ORIGINAL ARTICLE

More hostile dyslipidaemia in chronic kidney disease patients on maintenance haemodialysis than on conservative management

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Abstract

Objective: To study the pattern of dyslipidaemia in patients with stage-V chronic kidney disease on conservative management and those on maintenance haemodialysis.

Methods: This comparative observational study was conducted at the Jinnah Postgraduate Medical Centre, Karachi, from February to July, 2008, and comprised stage-V chronic kidney disease patients.

The patients were divided in two groups. Those who were on conservative management were placed in Group A, and those who were on maintenance haemodialysis were in Group B. Serum total lipid, cholesterol, triglycerides and high-density lipoprotein for both groups were assayed on chemical analyser and low-density lipoprotein was calculated by Friedwald equation. SPSS 17 was used for data analysis.

Results: Of the 120 patients, there were 60(50%) in each group. The mean age of patients in Group A was 46.33±14.56 years and in Group B was 43.4±14.1years. Of all, 64(53.3%) were men and 56(46.7%) were women. Mean systolic and diastolic blood pressure was 134±19.58mmHg and 83.6±14.14mmHg in Group A and 129±19.7mmHg and 79.7±12.1mmHg in Group B. Mean serum total lipid was significantly higher ($p<0.01$) whereas mean serum cholesterol was significantly lower ($p<0.01$) in Group B. Comparison of mean serum triglycerides between the groups was also statistically significant ($p<0.01$) and was high in Group B. Mean serum high-density lipoprotein was lower in Group B ($p<0.01$). The difference between serum low-density lipoprotein levels was statistically insignificant between the groups ($p=0.11$).

Conclusion: Pattern of dyslipidaemia in patients on maintenance haemodialysis was more hostile than those on conservative management, and posed increased risk of coronary heart disease.

Keywords: Dyslipidaemia, Chronic kidney disease, Haemodialysis, Conservative management. (JPMA 66: 928; 2016)

Introduction

Dyslipidaemia is a well-recognised complication of chronic kidney disease (CKD)1 and constitutes a characteristic pattern of disturbance, both in CKD patients on conservative management, i.e. CKD stage V,[1-4] and on maintenance haemodialysis (HD), i.e. CKD stage V-HD.[5,6] The presence of dyslipidaemia in this population makes them vulnerable to cardiovascular as well as cerebrovascular complications.

Dyslipidaemia of renal origin shows a characteristic pattern of raised serum triglyceride (TG) and low high-density lipoprotein (HDL) cholesterol levels. On the other hand, levels of very low-density lipoprotein (VLDL) cholesterol is typically high; and levels of total and low-density lipoprotein (LDL) cholesterol are mostly normal or may even be lower.[7] This is all because of impaired metabolism of HDL and TG-rich lipoprotein.

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Several mechanisms have been attributed to this pattern of dyslipidaemia. Firstly, due to the down regulation of lecithin-cholesterol acyltransferase (LCAT), maturation of HDL is impaired. Secondly, to a lesser extent, increased plasma cholesterol ester transfer protein (CEPT) plays a part. Thirdly, reduction in plasma concentrations of apolipoproteins (Apo) A-I and Apo A-II[8] and chronic inflammation[4] also contribute to reduce HDL levels. CKD-induced hypertriglyceridemia is caused by alteration in various mechanisms of lipid metabolism. It is primarily due to increase in plasma ApoC-III levels.[8] There is also down regulation of lipoprotein lipase, hepatic lipase and the VLDL receptor and upregulation of hepatic acyl-CoA cholesterol acyltransferase (ACAT).[2]

Principal features of renal dyslipidaemia remain essentially unchanged before and after initiation of HD[9] and the Apo protein profile mostly retains the same characteristics of dyslipidaemia. Both of the populations show reduced Apo A-I and Apo A-II levels, moderate elevations of Apo B and Apo E, and a significant increase of Apo C-III concentrations. HD patients have slightly lower concentrations of TG-rich lipoproteins compared to those who are not yet on dialysis, possibly due to an

attenuation of the dyslipidaemia on long-term HD.[9]

Lipid abnormalities are thought to be one of the contributing factors responsible for coronary artery disease (CAD), leading to high morbidity and mortality in this population of the patients.[3,10,11] Atherosclerotic heart disease (ASHD) is believed to account for approximately 55% of mortality and it contributes to a 20-fold increase in ischaemic heart disease (IHD) and 10-fold increase in stroke among patients with end-stage renal disease (ESRD). The risk for heart disease, both sub-clinical and clinical, exists even when the patients enter dialysis treatment. Two-thirds of all dialysis patients die within five years of initiation of dialysis treatment and approximately half of them die due to cardiovascular disease (CVD).[12]

