ASSESSMENT OF LIPID DYSFUNCTION IN PATIENTS ON MAINTENANCE HAEMODIALYSIS

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INTRODUCTION

Dyslipidaemia is highly prevalent in patients on maintenance haemodialysis (MHD), with predominance of the atherogenic triad, i.e., hypertriglyceridemia, elevated VLDL and reduced HDL.1 This mimics the lipid abnormalities of metabolic syndrome, which accelerate the progression of atherosclerosis and increase the risk for cardiovascular mortality.2 Patients with CKD are in the highest risk category, i.e., a coronary heart disease (CHD) risk equivalent, for risk factor management of CVD.3 The incidence of cardiovascular disease (CVD) is high in patients on haemodialysis.4 CHD risk factors in the general population remain predictive of CVD among patients with CKD.5 Cardiovascular disease is the leading cause of death in haemodialysis patients accounting for almost 50 percent of deaths.6 Many atherosclerotic cardiovascular disease (ASCVD) risk factors are more prevalent in end stage renal disease (ESRD) than in the general population. Of the traditional risk factors for ASCVD in patients with ESRD, dyslipidaemia may play a major role. Control of these risk factors may have a substantial impact in reducing the excess burden of CHD.7 Kidney Dialysis Outcome Quality Initiative (K/DOQI) states that patients on MHD with 1) Fasting triglycerides >5.65 mmol/L; 2) LDL >2.59 mmol/L and 3) Triglycerides ≥2.26 mmol/L, LDL-C <2.59 mmol/L, and non-HDL cholesterol >3.36 mmol/L, should be considered for treatment to reduce the cardiovascular complications in these patients.8

Cholesterol levels may be lower in MHD patients. In this setting, there is an inverse relationship between mortality and the cholesterol concentration.9 This pattern of reverse epidemiology, i.e., hypercholesterolemia associated with decreased mortality and low cholesterol concentration in MHD patients associated with increased CVD mortality has been associated with malnutrition inflammation atherosclerosis complex.10,11 Keeping in view, the mortality associated with CVD in haemodialysis patients and the association of cholesterol levels with CVD in MHD patients, we planned to study the lipid profile of patients on maintenance haemodialysis in our centre compared to healthy controls. This study was done to know the burden and the type of lipid dysfunction in our MHD patients to adopt appropriate measures to decrease CVD mortality in this population.

MATERIAL AND METHODS

This study was carried out in Nephrology Department Military Hospital Rawalpindi. Seventy patients (44
males and 26 females) on maintenance haemodialysis and 70 age and sex matched healthy volunteers were included. Individuals having hypertension, diabetes mellitus, ischaemic heart disease, nephrotic syndrome, hypothyroidism, chronic liver disease and patients taking lipid-lowering medications were excluded.

Clinical history and physical examination of each subject was carried out. The height and weight of all individuals were measured by measuring scale and weighing machine. Body mass index (BMI) was calculated in kg/m². Five ml of venous blood after overnight fast was collected for analysis of lipid parameters.

Serum total cholesterol (TC) was estimated by enzymatic cholesterol oxidase method CHOD-PAP12 and Serum triglycerides by lipase/GPO-PAP colorimetric method.15 Serum high-density lipoprotein cholesterol (HDL-C) by enzymatic colorimetric method. Low-density lipoproteins cholesterol (LDL-C) was calculated by Friedwald equation LDL-C=TC–(HDL-C+TG/2.2).14 Non-HDL-C was calculated by subtracting HDL-C from TC. All of them were done on chemistry analyser Selectra using reagent kits from Merck Co.

Data was analysed by using SPSS 15. Mean, SD and percent were calculated. Chi-square test was applied to determine the difference between MHD patients and controls with different grades of BMI. Independent student’s t-test was applied to know difference in lipid parameters among MHD patients and control groups and p value ≤0.05 was taken as significant.

RESULTS

One hundred-forty subjects, 70 in each of control and MHD patients groups completed the study. Forty-four individuals were male and 26 were females in each group (Figure-1). The age range of control and test subjects were 17–75 yrs with a mean (SD) of 46.99(15.2) vs 46.46(14.8) for MHD patients and controls respectively (Figure-2).

The MHD patients had lower BMI as compared to controls mean (SD) 20.07(3.66) vs 22.88(3.97) (Table-I). TC, LDL-C and Non-HDL-C of MHD patients were significantly lower compared with control groups as shown in Table-2. TC, LDL-C, and Non-HDL-C of male MHD patients were significantly lower compared with control group (Table-3). The same variables were higher in females of control group compared to MHD patients but the difference was not statistically different as shown in Table-4.

Fifty-four (77%) MHD patients had low serum TC levels, i.e., <4.5 mmol/l compared to 31 (40%) controls. The most common abnormality observed in haemodialysis patients was low HDL Cholesterol (81%) followed by increased Non-HDL-C (23%) and increased serum Triglycerides (19%).
Twenty-six (37%) of the haemodialysis patients would have required treatment for dyslipidaemia as per K/DOQI guidelines, 2 patients for hypertriglyceridaemia, 21 for increased LDL levels and 3 for increased Non-HDL levels.

**DISCUSSION**

We determined the lipid profile along with BMI of patients undergoing maintenance haemodialysis at our centre for cardiovascular risk assessment and to adopt appropriate measures to improve mortality in MHD patients.

