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DYSLIPIDAEMIA AMONG PATIENTS WITH END STAGE RENAL DISEASE IN MAKURDI, NORTH CENTRAL, NIGERIA

Dr. Monday O. Ogiator*[1], Joseph E. Ojobi[2] and Ochoche O. Ijachi[1]

[1]Department of Medicine, Benue State University Teaching Hospital.
[2]Department of Medicine, Federal Medical Centre, Makurdi.

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***Corresponding author: Dr. Monday O. Ogiator**

Department of Medicine, Benue State University Teaching Hospital.

ABSTRACT

Background: Chronic Kidney Disease (CKD) is a common public health problem with increasing prevalence and incidence. Dyslipidaemia is a commonly associated comorbidity in patients with CKD including end stage renal disease (ESRD). It has been shown to increase the risk of cardiovascular events which is a common cause of morbidity and mortality in these patients. In this study we aimed to determine the prevalence of dyslipidaemia among patients with ESRD seen at Benue State University Teaching Hospital, Makurdi. **Methodology:** This was a retrospective study which analysed data from patients with end stage renal disease managed at Benue State University Teaching Hospital, Makurdi from October, 1st 2012 to 31st December, 2015. **Results:** Out of the 118 patients studied, 59.3% were males while 40.7% were females. The mean age of the population was 45.9 ± 16.4. Seventy seven patients (65.3%) of the patients had dyslipidaemia. **Conclusion:** Over half of the Patients with ESRD had dyslipidaemia. Regular measurement of fasting serum lipids is essential in CKD to detect and treat abnormalities early as well as monitor progress of treatment

KEYWORDS: Chronic Kidney Disease, End Stage Renal Disease, Dyslipidaemia.

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem with increasing incidence and prevalence. End stage renal disease (ESRD) also known as CKD stage 5 is defined as needing dialysis or transplant. The prevalence of ESRD has increased in the past 10 years.[1] Cardiovascular disease (CVD) is a common feature in patients with ESRD. Infact the risk of CVD in patients with ESRD is similar to that of patients with previous CVD.[2] Additionally cardiovascular risk corresponds with decline in renal function. The leading cause of morbidity and mortality in patients with ESRD is cardiovascular disease.[3] As glomerular filtration rate declines, the relative risk of mortality from CVD increases.[4] The risk for CVD exists even as patients enter dialysis treatment. In the United States Renal Data System (USRDS) Wave 2 study, for example, the prevalence of ischaemic heart disease and cardiac failure was approximately 40% before renal replacement therapy, much higher than the 2 to 20% reported in the general population.[5] The annual mortality rate of dialysis patients is greater than 20%. The leading cause of morbidity and mortality in CKD is CVD, primarily atherosclerotic coronary artery disease. One potentially modifiable risk factor for CVD is dyslipidaemia.

As CKD progresses dyslipidaemia worsens, for instance in an evaluation of 2001 – 2010 National Health and Nutrition Examination Survey (NHANES), the prevalence of dyslipidaemia increased from 45.5% in CKD stage 1 to 67.8% in CKD stage 4.[6] Similarly, the use of lipid lowering agents increased from 18.1% in CKD stage 1 to 44.7% in CKD stage 4.[6]

Chronic Kidney Disease is associated with a dyslipidaemia comprising high triglycerides, low HDL-Cholesterol and altered lipoprotein composition. Since CVD is the leading cause of mortality in CKD and dyslipidaemia is a modifiable risk factor, treatment of dyslipidaemia is very important in CKD. Of more than 1000 haemodialysis patients studied only 20% had normal lipid levels.[7] A larger study evaluating dyslipidaemia in more than 21,000 dialysis patients found 82% prevalence of dyslipidaemia.[8]

Dyslipidaemia is a risk factor for atherosclerotic heart disease which is believed to account for 55% of mortality

and contributes to a 20 fold increase in ischemic heart disease and a 10 fold increase in risk of stroke among patients with ESRD.[9]

For instance in a study of 1041 dialysis patients, the prevalence of atherosclerotic risk factors of patients with ESRD was found to be higher when compared with that of normal adults. End stage renal disease patients had a high prevalence of diabetes (54%), hypertension (90%) left ventricular hypertrophy (LVH) - 22% hypertriglyceridaemia (36%) and low high density cholesterol (HDL-Cholesterol) – 33%.