There is an inverse relationship between CVD mortality and the low serum cholesterol concentration, attributed to malnutrition-inflammation-complex syndrome / malnutrition inflammation-atherosclerosis (MICS/MIA) complex.[5] In an attempt to reduce the burden of CVD in patients with CKD, aggressive management of cardiovascular risk factors like dyslipidaemia has been proposed.[13]

High cholesterol and TG plasma levels have been demonstrated to be independent risk factors for progression of renal disease. Recent studies indicate that statins also exert beneficial effects on the progression of renal impairment.[14] Several mechanisms have been proposed,[15] however exact mechanism behind the renoprotective effect of statin therapy is not well understood.

Dyslipidaemia is a major co-morbid in patients with CKD. Identifying such patients and proper management can minimise the complications related to dyslipidaemia.

The current study was planned to look into the pattern of dyslipidaemia in patients with CKD stage V and CKD stage V-HD.

Patients and Methods

This comparative observational study was conducted at the Jinnah Postgraduate Medical Centre (JPMC), Karachi, over six months from February 2008, and comprised CKD stage V and CKD stage V-HD patients.

Of the two equal groups, one comprised patients on conservative treatment (Group A) and the other had those on maintenance HD (Group B), with frequency of four-hour sessions two times a week, for at least three months. Informed consent was obtained from the participants.

Patients suffering from hypothyroidism, those already on lipid-lowering agents, obese having body mass index (BMI) of more than 30 and familial hyperlipidaemia were excluded.

Both groups were compared for serum total lipid, serum cholesterol, serum TG, serum HDL and serum LDL. Serum total cholesterol (TC) was estimated by enzymatic-cholesterol-oxidase-phenol-aminophenazone (CHOD-PAP) method and serum TGs by lipaseglycerol-3-phosphate-PAP (GPO-PAP) colorimetric method. Serum HDL was estimated by enzymatic colorimetric method. Serum LDL was calculated by Friedewald equation: LDL-C=TC-(HDL-C+TG/2.2). All of them were done on chemistry analyser Selecta using reagent kits.

Samples were collected using non-probability convenience technique. SPSS 17 was used for data analysis. Mean and standard deviation (SD) were computed for all quantitative variables in both groups. Frequency and percentage were calculated for gender. T-test was used to compare the mean significant difference between groups. $P<0.05$ was taken as significant.

Results

There were 120 patients in total; 60(50%) in each group. The mean age of patients in Group A was 46.33±14.56 years and in Group B was 43.4±14.1years (p=0.26). Overall, 64(53.3%) were men and 56(46.7%) were women. In Group A, there were 30(50%) women and 30(50%) men, whereas in Group B there were 26(43.3%) women and 34(56.7%) men (p=0.46). The mean weight was 50.6±13.8kg in group A and 50.1±12.5kg in Group B (p>0.05). Mean systolic blood pressure (BP) was 134±19.58mmHg and mean diastolic BP was 83.6±14.14mmHg in Group A, and 129±19.7mmHg and 79.7±12.1mmHg in Group B (Table-1).

Table-1: Comparison of demographic data between Group A and Group B (n=120).

Variables	Group A n=60	Group B n=60	P-Value
Mean Age (years)	46.33 ± 14.56	43.4± 14.1	0.26
Gender	Female=30	Female=26	
	Male=30	Male=34	0.46
Mean Weight (Kg)	50.63 ± 13.89	50.1± 12.5	0.82
Height (m)	1.59 ± 0.11	1.58± 0.1	0.60
Body mass index (kg/m2)	20.23 ± 4.9	20.02± 5.04	0.81
Mean Systolic Blood Pressure (mmHG)	134 ± 19.58	129 ± 19.7	0.16
Mean Diastolic Blood Pressure (mmHG)	83.6 ± 14.14	79.7 ± 12.1	0.10
Haemoglobin (Gm %)	9.14 ± 1.97	9.75 ± 1.23	0.04
Blood Urea Nitrogen (mg/dl)	50.8 ± 18.55	78.5 ± 27.4	<0.01
Serum Creatinine (mg/dl)	5.79 ± 1.19	8.9 ± 3.1	<0.01

Group A: On conservative management
Group B: On maintenance haemodialysis.

Table-2: Comparison of serum lipid levels between groups (n=120).

