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Dyslipidemia: Pattern in Chronic Kidney Disease Patients in a Teaching Hospital in Nigeria

Olokor Afeaje Benedicta and Unuigbe Evelyn I

Nephrology Unit, Department of Internal Medicine, University of Benin, Benin City, Nigeria

ABSTRACT

Background: Chronic kidney disease (CKD) is a common disease with a rising incidence, driven mainly by ageing, increased survival from cancers and major cardiovascular accidents. It is associated with numerous complications, one of which is dyslipidaemia, a traditional cardiovascular risk factor associated with increased cardiovascular mortality. The spectrum of dyslipidaemia in patients with CKD is distinct from that in the general population. This was a hospital based cross sectional case study aimed at determining the pattern of dyslipidaemia among chronic kidney disease patients and comparing the patterns in haemodialysing and dialysis-naïve patients.

Methods: One hundred and sixty patients were recruited for the study. All subjects had their renal functions assessed using serum creatinine and the Cockcroft-Gault formula to calculate glomerular filtration rates. They also had their lipid components assessed. Dyslipidaemia was defined using the National Cholesterol Education Program/Adult Treatment Panel III criteria.

Result: A hundred and sixty CKD patients were studied; of these113 (70.6%) were patients on haemodialysis and 47 (29.4%) were dialysis naive. The commonest dyslipidaemia encountered was a reduction in high density lipoprotein – cholesterol and was present in 117 (73.1%) CKD cases. The commonest patterns of dyslipidaemia were reduced HDL-C/ elevated triglyceride combination, reduced HDL-C alone and a combination of all 4 components (elevated total cholesterol /reduced HDL-C /elevated LDL-C /elevated triglyceride) with prevalences of 31.2 %, 22.5% and 12.5% respectively. Dyslipidaemia was common in both dialyzing and dialysis- naïve patients; it was present in 109 (96.3%) of haemodialysing patients as against 42 (89.4%) in non-dialysing patients.

Conclusion: A reduction in HDL- Cholesterol is the commonest dyslipidaemia in CKD even as early as CKD stage 1 and the commonest pattern is HDL-C/ Triglyceride combination. There is no significant difference in dyslipidemic patterns in haemodialysing and dialysis naïve patients.

Keywords: *Chronic kidney disease, pattern, Dyslipidaemia, Dialysis.*

INTRODUCTION

Chronic kidney disease (CKD) is a common disease with a rising incidence mainly driven by ageing, increased survival from cancers and major cardiovascular accidents, [1] as well as increasing prevalence of diabetes, hypertension and obesity. It is associated with numerous complications, one of which is dyslipidaemia. Dyslipidaemia, a traditional cardiovascular risk factor is associated with increased mortality risk in CKD patients.

Corresponding Author: **Dr. Olokor Afeaje Benedicta,** Department of Internal Medicine, University of Benin Teaching Hospital, P.M.B 1111, Benin City, Edo state, Nigeria. *E-mail:* sweetafe@yahoo.com

The World Health Organisation (WHO) defines dyslipidaemia as serum triglyceride (TG) >150-400 mg/dL (1.7-4.5 mmol/L), total cholesterol (TC) > 200 mg/dL (>5.2 mmol/L), low density lipoprotein (LDL) cholesterol > 135 mg/dL (>3.5 mmol/L), high density lipoprotein (HDL) cholesterol < 35 mg/dL (<0.9 mmol/L) in men or < 40 mg/dl (<1.0 mmol/L) in women and a ratio of total cholesterol to HDL-cholesterol >5 [2]. The National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III) defines dyslipidemia as total cholesterol >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) [3].

The spectrum of dyslipidemiain patients with CKD is different from that in the general population [1, 4]. This difference involves all classes of lipoproteins and occurs in all stages of CKD, including mild disease, patients without supportive treatment for CKD, and in patients on dialysis or after kidney transplantation [1, 5].

