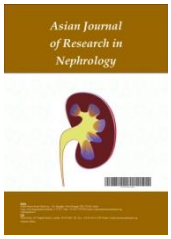

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Pattern of Dyslipidaemia among Patients with Diabetic Kidney Disease, in Northeastern Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Diabetic Diabetes mellitus is a chronic metabolic disorder of carbohydrates, lipids and protein resulting from absolute or relative lack of insulin. The myriad of metabolic derangements lead to development of complications such as DKD. Insulin deficiency is the common pathway in the development of dyslipidemia and chronic hyperglycemia. These two factors appear to combine to cause DKD. Dyslipidemia and its characteristics in T2DM patients have not been studied in northeastern Nigeria. This study describes the prevalence and pattern of dyslipidemia among DKD patients and compared with T2DM patients without kidney disease.
Materials and Methods: The study population consisted of adult T2DM patients recruited consecutively from the diabetes clinic of the University of Maiduguri Teaching Hospital, Maiduguri between the periods January to December 2021. Socio-demographic variables including age, sex, weight, BMI as well aslaboratory parameters were obtained from each study participant. Glomerular filtration wasestimated using the CKD-EPI equation and serum lipids were classified according to the WHO recommendation.

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Results: Out of318 study subjects recruited from the Diabetic clinic of University of Maiduguri Teaching Hospital; 194(61%) were females and 124(39%) were males. The mean age of the study population was 49.64±11.40 years and a mean duration of DM of 7.00±6.45 years. Mean HbA1C and Fasting blood glucose of the study population were 9.67±8.39% and 11.06±8.31mmol/L respectively. There were 126(39.6%) study participants who had DKD and the prevalence of hypercholesterolemia among them was 50% (total cholesterol > 5.2mmol/L) compared with 35.4% among study participants without DKD.

Conclusion: The present study showed that lipid abnormalities are common among DKD patients in northeastern Nigeria. Dyslipidemia is a known risk factor for cardiovascular disease and kidney disease progression. Identification and aggressive management of these disorders will help in slowing down the progression chronic kidney disease and prevention of other cardiovascular diseases.

Keywords: Dyslipidaemia; pattern; diabetic kidney disease; Northeastern Nigeria.

1. INTRODUCTION

Diabetes mellitus is a chronic disorder of carbohydrate, protein and lipid metabolism that is characterized by chronic hyperglycaemia and often leading to chronic complications such as retinopathy, nephropathy and cardiovascular disease [1]. Diabetic kidney disease is a leading cause of morbidity and mortality among patients with diabetes mellitus. It affects about 40% of patients with diabetes mellitus world-wide and it is the leading cause of end stage kidney disease in USA [1-4]. Azeez et al in has found a pooled prevalence of DKD to be 28% in Nigeria [5].Despite improvements in the management of diabetes mellitus, the prevalence of DKD has shown only modest decline compared to other long term diabetic complications in the United States in the period 1990-2010 [6]. Several factors such as duration of diabetes, age and presence of other complications have been shown to be associated with development of diabetic kidney disease [2]. Despite increasing knowledge about the pathogenesis and management of DKD, these poor outcomes suggest that the mechanisms underlying development and progression of DKD are still not fully understood. It has been shown that genetic factors, hyperglycemia and dyslipidemia are associated with DKD progression [6]. Abnormalities of lipid metabolism are inherently linked to hyperglycaemia in diabetes mellitus and increased VLDL, LDL and TG levels as well as decreased HDL are commonly seen [7,8]. The role of lipid nephrotoxicity in the pathogenesis of diabetic nephropathy was recognized by Kimmestiel and Wilson since 1930's [9]. Experimental studies conducted in diabetic rats showed that hypercholesterolemia worsens albuminuria, attracts macrophages into the glomeruli and resulted in extracellular matrix accumulation [10]. Triglyceride rich lipoproteins (TGRL) receptors have been expressed in podocytes, and mesangial cells stimulate the production of pro-inflammatory cytokines such as TNF-α, TGF-β and IL-6 [11]. This ultimately results in extracellular matrix accumulation and progressive interstitial fibrosis. In low and middle income countries such as Nigeria, many patients with DM are unable to pay for their treatment. This makes identifying factors such as dyslipidemia that promote progression of DKD more cost effective. In northeastern Nigeria, although the prevalence of DKD is similar to those reported from developed countries, DKD contribution to the burden of ESRD in the region is still evolving. The pattern of dyslipidemia among the diabetic patients with kidney disease has not been studied in this region. This study is aimed at describing the pattern of dyslipidemia among patients with DKD in northeastern Nigeria.

