Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 05, 2022

Original Research Article

Dyslipidemia in ChronicRenal Failure and Its Implications in Associated Cardiovascular Disease

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Abstract

Background & Objectives: Lipid disorders are one of the known metabolic changes associated with chronic renal failure (CRF) The prominent features of uremic dyslipidemia are an increase in plasma triglyceridesand cholesterol in nearly all lipoproteins, and a reduction in high-density lipoprotein (HDL) cholesterol. Cardiovascular disease (CVD) is a major cause of mortality in patients with chronic renal failure (CRF). One of the risk factors for cardiovascular disease is dyslipidemia as it accelerates atherosclerosis. Therefore it is essential to study uremic dyslipidemia, since optimal
treatment is essential for the prevention or delay of cardiovascular complications in patients with CRF.

Methods : Plasma lipid profile was studied in 30 patients of non diabetic chronic renal failure, 17 non-dialysed patient, 13 hemodialysis patients and compared to 25 healthy subjects. LDL was calculated using friedwald's formula.

Results : Plasma triglycerides (174±60.7 mg/dl Vs 97±17 mg/dl) and VLDL fraction (34.88± 12.15 mg/dl Vs 19.3±3.49 mg/dl) were significantly elevated in CRF patients compared to controls ($p < 0.001$). There was significant decrease in plasma HDL (36±5.1 Vs 48.8±10.3) in CRF patients compared to controls ($p < 0.001$). There was no significant difference in total cholesterol (187±43.5 Vs 185.2±24.51 mg/dl) in CRF and Controls ($p >0.05$). On comparing lipid profiles in CRF patients on conservative management and Hemodialysis there was significant increase in triglycerides in hemodialyis group (199.01±70 Vs 155.176±47mg/dl).

Conclusion:Uremic dyslipidemia is a specific Metabolic abnormality. Excess triglycerides and VLDL fraction was observed in patients of CRF both on conservative management and hemodialysis. Further, reduced level of HDL cholesterol was also observed both in conservative and hemodialysis group of CRF patients. Dyslipidemia observed in Uremic patients may contribute to accelerated atherosclerosis and further progression of chronic renal failure.

Keywords:Blood urea nitrogen ,Coronary heart disease ,Chronic kidney disease ,Chronic renal disease

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Introduction

Chronic renal failure (CRF) is an irreversible deterioration of renal function, which results from diminished effective functioning of renal tissue. Ensuing impairment of excretory, metabolic and endocrine functions of the kidney leads to the development of clinical syndrome of uremia. Cardiovascular disease is a major cause of morbidity and mortality among patients with chronic renal failure[1,2,3]. Majority of patients die from cardiovascular system complications. 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 chronic renal failure the most prevalent lipid disorders arehypertriglyceridemia and decreased HDL Concentration. LDL levels are usually normal or marginally increased[4,5,6]. Also there are reports available regarding accelerated atherosclerosis in chronic renal failure 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 HDL levels as one of risk factors for cardiovascular disease.Chronic renal failure is a syndrome, which results from progressive and irreversible destruction of nephrons regardless of the etiology, where the kidney is no longer able to maintain the biochemical homeostasis. The syndrome is complex and the biochemical changes and clinical signs are variable and mostly non-specific. Chronic renal failure may result from any destructive and progressive condition affecting both the kidneys. It implies failure of both the glomerular and tubular functions. By convention acquired tubular defects or isolated congenital defects are not included in the consideration of chronic renal failure. Chronic renal failure may be asymptomatic or symptomatic. Kidney has a tremendous reserve capacity. About 80% of renal function will be lost before the renal failure develops. Thus the GFR usually would have fallen to about 40 ml per minute, before the blood urea nitrogen or cretinine levels raise above the upper limits of normal Azotemia refers to the accumulation of nitrogenous waste products in the blood and is reflected as elevated blood urea nitrogen ‘Uremia’ is defined as symptomatic renal failure Stages of chronic kidney disease[9]

CARDIOVASCULAR ABNORMALITY:[7,8]

Cardiovascular disease is the leading cause of morbidity and mortality in patients with CRD at all stages. 30-45% of patients reaching ESRD already have advanced cardiovascular complications.

