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DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE POPULATION; A SINGLE CENTRE EXPERIENCE

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ABSTRACT

Background: Dyslipidemia is a major risk factor for cardiovascular disease in chronic kidney disease (CKD). **Objectives:** This study aimed at determining the prevalence of dyslipidemia among CKD patients in a tertiary hospital. **Methodology:** A comparative cross-sectional study of 160 CKD patients and an equal number of healthy controls. The Cockcroft-Gault formula was used in assessing renal function, lipid profile was also assessed and the National Cholesterol Education Program/Adult Treatment Panel III criteria used in the definition of dyslipidemia. **Results:** Mean age was 44.5 ± 15.7 years and 41.7 ± 14.6 years for cases and controls respectively. The prevalence of dyslipidemia was 94.4% amongst cases and 46.9% amongst controls with 73.1% of patients having reduced HDL-cholesterol, 66.2% elevated triglyceride, 25.6% elevated total cholesterol and 25% elevated LDL cholesterol in the CKD patients. The prevalence of dyslipidemia in the different stages of CKD I, II, III, IV and V were 33.3%, 66.7%, 94.2%, 97.5% and 95.2% respectively. **Conclusion:** Dyslipidemia is prevalent in CKD patients even in the early stages and becomes highly so as chronic kidney disease progresses.

INTRODUCTION

Chronic kidney disease (CKD) is a significant health problem worldwide and is increasing rapidly.[1] CKD is defined as a glomerular filtration rate (GFR) less than 60mL/min/1.73m^2 and/or kidney damage determined by abnormal findings in urine, such as proteinuria, albuminuria, haematuria, abnormal imaging, and/or histology, lasting for 3 months or more.[2]

In Nigeria, hospital-based studies have shown that CKD accounts for 2 – 10% of all admissions,[3-5] while in the United States 9.6% of non-institutionalized adults are estimated to have CKD.[6,7] Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with CKD.[8] Patients with CKD develop accelerated atherosclerosis and are at high risk of premature death from CVD. The increased predisposition of these patients to atherosclerosis is largely driven by inflammation, oxidative stress and dyslipidemia, features that are usually associated with CKD.[9]

Dyslipidemia is defined by the European Atherosclerosis Society[10] as total cholesterol (TC) of > 5.2mmol/l (>201 mg/dl), high density lipoprotein cholesterol (HDL-C) < 0.9mmol/l (<35 mg/dl), low density lipoprotein cholesterol (LDL-C) >3.5mmol/l (>135 mg/dl), triglyceride (TG) >1.75mmol/l (>154 mg/dl) and atherogenic index (AI) >5.8.

National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III) defines dyslipidemia as TC >5.17 mmol/l (>200 mg/dl), LDL-C >3.36 mmol/l (>130 mg/dl), HDL-C <1.03 mmol/l (<40 mg/dl) for males, <1.3 mmol/l (<50 mg/dl) for females and serum TG >1.7 mmmol/l (> 150 mg/dl).[11]

National guidelines have identified dyslipidemia and elevated levels of LDL-C in particular as a key risk factor for CVD risk modification for the general population.[12] It contributes to cardiovascular mortality which is ten to twenty times higher in dialysis patients than in the normal population, even after adjustments are made for age and sex.[13] There are some reports on the prevalence of dyslipidemia amongst Nigerian CKD patients. A 90.8% prevalence have been reported in dialysis-naïve CKD from North central Nigeria[14] while a report from North-western Nigeria showed severe dyslipidemia in pre-dialysis CKD patients (68.3% had elevated Tg, 63.5% reduced HDL, 22.2% elevated TC and 17.5% elevated LDL.[15]

Animal studies suggest that dyslipidemia worsens kidney function[13] and meta-analysis done of 13 small studies showed that lipid reduction preserves GFR and reduces proteinuria. Thus identification and treatment of dyslipidemia in CKD patients is of immense benefit.

This study aimed at determining the prevalence of dyslipidemia in CKD patients in South-south Nigeria.

MATERIALS AND METHODS

This was a comparative cross-sectional hospital-based study done in a tertiary hospital located in South-south Nigeria. CKD patients were recruited consecutively at presentation in the Nephrology clinic, Dialysis Unit and Accident and Emergency Units. Informed consent was obtained from all participants and ethical approval was obtained from the Hospital Ethics and Research Committee.

