STUDY OF LIPID PROFILE IN CHRONIC RENAL FAILURE PATIENTS UNDERGOING HAEMODIALYSIS: A HOSPITAL BASED STUDY

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ABSTRACT: INTRODUCTION: Chronic renal failure (CRF) is decrease in glomerular filtration rate (GFR) to <60 ml/min/1.73 m2 for >3 consecutive months with multiple etiologies. CRF results in profound lipid disorder which stems largely from dysregulation of high density lipoproteins (HDL) & triglyceride-rich lipoprotein metabolism. Many a time CRF patients live on hemodialysis on regular basis. Present study was done to know whether hemodialysis has any impact on the lipid profile of the CRF patients.

MATERIALS AND METHODS: Study were divided into 7 groups, Group-1: healthy controls (40), Group-2: CRF patients who never undergone hemodialysis (40), Group-3: CRF patients on hemodialysis (40), Group-4: Healthy males (28), Group-5: Healthy females (12), Group-6: males with chronic renal failure (28), Group-7: females with chronic renal failure (12). Sample analysed for high density lipoproteins (HDL), low density lipoproteins (LDL) & very low density lipoproteins (VLDL).

RESULTS: Among the various parameters tested triglyceride and VLDL levels were significantly higher in group-2 and3 as compared to controls ($p<0.0001$). HDL levels were significantly lower in group-2 compared to Group-1($p <0.0001$). HDL level was found reduced in group-3 as compare to Group-2($p=0.0035$). There was no significant change ($p=0.132$) observed in total cholesterol between healthy controls and CRF patients with hemodialysis. There is a significant change ($p=0.0309$) observed in LDL-c between CRF patients and controls and no significant change observed ($P=0.6070$) between Group-2 and Group-3.

CONCLUSION: CRF patients are at risk of cardiovascular diseases due to the elevation of various forms of lipids. Prescribing lipid lowering treatment in CRF patients with dyslipidemias for preventing future episode of cardiovascular events and will also preserve renal function.

KEYWORDS: Chronic renal failure (CRF), Hemodialysis, Lipid profile, Cardiovascular Diseases.

HOW TO CITE THIS ARTICLE: U. Sreenivasulu, S. N. Bhagyamma, R. Anuradha. "Study of Lipid Profile in Chronic Renal Failure Patients Undergoing Haemodialysis: A Hospital Based Study." Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 45, November 05, 2015; Page: 8131-8135, DOI: 10.18410/jebmh/2015/1091.

INTRODUCTION: Chronic renal failure (CRF) is a permanent and significant reduction in glomerular filtration rate or chronic irreversible destruction of kidney tissue.[1] It is characterized by a wide variety of biochemical disturbances and numerous clinical symptoms and signs.[2] The alteration includes Haematologic abnormalities, cardiovascular problems, gastrointestinal disturbances, neurologic disorder, osteodystrophy, skin disorder and altered sexual function.[3] Lipoprotein metabolism is altered in most patients with renal in sufficiency.[4] Dyslipidemias is a very common complication of Chronic Renal Failure (CRF). Disturbances in lipoprotein metabolism are evident even at the early stages of CRF and usually follow a downhill course that parallels the deterioration in renal function. Recently published studies indicate that dyslipidemias in these patients may actively participate in the pathogenesis of Cardiovascular disease (CVD) as well as in the deterioration of renal function.[5]

Submission 14-10-2015, Peer Review 15-10-2015, Acceptance 17-10-2015, Published 04-11-2015.
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DOI: 10.18410/jebmh/2015/1091

The characteristic lipid abnormalities seen in CRF patients are elevated triglycerides, normal/reduced total cholesterol (TC), decreased High Density Lipoprotein (HDL), normal Low Density Lipoprotein (LDL).[6] Progressive CRF not only leads to End stage renal disease (ESRD), but it is associated with high cardiovascular morbidity & mortality. In fact, patients with CRF are much more likely to die because of dyslipidemias than to progress to ESRD.[7] With the implication of plasma lipids in the Pathogenesis of atherosclerosis and ischemic heart disease, it becomes worthwhile to study the behavior of various lipid fractions in CRF patients.[8] CVD constitutes the major cause of death in patients with ESRD and it is still higher in Hemodialysis patients than in post-transplantation patients.[9] ESRD Patients on Hemodialysis have abnormalities in lipoprotein structure and metabolism and have a high incidence of cardiovascular diseases.[10] Keeping in view the different outcomes of the researchers regarding Hemodialysis modality in CRF patients, the present study was designed to see any impact of hemodialysis on lipid profile in CRF patients with and without Hemodialysis.

