ORIGINAL ARTICLE

EFFECT OF HAEMODIALYSIS AND FREQUENCY OF DIALYSIS SESSIONS ON SERUM LIPIDS AND BIOCHEMICAL PROFILE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Shazia Tauqeer, Raisa Naz, Nasir Hussain Shah Kazmi*, Muhammad Ayub**

Department of Physiology, *Medicine, Ayub Medical College, Abbottabad, **Department of Physiology, AJK Medical College, Muzaffarabad, Pakistan

Background: Different phenomenon such as loss or accumulation of various substances and dysregulation or alteration in number of metabolic pathways are responsible for aetiology and pathogenesis of chronic changes in chronic kidney disease (CKD). Haemodialysis or renal replacement therapy (RRT) does not correct the dyslipidemia of uraemia but may modify it. The objective of this study was to see the effects of haemodialysis and frequency of dialysis sessions on dyslipidemia and various biochemical markers in patients with CKD. **Methods:** This was a hospital based cross-sectional observational study conducted in Dialysis Unit of Ayub Teaching Hospital, Abbottabad. In our study renal functions and lipid profile of 30 healthy subjects as control group were compared with 56 cases of CKD undergoing haemodialysis with a frequency of 1, 4, 8, or 12 per moth. Serum lipid profile, renal function tests, serum and urinary albumin was estimated for both the groups. They were further analysed for serum markers before dialysis (pre-HD) and post dialysis, six months (post-HD). Statistical analysis was performed using SPSS-17. **Results:** Thirty (54%) subjects were males and 26 (46%) were females. The mean age of the patients was 45.48±14.78 years as against mean age of controls (46.78±13.95 years). Urea and creatinine were raised, and anaemia, hypocalcemia, hypoalbuminemia, hyponatremia, and hyperkalemia were observed. A significant elevation in serum total cholesterol, triglycerides, LDL and VLDL-C was seen. There was a reduction in HDL-C in pre-dialysis patients compared to controls. The difference between pre-HD and post-HD groups was unremarkable except for the serum potassium, chloride, urea, creatinine, total cholesterol, triglycerides and HDL-C. The effect of frequency of dialysis sessions was also not statistically significant. **Conclusion:** Regular treatment with dialysis may partially compensate for loss of renal function and decrease the accumulation of toxic metabolites, but cannot revert the overall physiological deficit.

Keywords: Uraemia, CKD, Haemodialysis, Renal replacement therapy (RRT)

Pak J Physiol 2018;14(1):3–6

INTRODUCTION

Chronic kidney disease is a global health problem with marked implications on individuals socioeconomic status and quality of life as well as economy of third world countries like India and Pakistan.[1] The CKD progression is associated with profound perturbations in metabolic pathways of several key enzymes and that eventually results in disordered internal milieu e;g azotemia, dysregulation of bone, minerals and lipid metabolism, anaemia, hypoalbuminemia[2] with ultimate deterioration in functional renal capacity and need for commencement of RRT.

There is growing evidence that abnormalities in lipid metabolism contribute to renal disease progression.[3] Moreover characteristic abnormalities of lipoproteins composition which are typically observed in renal failure population and also more pronounced in HD patients, provide a strong evidence of CVD.[4]

Serum lipids are affected in a way like TGs are markedly elevated in CRF because of increased hepatic production of TG-rich lipoproteins like very-low-density lipoproteins (VHDL)[4] and also because of dysregulation of TGs degradation pathway which results from insufficient beta-oxidation of free fatty acids (FFAs) in mitochondria.[5]

Serum total cholesterol is either normal, or increased modestly while HDL (high-density lipoprotein) levels are markedly decreased and are inversely associated with cardiovascular risk. HDL is decreased because of an increased catabolic rate due to predominant presence of sd-HDL (small dense HDL), which fails to undergo maturation normally because there is decreased production of lecithin cholesterol ester transfer protein (CETP) enzyme (CETP-acyltransferase) leaving CE as of poor quality, concomitant insulin resistance, TG rich HDL-3 particles, and oxidation prone pre b-HDL.[6]

These atherogenic changes and associated progression to ESRD is also accompanied by a shift towards increased size of LDL due to increase in the content of small dense sd-LDL particles which are also more atherogenic and proinflammatory.[7]