The primary outcome of the study was the estimation of the prevalence of dyslipidemia among CKD patients. Consenting CKD patients aged ≥ 18 years were recruited and patients were stratified based on the stage of CKD using the NKF/KDOQI staging.[2] Controls were apparently healthy individuals who had no symptoms suggestive of renal diseases and were neither hypertensive nor diabetic. They were age and sex matched hospital workers.

METHODOLOGY

A researcher-administered questionnaire was used in collecting data. Data on physical characteristics such as weight, height, and waist and hip circumference were recorded. Weight was measured in kilograms using hospital health scale ZT-120 with patients putting on light clothing without foot wears. The height was measured in meters using the same scale. The body mass index (BMI) defined as weight in kilogram divided by the square of patient's height in meters was calculated. The waist circumference in centimetres before breakfast was measured in the horizontal plane at the level of the natural waist line taken to be at the umbilicus using a non-stretchable tape, the hip circumference in centimetres was also measured in the horizontal plane at the level of maximum diameter and waist- hip ratio calculated.

All subjects were instructed to observe an overnight fast for 10-12 hours before blood sample collection. Each subject had their serum creatinine measured and GFR was estimated using the Cockcroft-Gault formula. Fasting blood glucose (FBG) and fasting serum lipids were also measured.

Measurement of total Cholesterol and HDL-C was done using the Cholesterol Oxidase method, triglycerides using the Glycerol phosphate oxidase reaction and LDL-C was calculated using the Frieldwald formula - LDL (mg/dl) = TC – (HDL + TG/5).

FBG was measured using an Accucheck glucometer and strips.

The controls were also assessed for the above-mentioned parameters.

Data obtained were entered into SPSS version 17 and analyzed. A univariate analysis describing the baseline socio-demographic characteristics of participants and prevalence rates were done. Continuous variables were presented as means and standard deviation (SD). Student's t test, cross tabulation, and Chi square test were used as appropriate. The confidence interval was set at 95% limit, with the level of significance, $p < 0.05$.

RESULTS

A hundred and sixty chronic kidney disease patients and an equal number of healthy adult controls were studied. The mean age of the study population was 44.5 ± 15.7 years for cases and 41.7 ± 14.6 years for controls. This difference in mean age was not significant (p=0.11). There were more males 101 (63.1%) than females.

The clinical and biochemical characteristics of the study population are shown in table 1. Mean BMI was less in cases (23.80 ± 4.78) when compared to controls (26.78±3.57) and these proportions were significantly different (p=0.01). The waist: hip ratio (WHR) of 0.93 ± 0.06 in cases was less than the ratio of 0.97±0.50 in controls, this difference was however not significantly different (*p*= 0.347). Mean FBG level was 105.88 ± 32.27mg/dl and 92.35 ± 9.86mg/dl in cases and controls respectively, this difference was statistically significant. (p= 0.01). Diabetes mellitus accounted for aetiology of CKD in 33 (20.6%) cases after chronic glomerulonephritis and hypertension which accounted for CKD in 57 (35.6%) and 53 (33.1%) cases respectively.

The mean values of the lipid components were consistently and significantly higher in cases compared to controls with the exception of HDL-cholesterol. Mean total cholesterol was 170.9 ± 47.8mg/dl in cases and 158.4 ± 48.9mg/dl in controls (*p*= 0.01). Mean HDL-cholesterol was significantly lower in cases compared to controls (33.7 ± 12.1 mg/dl in cases versus 69.0 ± 25.9 mg/dl in controls, *p*= 0.01). Mean LDL- cholesterol was 106.6 ± 41.1mg/dl and mean triglycerides was 153.3 ± 44.5 mg/dl in cases compared to 90.3 ± 49.5 mg/dl and 99.2 ± 49.9 mg/dl in controls respectively. These differences were also statistically significant (*p*=0.01) for both parameters.

Mean eGFR of 25.4 ± 18.01 mls/min in cases was significantly lower than mean eGFR of 94.0 ± 16.54mls/min in controls (*p*=0.01).

The prevalence of the different components of dyslipidemia is shown in table 2. Dyslipidemia was significantly more present in cases compared to controls (94.4% in cases, 46.9% in controls *p*= 0.01).

