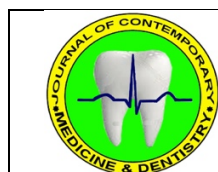


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Effect of Haemodialysis on Lipid Profile in Patients with Chronic Renal Failure

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Abstract

Background: Chronic renal failure (CRF) is a debilitating condition associated with high cardiovascular morbidity and mortality. Increased oxidative stress is the cause for accelerated atherosclerosis in CRF patients.

Objectives: To evaluate the effect of lipid profile in Pre-Hemodialysis patients. **Methodology:** Hospital based observational study was conducted tertiary care hospital. Total number of 40 cases who were on hemodialysis was taken and lipid profile was seen. **Result:** The concentrations of Blood urea, Serum creatinine were significantly elevated ($p > 0.001$) in Pre-hemodialytic patient. The mean concentrations of total Cholesterol were decreased in controls and increased in CRF patients during pre- hemodialysis sessions. The mean concentrations of LDL-C and VLDL-C were decreased in controls as compared to CRF patients during pre-hemodialysis.

Conclusion: CRF patients undergoing Hemodialysis show increased generation of reactive oxygen species, which leads to altered lipid profile, leading to lipid peroxidation, which can be controlled by using lipid lowering drugs and antioxidant therapy to the patients.

Keywords: Chronic renal failure (CRF), Dyslipidemia in (pre- hemodialysis) CRF patients

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Introduction

Chronic Renal Failure (CRF) is a pathophysiological process with multiple etiologies, resulting in the inexorable attrition of nephron number and function and frequently leading to End Stage Renal Disease (ESRD).¹ CRF leads to many complications over a period of time. The most common cause for mortality in these patients includes cardiovascular, cerebrovascular and peripheral vascular diseases. Death due to cardiovascular complication is 4 to 20-fold higher in CRF patients than any other cause in general population.² These complications are due to many metabolic and endocrinal disturbances among which dyslipidemia is one of the constant features of CRF. The patients with

impaired renal function exhibit significant alterations in lipoprotein metabolism, which in their most advanced form may result in the development of severe dyslipidemia.³ Lipid abnormalities, can be detected as early as renal function begins to decline.⁴ Lipid abnormalities and an enhanced oxidative stress in CRF patients accelerate the process of atherosclerosis resulting in cardiovascular complications. The present study is undertaken to assess the alterations in serum lipid profile which include TC, TG, VLDL-C, LDL-C and HDL-C. Present study was planned to evaluate the Lipid Profile in patients with CRF during pre- hemodialysis sessions and in healthy controls.

Materials and Methods

A case control study of Serum lipid profile, with CRF undergoing hemodialysis was carried out. Healthy controls and clinically diagnosed cases of CRF attending Dialysis unit of S.S. Hospital attached to S.S. Institute of Medical Sciences & Research Centre, Davangere were selected. The study was approved by the Institutional ethical committee and written Informed consent was taken from each subject. The cases and healthy controls voluntarily participated in the study. A total number of 80 subjects were participated in the study of which 40 were CRF patients on hemodialysis and 40 were healthy controls. Patients with liver diseases, infectious diseases, familial hyperlipoproteinemia, malignancies and on hypolipidemic drugs were excluded from the study. Under aseptic precautions, about 5 ml of blood was collected in a sterile vacutainer from selected CRF patients during pre- hemodialysis sessions. Serum was separated by centrifugation

and used for analysis of the following parameters.

- 1) Total cholesterol
- 2) Triglycerides
- 3) High density lipoprotein (HDL)
- 4) Low density lipoprotein (LDL)
- 5) Very low density lipoprotein (VLDL)

Student's unpaired 't'-test was used for comparing the means of two groups (cases & controls). Relationship between measurements was assessed by Karl Pearson's coefficient of correlation. For all the tests, a p-value of 0.05 or less was considered as statistical significance.

Results

There were 16 males and 24 females in control group while 5 males and 35 females were in the CRF group. Age wise distribution was according to the table- 1.