Plasma lipids and lipoprotein profiles in CKD are altered quantitatively, qualitatively, structurally and functionally [6] and this is usually influenced by progressive renal loss. With a decline in renal function, the lipid profile is altered initially in terms of reduced HDL which is due to a reduction in the plasma levels of ApoAI and ApoAII as well as primary proteins forming HDL. There is also a higher concentration of Apo-B due to lecithin-cholesterol-acyltransferase (LCAT) enzyme deficiency and moderately increased triglycerides (TG) serum concentrations, due to impaired clearance. [6-9]. The lipid profile in CKD patients varies widely depending on the level of kidney function and the degree of proteinuria [10]. Before end-stage renal disease (ESRD) sets in, CKD patients frequently have elevated TC and LDL-C levels, however as CKD advances to ESRD the prevalence of elevated TC and LDL-C levels decrease [10]. In dialysis patients LDL-C levels generally are lower than in the general population and half of all dialysis patients have either LDL-C levels over 100mg/dl (2.6mmol/L) or non-HDL-C levels over 130mg/dl (3.4mmol/L) [10]. HDL-C often is low in haemodialysis patients while triglycerides generally are moderately elevated. The classic lipid profile of late stage CKD includes hypertriglyceridemia, low HDL-C and low or normal LDL-C, a profile similar to that often seen in patients with diabetes and the metabolic syndrome [10].

There are no reports, to our knowledge, on the pattern of dyslipidaemia in CKD patients in our immediate geo-political area. This study, therefore, was aimed at determining the pattern of dyslipidaemia among CKD patients and also to compare the patterns in dialysing and dialysis naïve patients.

MATERIALS AND METHODS

This was a hospital-based cross sectional analytical study carried out in the University of Benin Teaching Hospital (UBTH). Patients with CKD were consecutively recruited for the study at presentation in the Nephrology, Dialysis, Accident and Emergency Units of UBTH. Informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Committee of University of Benin Teaching Hospital.

Patients were stratified based on the stage of CKD using the NKF/KDOQI staging[4]. One hundred and sixty CKD patients who presented at the Nephrology Clinic/Dialysis Unit/Accident and Emergency Unit of UBTH were recruited. They included both newly or previously diagnosed CKD patients who were either on conservative management or haemodialysis as the mode of renal replacement therapy (RRT) by way of haemodialysis. Controls in a ratio of 1: 1 were recruited. The controls were not known CKD patients and were neither hypertensive nor diabetic.

A researcher administered questionnaire was used to collect data from subjects. 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 glomerular filtration rate (GFR) was estimated using the Cockcroft-Gault formula.

Total serum cholesterol and HDL-C were measured using the cholesterol oxidase method, while serum triglycerides was measured using the Glycerol phosphate oxidase reaction.LDL- cholesterol was calculated using the Frieldwald formula ofLDL (mg/dl) = TC – (HDL + TG/5) [11].

Data obtained were entered into SPSS version 17 and analysed. Data are presented as means and standard deviation (SD). Student's t test and analysis of variance were used to determine the difference between the means and p value < 0.05 was considered significant.

RESULTS

Age and biochemical characteristics

CKD patients were aged between 18 to 80 years with a mean age of 44.5 ± 15.8 years while the controls had an age range of 22 to 70 years with a mean age of 41.8 ± 14.7 years (p = 0.109). The biochemical characteristics of CKD cases and controls are shown in table 1. The mean estimated glomerular filtration rate (eGFR) of cases and controls were 29.3 ± 18.0 mls / min and 94.0 ± 16.5mls/min respectively (p < 0.01). Mean total cholesterol was significantly higher in cases compared to controls (170.9 ± 47.8mg/dL versus 158.4 ± 48.9mg/dL respectively, p = 0.022). Mean HDL-Cholesterol, LDL-Cholesterol and triglyceride were 32.6 ± 8.7 mg/dl, 106.6 ± 41.3 mg/dl and 153.2 ± 44.5mg/dl for cases and 69.0 ± 25.9, 90.3 ± 49.5 and 99.2 ± 49.9 for controls respectively; all these differences were significant (p < 0.01 for each of the parameters).