Very low-density lipoproteins (VLDL) and chylomicrons (CMs) are raised as their lipolysis is

impaired partly because of decreased activity of lipoprotein lipase (LPL enzyme) and partly as a result of increased levels of apolipoprotein C III (apo C-III) where, Apo C III is an inhibitor of LPL, not hepatic lipase (HL) and is closely responsible for decreased catabolism of TG-rich lipoproteins and increased triglyceride levels in dialysis dependant CKD.[6] thus it would be expected to raise the levels of VLDL and CM remnants because of their decreased clearance.[6]

The abnormality of lipids metabolism in HD patients is mainly the disordered metabolic pathways resulting in dyslipidemia rather than marked hyperlipidemia.[7] Regular treatment with dialysis may partly compensate for the loss of renal function and decrease the accumulation of toxic metabolites, but cannot revert the overall physiological deficit.[8] The objective of this study was to see the effects of haemodialysis and frequency of dialysis sessions on dyslipidemia and various biochemical markers in patients with CKD.

MATERIAL AND METHODS

This comparative observational study was conducted in Dialysis Unit of Ayub Teaching Hospital Abbottabad over a period of 6 months. Informed consent from patients and ethical approval was obtained. Thirty subjects with normal renal function were randomly taken as control. The Pre-dialysis (Pre-HD) group consisted of 56 patients of stage V CKD with estimated GFR[9,10] <15 ml/min/1.73 m^2 undergoing haemodialysis and compared with the Post-haemodialysis (Post-HD) group after undergoing haemodialysis for 6 months.

General characteristics of the subjects were measured, history of diabetes, hypertension, familial hypercholesterolemia, haematological disorders cardiovascular disease and medication history of statins and fibrates, oral contraceptives, hormonal replacement therapy and steroids was recorded. Albumin, haemoglobin, triglyceride, HDL-C, LDL-C, TC, VLDL, haemoglobin (Hb), total calcium, phosphate, sodium, potassium, chloride serum and urinary albumin were evaluated before dialysis after dialysis and at interval of six months of maintenance haemodialysis for both groups.

Patients were not receiving any drugs interfering with lipid metabolism. Patients were dialyzed fortnightly, once, twice to thrice a week, depending on the need and biochemical parameters, for 2–4 hours during each schedule, with volumetric dialyzer machines using bicarbonate or acetate based buffer as a dialysate with blood flow of 250 ml/min and dialysate flow of 500 ml/min, using polysulfone based membrane dialyzers of 1.6 m^2 surface area (hollow fibre).

Data analysis was performed on SPSS-17. For continuous variables Mean±SD, and for categorical variables frequencies and percentages were calculated. Student's *t*-test and Chi-square test were applied and $p \leq 0.05$ was considered statistically significant.

RESULTS

Total number of subjects included in the study was 86. Fifty-six patients of CKD undergoing haemodialysis were cases and 30 subjects with normal renal function were controls. Among cases, 54% (n=30) were males and 46% (n=26) were females. The mean age of the patients was 45.48±14.784 years and age of controls was 46.78±13.953 years.

Raised urea, creatinine, anaemia, hypocalcemia, hypoalbuminemia, hyponatremia, hyperkalemia and a significant elevation in serum total cholesterol, triglycerides, LDL and VLDL-C, and reduction in HDL-C in pre-dialysis group patients compared to controls were observed (Table-1).

The effect of number of dialysis sessions (1, 4, 8, and 12 per month) was not statistically significant ($p>0.05$ for all four groups. There was marked variation in internal physiological homeostasis prior to commencement of RRT unaffected by number of dialysis sessions (Table-2). The differences between pre dialysis (pre-HD) and post dialysis, (post-HD) groups were unremarkable except for the serum potassium, chloride, urea, creatinine, serum total cholesterol and triglycerides (Table-3).