2. MATERIALS AND METHODS

This was a cross sectional prospective hospital-based study conducted at the Diabetes clinic of the University of Maiduguri Teaching Hospital, Maiduguri, northeastern Nigeria. Three hundred and eighteen (318) consecutive, consenting adult patients with type 2 diabetes, attending the diabetes outpatient clinic were recruited for the study from January 2021 to December 2021. "Their socio-demographic characteristics, duration of diabetes and biochemical parameters were obtained and recorded in a well-structured questionnaire. Anthropometric parameters such as weight, height and waist circumference were measured for each patient. Two blood pressure measurements were taken on the right arm in the sitting position and the average of two readings was recorded. Blood specimen was collected

after an 8-hour fasting for assay of electrolytes, urea, creatinine, serum lipids, glucose, glycated haemoglobin and uric acid. Early morning urine specimen was collected and immediately analysed using Medi-Test combi-9® (Macherey-Nagel, Germany) strip for protein, glucose and ketones. Urine samples were analysedwithin 30 minutes of collection with the test strips immersed into the urine for 10 seconds and read against the colour codes on the container after 30 to 60 seconds. Serum creatinine was analysed with Roche Cobas C311® clinical chemistry analyzer using photometric system at wave length of 505. EstimatedGlomerular filtration rates (eGFR) were calculated for each patient using the chronic kidney disease epidemiology collaboration formula with correction for black ethnicity (CKD-EPI equation)" [12].

2.1 Definition and KDIGO Classification of CKD

"Patients who had eGFR ≤ 60ml/minute/1.73M^2 were considered to have chronic kidney disease (CKD). Patients were also grouped based on the KDIGO GFR staging. G1: GFR >90 ml/min/1.73 m2; G2: GFR 60–89 ml/min/1.73 m2; G3a: GFR 45–59 ml/min/1.73 m2; G3b: GFR30-44, G4: GFR 15–29 ml/min/1.73 m2 , G5: GFR <15 ml/ min/1.73 m2 . Albuminuria level A1: <30mg/g, A2: 30-300mg/g, A3: >300mg/g. Patients who have GFR <60ml/min/1.73m2 and/or albuminuria >30mg/g are considered to have chronic kidney disease. Hyperfiltration is defined as GFR >120ml/min/1.73m2 and albuminuria <30mg/g in females and >130ml/min/1.73m2 and albuminuria <30mg/g in males" [12].

"Fasting Cholesterol and its sub-fractions as well as TG were determined using enzymatic methods with an automatic device Cholestech LDX^R(Cholestech Corporation, USA). LDL-c was calculated using the Friedewald formula for patients with TG levels < 400mg/dl" [13]. "Non-HDL-c, as a surrogate marker of apolipoprotein B (Apo B), was calculated as TC-HDL-c. American Association of Clinical Endocrinologistś Guidelines for the management of Dyslipidemia and prevention of Atherosclerosis [14] were used to classify isolated patterns of dyslipidemia as follows: high TC levels as values ≥5.2mmol/l, high LDL-c levels as ≥ 3.9mmol/l, low HDL-c levels as values < 1.0mmol/l in men and < 1.3mmol/l in women, and high TG as values ≥1.7mmol/l" [14] . Atherogenic dyslipidemia or combined dyslipidemia was defined as combination of any of the following: high TG, low LDL; high TG, high LDL; high LDL, low HDL; and isolated dyslipidemia were defined as: isolated hypercholesterolemia- combination of high TC and normal/ low TG and LDL; isolated hypertriglyceridemia – combination of high TG and normal/low TC and LDL; isolated high LDL-combination of high LDL and normal/low TG,TC while isolated low HDL was defined as combination of low HDL with normal LDL, TG and TC.

Hypertension: "hypertension was defined according to JNC 8 as systolic (SBP) and diastolic (DBP) blood pressure ≥140 and ≥90mmHg respectively, or history of current antihypertensive therapy" [15].

Anthropometric: "body mass index was classified as: normal (BMI 18.5-24.9), overweight (25.0-29.9), obesity (BMI ≥ 30)[16]. Truncal obesity was defined as waist circumference > 94 cm for males and > 80 cm for females" [17].

Type 2 diabetes mellitus: "this was defined as documented fasting plasma glucose ≥ 7.0mmol/l or 2 hour postprandial blood glucose ≥ 11.1mmol/l for the first time in a patient, with or without classical symptoms of DM; or presentation for the first time with symptoms of hyperglycemic crises and a documented random blood glucose ≥ 11.1mmol/l; and good glycemic target was defined as pre-prandial capillary plasma glucose between 4.4-7.2mmol/l and 2 hour postprandial capillary plasma glucose < 10.0mmol/l" [18]. Poor glycaemic control is defined as patients with HbA1C >7.5% and/or FBG >10mmol/l.