Table 1: Biochemical characteristics of cases and controls

BIOCHEMICAL PARAMETERS	CASES MEAN±SD	CONTROLS MEAN ± SD	P value
eGFR (mls/min)	29.3 ± 18.0	94.0 ± 16.5	<0.01
T CHOL (mg/dl)	170.9 ± 47.8	158.4 ± 48.9	0.022
HDL-C(mg/dl)	32.6 ± 8.7	69.0 ± 25.9	<0.01
LDL-C(mg/dl)	106.6 ± 41.3	90.3 ± 49.5	<0.01
TRIGLYCERIDE (mg/dl)	153.2 ± 44.5	99.2 ± 49.9	<0.01

BMI = Body mass index, GFR = Glomerular filtration rate, T CHOL = Total Cholesterol, HDL-C = High density lipoprotein cholesterol, LDL-C= Low density lipoprotein cholesterol

Table 2: Frequency of pattern of dyslipidemia in cases

DYSLIPIDEMIA	CASES n(%)	CONTROLS n (%)
↓HDL-C / ↑TRIGLYCERIDE	50(33.1)	1(1.2)
↓HDL-C ONLY	36(23.8)	15(18.5)
↑TOTAL CHOLESTEROL / ↓HDL-C / ↑LDL-C / ↑TRIGLYCERIDE	20(13.2)	0(0)
↑TRIGLYCERIDES	16(10.6)	27(33.3)
↑TOTAL CHOLESTEROL / ↑TRIGLYCERIDES / ↑LDL-C	8(5.3)	3(3.7)
↑TOTAL CHOLESTEROL / ↑TRIGLYCERIDES	6(4.0)	8(9.9)
↑TOTAL CHOLESTEROL / ↓HDL-C / ↑LDL-C	5(3.3)	1(1.2)
↓HDL-C / ↑LDL-C / ↑TRIGLYCERIDES	4(2.6)	1(1.2)
↑TOTAL CHOLESTEROL / ↓HDL-C / ↑TRIGLYCERIDE	2(1.3)	0(0)
↑LDL-C / ↓HDL-C	2(1.3)	0(0)
↑TOTAL CHOLESTEROL	1(0.7)	4(4.9)
↑LDL-C / ↑TRIGLYCERIDES	1(0.7)	5(6.2)

df = 14, p < 0.001 (with Yate's correction)
HDL-C = High density lipoprotein cholesterol, LDL-C= Low density lipoprotein cholesterol

Frequency and pattern of dyslipidaemia in cases and controls

The frequency and pattern of dyslipidaemia in cases and controls are shown in table 2. A reduction in HDL-C/ elevated TG and a reduced HDL-C only dyslipidaemia were the commonest pattern of dyslipidaemia in CKD patients accounting for 33.1% and 23.8% prevalence respectively whereas an elevated TG only dyslipidaemia was the commonest with a prevalence of 3.3%, followed closely by a reduction in HDL-C only dyslipidaemia having a prevalence of 18.5%. A combination of all four components (**'!**total cholesterol/**"'!**HDL-C/**'!**LDL-C/ **'!**triglyceride) was present in 13.2% of cases but

Table 3: LIPID components in the different CKD stages

CKD STAGES	HDL-C	TC MEAN ± SD	LDL-C	Tg
I	39.7 ± 0.6	166.4 ± 14.2	107.1 ± 17.8	103.2 ± 30.4
II	41.8 ± 8.4	185.4 ± 39.5	111.4 ± 33.2	161.0 ± 22.0
III	31.9 ± 9.4	173.9 ± 30.5	109.8 ± 27.9	152.8 ± 42.8
IV	32.8 ± 8.6	168.3 ± 59.6	104.1 ± 50.7	152.0 ± 48.4
V	31.5 ± 8.2	172.0 ± 36.6	107.4 ±32.6	165.5 ± 31.9

df = 11, p = 0.867

HDL-C = High density lipoprotein-cholesterol, LDL-C= Low density lipoprotein cholesterol, TC- Total Cholesterol.

