

A study of lipid profile in chronic kidney disease in pre- dialysis patients


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Introduction: Longitudinal studies have established that Cardiovascular Disease (CVD) occur more frequently and are the leading cause of death in Chronic Kidney Disease (CKD). Dyslipidemia has been established as an important risk factor in the pathogenesis of CVD in CKD patients. **Objectives:** Present study was aimed to evaluate (in CKD patients), Demography along with Prevalence and Pattern of Dyslipidemia and co-relation of Dyslipidemia with various CKD stages. **Methods:** Present **Cross-sectional study**, conducted in Department of Medicine, R.D. Gardi Medical College and CRG hospital, Ujjain, M.P. from 1st January 2015 to 31st July 2016. We studied 115 pre-dialysis CKD cases and 100 age & sex matched controls. CKD was diagnosed as per 2012 KDOQI Criteria. **Result:** In CKD cases, maximum 23.47% cases belonged to fifth decade. Mean age was 48.99 ± 16.74 . Male to Female ratio was 1.21: 1. Prevalence of individual dyslipidemias was High TC= 50.44%, High TG= 67%, High LDL-C= 42%, High VLDL-C= 67% and Low HDL-C= 73.9%. Overall, prevalence of dyslipidemia was 82.6%. Significant increase in TG and VLDL-C and significant decrease in HDL-C was observed. TC and LDL-C were non-significantly increased. TC, TG, LDL-C and VLDL-C were in increasing trend with progression of CKD stages (3-5) and increased in Subgroup II (ESRD) as compared to Subgroup I (Non-ESRD), the increase being significant in case of TG and VLDL-C. HDL-C value was in decreasing trend with progression of CKD stages and significantly decreased in Subgroup II as compared to Subgroup I. TC, TG, LDL-C and VLDL-C showed negative correlation with GFR while HDL-C showed positive correlation. TG, HDL-C and VLDL-C showed highly significant correlation. HDL-C showed strongest correlation, followed by TG. **Conclusion:** Patients with CKD are predisposed to accelerated atherosclerosis leading to increased CVD. This study confirms the presence of atherogenic lipid profile in CKD.

Keywords: Chronic Kidney Disease, Cardio Vascular disease, Dyslipidemia

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Introduction

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR)[1]. Cardio-Vascular Disease (CVD) is the leading cause of death, irrespective of race and ethnicity, and is mostly caused by cardio-metabolic risk factors and chronic kidney disease (CKD)[2].

In the United States, the prevalence of CVD in CKD patients reaches 63%, in contrast with only 5.8% in people without CKD, and this prevalence is directly correlated with the severity of CKD[3]. CVD accounts for 40% to 50% of deaths in dialysis patients.

In dialysis-dependent end-stage renal disease (ESRD) patients, the risk of cardiovascular (CV) mortality is 10-fold to 20-fold higher than in age and gender-matched control subjects without CKD[4]. The median survival of dialysis patients with baseline Heart Failure (HF) has been estimated to be 36 months, in contrast with 62 months for those without baseline HF[5]. Dyslipidemia has been established as a well-known traditional risk factor for CVD and large-scale observational studies have shown that total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) are most important independent predictors of cardiovascular morbidity and mortality [6]. Although there are many important risk factors playing a role in the pathogenesis of CVD in chronic kidney disease (CKD) patients, dyslipidemia represents one of the important and modifiable risk factor [7].

The prevalence of hyper-cholesterolemia ranges from 48% in CKD stage 1-2 to 80% in CKD stage 3-4[3]. Several prospective studies suggest that lipid abnormalities principally present in CKD is Hypertriglyceridemia along with increased Very-Low Density Lipoprotein Cholesterol (VLDL-C) and decreased HDL-C[8]. Abnormal lipid and lipoprotein concentrations in patients with CKD may be responsible for increased atherosclerosis and risk of CVD[9]. Elevated Triglyceride (TG) levels are due to impaired activity of Lipo-Protein Lipase (LPL) and direct inhibitory effect of various uremic 'toxins' on the enzymes involved in lipid metabolism [10]. Dyslipidemia has been observed to worsen with progression of CKD stages leading to increased Cardio-Vascular morbidity and mortality [11].

Objectives

01. To study the Demography in Pre-dialysis CKD patients (Study cases).
02. To study the prevalence of Dyslipidemia in Study cases.
03. To study the pattern of Dyslipidemia in Study cases.
04. To study the correlation of Dyslipidemia in Study cases with various stages of CKD.

Materials and Methods

Study Setting: The present study was conducted in the Department of Medicine, R.D. Gardi Medical College and CRG hospital, Ujjain, M.P. from 1st January 2015 to 31st July 2016. We studied 115 cases of CKD and 100 age & sex matched controls. CKD was diagnosed by clinical examination, biochemical analysis and sonological findings as per the 2012 Kidney Disease Outcomes Quality Initiative (KDOQI) Criteria.

