ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Impact of Hemodialysis on Lipid Related Ratios in Non- Diabetic Chronic Renal Failure Patients.

Sumathi ME[1]*, Asha B[2], and Mahesh V[3].

[1]Department of Biochemistry, Sri Devaraj Urs Medical College, Tamaka, Kolar, 563101, Karnataka, India.
[2]Department of Pharmacology, Sri Devaraj Urs Medical College, Tamaka Kolar, Karnataka, India.
[3]Department of Community Medicine, Sri Devaraj Urs Medical College, Tamaka Kolar, Karnataka, India.
Sri Devaraj Urs Academy of Higher Education and Research.

ABSTRACT

Chronic renal failure (CRF) is attributing to increased morbidity and mortality worldwide. Lipid abnormalities can be detected as early as renal function begins to decline. Dyslipidemia associated with CRF is often related to the type of renal replacement therapy. Approximately 20-40% of hemodialysis patients have been estimated to have elevated triglycerides and decreased HDL in addition to increased Lp(a) and oxidized LDL. We have done this study to estimate and compare traditional lipid profile with lipid related ratios among the conservatively managed patients and patients on haemodialysis. This cross sectional study was done in tertiary care teaching hospital and included 50 healthy controls and 60 CRF patients, among which 30 were on conservative management and remaining on haemodialysis. Lipid profile and cardiovascular specific lipid indices were done and noted in all patients. Total cholesterol (213±22.9), triglycerides (242.3±36.4) and VLDL (48.3±7.6) were significantly increased among CRF patients with conservatively management compared to those on haemodialysis ($p<0.001$). HDL levels were reduced significantly and lipid related indices were significantly increased ($p<0.001$) in patients on haemodialysis compared to conservatively managed patients. The specific markers for atherosclerosis such as reduced HDL and raised lipid related indices were observed among patients on haemodialysis, hence putting them at higher risk for cardiovascular complications.

Keywords: CRF, Hemodialysis, Lipids, Diabetic

Corresponding author

ISSN: 0975-8585

INTRODUCTION

The incidence of chronic renal failure (CRF) is increasing worldwide with high mortality and morbidity. [1] It is estimated that approximately 229 per million populations in India are suffering from End Stage Renal Disease (ESRD). One of the reasons could be due to rising incidence of diabetes and hypertension. [2]

CRF is a state which results from a permanent and usually progressive reduction in renal function in a sufficient degree to have adverse consequence on other systems. [3] The most common cause for mortality in these patients includes cardiovascular, cerebrovascular and peripheral vascular diseases. Death due to cardiovascular complications is 4-20 fold higher in CRF patients than any other cause in general population. These complications are due to many metabolic and endocrinal disturbances among which dyslipidemia is one of the constant feature of CRF. [4] Deaths due to CVD complications are attributed to lipid abnormalities associated with CRF. [1] Lipid abnormalities can be detected as early as renal function begins to decline (Glomerular Filtration Rate <50ml/min) but type and severity vary among different patients at different stages of disease. Most characteristic lipid abnormality is increased serum triglycerides, very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL) and low levels of high density lipoprotein (HDL). [4, 5] Dyslipidemia also play a significant role in the initiation and progression of glomerular and tubulointerstitial diseases. [1] Dyslipidemia associated with CRF is often related to the type of renal replacement therapy.

Mechanism of dyslipidemia associated with CRF involves many metabolic alterations such as hypertension and diabetes. Considering that there is no or few data available about the pattern of lipid abnormalities in non diabetic CRF patients and influence of hemodialysis on the lipid abnormalities. Hence we undertook this study to estimate traditional lipid parameters like total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c), non HDL-c and lipid related ratios like TG/HDL-c, TC/HDL, LDL-c/HDL-c and non HDL-c/HDL-c.

MATERIALS AND METHODS

A cross sectional study of serum lipid profile and lipid related ratios in chronic renal failure patients were carried out from February 2007 to February 2008. Controls and clinically diagnosed cases of CRF attending outpatient department (OPD) and dialysis units were included after obtaining written informed consent and the protocol was approved by the Institutional ethics committee.