Table 4: Pattern of dyslipidemia in the different stages of CKD

DYSLIPIDEMIA PATTERNS	PREVALENCE IN CKD STAGES 1 n (%)	2 n (%)	3 n (%)	4 n (%)	5 n (%)
↓HDL-C ONLY	1(33.3)	0(0)	10(19.2)	23(28.4)	2(9.5)
↓HDL-C/↑TRIGLYCERIDE	0(0)	1(33.3)	19(36.5)	23(28.4)	7(33.3)
↑TOTAL CHOLESTEROL /↓HDL-C / ↑LDL-C / ↑TRIGLYCERIDE	0(0)	0(0)	5(9.6)	12(4.8)	3(14.3)
↑TRIGLYCERIDES	0(0)	0(0)	4(7.7)	6(7.4)	6(28.6)
↑TOTAL CHOLESTEROL/ ↑TRIGLYCERIDES/↑LDL-C	0(0)	1(33.3)	2(3.8)	5(6.2)	0(0)
↑TOTAL CHOLESTEROL/ ↑TRIGLYCERIDES	0(0)	0	2(3.8)	4(4.9)	0(0)
↑TOTAL CHOLESTEROL/ ↓HDL-C / ↑LDL-C	0(0)	0	2(3.8)	3(3.7)	0(0)
↓HDL-C / ↑LDL-C / ↑TRIGLYCERIDES	0(0)	0	2(3.8)	1(1.2)	1(4.8)
↑TOTAL CHOLESTEROL/ ↓HDL-C / ↑TRIGLYCERIDE	0(0)	0	1(1.9)	0(0)	1(4.8)
↑LDL-C / ↓HDL-C	0(0)	0	2(3.8)	0(0)	0(0)
↑TOTAL CHOLESTEROL	0(0)	0	0(0)	1(1.2)	0(0)
↑LDL-C / ↑TRIGLYCERIDES	0(0)	0	0(0)	1(1.2)	0(0)

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

totally absent in controls. The patterns of dyslipidaemia that were least prevalent were elevated total cholesterol and LDL-C/triglycerides with a rate of 0.7% each.

The mean values of the lipid components of cases in the different CKD stages did not seem to vary significantly (p=0.867), these are shown in table 3, with the pattern of dyslipidaemia in the different stages seen in table 4.

present in 109 (96.3%) of dialyzing patients as against 42 (89.4%) in non-dialyzing patients. This difference was however not statistically significant (p<0.867) . A reduced HDL-C/**'!**triglyceride and reduced HDL-C were the frequently encountered pattern of dyslipidaemia in both groups while reduced total cholesterol and increased LDL/triglyceride was encountered in 0.9% of the dialysis group and none in the dialysis-naïve group (table 5). Reduced HDL-

Table 5: Frequency of pattern of dyslipidemia in cases

Dyslipidemia Pattern	Dialysis naïven (%)	Dialysing Casesn (%)
↓HDL-C / ↑TRIGLYCERIDE	13(31.0)	37 (33.9)
↓HDL-C ONLY	12(28.6)	24 (22.0)
↑TOTAL CHOLESTEROL /↓HDL-C / ↑LDL-C / ↑TRIGLYCERIDE	3 (7.1)	17 (5.6)
↑TRIGLYCERIDES	4 (9.5)	12 (11.0)
↑TOTAL CHOLESTEROL / ↑TRIGLYCERIDES /↑LDL-C	3 (7.1)	5 (4.6)
↑TOTAL CHOLESTEROL / ↑TRIGLYCERIDES	3 (7.1)	3 (2.8)
↑TOTAL CHOLESTEROL / ↓HDL-C / ↑LDL-C	1 (2.4)	4 (3.7)
↓HDL-C /↑LDL-C / ↑TRIGLYCERIDES	1(2.4)	3 (2.8)
↑TOTAL CHOLESTEROL /↓HDL-C / ↑TRIGLYCERIDE	1(2.4)	1 (0.9)
↑LDL-C / ↓HDL-C	1(2.4)	1 (0.9)
↑TOTAL CHOLESTEROL	0(0)	1 (0.9)
↑LDL-C / ↑TRIGLYCERIDES	0(0)	1 (0.9)
Total	**42**	**109**

