analytical, observational, cross sectional study.

### ***For diagnosis of CKD***

Diagnosis of CKD is done by both direct and indirect methods as per criteria. Direct method is by sonological evidence based on radiological opinion based on kidney size, volume, echogenicity, cortico-medullary differentiation and presence of structural kidney damage for greater than 3 months along with indirect evidence of decreased renal function by measuring the GFR by MDRD formula for duration of greater than 3 months. The staging of CKD is also done based on the GFR calculated by MDRD formula. The following criteria are used for diagnosis of CKD.

Clinical evidence of pallor, edema, hypertension, pleuritis, pericarditis, CCF pulmonary edema, and hypertensive retinopathy changes were noted.

Urine output below 500 ml was considered as oliguria and more than 3000 ml was considered as polyuria.

**Urine findings**

Proteinuria was considered as present when the heat test showed a definite cloud which did not get-dissolved on addition of glacial acetic acid. Urine pus cells more than 2-3 per high power field was considered abnormal.

**Biochemical findings**

The presence of Chronic Kidney disease was established based on presence of kidney damage and level of kidney function (GFR). Markers of kidney damage included abnormalities in the composition of blood i.e. elevated blood urea, serum creatinine.

**Ultra sonogram**

Evidence of CKD as by bilateral shrunken Kidneys or with loss of corticomedullary differentiation was taken as indicative of chronic renal failure based on the expert opinion of the consultant radiologist report.

**Statistical methods**

All data were collected and analysed statistically using appropriate tests. Independent sample t-test was applied after fulfilling the normality and equality of population

variance assumption. Pearsons Chi- square test is used to assess the association of different study parameters. Differences were considered statistically significant if P values were <0.05 and very significant if P<0.01.

**RESULTS**

**Table 1: Management strategies in the study population.**

Category	Number
Hemodialysis	50
Conservative management	90

Of the total 140 patients in the study 50 of them were on maintenance haemodialysis and 90 were on conservative management.

**Table 2: Staging of Chronic Kidney Disease (CKD) in the study population.**

Stage of chronic kidney disease	Number	Percentage
Stage 3	24	17.14
Stage 4	52	37.14
Stage 5	64	45.71

There are patients suffering from stage 3, 4 and 5 CKD enrolled into the study. Staging was done by calculating GFR thru the MDRD formula. No patients of stage 1 and 2 were found. Stage 5 included all patients undergoing haemodialysis and patients with GFR < 15ml/min/1.73 m<sup>2</sup> who are being managed conservatively at the time of the study.

**Table 3: Dyslipidemia and comparison with management strategies.**

Lipid profile	Number (%)	On hemodialysis	On conservative management	P value
Normal	48 (34.29%)	9	39	P< 0.0001 OR = 0.1765
Abnormal	92 (65.71%)	41	51	
<b>Total</b>	<b>140</b>	<b>50</b>	<b>90</b>	

**Table 4: Dyslipidemia vs. staging of CKD.**

Lipid profile	Stage of chronic kidney disease			P value
	Stage 3	Stage 4	Stage 5	
Abnormal	8 (33.33%)	37 (71.15%)	47 (73.43%)	$\chi^2 = 13.546$ p = 0.0011
Normal	16 (66.67%)	15 (28.85%)	17 (26.56%)	
<b>Total</b>	<b>24 (100%)</b>	<b>52 (100%)</b>	<b>64 (100%)</b>	

In the study population the prevalence of dyslipidemia as evidenced by abnormal lipid profile is 65.71% i.e. 92 patients had an abnormal lipid profile of which 41 patients were undergoing HD and 51 patients were under conservative management.

When comparing the prevalence of dyslipidemia with the staging of CKD, it was found that of the total 24 patients in CKD stage 3, 16(66.67%) of them had a normal lipid profile and 8 (33.33%) recorded an abnormal lipid profile. There is a statistically significant association of

prevalence of dyslipidemia with increase in staging of CKD.

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In our study the majority of the abnormality is seen in the triglyceride group with 68 (48.57%) patients having an

abnormality here. The abnormalities of total cholesterol and HDL cholesterol are seen in 32 (22.86%) and 30 (21.43%) patients respectively. About 18 (12.86%) patients had an abnormality in the LDL cholesterol group.

**Table 5: Comparison of dyslipidemia incidence in stage 5 CKD.**

Stage 5 CKD	Normal	Abnormal	P value
Conservative management	08	06	OR=0.1646 P=0.0056
On hemodialysis	09	41	

**Table 6: Mean parameters in lipid metabolism and variation with management strategy.**

Parameter	Total	On hemodialysis	On conservative management	p-value	t-value
Triglycerides	116.71±56.59	123.54±58.62	103.97±52.33	0.026	2.25
Serum cholesterol	156.62±51.62	158.42±53.35	151.56±49.93	0.86	0.171
HDL	43.15±16.	42.7±17.6	44±16	0.013	2.5
LDL	83.81±34.76	86.27±35.68	77.41±33.97	0.31	1.01

The mean TG values in the total study population are 116.71±56.59. The mean value of TG in patients under haemodialysis is higher (123.54±58.62) than those on the conservative management (103.97±52.33). The variation is statistically significant with P= 0.026.

#### **Total cholesterol**

There is a rise in the total cholesterol values in patients under haemodialysis (158.42±53.35) as compared to those under conservative management (151.56±49.93) with the mean value of the total study population is 156.62±51.62, but the rise is not statistically significant (p = 0.86).