Table-1: Serum lipids and biochemical profile in cases and controls (Mean±SD)

Variables	Controls	Cases	*p*
Sodium (mmol/l)	132.26±5.63	133.22±7.32	0.462
Potassium (mmol/l)	3.90±0.42	4.98±0.71	0.000
Chloride (mmol/l)	100.5±3.4	102.2±2.29	0.015
Calcium (mmol/l)	10.35±0.96	8.40±1.36	0.000
Serum urea (mg/dl)	33.69 ± 9.94	151.76±71.80	0.000
Creatinine (mg/dl)	0.74 ±0.89	9.53±2.95	0.000
Haemoglobin (mg/dl)	13.19±1.51	8.99±1.94	0.000
Albumin (mg/dl)	4.84±0.52	4.13±0.86	0.001
TC (mg/dl)	169.06±23.66	214.22±44.18	0.000
TG (mg/dl)	113.36±30.74	207.10±95.99	0.000
HDL-C (mg/dl)	52.98±8.93	44.29±9.68	0.000
LDL-C (mg/dl)	95.40±19.59	129.91±38.55	0.000
VLDL-C (mg/dl)	23.13±5.53	42.38±18.93	0.000

Table-2: Frequency of dyslipidemia and Hypoalbuminemia in patients undergoing 1, 4, 8 and 12 dialysis sessions per month [n (%)]

	No. of dialysis sessions				
Variable	1	4	8	12	*p*
Hypoalbuminemia	0 (0)	5 (9)	9 (16)	1 (1.78)	0.821
High TC	0 (0)	10 (18)	14 (25)	0 (0)	0.482
High TG	1 (1.78)	14 (25)	25 (44.6)	0 (0)	0.148
High LDL-C	1 (1.78)	19 (33.4)	29 (51)	1 (1.78)	0.398
Low HDL-C	1 (1.78)	14 (25)	21 (37.5)	2 (3.57)	0.774
High VLDL-C	2 (3.57)	14 (25)	24 (42.8)	0 (0)	0.148

Table-3: Serum lipids and biochemical profile in pre-HD and post dialysis, six months (post-HD) groups

Variables	Pre-dialysis (Pre-D) Mean± SD	Post Dialysis (Post-D) Mean± SD	*p*	Odds-Ratio (OR)	95% CI
Sodium. Na+ (mmol/l)	133.22±7.32	135.6±5.8	0.069	0.94	2.25–3.34
Potassium. K+(mmol/l)	4.98±0.71	3.8±0.36	0.001	1.21	0.82–1.01
Chloride. Cl -(mmol/l)	102.2±2.29	101.3±4.92	0.035	1.05	3.10–2.1
Calcium. Ca++ (mmol/l)	8.40±1.38	8.47±1.16	0.756	1.01	0.089–1.1
Serum UREA (mg/dl)	151.76±71.80	100.75±4.06	0.000	0.66	1.5–0.78
Creatinine (mg/dl)	9.53±2.95	6.95±1.19	0.000	0.72	0.83–1.02
Haemoglobin Hb (g/dl)	8.99±1.94	9.1±1.84	0.685	1.93	1.25–2.25
Albumin (mg/dl)	4.13±0.86	4.17±1.01	0.538	1.16	0.98–1.53
TC (mg/dl)	214.22±44.18	228.66±69.44	0.051	1.25	0.93–1.67
TG (mg/dl)	207.10±95.99	249.81±80.26	0.049	1.70	1.34–2.22
HDL-C (mg/dl)	44.29±9.68	40.78±7.19	0.031	1.1	0.85–1.43
LDL-C (mg/dl)	129.91±38.55	131.23±39.97	0.104	1.14	0.81–1.52
VLDL-C (mg/dl)	42.38±18.93	45.15±22.32	0.368	1.23	0.81–1.91

DISCUSSION

CKD is defined as irreversible kidney damage or greatly reduced renal functional capacity (measured clinically by decreased glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for 3 months or more.[9] Renal function is measured either by directly measuring GFR (mGFR) with the help of measuring the ability of kidneys to clear specific exogenous compounds such as Inulin and/or most frequently through the estimated GFR (e-GFR) by serum creatinine level.[10] For the maintenance of normal physiological environment this functional renal reservoir must be preserved. According to one study abnormalities of biochemical markers does not appear unless this reservoir has been reduced to less than 50% of the normal and need for HD arises when eGFR has been reduced to <15 ml/min/1.73 m^2.[9,10]