ISCHEMIC CARDIOVASCULAR DISEASE:

CRD at all stages constitute a major risk factor for ischemic cardiovascular disease, including occlusive coronary heart, cerebrovascular and peripheral vascular traditional and CRD – related risk factors. The CRD related risk include, anemia, hyperphosphatemia, hyperparathyroidism and a state of microinflamation. The inflammatory state elicits a rise in acute phase reactants such as inerleukin-6 and C- reactive protein. Other abnormalities augment myocardial ischemia. These include reduced myocardial tolerance to ischemia due to left ventricular hypertrophy and microvascular disease. Nitric oxide is an important mediator for vascular dilatation.It’s availability in CRD is decreased because of increased concentrations of asymmetric dimethyl – 1 arginine and also because nitric oxide is scavenged by reactive oxygen species

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CONGESTIVE HEART FAILURE.

Abnormal cardiac function secondary to myocardial ischemic disease and left ventricular hypertrophy together with salt and water retention in uremia often result congestive heart failure and pulmonary edema. A unique form of pulmonary congestion and edema may occur even in the absence of volume overload and is associated with normal or mildly elevated intracardiac and pulmonary capillary wedge pressure. It is due to increased permeability of alveolar capillary membranes.

HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY:

Hypertension is the most common complication of CRD and ESRD. It may develop early during the course of CRD and is associated with adverse out come in particular, more rapid loss of renal function and development of cardiovascular disease.Administration of EPO mayraise blood pressure and increase the requirement for antihypertensive drugs in CRD patients. Left ventricular hypertrophy and dilated cardiomyopathy are among the most ominous risk factors for excess cardiovascular morbidity and mortality in patients with CRD and ESRD and are thought to be related primarily to prolonged hypertension and ECFV overload. Absence of hypertension may signify the presence of salt wasting form of renal disease (e.g. medullary cystic disease, chronic tubulointerstitial disease, or papillary necrosis) or volume depletion due to gastrointestinal cause or diuretic therapy or reduced cardiac index.

MATERIALS AND METHODS

Cases of chronic renal failure admitted in the medical wards of VIMS Hospital, Bellary from December 2010 to june 2012 for study

INCLUSION CRITERIA:

All stable CRF Patients of chronic renal failure in all stages.

Diagnostic criteria for chronic renal failure

1. Clinical signs and symptoms of uremia
2. 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 (elevated blood urea, serum creatinine) or urine or abnormalities in imaging tests (ultrasonogram).
3. Ultrasonographic evidence of bilateral shrunken kidney/ loss of corticomedullary differentiation.

EXCLUSION CRITERIA:

1. Critically ill patients
2. Recent worsening of renal failure
3. Acute on chronic renal failure
4. Patients on lipid lowering drugs
5. Associated co-morbid conditions such as febrile illness

RESULTS AND OBSERVATIONS

Thirty patients of chronic renal failure and 25 normal subjects (controls) were taken for present study.Lipid levels like TC, TG, LDL and VLDL were estimated for both controls and CRF patients and were compared.