HDL: There is statistically significant fall in the levels of HDL in the study population with the mean value at 43.15±16.4 and the extent of fall is greater in the haemodialysis group (42.7±17.6) as compared to the conservative management group (44±16) (p = 0.013).

LDL: The mean value in the study group is 83.81±34.76 with a difference between patients under haemodialysis (86.27±35.68) from those under conservative management (77.41±33.97) (p = 0.31).

## **DISCUSSION**

The study consisted of 140 patients of which after evaluation represented the study population adequately in terms of age and sex. The mean age of the population of the study was 55.14±12.27 years. The mean age of the patients undergoing dialysis was 54.4±22.75 years and those under conservative management was 56.42±18.65 years. The variation in distribution of age is not

statistically significant and the study population ideally represents the reference population.

It has been observed that the representation of either sex is adequate in the study group with a total of 89 (63.57%) patients being male and 51 (36.43%) patients being female. Of the patient population undergoing HD i.e. 50 patients, 32 (64%) were male and 18 (36%) female. There is no statistically significant variation in population representation in the study.

The prevalence of dyslipidemia in non-diabetic CKD as calculated in this study is found to be 65.71% in patients with CKD without any prior history of diabetes. A study among Nepalese population with CKD recorded a higher prevalence of dyslipidemia among CKD patients when compared to the non-CKD control group, and the difference was statistically significant.<sup>10</sup>

In the general study population there is marked elevation of triglycerides in 68 (48.57%) patients. A study by Saroj K et al reported a prevalence of 36.6% and a study in Khatmandu, Nepal also showed a prevalence of 35.58% of hypertriglyceridemia in CKD.<sup>10,11</sup>

The cause for hyper triglyceridemia in chronic kidney disease patients has not been delineated. Available data derived from kinetic studies with intralipid administration have demonstrated that in the reduced catabolism of triglycerides, the predominant defect may be due to deficiency of lipoprotein lipase or hepatic triglyceride lipase or both. These enzymes are the primary mediators of the process. Reasons for decrease in activity of these enzymes are not clear, possibly due to;

- Presence of circulatory inhibitor of lipolytic enzymes in the serum
- Changes in apoprotein concentrations which can affect lipoprotein lipase activity
- Insulin resistance seen in renal insufficiency
- Alteration of lipoprotein substrate.<sup>12,13</sup>

Hypercholesteremia was found in 32 (22.86%) patients and decrease in HDL cholesterol was found in 30 (21.43%).

Saroj K et al found about 34.4% of the CKD study patients to have hypercholesteremia and 34.1% had low levels of HDL cholesterol.<sup>11</sup> The reports conducted in Khatmandu, Nepal by Poudel B et al showed a prevalence of 33.75% of hypercholesteremia.<sup>10</sup>

Anderson et al found hypercholesteremia in 20% of the patients in their study.<sup>14</sup> Hypercholesteremia is a significant risk factor for CAD. But, Gerald Appel found low values of cholesterol in CKD patients.<sup>15</sup>

Goldberg et al found decrease in HDL concentrations in CKD patients as compared to controls in contrast to Rapoport and Aviram study showed no decrease in HDL concentrations in CKD patients.<sup>16,17</sup>

The LDL cholesterol is abnormal is only observed in 18 (12.86%) of the study population whereas Saroj K et al reported a larger figure of 35% of the study population to have undesirable LDL levels and Poudel et al reported an even higher prevalence of 38.03%. But abnormality in uremia is mainly qualitative.<sup>10,11</sup>

A total of 50 patients were on haemodialysis and 90 patients were on conservative management. There was an increased incidence of dyslipidemia in patients under haemodialysis, 41 of the 50 patients, as compared to 51 out of 90 patients under conservative management ( $P < 0.0001$ ; OR = 0.1765).

Kronberg F et al found out that hypertriglyceridemia is more prevalent in the dialysis group than conservative management group and in the dialysis group more prevalent in the peritoneal dialysis patients maybe owing to significant amounts of glucose being absorbed from the dialysis fluid.<sup>18</sup>

The patients who were on haemodialysis were suffering from chronic kidney disease from long time compared to patients on conservative management. Probably that might have contributed to increase number of lipid abnormalities in those patients.

There was a general worsening of lipid profile in patients as the severity of CKD increased as evidenced by the prevalence of dyslipidemia increases with increase in grading of CKD.

In the present study 24 patients (17.14%) were in stage 3, 52 (37.14%) patients belonged to stage 4 and 64 (45.72%) patients were categorized as stage 5 or end stage renal disease. The prevalence of dyslipidemia increases as the chronic kidney disease progresses. There is statistically significant association between the parameters ( $P = 0.009$ ).

According to Vaziri and Moradi CKD causes profound dysregulation of lipoprotein metabolism, resulting in lipoprotein abnormalities. Dyslipidemias develop during early stages of CKD, but progress rapidly with progression of CKD.<sup>19</sup>

There is also increased incidence of dyslipidemia in stage 5 CKD as most of the patients undergo regular haemodialysis. And this increased incidence of dyslipidemia in stage 5 CKD may also be due to the long duration of illness. This has to be confirmed by further studies.

No cases have been excluded from the study after enrolling due to complications or death during the study.

## CONCLUSION

The study concludes that, the prevalence of dyslipidemia in non-diabetic CKD is high enough to pose a health problem in the society and this problem of dyslipidemia increases with the severity of CKD. A high degree of abnormality is found in triglycerides in the form of hypertriglyceridemia in non-diabetic CKD patients. Haemodialysis could be a potential risk factor for development of dyslipidemia in non-diabetic CKD as the prevalence is high in this group of patients compared to conservative management group.

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