BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

Hypercholesterolemia Due to Chronic Renal Failure in Diabetic Sudanese Patients

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ABSTRACT

This study was conducted to compare the quantitative and qualitative aspects of serum cholesterol in chronic renal failure (CRF) patients due to diabetes with that of CRF in patients due to other causes, and assessing the possibility for developing atherosclerotic cardiovascular disease. The study was conducted in 80 Sudanese patients on haemodialysis and peritoneal dialysis, 40 of them had CRF due to Diabetes mellitus and others had CRF due to other causes. Additional 40 health Sudanese served as control. Serum samples were analyzed using standard colorimetric methods to detect concentration of the total cholesterol, triglycerides, high density lipoprotein. In CRF patients due to diabetes mellitus there was significant increase in serum cholesterol level, also there was consequent decrease in high density lipoprotein. The mean of total cholesterol was 255 mg/dl in the first group and in the second was 183 mg/dl, triacylglycerols was 177 mg/dl for the first group and for the second group was 163 mg/dl, low density lipoproteins was 187 mg/dl for the first group and for the second group was 113 mg/dl, high density lipoprotein cholesterol was 27 mg/dl for the first group and 31 mg/dl for the second group. There was no effect of sex, age and the duration of renal failure. This study demonstrated the effect of diabetes mellitus on lipoprotein level in patients with CRF as one of the atherosclerotic risk factor.

Keywords: chronic renal failure, diabetes mellitus, hyperlipaemia.

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Received 30 December 2014, Accepted 08 January 2015

Please cite this article as: Modawe GA *et al.*, Hypercholesterolemia Due to Chronic Renal Failure in Diabetic Sudanese Patients. British Journal of Medical and Health Research 2015.

INTRODUCTION

Chronic renal disease (CRD) is a patho-physiologic process with multiple etiologies, resulting in the inexorable attrition of nephron number and function and frequently leading to end-stage renal disease (ESRD). In turn, ESRD represents a clinical state or condition in which there has been an irreversible loss of endogenous renal function, of a degree sufficient to render the patient permanently dependent upon renal replacement therapy (dialysis of transplantation) in order to avoid life – threatening uremia[1]. Wide geographical variations in the incidence of disorders causing CRD exist. The most common cause of glomerulonephritis in sub-Saharan Africa is malaria. Schistosomiasis is a common cause of renal failure due to urinary tract obstruction in parts of the Middle East, including southern Iraq[2]. Glomerulonephritis is most common cause of chronic renal failure in Sudan[3, 4]. In United States of America, diabetes and hypertension are the leading underlying etiologies of both CRD and ESRD[1]. Diabetes mellitus can have profound effects on the renal system. Approximately 45%of patients with type 1 will develop progressive deterioration of kidney function (diabetic nephrophthy) within 15-20 years after diagnosis. Early treatment of diabetes that focuses on tight control of blood glucose and prevention of high blood pressure may prolong the onset of chronic renal failure[5]. The term hyperlipidaemia is applied when the plasma cholesterol or triglyceride level are increased. The degree of cholesterol or triglyceride elevation is a reflection of altered lipoprotein level, which are often classified as lipoprotein phenotypes. The most common forms of hyperlipidemia seen in clinical practice are not the primary (familial) types, but those secondary to other disorders, such as alcohol consumption, chronic severe uncontrolled diabetes mellitus (diabetic lipaemia), nephrosis and glycogenesis, drugs, nephritic syndrome and obstructive liver disease[5]. Patients with chronic renal disease suffer from a secondary form of complex dyslipidemia. The most important abnormalities are an increase in serum triglyceride level and increased plasma low density lipoprotein (LDL) cholesterol, which is the first lipid abnormality to appear in nephritic patients. Some patients exhibit evidence of decreased lipoprotein lipase activity and develop hyper-triglycerdaemia from over production of very low density lipoprotein (VLDL) chronic renal disease also promote its progression and the development of atherosclerosis. The objective of this study was to compare lipid profile in patients with chronic renal failure (CRF) due to diabetes mellitus to lipid profile in patients with renal failure due to other causes.

MATERIALS AND METHODS

Subjects: Subjects included in this study were 40 chronic renal failure diabetic patients (group A), with age range between 20-80 years, they were attending Khartoum Dialysis Unit

in Khartoum University Center for Kidney Dialysis and Transplantation,this study carried out from May to October 2013. Other 40 Sudanese patients with chronic renal failure due to other cause (group B), and 40 healthy Sudanese people (group C) from Alneelain University and from people working at Khartoum Dialysis Unit in Khartoum University Center for Kidney Dialysis and Transplantation.