Table –1: Age wise distribution

Age (Years)	Cases		Controls	
	No.	%	No.	%
22-34	10	25	8	20
35-44	11	27.5	12	30
45-54	8	20	10	25
55-64	9	22.5	7	17.5
65-74	2	5	3	7.5
Total	40	100	40	100
Mean ± SD	43.6 ± 12.4		44.6 ± 11.8	
p values	0.69 NS			

Table –2: Comparison of Serum Lipid Profile

Parameter	Controls	Cases	Mean Difference	p* Values
	Mean ± SD	Mean ± SD		
TC mg/dl	168.70 ± 11.40	184.60 ± 35.60	5.71	0.331 NS
TG mg/dl	116.30 ± 30.0	206.20 ± 73.0	88.88	0.001 *
HDL-C mg/dl	44.50 ± 3.20	41.20 ± 0.50	0.93	0.268 NS
LDL-C mg/dl	99.10 ± 10.90	100.20 ± 19.0	16.01	0.001 *
VLDL-C mg/dl	25.80 ± 7.10	41.20 ± 15.0	17.32	0.001 *
TC/HDL -C	3.80 ± 0.40	4.20 ± 0.50	0.17	0.121 NS

SD- Standard deviation; * Significant, NS-Not Significant

The mean serum concentrations of TC, TG, HDL-C, LDL-C, VLDL-C were in the range of 168.70 ± 11.40, 116.30 ± 30.0, 44.50 ± 3.20, 99.10 ± 10.90, 25.80 ± 7.10, respectively in controls and 184.60 ± 35.60, 206.20 ± 73.0,

41.20 ± 0.50, 100.20 ± 19, 41.20 ± 15, respectively in cases. Statistical analysis by unpaired 't'- test showed that the mean levels of TG, LDL-C, VLDL-C were increased in pre-hemodialysis when compared to controls and

were statistically highly significant ($p < 0.001$) except for TC and HDL-C which were not statistically significant. The ratio of TC/HDL was in the range of 3.80 ± 0.40 in controls and 4.20 ± 0.50 in cases and it was not statistically significant (Table-2).

Discussion

CRF is one of the leading causes for increased morbidity and mortality in general population. Deaths due to cardiovascular complications in CRF patients are 20 times higher when compared to other causes. Patients with CRF display a clinical picture of atherosclerosis. Disorders of lipoprotein metabolism, in hemodialysis are important mechanisms of atherogenesis in CRF. In the present study the mean concentrations of blood urea, serum creatinine in controls were in the range of 28.56 ± 7.60 mg/dl and 1.30 ± 0.37 mg/dl, respectively. In patients with CRF during pre-hemodialysis sessions the mean concentrations were 68.48 ± 19.14 mg/dl and 29.75 ± 9.71 mg/dl, respectively. The mean concentrations were increased in pre-hemodialysis compared to controls. This is in accordance with studies of Meerashivshankar, et al;⁵ and Nitin S Nagane.⁶ CRF is characterized by a gradual decrease in nephron number and function. Decrease in the concentrating ability of kidney leads to accumulation of urea and creatinine.⁶ The mean concentrations of TG in controls and in patients with CRF during pre-hemodialysis sessions were in the range of 116.30 ± 30.0 mg/dl, 206.20 ± 73.0 mg/dl respectively. The mean concentrations were decreased in controls and increased in CRF patients during pre-hemodialysis session which were statistically highly significant ($p < 0.001$ HS). This is in accordance with the studies of A Altaf, et al;⁷ and NS Nagane, et al;⁶.

Plasma TG start to increase in early stages of CKD and show the highest concentration in nephrotic syndrome and in dialysis patients especially those who are treated with peritoneal dialysis. It is known that CKD causes insulin resistance which can, in turn, promote hepatic VLDL production. Thus, it could be hypothesized that the insulin resistance driven overproduction of VLDL may significantly contribute to the development of hypertriglyceridemia in patients with CKD.³

In hemodialysis patients, the repeated use of low molecular heparins for anticoagulation may lead to a defective catabolism of TG-rich lipoproteins as heparin releases LPL from endothelial surface and thus its chronic use may result in LPL depletion. The use of flux polysulfone membrane or cellulose triacetate membrane is accompanied by a significant reduction in serum TG.³ The cause of decreased lipase activities in uremia is thought to be depletion of the enzyme pool induced by frequent heparinization in hemodialysis patients, an increase in the plasma Apo C-III/ apo C-II ratio, and the presence of other lipase inhibitors in plasma. Apo C-II is an activator of LPL, whereas apo C-III is an inhibitor of LPL. The increased apo C-III/ apo C-II ratio is usually due to disproportionate increase in plasma apo C-II.⁸ LPL bound to the endothelium may be released by heparin which is given during hemodialysis process. Also flux biocompatible dialysis membrane may be responsible for increasing the LPL activity during dialysis.⁶ The mean concentrations of TC in controls and in patients with CRF during pre-hemodialysis sessions were in the range of 168.70 ± 11.40 mg/dl, 184.60 ± 35.60 mg/dl and, respectively. The mean concentrations were decreased in controls and increased in CRF patients during pre-hemodialysis sessions which were statistically highly significant ($p < 0.001$). This is in accordance with the studies of A Altaf, et al;⁷ and NS Nagane, et al;⁶. Serum cholesterol is positively correlated with the incidence of atherosclerosis and coronary vascular disease.⁹