METHODS: A total of 80 subjects were used for this study. Forty of them (28 males and 12 females) who were apparently healthy were used as control while the remaining 40(28 males and 12 females) were patients with chronic

renal failure undergoing dialysis treatment. The age group included individuals from 35 years to 65 years. In order to understand the influence of dialysis on lipid profile, the patients were divided into 2 groups: those who have CRF but undialysed and those who are undergoing Hemodialysis. Thus, study was divided into 7 groups. Group-I (healthy controls), Group-2 (CRF patients who never undergone hemodialysis) and Group-3 (CRF patients on hemodialysis), Group-4 (Healthy males), Group-5(Healthy females), Group-6(males with chronic renal failure) Group-7(females with chronic renal failure). Exclusion criteria include, known case of acute renal failure/hypertension/ischemic heart disease, taking drugs that affect lipids and lipoproteins level.

Sample Collection: Blood samples were collecting from Government General Hospital, Anantapuramu, Andhra Pradesh. 5 ml of venous blood samples collected in plain tubes in the morning after an overnight fast. After collection, samples were centrifuged and serum was analysed for estimation of Serum total cholesterol (TC), triglycerides (TGs), HDL cholesterol (HDL-C), LDL cholesterol (LDL-C), Blood urea and Serum creatinine, using commercially available kits on semi auto analyzer of Clinical Biochemistry Laboratory. The serum total cholesterol were analyzed using cholesterol oxidase method,[11] triglyceride assessment was carried out by glycerol kinase method,[12] High Density Lipoprotein Cholesterol (HDL-C) were analyzed using cholesterol HDL precipitating reagent method,[13] Very Low Density Lipoprotein Cholesterol (VLDL-C) were calculated by dividing the triglyceride concentration by 5. While Low Density Lipoprotein Cholesterol (LDL-C) using Frieldwald's formula.[14] The Blood urea was estimated by Diacetyl monoxime (DAM)method,[15] serum creatinine was estimated by Jaffe's method.[16]

Ethics: Before doing the study Ethics Committee approval has taken in the Govt. Medical College, Anantapuramu.

STATISTICAL ANALYSIS: In data analysis, comparison of parameters in between two study groups and in between control group and study groups were done by using Unpaired t-test. All the data are expressed in mean and standard deviation. For the statistical significance, student 't' test was performed using Graph pad software. Test of probability less than 0.05 ($p<0.05$) was regarded significant.

RESULTS: In the present study the mean serum triglyceride was significantly elevated in CRF patients when compared with control ($p<0.0001$); patients of CRF with hemodialysis have elevated triglyceride level. There is a statistical significant difference observed between total cholesterol level in CRF patients and control groups ($p=0.0239$) and also significant difference observed between CRF patients and hemodialysis patients ($p=0.0239$). HDL cholesterol levels reduced in CRF patients with compared to controls ($p<0.0001$) and there is statistical difference is observed between CRF patients and with hemodialysis patients ($p=0.0035$). There is significant difference observed in LDL cholesterol levels between CRF patients and controls ($p=0.0309$) and there no statistical significant difference observed between CRF patients hemodialysis patients ($p=0.6070$).VLDL cholesterol levels found to be higher in CRF patients as compared to the controls ($p <0.0001$) as shown intable-2 and there is statistical significant difference observed in vldl between CRF patients and with hemodialysis CRF patients ($P<0.0001$) as shown in table-3. There is statistical significant difference observed in TGs, VLDL, HDL values between group-4 and group-6 and also no significant difference observed in Total cholesterol, LDL values as shown in table-4. There is statistical significant difference observed in TGs, vldl values between group-5 and group-7 and also no significant difference observed in Total cholesterol, LDL values as shown in table-5.

CRF= chronic renal failure, HD= Hemodialysis. pts= patients Total cholesterol (TC), triglycerides (TGs), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), Very low density lipoproteins(VLDL) NS-not significant, ESS-extremely statistically significant, SS- statically significant.