A reduction in HDL-C was the most prevalent dyslipidemia encountered amongst the cases and was present in 117 (73.1%) cases as against 18 (11.2%) in controls, while elevated triglyceride was present in 106 (66.2%) cases compared to 43 (26.9%) in controls; these differences were both statistically significant (*p*=0.01 respectively). Elevated total cholesterol(TC) was seen in

41 (25.6%) of cases and elevated LDL-cholesterol in 40 (25%) of cases in comparism with that of controls in which TC and LDL-C were elevated in 29(18.1%) and 26(16.2%) respectively. This however was not statistically significantly different; elevated triglyceride was the commonest form of dyslipidemia amongst controls seen in 26.9%.

The prevalence of dyslipidemia in the different stages of CKD I, II, III, IV and V were 33.3%, 66.7%, 94.2%, 97.5% and 95.2% respectively. Dyslipidemia was most prevalent in CKD stage 4 where 97.5% of cases had dyslipidemia. CKD stage 1 had the least prevalence of dyslipidemia, a reduced HDL-C which was most prevalent in cases was also the only lipid abnormality seen in this stage. Using the Spearman rank order a moderate negative correlation was seen between the estimated GFR and the prevalence of dyslipidemia. This correlation was statistically significant (r_s (8) = -.430, p =.000) this is shown in table 3.

There was no statistically significant difference in the prevalence of dyslipidemia between genders (p =0.821) as seen in table 4, neither was the difference in occurrence of dyslipidemia among the different aetiologies of CKD statistically significant (p = 0.832).

Table 1: Clinical and Biochemical Characteristics of Study Population.

VARIABLE	CASES (n=160) Mean±SD	CONTROLS (n=160) Mean±SD	*t*-value	*p*-value
Age (years)	44.5±15.7	41.7±14.5		0.019
BMI (kg/m2)	23.80 ± 4.78	26.78 ± 3.57	6.319	0.01
WAIST-HIP RATIO	0.93 ± 0.06	0.97 ± 0.50	0.941	0.347
FASTING BLOOD GLUCOSE (mg/dl)	105.88 ± 32.27	92.35 ± 9.86	-5.071	0.01
ESTIMATED GFR (mls/min)	25.4 ±18.01	94.0±16.54	-34.73	0.01
TOTAL CHOL(mg/dl)	170.90 ± 47.84	158.42 ± 48.89	-2.303	0.022
HDL-CHOLESTEROL(mg/dl)	33.69 ± 12.09	69.04 ± 25.97	15.610	0.01
LDL-CHOLESTEROL((mg/dl))	106.56 ± 41.26	90.39 ± 49.62	-3.170	0.01
TRIGLYCERIDES (mg/dl)	153.29± 44.52	99.21 ± 59.69	-9.187	0.01

BMI – Body Mass Index, PCV- Packed Cell Volume, Total CHOL – Total Cholesterol, GFR – Glomerular filteration rate.

Table 2: Prevalence of Dyslipidemia And Abnormalities In The Lipid Profile Components Amongst Study Population.

PARAMETERS	CASES n (%)	CONTROLS n (%)	p-value
PRESENCE OF DYSLIPIDEMIA	151(94.4)	75 (46.9)	0.01
ELEVATED TOTAL CHOLESTEROL	41(25.6)	29(18.1)	0.105
REDUCED HDL – C	117(73.1)	18(11.2)	0.01
ELEVATED LDL – C	40(25)	26(16.2)	0.053
ELEVATED TRIGLYCERIDE	106(66.2)	43(26.9)	0.01

HDL-C = High density lipoprotein cholesterol, LDL-C- Low density lipoprotein cholesterol

Table 3: **Prevalence of Dyslipidemia In the Different Stages of CKD.**

ESTIMATED GFR(mls/min)	NO OF CASES IN EACH STAGE	PREVALENCE OF DYSLIPIDEMIA n(%)
>90	3	1(33.3)
60 - 89	3	2(66.7)
30 -59	52	49(94.2)
15-29	81	80(97.5)
<15	21	20(95.2)

rho = -.430, p<0.05

Table 4. Prevalence of Dyslipidemia amongst gender.

