DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE

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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 uraemia 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 triglyceride-rich 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:

1. Patients of chronic kidney disease on conservative treatment.
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;

AGE GROUP	NO. OF CASES	%	SEX			
			MALE		FEMALE	
			NO.	%	NO.	%
20-29	4	8	3	6	1	2
30-39	12	24	5	10	7	14
40-49	14	28	8	16	6	12
50-59	8	16	6	12	2	4
60-70	12	24	8	16	4	8

Table-1: Age and Sex distribution of cases

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S.NO.	FINAL DIADNOSIS	NO OF CASES
1	CHRONIC GLOMERULONEPHRITIS	30
2	HYPERTENSIVE NEPHROSCLEROSIS	12
3	POLYCYSTIC KIDNEY DISEASE	6
5	OBSTRUCTIVE UROPATHY	2

Table-2: Final diagnosis in cases

Sample 1		
Variable	SERUM_CREATININE	
Select	group=1	
Sample 2		
Variable	SERUM_CREATININE	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	9.6300	0.9160
95% CI for the mean	8.7448 to 10.5152	0.8224 to 1.0096
Variance	9.7026	0.0514
Standard deviation	3.1149	0.2267
Standard error of the mean	0.4405	0.0453
F-test for equal variances	P < 0.001	
T-test (assuming equal variances)		
Difference	-8.7140	
95% CI of difference	-9.9615 to -7.4665	
Test statistic t	-13.922	
Degrees of Freedom (DF)	73	
Two-tailed probability	P < 0.0001	

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

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.

Sample 1		
Variable	HB%	
Select	group=1	
Sample 2		
Variable	HB%	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	6.3100	13.6160
95% CI for the mean	5.7327 to 6.8373	13.3313 to 13.9007
Variance	3.4421	0.4756
Standard deviation	1.8553	0.6896
Standard error of the mean	0.2624	0.1379
F-test for equal variances	P < 0.001	
T-test (assuming equal variances)		
Difference	7.3060	
95% CI of difference	6.5393 to 8.0727	
Test statistic t	13.990	
Degrees of Freedom (DF)	73	
Two-tailed probability	P < 0.0001	

Table-4: Comparison of Mean Haemoglobin values in both groups

The mean HB is 6.3 gm% in patients of CKD and is 13.6 gm% in control subjects.

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Sample 1		
Variable	TOTAL_CHOLESTEROL	
Select	group=1	
Sample 2		
Variable	TOTAL_CHOLESTEROL	
Select	group=2	

	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	213.5600	186.7600
95% CI for the mean	205.4657 to 221.6543	182.8635 to 190.6565
Variance	811.1902	89.1067
Standard deviation	28.4814	9.4396
Standard error of the mean	4.0279	1.8879

F-test for equal variances	P < 0.001
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T-test (assuming equal variances)

Difference	-26.8000
95% CI of difference	-38.4939 to -15.1061
Test statistic t	-4.568
Degrees of Freedom (DF)	73
Two-tailed probability	P < 0.0001

Table 5: Comparison of Mean Total Cholesterol level in both

The mean total cholesterol is 213.5 mg/dl in patients of CKD and is 186.7 mg/dl in control subjects.

Sample 1	
Variable	TRIGLYCERIDE
Select	group=1
Sample 2	
Variable	TRIGLYCERIDE
Select	group=2

	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	218.7400	87.0400
95% CI for the mean	200.4702 to 237.0098	84.1815 to 89.8985
Variance	4132.6453	47.9567
Standard deviation	64.2857	6.9251
Standard error of the mean	9.0914	1.3850

F-test for equal variances	P < 0.001
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T-test (assuming equal variances)

Difference	-131.7000
95% CI of difference	-157.4848 to -105.9152
Test statistic t	-10.180
Degrees of Freedom (DF)	73
Two-tailed probability	P < 0.0001

Table-6: Comparison of Mean Triglyceride 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.

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Sample 1		
Variable	HDL	
Select	group=1	
Sample 2		
Variable	HDL	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	31.5640	46.5200
95% CI for the mean	30.6578 to 32.4702	44.8051 to 48.2349
Variance	10.1681	17.2600
Standard deviation	3.1887	4.1545
Standard error of the mean	0.4510	0.8309
F-test for equal variances	P = 0.117	
T-test (assuming equal variances)		
Difference	14.9560	
95% CI of difference	13.2300 to 16.6820	
Test statistic	17.270	
Degrees of Freedom (DF)	73	
Two-tailed probability	P < 0.0001	

Table-6: Comparison of Mean HDL 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.