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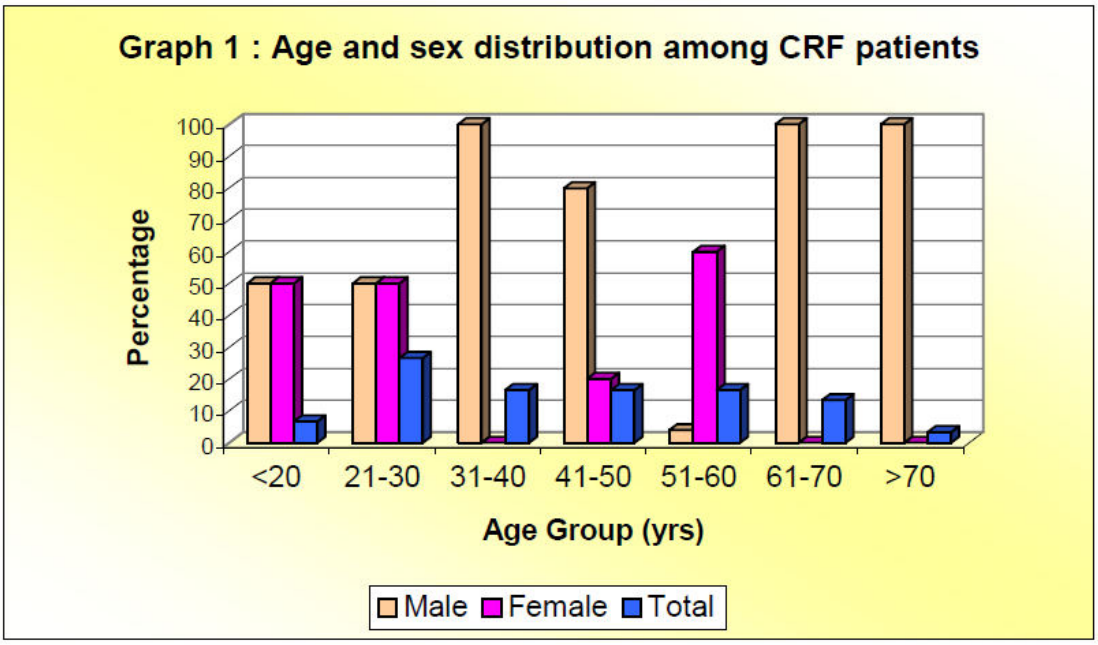
TABLE 1 : AGE AND SEX DISTRIBUTION AMONG CRF PATIENTS

Age group	Total no of cases	Percentage	Male	Percentage	Female	Percentage
<20	2	6.6	1	50	1	50
21-30	8	26.6	4	50	4	50
31-40	5	16.6	5	100	0	0
41-50	5	16.6	4	80	1	20
51-60	5	16.6	2	40	3	60
61-70	4	13.3	4	100	0	0
>70	1	3.3	1	100	0	0
Total	30		21		9	



In the present study, 30 patients of CRF were included, out of which 21 patients (70%) were male and 9 patients (30%) were females. On decade wise grouping, we found maximum number of patients between 21-30 years (26.6%) . The mean age for the total number of patients was 42.7. The mean age for male patients was 45.3.The mean age for female patients was 36.6. Male to female ratio in the study group was 2:3:1

TABLE 2: BIOCHEMICAL DATA IN CONTROLS AND CRF PATIENTS. (MEAN±SD)MG/DL.

Groups	Blood urea	Serum creatinine
Controls (n=25)	15.7±5.3	0.82±0.33

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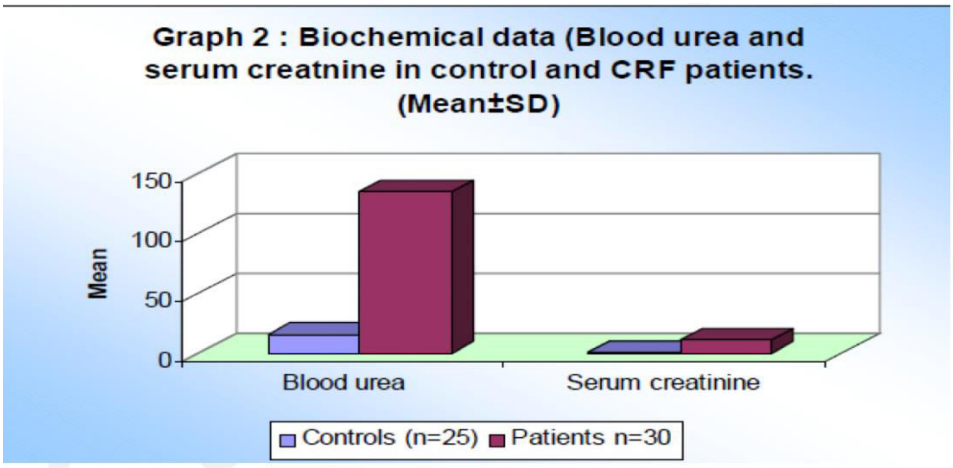
Patients n=30	135.23±41.64	10.96±4.73
t-value*	14.235	10.681
Significance	<0.001	<0.001

*Student's t-test (unpaired) P<0.001 highly significant



In Table 2 Mean values for urea in controls and patients showed aconsiderable difference, which was found to be highly significant (P<0.001). Creatinine levels in CRF patients were very high as compared to controls. This difference was statistically significant (P<0.001). Table 3 : Biochemical (lipid profile) data in controls and CRF patients (Mean± SD)mg/dl.