Among them up regulation of hepatic enzymes Hydroxy-3-methylglutaryl-CoA reductase and cholesterol 7 α -hydroxylase are important. Heavy proteinuria in CRF patients can lead to up regulation of HMG CoA reductase. In addition LDL receptor deficiency may play a central role in the genesis of the associated hypercholesterolemia in CRF patients.⁶

The mean concentrations of HDL-C in controls and in patients with CRF during pre-hemodialysis sessions were in the range of 44.5 ± 3.20 mg/dl, 41.20 ± 0.50 mg/dl, respectively. The mean concentrations of HDL-C were increased in controls compared to CRF patients during pre-hemodialysis sessions. The results were statistically highly significant in both ($p < 0.001$). The results are in accordance with

the studies of NS Nagane et al;⁶. Patients with CKD have, generally reduced plasma HDL-C levels compared to individuals with normal renal function. Thus, patients with impaired renal function usually exhibit decreased levels of apolipoprotein AI and AII, diminished activity of LCAT as well as increased activity of cholesteryl transfer protein that facilitates the transfer of cholesterol esters from HDL to TG-rich lipoproteins thus reducing the serum concentrations of HDL-C.¹⁰

Impaired maturation of cholesterol ester –poor HDL 3 to cholesterol ester rich cardioprotective HDL 2 and other factors may be responsible for progressive decline in the level of HDL-C in CRF.¹¹

Hemodialysis procedure may also have a contributory role in the reduced HDL-C levels of dialysis patients. Thus, in dialysis patients the type of membrane and dialysate used in hemodialysis procedure may influence the HDL-C levels. It has been shown that the use of high-flux instead of low flux membrane is associated with an increase in apolipoprotein AI and HDL-C values.³

The mean concentrations of LDL-C and VLDL in controls are in the range of 99.10 ± 10.90 mg/dl, 25.80 ± 7.10 mg/dl, respectively. In patients with CRF during pre- hemodialysis sessions were 100.20 ± 19.0 mg/dl and 41.20 ± 15.0 mg/dl, respectively. The mean concentrations of LDL-C and VLDL-C were decreased in controls as compared to CRF patients during pre-hemodialysis. The results were statistically highly significant ($p < 0.001$) in both. The results are in accordance with the studies of Nitin S Nagane and Jayashree Ganu⁶. There are qualitative changes in LDL-C in patients with CKD and dialysis patients. The proportions of small density LDL and IDL, which are considered to be highly atherogenic are increased. Increased sdIDL is a subtype of LDL that has high propensity to penetrate the vessel wall, become oxidized and triggers the atherosclerotic process. Because of decreased hepatic triglyceride lipase activities in hemodialysis patients, the conversion of IDL to LDL is impaired and IDL accumulates in plasma. IDL and small density LDL have high affinity for macrophages, which theoretically promote their entry into the vascular wall to participate in the formation of foam cells and

atherosclerotic plaque. The plasma levels of apo B, which is the major apolipoprotein of LDL and IDL, are strongly correlated with levels of these lipoproteins.⁸ The mean ratio of TC/HDL-C in controls, and in patients with CRF during pre- hemodialysis sessions were 3.80 ± 0.40 , 4.20 ± 0.50 , respectively. The cause for the decrease in lipoprotein concentrations could be due to removal of lipoproteins by repeated dialysis and decreased peripheral resistance to insulin after initiation of dialysis.¹¹

Conclusion

This study demonstrates that there is an increased risk of cardiovascular complications in patients undergoing hemodialysis. CRF patients undergoing hemodialysis shows an increased altered lipid profile. These effects can be reduced by advising proper diet or by using lipid lowering drugs. Supplementation of antioxidants and use of vitamin E coated dialysis membranes would significantly reduce the oxidative stress and thus minimize the risk of cardiovascular and cerebrovascular complications as well as improve the general wellbeing and lower the cost of health care in hemodialysis patients.

Conflict of Interest: None declared

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Ethical Permission: Obtained

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