Study Design: The present study was a Cross-sectional observational study.

Inclusion Criteria: All patients of Chronic Kidney Disease with age 18 years or above, who give consent for study.

Exclusion Criteria

01. Patients who do not fill the above criteria.
02. Patients with End Stage Renal Disease (CKD-Stage 5) on Hemodialysis.
03. Patients with Diabetes Mellitus.
04. Patients already on lipid lowering drug therapy.

Sampling methods: Blood samples were drawn from all the patients by venipuncture in cubital fossa after a minimum of 12 hours of fasting. About 10 ml of blood was drawn & transfused to dried glass vials. Serum was separated within 2 hours after collection and centrifuged at 5000 rpm for 10 minutes. The supernatant clear serum was then pipetted out and stored in dry thin walled vials at 40°C. The samples were analysed on the same day.

Laboratory procedures: Study of lipid profile was done by VITROS slide method.

Ethical Clearance: Ethical clearance for the study was obtained from Ethical Committee, RD Gardi Medical College, Ujjain

Any Scoring System: None

Surgical procedure, if any: None

Statistical analysis: Statistical software SPSS 23.0 was used for the analysis of data.

Results

Table-1: Age&Gender-Wisedistribution& mean age of Study group and Control group.

S. No.	Age group (in years)	Study group (n=115)		Control group (n=100)	
		No. of cases	Percentage	No. of cases	Percentage
1	18-20	1	0.86	5	5
2	21-30	18	15.65	28	28
3	31-40	21	18.26	11	11
4	41-50	27	23.47	14	14
5	51-60	23	20	19	19
6	61-70	14	12.17	19	19
7	>70	11	9.56	4	4
8	Male	63	54.8	54	54
9	Female	52	45.2	46	46
10	M:F	1.21 : 1		1.17 : 1	
11	Mean age (Overall)	48.99±16.74 (20-92)		44.12±17.61 (18-76)	
12	Mean age (Male)	53.55±16.37 (21-92)		44.89±18.99 (18-76)	
13	Mean age (Female)	43.46±15.59 (20-76)		43.21±16.01 (21-72)	

Table-2: Biochemical Parameters in Study group and Control group.

S. No.	Biochemical Parameter	Study group (n=115)		Control group (n=100)		P-value for Independent t- test
		Mean	S.D.	Mean	S.D.	
1	Blood Urea	204.75	84.12	14.11	4.34	0.000
2	Serum Creatinine	8.34	4.55	0.75	0.29	0.000
3	Serum Total Proteins	6.08	0.62	6.80	0.46	0.000
4	Serum Albumin	3.33	0.53	4.23	0.33	0.000
5	Serum Sodium	138.35	7.12	139.85	5.29	0.081
6	Serum Potassium	5.51	1.27	4.28	0.71	0.000
7	Serum Calcium	8.30	1.29	8.93	0.77	0.000
8	Serum Phosphorus	7.29	2.13	3.66	0.83	0.001
9	Hemoglobin	7.60	2.54	12.02	1.56	0.000

A statistically highly significant increase in levels of Blood Urea, Serum Creatinine, Serum Potassium and Serum Phosphorus, while a statistically highly significant decrease in levels of Serum Total Proteins, Serum Albumin and Serum Calcium was observed in Study group. Serum Sodium level was decreased in Study group, but not significantly.

Table-3: Prevalence of Individual & Overall Dyslipidemia in Study and Control group. Chi-square test was applied.

Lipid profile parameter		Study Group		Control Group		p-value
		No. of cases	(%)	No. of cases	(%)	
TC	<200	57	49.56	73	73	0.000
	≥200	58	50.44	27	27	
TG	<150	38	33	70	70	0.000
	≥150	77	67	30	30	
HDL-C	<40	85	73.9	20	20	0.000
	40-60	30	26.1	80	80	
LDL-C	<130	67	58	69	69	0.103
	≥130	48	42	31	31	
VLDL-C	<30	38	33	90	90	0.000
	≥30	77	67	10	10	
Overall	N	20	17.5	54	54	0.000
	AB	95	82.6	46	46	

N=Normal Lipid profile. AB=Abnormal Lipid profile. Prevalence- High TC = 50.44%, High TG = 67%, High LDL-C = 42%, High VLDL-C = 67% and Low HDL-C = 73.9%, statistically significant difference in prevalence being observed in all parameters except LDL-C. Overall, prevalence of Dyslipidemia= 82.6%

Mean value of TC, TG, LDL-C & VLDL-C was increased in Study group. The increase was Highly Significant in case of TG & VLDL-C, while Non-Significant in case of TC & LDL-C. HDL-C was Significantly decreased in Study group. Mean values of TC, TG, LDL-C and VLDL-C were in increasing trend with progression of CKD stages (3 to 5), while HDL-C value was in decreasing trend.