Dialysis is a process of separating the soluble crystalloids from the colloid in a mixture by means of a dialyser. Unfortunately, there is not any definitive cure for CKD. If it is not treated it eventually progresses to end-stage renal disease (ESRD).[8] In the present study we tried to explore the various aetiopathological, physiological, and biochemical markers in ESRD and effects of dialysis on this organ dysfunction. We observed raised creatinine, urea, anaemia, hypocalcemia, hypoalbuminemia, hyperkalemia. A significant elevation in serum total cholesterol, triglycerides, LDL and VLDL-C, and reduction in HDL-C values, a typical proatherogenic profile responsible for high cardiovascular mortality in CKD population was seen as compared to controls, and is consistent with other studies.[11] Both K^+ and Cl^- showed statistically significant decrease in serum levels during dialysis. Na^+ and Ca^{++} did not exhibit any reduction, rather mild but not statistically significant (p=0.069) increase in sodium level was seen. Similar results were reported in an Indian population.[12,13] Serum urea and creatinine decreased markedly as a result of dialysis treatment showing significant impact of HD on residual renal function (p=0.000). Similar results were observed by Varan *et al*.[14]

In our study serum haemoglobin and albumin were significantly lower in pre-dialysis group as a marker of anaemia and cachexia of chronic inflammation in CKD[15]. Haemoglobin and serum albumin were unaffected by maintenance haemodialysis in post-HD group. Our study aimed to delineate any association between uremia and dyslipidemia. We found statistically significant elevation in total cholesterol and in triglyceride levels and reduced HDL levels in post-HD group compared to pre-HD group. Serum LDL and VLDL increased but not statistically significant, quite consistent with the results observed by Kapil Gupta *et al*[16] who found a negative correlation between hyper-triglyceridemia and plasma cholesterol levels and duration of HD, subjecting patients on HD to a greater risk of atherosclerotic events. TG rises as a result of reduced hepatic and plasma lipoprotein lipase activity, and there is an inverse relationship between triglycerides and HDL-C levels.[2,3] The reduced HDL levels may be due to hypertriglyceridemia which stimulates the TG enhancement and relatively depletion of cholesterol content of HDL particles, thus altering the shape of HDL-C particles and correspondingly reduction in plasma HDL-C levels in addition to Lecithin cholesteryl ester transferase (LCAT) deficiency which stimulates the reverse transfer of HDL from the peripheral tissues to the liver.[17]

The VLDL-C and LDL-C were significantly higher in pre-dialysis group as compared to controls. With repeated maintenance hemodialysis post-HD group, there was not further significant alteration in the levels of plasma LDL-C and VLDL-C. These results are consistent with those of the earlier reported.[16,18]

We observed no statistically significant relationship among different groups suggesting more or less frequent dialysis sessions did not have any impact on serum albumin and lipid profiles. The number of patients undergoing 1 and 12 dialysis sessions were less as compared to 4 and 8 sessions per month because of high mortality in patients requiring more frequent dialyses and financial constraints on family.[19] Those

requiring less frequent dialyses had better renal function profile.

HD usually results in elevation of TG-rich lipoproteins, and serum TC, reduced HDL-C, while LDL-C and VLDL-C levels remain within normal range as explained earlier.[20] However, sub-fractions of lipoproteins, e.g., apolipoprotein-B containing sub-fractions usually show high sd-LDL (small dense LDL) levels.[20] Underlying pathophysiological mechanisms are similar to pre-dialysis ESRD patients. Unfortunately, there is no definitive cure for CKD. If it is not treated it eventually progresses to ESRD.[3] Timely commencement of RRT is imperative to halt the disease progress and to prevent the complications of uraemia in CRF that leads to a significant disease morbidity and finally death.[9]

CONCLUSION

Regular treatment with dialysis may partially compensate for loss of renal function and decrease the accumulation of toxic metabolites, but cannot revert the overall physiological deficit.