A total number of 110 subjects participated in the study, of which 60 were CRF cases and 50 were healthy controls. Clinically diagnosed cases of chronic renal failure > 20 years of age were included. Among 60 CRF cases, 30 were on maintenance hemodialysis for a period of 5 months to 3 years. These patients were undergoing hemodialysis for 3-4 hours three times a week. Remaining 30 patients were on conservative line of treatment. 50 normal healthy individuals without any major medical illness were included. We excluded patients with diabetes mellitus, familial hyper lipoproteinemias, hepatic dysfunction and patients on hypolipidemic drugs. About 5ml of venous blood was drawn under aseptic precautions in a sterile bulb from selected subjects after period of overnight fasting of 12 hrs, serum was separated by centrifugation and used for analysis. Total cholesterol was estimated by cholesterol oxidase- peroxidase method, Triglycerides by Glycerol oxidase and peroxidase method, HDL by precipitation method and LDL and VLDL was calculated by Fried Wald's formula after considering its limitations. Other lipid ratios like LDL-c/HDL-c, TC/HDL-c, TG/HDL-c, Non HDL, Non HDL-c/HDL-c were calculated. Lipid profile was analyzed by using ERBA kits in microlab semi-autoanaylzer of MERCK Company. All the reagents used in the estimation were of analytical grade. The subjects were categorized into Group I(controls), Group II (Conservative treatment) and Group III (hemodialysis).

Statistical Analysis

Descriptive data is represented as mean and standard deviation (SD). Comparison of biochemical parameters between the three groups is done using one way ANOVA. Comparison of lipid parameters and lipid ratios was done between conservative and hemodialysis patients by using unpaired t test.

ISSN: 0975-8585

RESULTS

The baseline demographic characteristics of patients in all three groups were comparable. The lipid profile among the study groups was significant as shown in table 1. The lipid profile and lipid related indices between conservatively managed patients and patients on haemodialysis were shown in table 2.

Table 1 Lipid profile among study groups

Parameters	Group I (n=50) (Controls)	Group II (n=30) (Conservatively managed patients)	Group III (n=30) (Hemodialysis patients)	P value
Total cholesterol (mmol/L)	182±22.7	213±22.91	197.6±22.7	0.001
Triglycerides (mmol/L)	115±30.1	242.3±36.4	196.83 ± 21.83	0.001
HDL (mmol/L)	44.3±5.0	40± 4.0	32.2±3.08	0.001
LDL (mmol/L)	115.4±23.4	125.2±18.4	125.4±22.4	0.001
VLDL (mmol/L)	22.9±6.0	48.38±7.6	39.2±4.37	0.001
TC/HDL	4.12±0.63	5.36±0.73	6.18±1.0	0.001
TG/HDL	2.65±0.8	6.11±1.05	7.35±6.12	0.001
LDL/HDL	2.64±0.63	3.16±0.58	3.93±0.91	0.001
Atherogenic Index of Plasma (AIP)	0.92±0.3	1.79±0.18	1.88±0.37	0.001

Table 2: Comparison of lipid profile and lipid related indices between group II and III

Parameters	Group II (n=30) (Conservatively managed patients)	Group III (n=30) (Hemodialysis patients)	P value
Total cholesterol (mmol/L)	213±22.91	197.6±22.7	0.001
Triglycerides (mmol/L)	242.3±36.4	196.83±21.8	0.001
HDL (mmol/L)	40± 4.0	32.2±3.08	0.001
LDL (mmol/L)	125.2±18.4	125.4±22.4	>0.05
VLDL (mmol/L)	48.38±7.6	39.2±4.37	0.001
TC/HDL	5.36±0.73	6.18±1.0	0.001
TG/HDL	6.11±1.05	7.35±6.12	0.001
LDL/HDL	3.16±0.58	3.93±0.91	0.001
AIP	1.79±0.18	1.88±0.37	0.001
Non HDL	173.75±22.5	165.36±22.79	0.001
Non HDL/HDL	4.39±0.73	5.19±1.03	0.001

DISCUSSION

The present study includes 110 subjects of which 60 were chronic renal failure patients and 50 were normal healthy individuals.