Sample 1		
Variable	LDL	
Select	group=1	
Sample 2		
Variable	LDL	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	138.2080	122.7440
95% CI for the mean	130.2658 to 146.1492	119.2860 to 126.2020
Variance	780.7971	70.1784
Standard deviation	27.9427	8.3773
Standard error of the mean	3.9517	1.6755
F-test for equal variances	P < 0.001	
T-test (assuming equal variances)		
Difference	-15.4640	
95% CI of difference	-26.8834 to -4.0446	
Test statistic t	-2.690	
Degrees of Freedom (DF)	73	
Two-tailed probability	P = 0.0096	

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.

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Sample 1		
Variable	VLDL	
Select	group=1	
Sample 2		
Variable	VLDL	
Select	group=2	

	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	43.7880	17.4190
95% CI for the mean	40.1407 to 47.4353	16.8421 to 17.9899
Variance	164.7043	1.9331
Standard deviation	12.8337	1.3903
Standard error of the mean	1.8150	0.2731

F-test for equal variances	P < 0.001
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T-test (assuming equal variances)

Difference	-25.3720
95% CI of difference	-31.5197 to -21.2243
Test statistic	-10.210
Degrees of Freedom (DF)	73
Two-tailed probability	P < 0.0001

Table-8: Comparison of Mean VLDL level in both groups

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

Sample 1		
Variable	LDL_HDL	
Select	group=1	
Sample 2		
Variable	LDL_HDL	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	4.4401	2.6612
95% CI for the mean	4.1291 to 4.7510	2.5269 to 2.7956
Variance	1.1970	0.1060
Standard deviation	1.0941	0.3256
Standard error of the mean	0.1547	0.0651
F-test for equal variances	P < 0.001	
T-test (assuming equal variances)		
Difference	-1.7788	
95% CI of difference	-2.2259 to -1.3319	
Test statistic t	-7.932	
Degrees of Freedom (DF)	73	
Two-tailed probability	P < 0.0001	

Table-9: Comparison of Mean LDL /HDL ratio in both groups

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

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Sample 1		
Variable	TG_HDL	
	TG/HDL	
Select	group=1	
Sample 2		
Variable	TG_HDL	
	TG/HDL	
Select	group=2	
	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	7.0295	1.8897
95% CI for the mean	6.3582 to 7.7009	1.7787 to 2.0008
Variance	5.5808	0.0723
Standard deviation	2.3624	0.2689
Standard error of the mean	0.3341	0.0538
F-test for equal variances	P < 0.001	
T-test (assuming equal variances)		
Difference	-5.1398	
95% CI of difference	-6.0877 to -4.1920	
Test statistic t	-10.807	
Degrees of Freedom (DF)	73	
Two-tailed probability	P < 0.0001	

Table-10: Comparison of mean TG/LDL ratio in both groups

The mean TG/HDL ratio is 7.02 in patients of CKD and is 1.88 in control subjects.

Sample 1		
Variable	TG_LDL TG/LDL	
Select	group=1	
Sample 2		
Variable	TG_LDL TG/LDL	
Select	group=2	

	Sample 1	Sample 2
Sample size	50	25
Arithmetic mean	1.6642	0.7110
95% CI for the mean	1.4743 to 1.8541	0.6864 to 0.7356
Variance	0.4465	0.0036
Standard deviation	0.6682	0.0596
Standard error of the mean	0.0945	0.0119

F-test for equal variances	P < 0.001
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T-test (assuming equal variances)

Difference	-0.9532
95% CI of difference	-1.2210 to -0.6854
Test statistic t	-7.094
Degrees of Freedom (DF)	73
Two-tailed probability	P < 0.0001

Table-11: Comparison of mean TG/LDL ratio in both groups

The mean TG/LDL ratio is 1.66 in patients of CKD and is 0.71 in control subjects.

MEAN	CASES	CONTROLS
TOTAL CHOLESTEROL	213.5	186.7
TRIGLYCERIDES	218.74	87.04
HDL	31.5	46.5
LDL	138.2	122.7
VLDL	43.78	17.41

Table-12: Comparison of all Variants of Lipid Profile in both groups

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 186.76mg/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 6.31g/dL.
- Mean serum creatinine value was 9.63 mg/dL.

- Mean total cholesterol value was 213.56mg/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 213.56mg/dL in cases and 186.76mg/dL in control, similar study was done by Oliver and Boyd ¹³ determined the level of total cholesterol between 100-250 mg%. Soperry¹²⁰ reported the range of 192-382 mg% in normal individuals, Naht, Gupta and Iyer¹⁴ 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 & Zulianiet al¹⁵ and Roovoets et al¹⁶. 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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