Table-4: Prevalence of CKD cases and mean value of various Lipid Profile parameters in various CKD stages.

CKD Stages	No. of cases		TC	TG	HDL-C	LDL-C	VLDL-C
1	0		-	-	-	-	-
2	0		-	-	-	-	-
3 (3a+3b)	5	Mean	196.80	147.00	40.60	114.40	27.20
		SD	24.22	57.63	5.86	19.53	11.34
4	29	Mean	199.28	151.28	38.17	118.72	30.48
		SD	43.59	69.86	7.40	39.14	15.90
5	81	Mean	206.10	194.44	34.73	125.41	37.44
		SD	44.33	58.78	4.99	38.39	11.31
Total (Study group)	115	Mean	203.97	181.50	35.85	123.24	35.24

		SD	46.46	64.37	5.95	37.89	12.98
		p-value	0.096	0.000	0.044	0.133	0.000
Control Group	100	Mean	195.36	117.11	51.19	116.37	19.78
		SD	27.81	30.84	10.00	28.81	4.88

Note: p-value=compared to Control group

Table-5: Prevalence of CKD cases and mean value of various Lipid Profile parameters in two Sub-groups (I and II) of Study group. Sub-group I = CKD Stages 1 to 4 (Non- ESRD). Sub-group II=CKD Stage 5 (ESRD).

Sub-group	No. of cases		TC	TG	HDL-C	LDL-C	VLDL-C
I	34	Mean	198.91	150.65	38.53	118.09	30.00
		SD	41.04	67.42	7.17	36.72	15.22
		p-value	0.641	0.008	0.000	0.780	0.000
II	81	Mean	206.10	194.44	34.73	125.41	37.44
		SD	44.33	58.78	4.99	38.39	11.31
		p-value	0.060	0.000	0.000	0.081	0.000
		p'-value	0.419	0.001	0.007	0.347	0.013
Control group	100	Mean	195.36	117.11	51.19	116.37	19.78
		SD	27.81	30.84	10.00	28.81	4.88

In both Subgroup I and Subgroup II as compared to Control group, mean TG & VLDL-C were increased (statistically highly significant), HDL-C was decreased (statistically highly significant).TC & LDL-C were increased but not significantly.

In Subgroup-II (ESRD) as compared to Subgroup-I (Non-ESRD), mean TG and VLDL-C were increased (statistically highly significant), while value of HDL-C was decreased (statistically highly significant). TC and LDL-C were increased but not significantly.

Note: p-value=compared to Control group. p'-value=compared to Sub-group I.

Table-6: Correlation of Lipid profile parameters with GFR. (n=115)

GFR		GFR	TC	TG	HDL-C	LDL-C	VLDL-C
GFR	Pearson Correlation	1	-0.100	-0.307	0.324	-0.109	-0.276
	p-value		0.286	0.001	0.000	0.246	0.003

TC, TG, LDL-C and VLDL-C showed negative correlation with GFR while HDL-C showed positive correlation. TG, HDL-C and VLDL-C showed statistically highly significant correlation while TC and LDL-C showed non-significant correlation. The strongest correlation was observed with HDL-C (0.324), followed by TG (-0.307).

Note: Mean GFR= 11.75 ± 7.93 mL/min/ 1.73 m²

Discussion

Age and Gender- In Study group, maximum 23.47% cases were in fifth decade; mean age was 48.99 ± 16.74 & Male: Female ratio was 1.21: 1. In Control group, maximum 28% cases were in third decade; mean age was 44.12 ± 17.61 & Male: Female ratio was 1.17: 1.

Similar observations were obtained by Aharwar et al in 2015 with mean age of patients and controls was 47±16 yrs and 47.68.46±15.95 yrs respectively & Male: Female ratio 1.27: 1 [12]. Avasthi G et al in 2001 obtained similar age distribution [13]. Jungers P et al in 1996 had similar Gender distribution with a marked preponderance of males [14].

Lipid profile parameters

Prevalence: The prevalence of individual dyslipidemias was High TC = 50.44%, High TG = 67%, High LDL-C value = 42%, High VLDL-C = 67% and Low HDL-C = 73.9%, statistically significant difference in prevalence being observed in all parameters except LDL-C.

Garg et al in 2015 in their study of 100 CKD patients observed that 97% had elevated TG values, 61% had elevated TC values, 34% had elevated LDL-C values and 87% had low HDL-C values [15].

Overall, prevalence of Dyslipidemia was 82.6% in CKD patients, which was significantly higher as compared to Control group (46%). The NHANES study in United States observed prevalence of dyslipidemia varying from 48% in CKD stage 1-2 to 80% in CKD stage 3-4 [3]. This is in concordance with the present study as the Study group comprised of patients in CKD stages 3 to 5 only.