Blood samples: Fasting venous blood samples from each patient (5ml) and control were obtained using disposable syringes. The blood was allowed to clot for one hour at room temperature and centrifuged at 5000 r.p.m. for 10 minutes to separate serum from blood cells. Sera were kept at tightly covered containers at -20^{o}C and used later for estimation of serum total cholesterol, triglyceride and serum HDL cholesterol.

Biochemical methods: Serum biochemical assays were performed using standard methods. Sera samples were analyzed for metabolites (total serum cholesterol, triglycerides and serum high density lipoprotein cholesterol). They were analyzed using commercial kits (Linear chemicals, Spain) using Corning colorimeter model 252. Serum low density lipoprotein cholesterol concentration (mg/dl) was calculated according to Friedwald equation as follows:

$$\text{LDL} = \text{serum cholesterol conc.} - \text{HDL} - \frac{\text{Serum triacylglycerol cone}}{5}$$

All standards and controls were of human origin with known biochemical values and were supplied by the manufacturer.

RESULTS AND DISCUSSIONS

In this study, the lipid profile of forty Sudanese patients with chronic renal failure due to diabetes mellitus (group A) has been compared to the lipid profile of forty Sudanese patients with renal failure due to other causes (group B) and forty healthy people used as the control group (group C). Patients were randomly selected from Khartoum Dialysis Unit and Khartoum University Centre of Kidney Dialysis and Transplantation. The range of age was from 25-75 years for all groups and the mean of age was as follows: group A 54 years, groups B 43 years and group C 46 years. The distribution of sex and the study groups was as follows: group A: 25 male and 19 females. Table (1) show that group (A) had the highest level of serum total cholesterol concentration in the study groups, followed by group (B), while group (C) represents the normal value. There was significant difference between group (A) and group (B) also between group (A) and group (C), while there is no significant difference between group (B) and group (C). Table (2) show that group (A) had the highest level of serum triglyceride concentration, followed by group (B), while group (C) represent the normal level. There is significant difference between group (A) and group (C) only. Table (3) show that group (A) had the highest level of serum low density lipoprotein cholesterol

concentration among the study groups. There is significant difference between group (A) and group (B) (and between group (A) and group C), but there is no significant difference between group (B) and group (C). Table (4) show that group (A) had the lowest level of serum high density lipoprotein cholesterol concentration among the study groups. There is significant difference between group (A) and group (C) and group (B) and group (C). Patients with CRF due to any cause have hyperlipidaemia mainly hypercholesterolemia[6]. They suffer from a secondary form of complex dyslipidaemia also hyperlipidaemia promotes progression of CRF to end state renal disease (ESRD) and the development atherosclerosis. Therefore, renal patients with dyslipidaemia should be subjected to lipid lowering therapy[7]. Patients with diabetes mellitus have abnormal plasma lipid levels and frequently may develop severe triglyceridaemia chylomicronaemia syndrome and they are at increased risk of coronary, cerebral and peripheral vascular disease because of possible presence of structural and functional abnormalities that may impair the lipid metabolism and transport system in diabetic patients[8]. Patients who have chronic renal failure due to diabetes are expected to have higher levels of cholesterol and other lipids than patients with chronic renal failure without diabetes; this may be explained by the synergetic effect of both diabetes and renal failure on lipid metabolism[6]. Table (1) show that group (B) has high level of serum total cholesterol when compared with the healthy people (group C); this finding is in agreement with previous studies[6, 9]. Hyperlipidemia is a common finding in renal disease especially nephritic syndrome in which hypercholesterolemia is one of the criteria for diagnosis of renal disease. Group (A) had significantly higher level of serum total cholesterol. This could be explained by the effect of both CRF and D.M. on lipid metabolism which may act synergistically to raise serum total cholesterol. The results agree with previous studies[6]. The serum total cholesterol concentration in group (A) was significantly higher than the normal group (C) and this might indicate great risk for atherosclerosis and vascular disease. These patients need treatment of hyperlipidemia as well as protective measures. Table (3) shows that LDL cholesterol concentration is greatly increased in group (A), this account for the significant increase of total cholesterol level in these patients and may indicate that the type of cholesterol increase in the blood of group A is bad cholesterol and this agree with previous studies[10]. This indicates that these patients (group A) are at increased risk for atherosclerosis and vascular disease and may need management. Group (B) had also significant increase in LDL cholesterol, this also agree with the results obtained in previous studies[10, 11] and need management. Table (4) show that group A) had the lowest level of serum HDL cholesterol concentration. This high level of HDL is protective against atherosclerosis and vascular disease while the decrease in the level of HDL increases the risk factor for these conditions [6,