After adjustment for age, race, gender and atherosclerotic CVD, the prevalence of low HDL-C and hypertriglyceridaemia were still found to be more common among patients with ESRD than among normal subjects[7]. Among patients with ESRD, a number of lipid abnormalities have been identified. Reports from several studies suggests that the kind of dyslipidaemia is often related to the type of renal replacement therapy.[10]

Approximately 20 – 40% of haemodialysis patients have been estimated to have elevated triglycerides and reduced HDL-Cholesterol (HDL-C).[11,12] Additionally, increased oxidized low density lipoprotein cholesterol (LDL-C) levels and increase lipoprotein LP (a) levels have been reported with 34% of patients having elevated levels.[13,14,15]

Peritoneal dialysis is associated with a relatively more atherogenic lipid profile than haemodialysis. In reported studies, 20-40% of peritoneal dialysis patients have been shown to have elevated total cholesterol and LDL-C and 25 – 50% of patients have been reported to have elevated triglycerides and low HDL-C.[15,16,17]

Beyond simply measuring lipid levels, emerging evidence suggests that lipoprotein size and composition is altered in CKD with increased small dense LDL and decreased larger LDL particles in CKD patients compared to controls.[18] Small dense LDL is more atherogenic than larger LDL particles. Reis A et al[19] compared LDL particle composition between subjects with stage 4 and 5 CKD and non CKD controls and found similar total lipid and cholesterol content, but altered content of various lipid subclasses for example decreased phosphatidylcholine, sulfatides and ceramides and increased N-acyltaurines. Many of these lipids species are known to have either pro or anti – atherogenic properties and thus could directly affect atherogenesis.[19]

Also CKD leads to a down regulation of lipoprotein lipase and the LDL-receptor. In addition increased triglycerides in CKD are due to delayed catabolism of triglycerides and lipoproteins with no differences in production rate.[20]

Decreased lecithin –Cholesterol acyltransferase (LCAT) activity and increased cholesterylester transfer protein (CETP) activity contribute to decreased HDL-Cholesterol levels. Beyond decreased HDL cholesterol levels, the HDL in CKD is less effective in its anti-oxidative and anti-inflammatory functions.[21] CKD also causes insulin resistance which may contribute to low HDL level. Low HDL levels is associated with cardiovascular risk both in the general population and in patients with CKD.[22] Although HDL levels may be in part be genetically determined, insulin resistance and CKD are associated with low HDL levels because as glomerular filtration rate declines, insulin sensitivity decreases.[23]

In this study we aimed to determine the prevalence of dyslipidaemia among patients with ESRD seen at Benue State University Teaching Hospital This is important because dyslipidaemia is a modifiable risk factor for CVD known to be a common cause of morbidity and mortality in patients with CKD.

MATERIALS AND METHODS

This was a retrospective study where records of patients managed for ESRD between December, 2012 and December 2015 were retrieved and reviewed. Ethical clearance was obtained from the ethics committee of Benue State University Teaching Hospital

The records of all patients with ESRD seen by the Nephrology unit of Benue State University Teaching Hospital from 1st October, 2012 to 31st December, 2015 were reviewed.

Benue State University Teaching Hospital is a tertiary healthcare facility located in Makurdi, North Central Nigeria.

Data obtained from each patient included age, gender, weight, height, body mass index (BMI) serum creatinine, serum total cholesterol, HDL Cholesterol, low density cholesterol and Triglycerides (TG). Estimated Glomerular Filtration Rate (eGFR) was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine equation.[24,25]

CKD Stage 5 (ESRD) was defined as eGFR ≤ 15mls/min or patients already undergoing dialysis or has had renal transplant.

Dyslipidaemia was defined using the standardized definition for dyslipidaemia according to the National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III: The third report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol on adults as follows.[26]

Total Cholesterol >5.17mmol/L (>200mg/dl)
LDL-C > 3.36mmol/L (>130mg/dl)
HDL-C <1.03mmol/L (<40mg/dl) for mates

<1.13 (<50mg/dl) for females
Serum TG >1.7mmol/L (>150mg/dl)

Statistical Analsysis
The Statistical Package for Social Sciences (SPSS Inc. Chicago II) version 21.0 statistical software was used for data analysis.

Quantitative variable (age, BMI, eGFR, lipid indices) were expressed as means ± standard deviation while categorical variables were expressed as proportions. The t-test and the chi-square test were used in the comparison of means and proportions respectively.

P-value <0.05 was considered statistically significant.

RESULTS

The study population comprised 118 subjects, 70(59.3%) were males while 48.(40.7%) were females (Fig.1). The mean ages of males and females were 47.1 ± 17.7 and 45.9 ± 19.4 years respectively. There was no statistically significant difference between the two values. 69% of the study population were less than 50 years of age (Table 1).

Mean BMI was 23.0 ± 3.7kg/m^2 for males and 22.8 ± 3.1km/m^2 for females. The different was not statistically significant p (0.491).

Dyslipidaemia was present in 77(65.3%) of which 46(39%) were males and 31 (26.3%) were females (Table 3).

Twenty One (17.8%) had elevated total cholesterol, 12 (10.27) had elevated LDL-Cholesterol while 44(37.3%) had elevated TG/HDL- Cholesterol.