REFERRENCE

1. Raju SSK, Lalitha DL, Kiranmayi P. A study of lipid profile and lipid peroxidation in chronic kidney disease with special reference to hemodialysis. J Clin Res Bioeth 2013;4:143.
2. Lodh M, Lal S, Goswami B, Karmakar P, Parida AK. Dyslipidemia in chronic renal failure: Cause or effect? Asian J Med Sci 2016;7(5):42–6.
3. Vaziri ND, Norris K. Lipid disorders and their relevance to outcomes in chronic kidney disease. Blood Purif 2011;31:189–96.
4. Attman PO, Samuelsson O, Johansson AC, Moberly JB, Alaupovic P. Dialysis modalities and dyslipidemia. Kidney Int Suppl 2003;84:S110–2.
5. Cibulka R, Racek J. Metabolic disorders in patients with chronic kidney failure. Physiol Res 2007;56:697–705.
6. Kaysen GA. Dyslipidemia in chronic kidney disease: Causes and consequences. Kidney Int 2006;70:S55–8.
7. Vaziri ND. Dyslipidemia of chronic renal failure: the nature, mechanisms, and potential consequences. Am J Renal Physiol 2006;290:262–72.
8. Cibulka R, Racek J, Vesela E. The importance of L-carnitine in patients with chronic renal failure treated with hemodialysis. Vnitr Lek 2005;51:1108–13.
9. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, *et al*. National kidney foundation practice guidelines for chronic kidney disease: evaluation, classification and stratification. Ann Intern Med 2003;139(2):137–47.
10. Salgado JV, Neves FA, Bastos MG, França AK, Brito DJ, Santos EM, *et al*. Monitoring renal function: measured and estimated glomerular filtration rates-a review. Braz J Med Biol Res 2010;43(6):528–36.
11. Addabbo F, Mallamaci F, Leonardis D, Tripepi R, Tripepi G, Goligorsky MS, *et al*. Searching for biomarker patterns characterizing carotid atherosclerotic burden in patients with reduced renal function. Nephrol Dial Transplant 2007;22:3521–6.
12. Sreenivasulu U, Bhagyamma SN, Anuradha R. Study of serum electrolyte changes in end stage renal disease patients before and after hemodialysis sessions: a hospital based study. Sch Acad J Biosci 2016;4(3B):283–7.
13. Shankalia DM, Tanna AC. Role of hemodialysis in renal failure to correct biochemical parameters. Indian J Appl Res 2013;3(6):414–6.
14. Varan HI, Dursum B, Dursum E, Ozben T, Suleymanlar G. Acute effects of hemodialysis on oxidative stress parameters in chronic uremic patients: comparision of two dialysis membranes. Int J Nephrol Renovasc Dis 2010;3:39–45.
15. Akdag I, Yilmaz Y, Kahvecioglu S, Bolca N, Ercan I, Ersoy A, *et al*. Clinical value of the malnutrition-inflammation-atherosclerosis syndrome for long-term prediction of cardiovascular mortality in patients with end-stage renal disease: A 5-year prospective study. Nephron Clin Pract 2008;108:C99–105.
16. Gupta K, Mahajan R. Coronary risk factors in maintenance hemodialysis patients: Who is the culprit –hemodialysis or chronic renal failure? Int J Appl Basic Med Res 2011;1(1):11–4.
17. Jones MK, Catte A, Li L, Segrest JP. Dynamics of activation of lecithin: cholesterol acyltransferase by apolipoprotein A-I. Biochemistry 2009;48(47):11196–210.
18. Maheshwari N, Ansari MR, Darshana MS, Lal K, Ahmed K. Pattern of lipid profile in patients on maintenance hemodialysis. Saudi J Kidney Dis Transpl 2010;21:565–70.
19. Zoccali C, Kramer A, Jager KJ. Chronic kidney disease and end-stage renal disease–a review produced to contribute to the report 'the status of health in the European Union: towards a healthier Europe' NDT Plus 2010;3:213–24.
20. Tsimihodimos V, Dounousi E, Siamopoulos KC. Dyslipidemia in chronic kidney disease: An approach to pathogenesis and treatment. Am J Nephrol 2008;28:958–73.

Address for Correspondence:

Dr Shazia Tauqeer, Department of Physiology, Ayub Medical College, Abbottabad, Pakistan. **Cell:** +92-333-5286502
Email: shazia_tauqeer@hotmail.com

Received: 15 Aug 2017 Reviewed: 27 Dec 2017 Accepted: 2 Jan 2018