TABLE 3: SHOWING THE ELECTROCARDIOGRAPHIC CHANGES

Particulars	Frequency	Percentage
LVH	18	60 %
NO LVH	12	40 %
Total	30	100 %

In the present study, out of the 30 patients with CRF, 18 patients (60%) had Left Ventricular Hypertrophy and 12 patients (31%) had no signs of left ventricular hypertrophy.

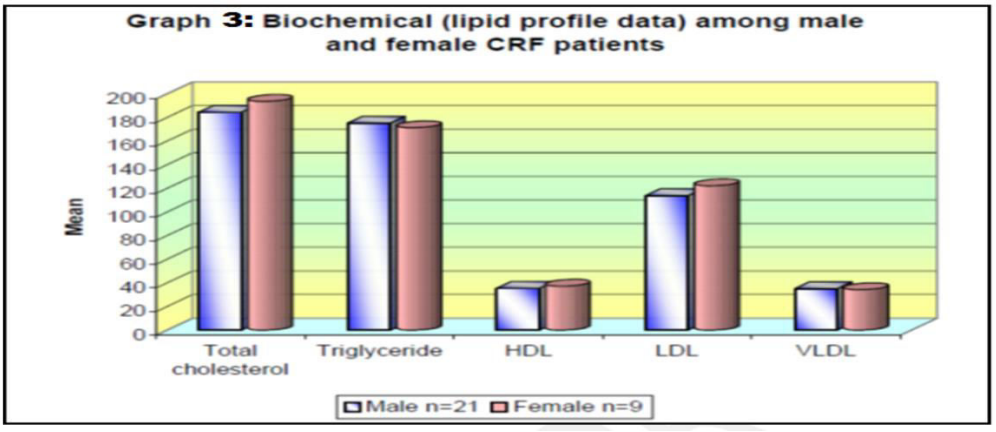


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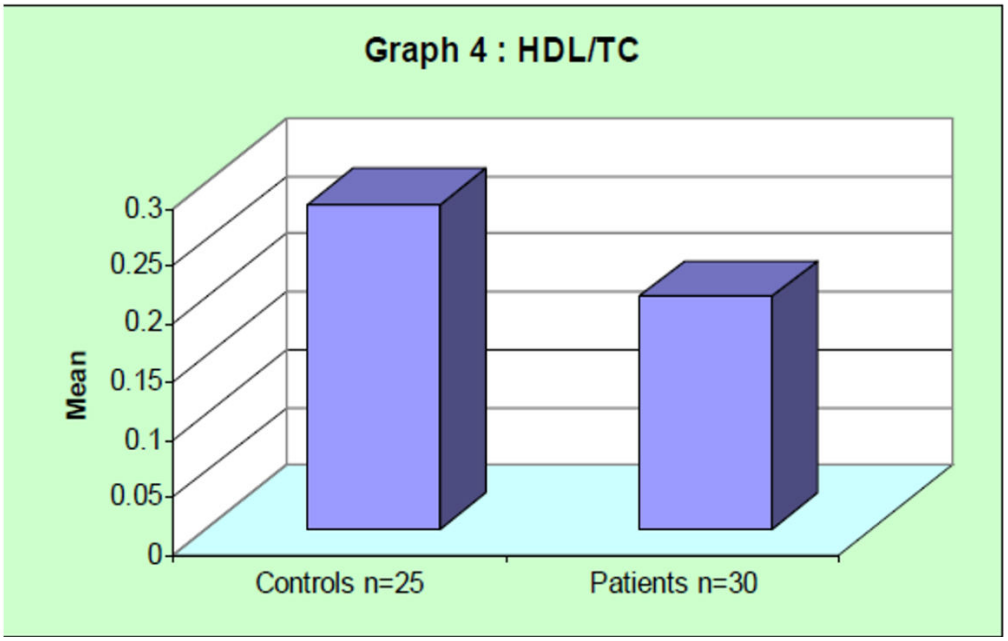
TABLE 4: SHOWS COMPARISON OF BIOCHEMICAL MEAN VALUES OF TC, TG,HDL, AND HDL/TC

Table-4 : (Mean ±SD)mg/dl.