The mean values of blood urea, serum creatinine, serum sodium and potassium in controls were in the range of 30.3 ± 16.0 mg/dl, 1.3 ± 0.4 mg/dl, 140 ± 5.2 mmol/L and 3.5 ± 0.4 mmol/L respectively. In cases they were in the range of 105.8 ± 40.7mg/dl, 6.7 ± 3.6 mg/dl, 133.1 ± 7.3 mmol/L and 4.7 ± 0.8 mmol/L respectively. The mean values were increased in cases when compared to controls except for serum sodium (p value <0.001). There were no significant differences in these parameters between conservatively managed patients and patients on haemodialysis.

The mean value of triglycerides in conservatively managed patients was 242.3±36.4 when compared to patients on hemodialysis (196.83 ±21.8) which was significant (p<0.001). Hypertriglyceridemia is a common feature of CRF due to increased synthesis by promoting heapatic VLDL production and /or diminished clearance from circulation. [6-8]

The total cholesterol in conservatively managed patients was 213±22.91 and was significantly high (p=0.001) compared to patients on hemodialysis (197±22.7). CRF is associated with hypercholesterolemia which is due to associated proteinuria and renal insufficiency per se. Proteinuria leads to alteration in gene expression for HMG-CoA reductase which results in increased activity of HMG-CoA reductase leading to

hypercholesterolemia. Homeostasis of cholesterol is maintained by LDL receptor mediated cholesterol uptake. Renal insufficiency or in combination with heavy proteinuria leads to acquired LDL receptor deficiency which plays a central role in the genesis of the associated hypercholesterolemia in CRF. [6]

VLDL among conservatively managed CRF patients was significantly high (48.38±7.6) compared to patients on hemodialysis (39.2±4.37). CRF is associated with increased VLDL levels due to dysregulation of Lipoprotein lipase (LPL), hepatic lipase, VLDL receptor, hepatic Acyl CoA Cholesterol acyl transferase (ACAT) and LDL receptor related protein (LRP) expression / activities and impaired HDL metabolism leading to increased level of VLDL-C. [9, 10]

HDL levels are significantly decreased in patients on hemodialysis (32.2±3.08) when compared to patients managed conservatively (40±4.0). In CRF patients HDL levels tend to decrease due to decreased activities of LPL, hepatic triglyceride lipase (HTGL), Lecithin cholesterol acyl transferase (LCAT) and increased concentration of Cholesterol ester transport protein (CETP) and decreased apolipoprotein concentrations. LPL generates precursor of HDL during lipolysis of TG rich lipoproteins and HTGL promotes conversion of HDL_2 to HDL_3, thereby they maintain the normal HDL-C concentration. LCAT is the key enzyme which keeps the chemical gradient of cholesterol from cells to plasma. LCAT activity is also decreased in patients with CRF especially on haemodialysis. Reduction of plasma LCAT activity may be due to reduced hepatic production and its inhibition by an unknown uremic toxin leading to decreased HDL-C concentration. HDL-C metabolism is also regulated by cholesterol ester transport protein, which transfers cholesterol ester from HDL to TG rich lipoproteins in exchange of TG. [6]

We also calculated TC/HDL, TG/HDL, LDL/HDL, AIP, Non HDL and non HDL/HDL. Mean values of all indices were significantly increased in patients on hemodialysis when compared to conservatively managed CRF patients except for non HDL which was significantly decreased in group II patients. These indices are specific risk factors for atherosclerosis. Our study results are in accordance with many studies which have demonstrated dyslipidemia among CRF patients. [11-14] There are some studies which have concluded the higher atherogenic risk among patients on conservative management based on higher TC, TG, VLDL and LDL and lower HDL levels. [15-17] In our study we have looked for specific atherogenic indices which are significantly increased among patients on hemodialysis due to more reduction in HDL.