Our haemodialysis patients had significantly lower BMI (p=0.001). Several other studies have shown similarly lower BMI in MHD patients as compared to controls. We found 49% normal weight, 13% overweight and 1% obese patients undergoing haemodialysis in comparison to 59% normal weight, 24% overweight and 17% obese individuals under going haemodialysis as reported by Torun and associates. Thirty-seven percent of MHD patients had BMI less than 18.5kg/m². This indicates increased prevalence of malnutrition in our MHD patients according to WHO guidelines for adults. Survival among haemodialysis patients is enhanced in over weight individuals. Every one-unit increase in the BMI is associated with a reduction of 30 percent in the relative risk of dying.

TC and LDL-C was significantly lower in MHD patients as compared to healthy controls (p=0.0001). Among male haemodialysed patients similar observation was recorded. Kalantar-Zadeh et al also observed low total cholesterol, LDL-C and HDL-C in MHD patients compared to healthy controls similar to our study.

Other common lipid abnormality observed in our haemodialysis patients was low HDL-C levels. However serum HDL-C was non-significantly lower in MHD patients as compared to controls. HDL-C <40 mg/dl (1.03 mmol/l) was found in 81% of MHD patients in contrast to 51% incidence found by Pennell P et al and 33% in CHOICE study.

Non-HDL-C >3.36 mmol/l were found only in 23% of our MHD patients. Pennell and Co workers (2006) found 54% patients having Non-HDL alone at the level of ≥ 3.36 mmol/l. Non-HDL Cholesterol is reported to be uninfluenced by non-fasting state and thus has the advantage in haemodialysis patients in whom fasting samples are difficult to obtain for lipid analysis.

Only 19% of our haemodialysis patients had serum TG levels more than 2.26 mmol/l. In CHOICE study 36% of haemodialysed patients had hypertriglyceridaemia where as Pennell and coworkers found the incidence to be 52%. Non-fasting sample collection by Pennell may be the cause of this difference as triglyceride levels increase after meals.

MHD female patients in our study had lower TC, LDL-C, HDL-C and Non-HDL-C compared to healthy control females but the difference was not statistically significant. Small sample size may be one reason for this observation. The other reason may be that mean age of our female patients on MHD was 51 years and almost 80% of these were postmenopausal. After menopause serum total cholesterol and LDL cholesterol increase and HDL cholesterol decreases. This is secondary to decreased levels of oestrogen. Females are likely to have early menopause in ESRD and have unfavourable lipid profile for CVD in ESRD.

In our study 37% of the haemodialysis patients would have required treatment as per K/DOQI guidelines versus 57% in Pennell P study. This high percentage of MHD patients having low cholesterol and lower percentage qualifying treatment for hyperlipidaemia again indicates malnutrition. Our general population also has lower incidence of hyperlipidaemia.

Total and LDL hypercholesterolemia as well as hypertriglyceridaemia have a paradoxical association with better survival. Low serum cholesterol in MHD patients is associated with increased CVD mortality. This pattern of reverse epidemiology for CVD risk factors has been associated with malnutrition-inflammation-complex syndrome / malnutrition inflammation-atherosclerosis complex (MICS/MIA). Malnutrition and inflammation are common in CKD patients, associated with high short-term mortality in haemodialysis patients and appear to be the main cause of worsening ASCVD in CKD patients.

Malnutrition may lead to inflammation and vice versa. Malnourished dialysis patients are hypocholesterolemic, deficient of antioxidants and are predisposed to infection that may decrease the ability to remove circulating endotoxins. Based upon the lipoprotein-endotoxin hypothesis, there is an optimum serum lipoprotein concentration below which lipid reduction is detrimental as it leads to decreased ability of lipoproteins to bind lipopolysaccharide; this, in turn, may prevent lipoproteins from neutralizing the detrimental effects of endotoxin. Uraemia and renal replacement therapies result in markedly enhanced oxidative...
stress, the production of complement fragments and cytokines, increased adhesion molecules in endothelial cells, and other pro-inflammatory factors. These factors may provide the proper milieu for the development of accelerated atherosclerosis. 

Successful management of MICS may ameliorate the cardiovascular mortality and poor outcome in dialysis patients. Because MICS is multifactorial, its correction will require an integral approach rather than a single intervention. The early stage of chronic renal failure may be the ideal time to start therapeutic interventions.

Routine counselling and encouragement for physical activity in MHD patients has the potential to improve physical functioning, and optimise quality of life. For MHD patients, incorporation of exercise into the dialysis session may increase patient participation and tolerance of exercise. A study in normal adults concludes that a regular exercise program can improve plasma lipid and lipoprotein patterns, results, which should be applicable to haemodialysis patients as well. MHD patients can adhere to long-term physical training programs on the non-dialysis days, as well as during haemodialysis with considerable improvements in physical fitness and health.

Further studies are needed in different haemodialysis centres in large number of patients especially in female patients in our country to know the impact of different strategies adopted to ameliorate malnutrition, inflammation and cardiovascular disease in haemodialysis patients in our set-up.

In conclusion, hypocholesterolaemia and decreased HDL-C along with low BMI are prevalent in our MHD patients. This may increase mortality in these patients through malnutrition inflammation atherosclerosis process leading to CVD complications. Dietary education of MHD patients, improvement in dialysis practices and inclusion of exercise programmes in dialysis centres is likely to improve CVD mortality in MHD patients.

REFERENCES

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