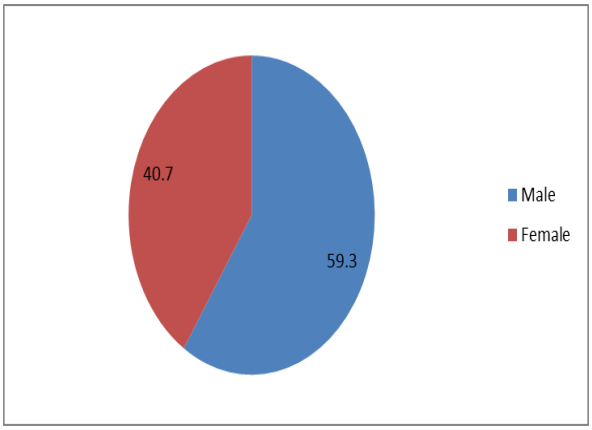

Figure 1: Sex Distribution of Patients.

Table 1: Age Distribution of Patient.

Age	Frequency	Percentage
18 – 33	30	25.4%
34 – 49	39	33.1
50 – 65	32	27.1
>65	17	14.4
Total	**118**	**100**

Table 2: Total Cholesterol.

Sex	Normal	Elevated
Male	58	12
Female	39	9
Total	97	21

Table 3: LDL – Cholesterol.

Sex	Normal	Elevated
Male	63	7
Female	43	5
Total	106	12

Table 4: Triglycerides/HDL – Cholesterol.

Sex	Normal	Elevated	Total
Male	43	27	70
Female	31	17	48
Total	74	44	118

Table 5: Two by Two Table of Gender versus Lipid Status.

Sex	Dyslipidaemia	No Dyslipidaemia	Total
Male	46(39.0)	24(20.3)	70
Female	31(26.3)	17(14.4)	48
Total	77(65.3)	41(34.7)	118

OR-1.051, X^2 – 0,016, df-1, P value- 0.89

DISCUSSION

The majority of our study population were males 70 (59.3%). This is similar to some studies which reported higher prevalence of CKD in men.[27] Although some studies report higher prevalence in women.[28] This depends on factors such as the stage of CKD being considered and the underlying aetiology of the disease.

Age distribution of the patient revealed that most of them were in their productive years less than 50 years (Table 1) This is similar to several studies done in Nigeria, Africa and developing countries.[29,30,31,32] This is due to a number of reasons. First there is high prevalence of childhood infections in Africa and Sub- Saharan Africa including Nigeria leading to chronic glomerulonephritis which is a cause of ESRD in Nigeria[33,34] Also Human Immunodefiency Virus (HIV) which is so prevalent in Nigeria contributes to HIV associated nephropathy (HIVAN) which is also a common cause of ESRD,[35] In addition use of nephrotoxic agents like Non Steroidal Anti Inflammatory Drugs (NSAIDS), herbal medications, mercury containing soaps/creams is very common in our environment. The use of these agents can cause renal damage leading to ESRD.[36] Other reasons are late presentation to nephrologist as well as poor control of blood pressure and blood glucose levels in patients that are hypertensive and diabetic respectively.

Other studies especially in advanced countries where common causes of CKD are non communicable diseases like diabetes mellitus and hypertension reported higher mean ages for CKD.[37,38,39]

The prevalence of dyslipidaemia was higher among male patients. Interestingly the male patients had a higher mean BMI (23.0 ± 3.7kg/m^2) compared with 22.8 ± 3.1kg/m^2 for females. Whether or not this is responsible for the higher prevalence of dyslipidaemia is not clear as there may be a complex interaction of other factors.

Among patients with dyslipidaemia majority had low HDL/high TG, (44(37.3%) compared with 21(17.8%) and 12 (10.2%) for elevated total cholesterol and LDL Cholesterol respectively). This is consistent with reports from other studies of dyslipidaemia in ESRD Patients.[40,41]

Dyslipidaemia has been implicated as a risk factor for atherosderostic vascular disease in dialyzed patients. Haemodialysis is associated with hypertriglyceridemia and low serum HDL-Cholesterol.[42,43,44] Insulin resistance and CKD are associated with low HDL levels because as glomerular filtration rate declines, insulin sensitivity decreases.[23]

Plasma LDL-Cholesterol is usually not elevated as obtained in this study, only 12 patients had elevated LDL-Cholesterol.

The cause of hypertriglyceridemia is increased production of Apo B protein and a marked decrease in the metabolism of VLDL primarily as a result of decreased endothelial cell dilapidation of VLDL.[38]

CONCLUSION

Abnormalities in serum lipid indices are common in patients with ESRD. If left untreated, they can increase the risk of cardiovascular events and worsen the overall prognosis in such patients. Early detection and prompt commencement of therapy is essential.

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