CONCLUSION

This study demonstrates that there is increased risk of cardiovascular complications in CRF patients particularly in patients who are on hemodialysis due to exacerbated reduction in HDL levels. The increased atherogenic indices among hemodialysis patients lead to accelerated atherosclerosis and increase in cardiovascular risks.

REFERENCES

[1] A Chijioke, A Makusidi, A Shittu, M Sanni, S Biliaminu, M Abdul-Rahman et al., Pattern of Lipid Profile In Dialysis Naive Chronic Kidney Disease Patients From Ilorin, Nigeria. The Internet Journal of Nephrology. 2009 ; 6(1).

[2] Singh AK, Farag MK Youssef, Mittal VB, Subramanian K K, Keithi Reddy SR, Acharya VN. Epidemiology and risk factors of chronic kidney disease in India – results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. Nephrology 2013: 14:114-24

[3] Winearls CG. Chronic Renal failure In : Warrell DA, Cox TM, Firth JD, Benz EJ, Eds. Oxford text book of Medicine 4th edn, Vol 3. New York, Oxford University press; 2003:263-278.

[4] Oda H, Keane WF. Lipid abnormalities in end stage renal disease. Nephrol Dial Transplant 1998;13(1):45-49.

[5] Wanner C. Importance of hyperlipidaemia and therapy in renal patients. Nephrol Dial Transplant 2000;15(5):92-96

[6] Vaziri ND. Dyslipidemia of chronic renal failure: The nature, mechanisms and potential consequences. Am J Physiol Renal Physiol 2006;290:262-272.

[7] Ma KW, Greene EL, Raij L. Cardiovascular risk factors in chronic renal failure and hemodialysis populations. Am J Kidney Dis 1992;19(6):505-513.

[8] Prinsen BHCMT, Velden MGMDS, de Koning EJP, Koomans HA, Berger R, Rabelink TJ. Hypertriglyceridemia in patients with chronic renal failure : possible mechanisms. Kidney Int 2003;63(84):S121-S124.
[9] Lee DM, Gibson CK, Samuelsson O, Attman PO, Wang CS, Alaupovic P. Lipoprotein particle abnormalities and the impaired lipolysis in renal insufficiency. Kidney Int 2002;61:209-18.
[10] Bagdade J, Casaretto A, Albers J. Effects of chronic uremia, hemodialysis and renal transplantation on plasma lipids and lipoproteins in man. J Clin lab med 1976;87(1):37-47.
[11] Alam SM, Bhatt AK. Abnormal lipoprotein in uraemic patients treated conservatively and by maintenance hemodialysis. JAPI 1991;39(2):170-171.
[12] Shah B, Nair S, Sirsat RA, Ashavaid TF, Nair KG. Dyslipidemia in patients with chronic renal failure and in renal transplant patients. J Prostgrad Med 1994;40(2):57-60.
[13] Lee P, O'Neal D, Murphy B, Best J. The role of abdominal adiposity and insulin resistance in Dyslipidemia of chronic renal failure. Am J Kidney Dis 1997;29(1):54-65.
[14] Massy ZA, Khoa TN, Lacour B, Descamps-Latscha, Man NK, Jungers P. Dyslipidemia and the progression of renal disease in chronic renal failure patients. Nephrol Dial Transplant 1999;14:2392-2397.
[15] Avram MM, Goldwasser P, Burrell DE, Antignani A, Fein PA, Mittman N. The uremic dyslipidemia : a cross-sectional and longitudinal study. Am J Kidney Dis 1992;20(4):324-335.
[16] Attman PO, Alaupovic P, Tavella M, Gibson CK. Abnormal lipid and apolipoprotein composition of major lipoprotein density classes in patients with chronic renal failure. Nephrol Dial Transplant 1996;11:65-69.
[17] Das BS, Misraf SK, Rao VM, Satpathy SR, Bose TK. Serum lipid in chronic renal failure. JAPI 1984;32(12):1019-1021.