Groups	Conservative treatment n=17	Dialysis n=13	t-value	p-value
Total cholesterol	192.529±50.17	180.385±32.66	0.7595	N.S
Triglycerides	155.176±47	199.01±70	2.052	Sig P<0.05
HDLc	36.1±5.76	35.7±5.20	0.1964	N.S
LDLc	125.38±44.3	104.87±25.10	1.492	N.S
VLDLc	31.27±9.525	39.82±14	1.991	N.S
HDL/TC	0.20±0.053	0.202±0.0405	0.1130	N .S



Mean total cholesterol in patients on conservative treatment was 192.529±50.17 mg/dl and for patients on Hemodialysis it was 18038±32.66 and this difference was statistically not significant (P>0.05). TG- Mean triglycerides in patents of CRF on conservative treatment and Hemodialysis group are 155.176±47 and 199.01±70mg/dl respectively. This difference was statistically significant (P<0.05). HDLc: Mean HDL value in conservative treatment group and those on Hemodialysis are 36.1±5.76 mg/dl and 35.7±5.20 respectively and this difference was statistically not significant. LDL:- Mean LDL value in CRF patients on conservative group and Hemodialysis group are 125.38±44.3mg/dl and 104.87±25.10 respectively and this difference was statistically not significant.VLDL:- Mean VLDL values for conservative and Hemodialysis group are 31.27±9.525 mg/dl and 39.82±14mg/dl respectively and this difference was statistically not significant.HDL/TC:- The difference in mean values of HDL/TC in both conservative treatment and Hemodiailysis group was also statistically not significant.

Table 5: Biochemical (lipid profile) data among male and female CRF patients

Lipid patients mg/dl	Male (n=21) Mean ±SD	Female (n=9) Mean±SD	t’	p-value
Total cholesterol	184.47±46.8	193.7±33.57	0.533	N.S
Triglyceride	175.38±55.03	171.44±72.16	0.1637	N.S

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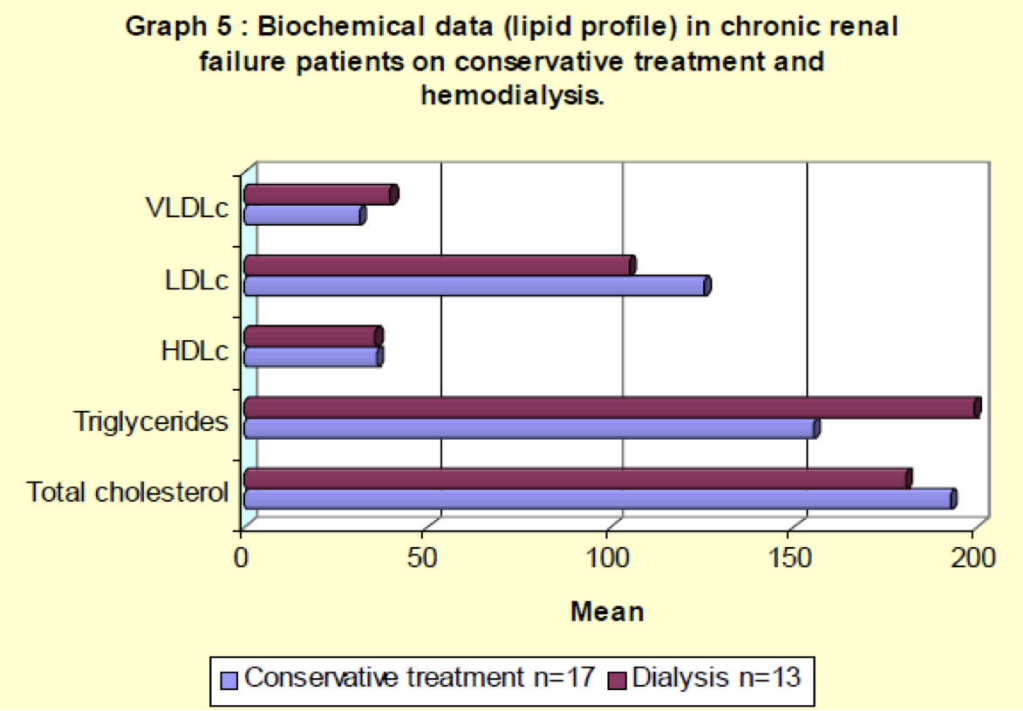
HDL	35.3±5.45	37.2±3.94	0.9416	N.S
LDL	114.01±41.72	122.27±28.01	0.5412	N.S
VLDL	35.13±11.03	34.29±14.43	0.1743	N.S

Table 5:Shows Biochemical (lipid profile) data among male and female CRF patients.
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 theses differences were statistically not significant P(<0.05).