Summarizing the observations (irrespective of CKD stage): In present study, mean value of TC, TG, LDL-C & VLDL-C was increased in Study group. The increase was statistically Highly Significant in case of TG & VLDL-C, while Non- Significant in case of TC & LDL-C. HDL-C was statistically significantly decreased in Study group.

Shah B et al in 1992 studied Lipid profile in CKD patients and observed no change in TC, HDL-C and LDL-C but there was significant increase in TG level [16]. Koch et al in 1994 observed significant decrease in HDL-C but no change in values of TC, LDL-C and TG [17]. Crook et al in 2003 obtained significant increase in LDL and VLDL-C with significant decrease in HDL-C [18].

Raju et al in 2013 in their study of 95 CKD patients obtained significant increase in TG and VLDL-C levels and statistically significant decrease in HDL-C levels, but no change in TC and LDL levels[8]. Mannagi et al in 2014 in their study of 30 CKD patients obtained significant increase in TG and LDL-C [19].

Aharwar et al in 2015 in their study of 100 CKD patients obtained significant increase in TG and VLDL-C and significant decrease in HDL-C levels. The values of TC and LDL-C were increased but not significantly [12]. The observations of Lipid profile parameters in present study are, thus, similar to that obtained by Raju [8] et al and Aharwar [12] et al.

Summarizing the observations in various stages of CKD: In present study, values of TC, TG, LDL-C and VLDL-C were in increasing trend with progression of CKD stages (3 to 5), while HDL-C value was in decreasing trend.

In both Subgroup I and Subgroup II as compared to Control group, mean TG & VLDL-C were increased (statistically highly significant), HDL-C was decreased (statistically highly significant).TC & LDL-C were increased but not significantly.

In Subgroup-II (ESRD) as compared to Subgroup-I (Non-ESRD), mean TG and VLDL-C were increased (statistically highly significant), while value of HDL-C was decreased (statistically highly significant). TC and LDL-C were increased but not significantly.

A study by Bhagwat et al, 1997 observed dyslipidemia to be independent of serum creatinine levels [20]. A study by Rao et al, 2010 observed significantly high VLDL-C levels in all stages of CKD 1-5; high TC, LDL-C, TG & HDL-C levels in earlier CKD stages while showing decreasing levels in CKD stage 5[21]. Noor et al (2014) observed increase in the values of TC, TG and VLDL-C while decrease in the values of HDL-C with progression of CKD stages.

Values of LDL-C showed decreasing trends in CKD stage 4 and 5 [22]. Aharwar et al (2015) observed value of TG, LDL-C and VLDL-C to be progressively increasing with successive CKD stages while HDL-C value to be progressively decreasing with successive CKD stages. TC value was showing increasing trend from CKD Stage 2 to 4 but in Stage 5, value was lower than Stage 4 [12]. A recent study by Garg et al, 2015 showed statistically significant increase in the values of TG, TC, VLDL-C and TC/HDL-C with the progression of the stages of CKD [15].

Thus, the observations of Lipid profile parameters in various stages of CKD in present study were, more or less, similar to those obtained by Aharwar [12] et al, Garg et al[15] and Noor [22] et al.

Correlation with GFR:In study group, TC, TG, LDL-C and VLDL-C showed negative correlation with GFR while HDL-C showed positive correlation i.e. with decreasing GFR, HDL-C level were also decreasing.

TG, HDL-C and VLDL-C showed statistically highly significant correlation while TC and LDL-C showed non-significant correlation.

The strongest correlation was observed with HDL-C (0.324), followed by TG (-0.307). Aharwar et al (2015) also observed negative correlation of TC, TG, LDL-C and VLDL-C with GFR while positive correlation of HDL-C with GFR. But they observed the strongest correlation with TG (-0.543)[12].

Conclusion

Patients with CKD are predisposed to accelerated atherosclerosis leading to increased cardiovascular complications. Several factors contribute to atherogenesis, most notable among which is dyslipidemia. TC, TG, LDL-C, VLDL-C increase and HDL-C decrease in CKD, however significant derangement is seen in levels of TG, VLDL-C and HDL-C.

Dyslipidemia in CKD tends to worsen as the disease (stage of CKD) progresses with statistically significant increase in the values of TG and VLDL-C and statistically significant decrease in the values of HDL-C from Non-ESRD stages to ESRD. TC and LDL-C also increase with the progression of disease but not significantly.

What this study adds to existing knowledge?

This study reconfirms the presence of atherogenic lipid profile in patients of CKD leading to increased cardiovascular risk. The dyslipidemia tends to worsen with progression of CKD from Non-ESRD to ESRD, the most notable lipid abnormality being Low HDL-C.

Limitations

Most of the patients in our study presented in late stages of CKD (3-5). The sample size of study was small.

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