CRF= chronic renal failure, HD=Hemodialysis. pts= patients, Total cholesterol (TC), triglycerides (TGs), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), Very low density lipoproteins(VLDL) NS-not significant, ESS-extremely statically significant, SS- statically significant.

Total cholesterol (TC), triglycerides (TGs), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), Very low density lipoproteins (VLDL), NS -not significant, SS- statically significant ESS-extremely statically significant.

DISCUSSION: Chronic Renal Failure (CRF) is a worldwide health problem and is the leading cause of morbidity and mortality in the developed world. Patients with CRF are at high risk for cardiovascular disease (CVD) and cerebrovascular disease (CBVD), and they are more likely to die of CVD than to develop end stage renal disease (ESRD). CRF is associated with premature atherosclerosis and increased incidence of cardiovascular morbidity and mortality. Several factors contribute to atherogenesis and cardiovascular disease in patients with CRF, the notably among all is dyslipidemias.[14] Chronic renal failure, per se, primarily affects the metabolism of high-density lipoprotein (HDL) and triglyceride (TG)-rich lipoproteins. Other studies[15,16,17] said that dyslipidaemia develops early in renal failure and it becomes more pronounced as the renal disease progresses because of imbalance between lipoprotein synthesis and degradation. The result in the table-2 shows a significant increase in serum TG level in patient with CRF when compared with control groups due to down regulation of skeletal muscle and adipose tissue Lipoprotein lipase (LPL), hepatic lipase, and VLDL receptor and of hepatic Lipoprotein lipase (LPL) is collectively responsible for hypertriglyceridemia, impaired clearance and elevated

plasma levels of VLDL, IDL, and chylomicron remnants. Plasma triglyceride concentration is frequently elevated in patients with CRF.[18,19] In fact, serum TG is elevated due to an enhanced production of TG-rich lipoproteins such as VLDL by the liver, in addition dysfunction of TG degradation result from insufficient mitochondrial beta-oxidation of fatty acids.[20] Table-2 shows slight elevation of plasma total cholesterol and LDL concentration in patients with CRF when compared to controls. Studies show the total cholesterol and LDL are only occasionally elevated.[21] Increased LDL may promote nephropathy and atherosclerosis.[20] Table-2 shows that The VLDL values of CRF patients are higher than those of control with statistically significant. Increase insulin resistant state impairs the normal suppression of fatty acids released from adipose tissue in the post prandial state enhances hepatic VLDL secretion.[22] The results in Table-2 shows Plasma HDL concentration in renal failure patients is found to be reduced, this is because chronic renal failure results in profound dys-regulation of several key enzymes and receptors involved in the metabolism of lipoproteins, particularly those of HDL, Down-regulation of lecithin-cholesterol acyl transferase (LCAT), apoA-1, and hepatic lipase together with up-regulation of cholesterol ester transfer protein(CETP) are largely responsible for the reduction in HDL cholesterol, impaired maturation of cholesterol ester-poor HDL- 3 to cholesterol ester-rich HDL-2, increased HDL triglycerides, and depressed plasma apoA.[23] Dyslipidemia in hemodialysis patients**:** cardiovascular disorders are one of the most serious problems in chronic hemodialysis patients. The mortality due to cardiovascular disease in hemodialysis patients is estimated to be 9% annually and is 30 times higher than that observed in the general population.[24] The main lipid abnormality in this patient group is a rise in triglyceride and triglyceride-rich remnant lipoprotein levels. Table-3 shows TGs and VLDL values in hemodialysis are higher than those of CRF patients (without hemodialysis). In hemodialysis patients, post heparin plasma lipoprotein lipase activity and hepatic lipase activity have been reported to be reduced, while the apo CII/apo CIII ratio is decreased. A possible disturbance in both enzymes, accompanied by an increase in apo CIII in VLDL, results in a prolonged half-life of the VLDL particles, which may explain the observed hypertriglyceridemia in these patients.[25] LDL levels are generally within normal limits However, as with other lipoproteins, LDL is not homogeneous and there are variations in size, density and composition.[26,27] Another frequently seen impairment of lipid metabolism in the CRF patient group, which includes HD patients, is a reduction in HDL cholesterol and impaired HDL metabolism appear in the form of decreased Apo AI, impair HDL maturation.[28,29] Another reason for lowered HDL and impairment in its metabolism is Lecithin-Cholesterol acyl transferase (LCAT deficiency).[30,31]