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

Dyslipidaemia in dialysis-naïve and haemodialysis subjects

There were 113 (70.6%) CKD subjects on HD and 47 (29,4%) were dialysis-naïve. The frequency & pattern of dyslipidaemia in the two groups are shown in tables 5 and 6 respectively. Dyslipidaemia was

C was the commonest abnormality in the lipid profile encountered amongst both dialyzing and non-dialyzing cases and was present in 86 (76.1%) dialyzing cases as against 31 (66%) in non-dialyzing cases (table 6). This difference was not statistically significant (p=0.187). Elevated triglyceride was the next most

Table 6: Specific LIPID profile abnormalities in dialysing ad non-dialysing chronic kidney diseases cases

Lipid Abnormalities	Dialyzing n(%)	Non-Dialyzing n(%)	p-value
Presence of Dyslipidemia	109(96.5)	42(89.4)	0.867
Elevated Total Cholesterol	31(27.4)	10(21.3)	0.416
Reduced HDL – C	86(76.1)	31(66)	0.187
Elevated LDL – C	32(28.3)	8(17)	0.133
Elevated TRIGLYCERIDE	78(69)	28(59.6)	0.249

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

common dyslipidaemia noted in 78 (69%) dialyzing cases and 28 (59.6%) in non-dialyzing cases; the difference was not statistically significant either (p = 0.249). Elevated total cholesterol and LDL-cholesterol were present in 41 (25.6%) and 40 (25%) respectively in dialyzing cases and 29(18.1%) and 26(16.2%) in non-dialyzing cases. This also was not statistically significantly different.

Thus, the pattern of dyslipidaemia in the dialysing and dialysis-naïve cases was similar. HDL-C/triglyceride combination and reduced HDL-C were the most prevalent pattern of dyslipidaemia in both groups.

DISCUSSION

Dyslipidaemia is a potentially modifiable traditional risk factor for cardiovascular disease in CKD patients. It contributes to cardiovascular mortality in them and occurs due to altered lipid metabolism which characterises CKD, seen even in the early stages. The results of this study show significant differences in the mean values of each lipid component when compared between the cases and controls. The mean values of the different components among the cases 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[12]. This difference may be due to sample size of both studies; Khalid *et al* studied 50 CKD patients who were strictly dialysis-naïve while this study took into consideration 150 dialysing and dialysis-naïve patients.

In this study, the most prevalent pattern of dyslipidaemia in CKD patients was the combination of reduced HDL-C and elevated triglycerides with a prevalence of 31.2%, about a third of the cases. This trend is observed in both the haemodialysis (HD) patients and dialysis naïve patients as the commonest in both groups. This finding is in keeping with that reported by Attman et al in which the most prevalent dyslipidaemia combinations were a reduced HDL-C and elevated triglycerides[13]. This pattern is due to the fact that dysregulation in lipoprotein metabolism in CKD is first expressed as a reduction in Apo lipoprotein I and II which usually enhance HDL-C production resulting in low levels; accompanied by a defect in breakdown and clearance of triglyceride rich apoB containing lipoproteins [14, 15]. The next most common was reduced HDL-C alone occurring in 23.8%. Dyslipidaemia affecting all the components of the lipid profile followed in line with a prevalence of 13.3%. Other combinations contributed to the minority with elevated total cholesterol and the combination of elevated LDL-C and triglycerides accounting for just 0.7% each.

In the HD and dialysis-naïve patients, the prevalence of a reduced HDL-C and hypertriglyceridemia were 76% and 69%; and 66% and 59.6% respectively; these rates were high and similar in the two groups but were not statistically significant. The rates are at variance to the report of Biara*et al* in which the prevalence of a reduced HDL-C and hypertriglyceridemia in dialysing and haemodialysis-naïve patients were 60% and 90%; and 10% and 80% respectively [16].