GENDER	DYSLIPIDEMIC n (%)	NON-DYSLIPIDEMIC n(%)
Male	95(94.0)	6(6.0)
Female	56(95.4)	3(4.6)

Df =1, p = 0.821

DISCUSSION

The mean age of cases in this study was 44.49±15.75years giving an age range that suggests that most of the CKD patients were in their prime working age. This is in keeping with findings of previous studies.[16]

There were more males than females in a ratio 1.7: 1, this also is in agreement with the findings of a study in South western Nigeria[16] in which the male to female ratio of CKD was 1.42:1. A plausible explanation for this could be the higher prevalence of risk factors for CKD in males. The commonest etiology of CKD was hypertension, chronic glomerulonephritis and DM accounting for 35.6%, 33.1% and 20.6% respectively, this is in keeping with a study carried out at Port-Harcourt in which the same etiological factors took the lead although at lesser prevalences.[17]

Our findings also agree with the documented evidence that dyslipidemia is highly prevalent in CKD.[14,15,16] Using the NCEP ATP III[11] cut off values for hypercholesterolemia, 94.4% of the study population had dyslipidemia which was higher than that observed in controls 46.9% (p<0.01).

HDL-C was noted to be the earliest affected component of the lipid profile accounting solely for the dyslipidemia observed amongst cases in CKD stage 1. In stage 1, 33.3% of cases had dyslipidemia and this was reduced HDL-C. Elevated Tg was also noticed in the earlier stages of CKD; CKD stage 2 with a prevalence as high as 66.7% these are in keeping with findings from earlier documented studies.[18]

The prevalence of dyslipidemia in the different components of the lipid profile in this study showed that 73.1% had reduced HDL-C, 66.2% had hypertriglyceridemia, 25.6% had hypercholesterolemia, and 25% had elevated LDL-C. These prevalence values were higher than those observed in the control group with 11.2% having reduced HDL-C, 26.9% hypertriglyceridemia, 18.1% hypercholesterolemia, and 16.2% had elevated LDL-C. This however differs slightly from that reported by Chijioke et al in Ilorin in which 90.8% had hypercholesterolemia, 81.7% had hypertriglyceridemia, and 75.8% reduced HDL-C,[14] this may have been due to differences in studied population as all stages of CKD was evaluated but is comparable to a study done in Maiduguri[15] where 63.5% had reduced HDL-C, 68.3% had hypertriglyceridemia, 22.2% had hypercholesterolemia, and 17.5% had elevated LDL-C.

Results of this study also differed from that reported by Khalid *et al* in which elevated Tg had a prevalence of 46%, reduced HDL-C 16% and elevated total cholesterol 16%, however the mean values of the different components were lower in this study (153.29 ± 44.52mg/dl, 33.69 ± 12.09 mg/dl and 170.90 ± 47.84 mg/dl for triglyceride, HDL-C and total cholesterol respectively) when compared to that reported by Khalid *et al* in which mean values were 225.87 mg/dl, 30.62 mg/dl and 264.5 mg/dl for triglyceride, HDL-C and total cholesterol respectively.[18] This may also be due to the fact that the study by Khalid *et al* was carried out in a smaller population – 50 CKD patients who were not on dialysis.

Reduced HDL-C levels and increased triglyceride rich lipoproteins are the major lipid abnormalities. Reductions in plasma concentrations of apoprotein (Apo) A-I and Apo A-II are thought to play a large role in the low HDL cholesterol (HDL-C) levels. ApoA-I and ApoA-II are mandatory components of the HDL particle. Patients with CKD have been shown to have reduced genetic expression of these apoproteins at sites of HDL production in the liver. Another factor contributing to low HDL-C levels is the profound inflammation present in these patients. Chronic inflammation results in decreased albumin levels. Albumin serves as a carrier of free cholesterol from the peripheral tissues to HDL, and a reduction in albumin may contribute to reduced HDL-C levels. The increased plasma triglyceride levels can be explained in part by significant increases in plasma ApoC-III levels. Apoprotein C-III is a potent inhibitor of the enzyme lipoprotein lipase, which is responsible for the degradation of triglyceride-rich particles.[19]

A plasma concentration of LDL-C is usually normal and only occasionally elevated in ESRD patients. Mean estimated GFR was lower in cases than controls, 26.26 ± 18.01ml/min as against 96.41 ± 16.54 ml/min as is expected (p<0.01),

CONCLUSION

In conclusion, this study had shown that dyslipidemia is highly prevalent in our CKD patients and their prevalence increased with severity of CKD. The earliest and commonly affected components of the lipid profile were HDL-C and triglycerides.

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