CONCLUSION: CRF patients with and without hemodialysis are at greater risk of development of dyslipidemias, characterized by hypertriglyceridemia, elevated VLDL and decreased HDL levels without any discrimination of sex. Hemodialysis can effectively reduce the accumulation of nitrogenous waste products but fails to clear dyslipidemias generated during the course of CRF. But still the patients on hemodialysis are still exposed to several of the metabolic consequences of renal failure. On the basis of the findings of the present study, it is further suggested that prescribing lipid lowering treatment in CRF patients with dyslipidemias for preventing future episode of cardiovascular events could help and will also preserve renal function. A strict monitoring lipid profile and lipoproteins can reduce the morbidity and mortality rate and will also improve the quality of life of CRF patients.

ACKNOWLEDGEMENTS: We acknowledge the support and cooperation from the patients and healthy controls enrolled in the study. We also thankful to the principal madam Dr.Myreedy neeraja M.D., and laboratory staff of Biochemistry Department for their valuable help and support.

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Characteristics	Group-1: Healthy controls	Group-2: CRF pts without HD	Group-3: CRF pts with HD
No.of participants	40	40	40
Age(years)Mean±SD	47.2±9.6	47.5±11.09	47.5±11.09
Sex(male/female)	28/12	28/12	28/12
Diabetes mellitus (%)	-	15(37.5%)	15(37.5%)
Blood urea(mg/dl)	29.5±6.22	127.4±6.7	100.75±4.06
Serum creatinine(mg/dl)	1.07±0.21	8.05±1.19	6.29±1.18

Table 1: The baseline characteristics of study population

Parameters (mg/dl)	Group-1:Healthy controls	Group-2:CRF pts without HD	t-value	p-value
TC(mg/dl)	175.3±13.3	182±15.7	3.83	P=0.0003 SS
HDL-c(mg/dl)	44.6±5.9	33.5±3.7	10.0	<0.0001 ESS
LDL-c(mg/dl)	104.5±14.6	111.9±15.5	2.19	P==0.0309 SS
TGs(mg/dl)	132.2±9.8	181.6±15.8	24.18	<0.0001ESS
VLDL	26.15±2	36.5±3.5	16.3	<0.0001 ESS

Table 2: Revealed the Lipid profile parameters among control and CRF patients with and without Hemodialysis (In Mean±Standard deviation)

Parameters	Group 2: CRF patients without HD	Group 3:CRF patients with HD	t-value	p-value
TC	182±15.7	178.6±14.3	2.30	0.0239 SS
HDL-c	33.5±3.7	28.3±2.09	3.010	0.0035 SS
TGs	181.6±15.8	199.2±10.1	4.158	<0.0001 ESS
LDL-c	111.9±15.5	110.2	0.5164	0.6070 NS
VLDL	36.5±3.5	40±1.85	5.59	<0.0001 ESS

Table 3: Revealed Lipid profile parameters among CRF patients without Hemodialysis and on Hemodialysis

Groups	TC(mg/dl)	HDL-c(mg/dl	TGs(mg/dl)	LDL-c(mg/dl)	VLDL(mg/dl)
Group-4	177±13.4	43±6.1	132.07±11.4	107.6±14.4	26.3±2.29
Group-6	183.5±17.4	34.7±3.5	183.7±18.2	111.5±17.6	37.1±4.03
t-value	1.56	6.2	12.7	0.9075	12.3
p-value	0.1232 NS	<0.0001 ESS	<0.0001 ESS	0.3682 NS	<0.0001 ESS

Table 4: The mean±SD of TC, HDL-c, LDL-c, TGs, VLDL of the male subjects

Groups	TC(mg/dl)	HDL-c(mg/d)	TGs(mg/dl)	LDL-c(mg/dl)	VLDL(mg/dl)
Group-5	171.4±12.7	48.4±3.1	129.2±5.46	97.2±12.6	25.7±1.05
Group-7	178.7±9.4	30.6±2.3	175.9±5.5	112.7±9.19	35.2±1.1
t-value	1.6005	15.9	20.8	3.45	21.6
p-value	P=0.1238 NS	P<0.0001 ESS	P<0.0001 ESS	P=0.0023 SS	P<0.0001 ESS

Table 5: The mean ± SD of TC, HDL-c, LDL-c, TGs, VLDL the female subjects