The results of this study agree with the reports that a reduction in HDL-C is the earliest lipid profile abnormality seen in CKD patients occurring as early as CKD stage 1. Using the NCEP ATP III[3] cut off values for hypercholesterolemia; reduced HDL-C was the earliest affected component of the lipid profile accounting solely for the dyslipidaemia observed amongst cases in CKD stage 1. In stage 1, 33.3% of cases had dyslipidaemia and this was reduced HDL-C. This early lipid abnormality is due to a substantial dysregulation of the synthesis and activity of HDL and metabolism of Tg rich apolipoprotein (apo) B containing lipoproteins seen in CKD [12].

CONCLUSION

Dyslipidaemia is prevalent in CKD patients and all the lipid components are affected. The earliest affected component of the lipid profile is HDL-C. The commonest lipid abnormality pattern is HDL-C / triglycerides. There were no significant differences in the pattern of dyslipidaemia amongst dialysing and dialysis-naïve patients. Early screening for lipid abnormalities in CKD will be beneficial in reducing the risk of cardiovascular in them.

REFERENCES

1. Coresh J, Byrd-Holt D, Astor BC , Briggs JP, Eggers PW, Lacher DA *et al*. Chronic kidney disease awareness, prevalence, and trends among US adults, 1999 to 2000. J. Am Soc Nephrol. 2005; 16: 180-188.
2. Report of WHO Scientific Group; Cardiovascular disease risk factors; new areas for research. WHO Technical Report Series. No 841. WHO Geneva 1994.
3. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285-286.
4. Hassan T. Inferential statistics. *In:* Bankole MA (Ed) Handbook of Research Methods in Medicine. National Postgraduate Medical College of Nigeria. 1991; 171-211.
5. Greenwald I. The chemistry of Jaffe's reaction for creatinine II. The effect of substitution in the creatinine molecule and a possible formula for the red tautomer. J. Am. Chem. Soc., 1925, 47 (5):1443–1448.
6. Montague T and Murphy B. Lipid management in chronic kidney disease, haemodialysis, and transplantation. EndocrinolMetabClin North Am.2009; 38: 223–234.
7. Wanner C and Quaschning T. Dyslipidaemia and renal disease: pathogenesis and clinical consequences. CurrOpinNephrol Hypertens. 2001; 10: 195–201.
8. Attman PO and Samuelsson O. Dyslipidaemia of kidney disease. CurrOpinLipidol. 2009; 20: 293–299.
9. Roberto Scarpioni, Marco Ricardi, Vittorio Albertazzi and Luigi MelfaTreatment of dyslipidaemia in chronic kidney disease: Effectiveness and safety of statins. World J Nephrol 2012 December 6; 1(6): 184-194.
10. Weiner DE and Sarnak MJ. Managing Dyslipidaemia in CKD. J Gen Intern Med 2004; 19 (10): 1045-1052.
11. Bergmeyer H and Grassl M, editors. Methods of enzymatic analysis. Metabolites 3: Lipids, amino acids and related compounds, 3rd edition. Weinheim: Wiley-VCH; 199
12. Khalid M, Masood J, Muhammad A, Muhammad N and Abdul Q: Pattern of Dyslipidaemia in patients with CRF. Prof. Med J 2006;13 (1): 79-84.
13. Attman PO, Samuelsson O, Johansson AC, Moberly JB and Alaupovic P. Dialysis modalities and dyslipidaemia. Kidney Int. Suppl 2003; 63: S110-S112.
14. Victor B. Dyslipidaemia in Chronic Renal Failure. International Federation of Clinical Chemistry and Laboratory Medicine Annual Report 2009 1,2.
15. Attman PO, Knight-Gibson C, Tavella M, Samuelsson O and Alaupovic P. The compositional abnormalities of lipoproteins in diabetic renal failure. Nephrol Dial. Transplant. 1998;13: 2833-2841.
16. Biara D, Joshi V, Shah T, Gandha K and Modi N. Impact of hemodialysis on lipid profile among chronic renal failure patients. Int. J Sci, Research pub, 2013 (3) 7;2250-3135