[12]. It was notice that group A had significantly lower level of HDL than group B so this showed renal failure and diabetes severely affected the level of HDL. Table (2) show that both group A and B both had increased level of TG so renal failure due to any cause can lead to increased TG level as shown in the previous studies[6]. But no significant difference between group A and group B was observed. Lipoproteins disturbance in patients with CRF receiving haemodialysis appears to be independent of length of dialysis, also age and sex do not affected the concentration of lipid profile[13]. It was found that haemodialysis patients have a statistically significant higher triglycerides and VLDL-C level and low HDL-C level compared to normal healthy controls. There were no statistically significant differences in total cholesterol (TC) or LDL-C level who found that total cholesterol and LDL-C level were significantly lower in the dialysis patients compared to normal controls. It was found that both haemodialysis groups (diabetic and non-diabetic) have a significantly higher triglycerides and VLDL-C levels and significantly lower HDL-C level compared to normal controls. The atherogenic indices (TC/HDL-C and LDL-C/HDL-C ratios) are also significantly higher in both groups of haemodialysis patients compared to controls. There were no statistically significant differences in total cholesterol or LDL-C levels. These results in general are in line with the results comparing lipid profile of all haemodialysis patients to normal controls indicating that patients with diabetic nephropathy generally share the characteristic features of dyslipidaemia of chronic renal failure[6]. In general the results show that both groups of haemodialysis patients (diabetic and non-diabetic) have significantly higher triglycerides and VLDL-C, and lower HDL-C levels compared to the control group, From the results it is found that both groups of haemodialysis patients (diabetic and non-diabetic) have significantly higher levels of triglycerides compared to normal healthy controls indicating that, regardless of the cause, CRF leads to hypertriglyceridaemia as shown in the studies of[6, 14]. The results also show that there were no significant differences in triglycerides and VLDL-C levels between diabetic and non-diabetics. The results also show that diabetic haemodialysis patients had significantly lower HDL-C levels compared to non diabetics, so despite the similarities in lipid profile between diabetic and non diabetic haemodialysis patients, the abnormalities are more marked in diabetic haemodialysis patients than in non diabetic haemodialysis patients reflecting the additional impact of diabetes on severely affected the level HDL-C. The results also show that there wre no significant differences in total cholesterolor LDL-C concentrations between diabetic or non diabetic renal failure patients or in comparison with normal healthy controls. This support the results of many studies that end-stage renal disease does not necessarily cause increase in total cholesterol or LDL-C levels. The results also show that diabetic haemodialysis patients had significantly

higher (TC/HDL-C) and (LDL-C/HDL-C) ratios compared to non diabetic haemodialysis patients who also had significantly higher ratios compared to controls. Thus diabetic haemodialysis patients have great chance for developing atherosclerotic cardiovascular disease compared to non diabetic haemodialysis patients who are at great risk of developing atherosclerotic cardiovascular disease compared to normal controls.

Table 1: Total cholesterol concentration among chronic renal failure patients due to diabetes mellitus, or other causes and control group.

Group	No./group	Mean ±SD	Comparison	P-value
A	40	255±91	AB	0.00
B	40	183±53	AC	0.00
C	40	198±76	BC	0.199

*The mean difference is significant at the P value <0.05

Table 2: Triglyceride concentration among chronic renal failure patients due to diabetes mellitus, chronic renal failure due to other cause and control group.

Group	No./group	Mean ±SD	Comparison	P-value
A	40	177±82	AB	0.682
B	40	163±77	AC	0.000
C	40	109±50	BC	0.050

*The mean difference is significant at the P value <0.05

Table 3: Low density lipoprotein concentration among chronic renal failure patients due to diabetes mellitus, chronic renal failure due to other cause and control group.

Group	No./group	Mean ±SD	Comparison	P-value
A	40	187±84	AB	0.00
B	40	113±49	AC	0.00
C	40	92±34	BC	0.199

*The mean difference is significant at the P value <0.05

Table 4: High density lipoprotein concentration among chronic renal failure patients due to diabetes mellitus, chronic renal failure due to other causes and control group.

Group	No./group	Mean ±SD	Comparison	P-value
A	40	27±8	AB	0.103
B	40	31±8	AC	0.00
C	40	44±8	BC	0.199

*The mean difference is significant at the P value <0.05

CONCLUSION

Patients with CRF due to D.M. had more severe hyperlipidemia than patients with CRF due to other causes. The increase in total cholesterol level in patients with CRF was mainly due to elevation in LDL fraction which was high in group A.

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