DISCUSSION

The results of the study on the lipid disorders in patients with chronic renal failure show that there are significant alterations in the lipid profiles of these patients as compared to controls.

Table 6 : Comparative study of lipid profiles in chronic renal failure with previous studies:

Lipids	Avasthi et a[9] Mean ±SD	Present study Mean ±SD	Controls Mean ±SD
TC	204±50.54	187±43.5	185±24.5
TG	181±21.8	174±60.7	97±17

Avasthi et al studied 20 patients of chronic renal failure. During investigation all the patient were placed on conservative treatment for renal failure They reported mean triglyceride levels of 181±21.87 and total cholesterol of 204±50.54 mg/dl respectively.

Table 7:sex distribution:

Avasthi et al[9]			Present study		
Male	Female	M:F	Male	Female	M:F

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13	7	1.8:1	21	9	2.3:1

In study conducted by Avasthi et al male to female ratio was 1.8:1

Table 8: Lipid profile data(mean ±SD)

S M Alam et al[10]			Present study		
Lipid	Uremia	H.D	Uremia	H.D	Controls
TC	232.3±56.4	160.8±56.4	192.5±50.17	180.38±32.66	185.2 ±24.2
TG	243.7±119	145.4±24.3	155.176±47	199.01±70	97±17
HDLc	19.0±6.1	12.17±5.1	36.1±5.76	35.7±5.20	48.8±10.3
LDLc	-	-	125.38±44.3	104.87±25.10	116.8±26.78
VLDLC	-	-	31.27±9.525	39.82±14	19.3±3.49

H.D = Heamodylisis, S.M. Alam et al Studied serum lipid and lipoprotein fractions in ESRD patients (35 patients), twenty patients were being treated conservatively and 15 were being hemodialyzed twice weekly. The mean TG, HDLc of this study are shown in Table 13. Serum triglycerides were elevated in conservatively managed group. It was also noted that HDLc was markedly decreased in both conservative and hemodialys is group.

Table 9:sex distribution:

S. M. Alam et al[10]			Present study		
Male	Female	M:F	Male	Female	M:F
22	13	1.7:1	21	9	2.3:1

Table 14 Shows comparison of sex distribution in study conducted by SM Alam et al with present study.

Table 10: shows comparison of distribution of patients in conservatively managed group and Hemodialysis group in study conducted by SM Alam et al with present study.

Group	S. M. Alam et al[10]			Present study		
	Male	Female	Total	Male	Female	Total
Conservative	13	7	20	11	6	17
Hemodialysis	9	6	15	10	3	13

Table 11: Lipid profile data(mean ±SD)

John D. Bagdade et al[11]			**Present study**		
Lipid	Uremia	H.D	Uremia	H.D	Controls
TC	209±44	196±31	192.5±50.17	180.38±32.66	185.2 ±24.2
TG	209±91	210±127	155.176±47	199.01±70	97±17
HDLc	35±23	38±18	36.1±5.76	35.7±5.20	48.8±10.3

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John D. Bagdade et al Studied lipid profile in 27 patients of CRF, 13 patients not on dialysis, 14 patients on dialysis who had stable chronic uremia. The results of this study is shown in table 16. Triglycerides were found to be elevated in both non – dialysed and dialysed CRF patients and HDLc was found to be decreased (<40 mg/dl) in both dialysed and undlialysed groups.

	John D . Bagdade et al[11]	Present study
Serum creatinine (mg/dl)	12.1±3.3	10.96±4.73

Mean serum creatinine values in study conducted by John D Bagdaded et al was 12.1±3.3 mg/gl and it was 10.9±4.73 in present study .