	Group A n=60	Group B n=60	P-Value
Serum Total Lipid (mg/dl)	379.5±132	538.47±66.8	<0.01*
Serum Cholesterol (mg/dl)	109.63 ± 54.6	70.93 ± 33.2	<0.01*
Serum Triglycerides (mg/dl)	118 ± 40.6	156.1 ± 49.3	<0.01*
Serum HDL Level (mg/dl)	32.27 ± 3.45	26.5± 4.64	<0.01*
Serum LDL Level (mg/dl)	48.3 ± 25.9	55.67 ± 29.6	0.14

* Significant mean difference
Group A: On conservative management
Group B: On maintenance haemodialysis
HDL: High-density lipoprotein
LDL: Low-density lipoprotein.

Mean serum total lipid was significantly higher in Group B (p<0.01) whereas mean serum cholesterol was significantly lower(p<0.01)in Group B. Comparison of mean serum TGs between groups was also statistically significant (p<0.01) and high in Group B. Mean serum HDL was lower in Group B (p<0.01). The difference between serum LDL levels was statistically insignificant between the groups (p=0.11).

Discussion

In our study serum HDL levels in both CKD groups were found low, similar to other studies.[16] However, TG and total lipid levels in both groups were found to be within normal limit. This finding in association with decreased BMI, urea, creatinine and haemoglobin levels may suggest a role of overall low socio-economic status of our patients, which may result in more malnourishment, lack of adequate management and under-dialysis as compared to their counterparts in the world. In addition, this can be a part of reverse epidemiology.[17,18] Like ours, most of the studies done to explore reverse epidemiology in CKD population reported no inverse relationship with HDL as it was found with other lipids. The likely explanation for this could be that cholesterol esters in HDL are primarily received from albumin[19] (an important marker of nutritional status) and therefore malnutrition is associated with low HDL. This also explains why other lipoproteins are low in malnutrition. Similar results were found in another study from Pakistan.[6]

In our study, we found that pattern of dyslipidaemia in patients on maintenance HD was more hostile, with high serum total lipid and TG levels and low serum HDL level and serum cholesterol level than patients on conservative management. There are very few studies done in this regard. For instance, Attman PO[9] found that the dyslipidaemia remains essentially unchanged in both groups of patients while HD patients have slightly lower concentrations of TG-rich lipoproteins, possibly representing an attenuation of the dyslipidaemia on long-term HD.[9] Difference in the results of our study can be explained by overall difference in the pattern of dyslipidaemia in our CKD population,[6] which is attributed to malnutrition, along with inadequate frequency of haemodialysis, high inflammation levels, a decreased appetite and hypo-caloric levels.

About two-thirds of all dialysis patients die within five years from the initiation of dialysis treatment.[20] Causes of death are diverse; however, approximately half of all HD patients die of CVD.

Total and LDL hypercholesterolemia as well as hypertriglyceridemia have a paradoxical association with better survival in HD patients.[20] Low serum cholesterol in HD patients is associated with increased CVD mortality. This pattern of reverse epidemiology for CVD risk factors has been associated with MICS/MIA.[21] Both malnutrition and inflammation which are common in these patients are associated with high short-term mortality in HD patients and appear to be the main cause of worsening atherosclerotic CVD in these patients.[22]

Another study suggests the possibility of reverse epidemiology in HD patients concerning lipids could possibly be due oxidative stress.[23] Reactive oxygen species (ROS) production that is not balanced by antioxidant control is associated with oxidative stress. Uraemia and HD increase oxidative stress, with malnutrition causing deficiency of antioxidant providing proper environment for the development of accelerated atherosclerosis. Furthermore, oxidative injury has been reported to alter lipids in both the general population and HD patients and is involved in CVD acceleration.[24]

Successful management of MICS may ameliorate the cardiovascular mortality and poor outcome in these patients.[21] Treatment for CKD patients with MICS needs to focus short-term on inflammation and malnutrition through dietary counselling and medication. Once MICS is controlled, a more long-term therapy may need to look at controlling lipids associated with CVD risk. Statins can help control lipids. They may also help control inflammation which in turn may help to regulate appetite and increase albumin levels. The early stage of CKD may be the ideal time to start therapeutic interventions.[25]

The study had its limitations, including a small sample size. If this study was conducted on larger number of patients and if done with the collaboration of many hospitals, more significant results would be obtained.

Patient in haemodialysis group in our study were on twice per week haemodialysis i.e. they were under-dialysed.