Table 12: Lipid profile data (mean ±SD)

LS Ibels et al[12]			Present study		
Lipids	Uremia	H.D	Uremia	H.D	Controls
TC	236±24	216±57	192.5±50.17	180.38±32.66	185.2 ±24.2
TG	273.±57	237±112	155.176±47	199.01±70	97±17
HDLc	22±6	24±9	36.1±5.76	35.7±5.20	48.8±10.3
LDLc	131±42	116±34	125.38±44.3	104.87±25.10	116.8±26.78
VLDLC	55±40	47±28	31.27±9.525	39.82±14	19.3±3.49

LS Ibels et al studied serum lipoprotein fractions in patients of CRF of Conservatively managed group, those on short term and long term maintenance hemodialysis .

CONCLUSIONS

In this study alteration in different lipoprotein fractions in chronic renal failure patients were studied and also difference in lipid profile in chronic renal failure patients on conservative treatment and hemodialysis were also studied. There is significant increase in triglyceride and VLDL concentration in chronic renal failure patients. The HDL-cholesterol level was found to be significantly lower in CRF patients compared to control group .Total cholesterol and LDL was not significantly raised in patients of CRF compared to controls.The HDL/TC ratio was significantly reduced in CRF patients.On comparison of chronic renal failure patients on hemodialysis and patients on conservative treatment, there is significant increase in triglyceride levels. However total cholesterol and LDL levels were not significantly increased in Hemodialysis patients as compared to patients on conservative treatment.The significant increase of triglyceride, VLDL and reduction in HDL and HDL/TC ratio in chronic renal failure patients is the cause for increase in cardiovascular abnormalities in CRF patients. Significant reduction in HDL and HDL/total cholesterol ratio are the important predictive indices for the risk of developing coronary artery disease in all group of patients with chronic renal failure. This may be major contributory factor for enhanced atherogenesis in these patients. The present study shows that patients with chronic renal failure have higher left ventricular mass index and higher prevalence of left ventricular hypertrophy (LVH), which is more marked in patients with severe renal failure.

References

1. King W. MA, Edward L. Greene, Leopold Raij Cardiovascular risk factors inchronic renal failure and hemoaialysis populations Am J kidneyDis.1992;6:505-513.
2. Eggers PW: Mortality rates among dialysis patients in Medicare's end- stagerenal disease program. Am J. kidney Dis. 1990; 15: 414-421.
3. Rostand SG, Kirk KA, Rutsky EA: Relationship of coronary risk factors tohemodialysis-associated ischemic heart disease, kidney Int.1982;22:304-308.
4. Lidner A, Charra B, Sherrard D. Accelerated atherosclerosis in prolongedmaintainance hemodialysis. N Engl J Med 1974;290:697-701

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5. Tetsuo Shoji, Eiji Ishimura, Masaaki Inaba, Tsutomu Tabata, yoshikiNishizawa. Atherogenic Lipoproteins in End-stage renal disease. Am J kidneydis 2001;38:S30-S33.
6. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovasculardisease in chronic renal disease. Am J kidney dis 1998; 32: S112-S119.
7. Karl Skorecki, Jacob Green, Barry M Brenner. Chronic renal failure. Kasper,Braunwald, Fauci, Hauser, Long O, Jameso; in Harrison's principles ofinternal medincine. 18th ed, Mc Graw Hill 2011. 1653-1663.
8. Cheung AK., Sarnak MJ, Yan G. kidney Int2000;58:353-62
9. G. Avasthi, Devinder Mittal, G.L.Soni. lipid profile of patients of chronicrenal failure. Indian J. Med res 1986;84:612-616
10. SM Alam, AK Bhatt, Abnormal lipoprotein in uremic patients treatedconservatively and by maintainance hemodialysis. J Assoc phy India1991;99:170-171
11. John D. Bagdade, John J. Albers. Plasma high density Lipoprotein concentrations in chronic hemodialysis and renal transplant patients N Engl JMed 1977;1436-39
12. L.S Ibels, L.A Simons, J.O King, P.F Williams,F.C Neale, JH Stewart et alstudies on the nature and causes of hyperlipidemia in uremia, maintenancedialysis and renal transplantation. Quart J Med 1975;176:601-614