2.2 Statistical Analysis

Data collected were entered into a computer and analyzed using the Statistical Package for Social Sciences (SPSS Inc Chicago IL USA) version 21. Continuous variables were expressed as mean (±SD) and association between them was determined using student t test. Discrete variables were expressed as percentages and proportions and their association was determined using Chi squared test. Probability (P) values<0.05 were considered significant. Results are presented as Tables where appropriate. Analysis for risk factors was done using binary logistic regression.

3. RESULTS

A total of 318 subjects were recruited from the Diabetic clinic of University of Maiduguri Teaching Hospital, Maiduguri between January to December 2020. There were 194(61%) females and 124(39%) were males. The mean age of the study population was 49.64±11.40 years and a mean duration of DM of 7.00±6.45 years. Mean HbA1C and Fasting blood glucose of the study population were 9.67±8.39% and 11.06±8.31mmol/L respectively. Total cholesterol, LDL, TG and HDL were 4.99±2.19 mmol/L, 3.09±1.04mmol/L, 1.82±0.96 mmol/L and 1.17±0.43mmol/L respectively.

Out of the study population, 126(39.6%) had DKD whereas 192(60.4%) had normal kidney function. The characteristics of patients with DKD as compared with those without DKD are as shown in Table 1.

Out of the 126 study participants who developed DKD, 111(88.1%) had HbA1C > 7.5% and 50% of them had total cholesterol > 5.2mmol/L. Other results as shown in Table 2.

Table 1. Socio-demographic and biochemical characteristics of study subjects with DKD and those without DKD

Variables	DKD(n=126)	No DKD(n=192)	*P*
Age(years)	52.44±10.43	47.81±11.66	0.000
Sex Male	37(29.4%)	87 (45.3%)	X^2=8.133
Female	89(70.6%)	105(54.7%)	P=0.004
Duration of DM(years)	8.19±6.66	6.22±6.21	0.007
Weight(Kg)	77.99±13.72	76.22±17.77	0.318
BMI(Kg/M^2)	28.05±5.78	27.15±6.09	0.182
Waist Circumference(cm)	91.42±14.28	91.28±16.51	0.934
HbA1C(%)	10.26±8.06	9.78±8.61	0.619
Fasting blood glucose(mmol/L)	10.61±5.72	11.36±9.64	0.430
Total Cholesterol(mmol/L)	4.96±1.19	5.01±2.67	0.809
HDL(mmol/L)	1.17±0.48	1.18±0.40	0.898
TG(mmol/L)	1.99±0.97	1.69±0.94	0.006
LDL(mmol/L)	3.18±1.10	3.04±0.99	0.259

Table 2. Showing the prevalence of poor glycaemic control, blood pressure control and lipid abnormalities among study participants

Variables	All(n=318)	DKD(n=126)	No DKD(n=192)	χ^2, *P* value
HbA1C >7.5%	261(82.1%)	111(88.1%)	150(78.1%)	5.140, 0.025
Systolic BP >140mmHg	129(40.6%)	60(47.6%)	69(35.9%)	4.306, 0.047
Diastolic BP >90mmHg	122(38.4%)	51(40.5%)	71(37%.0)	0.393, 0.557
Total cholesterol >5.2mmol/L	131(41.2%)	63(50.0%)	68(35.4%)	6.679, 0.011
Triglyceride >4.5mmol/L	6(1.9%)	3(2.4%)	3(1.6%)	0.275, 0.685
Low Density Lipoprotein >3.5mmol/L	110(34.6%)	51(40.5%)	59(30.7%)	3.627, 0.038
High Density Lipoprotein <0.9 (Females)&<1mmol/L(males)	104(32.7%)	49(38.9%)	55(28.6%)	3.63, 0.038
PCV <30%	54(17.0%)	44(34.9%)	10(5.2%)	47.03, 0.000
Proteinuria	130(40.9%)	77(61.1%)	53(27.6%)	35.34, 0.000
BMI>26Kg/M^2	211(66.4%)	92(73.0%)	119(62.0%)	4.151, 0.027
Uric acid >420mmol/L	128(40.3%)	91(72.2%)	37(19.3%)	88.69, 0.000

4. DISCUSSION

This cross sectional descriptive study evaluated the prevalence and pattern of lipid abnormalities among study participants with DKD and compared with T2DM patients who had no evidence of DKD in Maiduguri northeastern Nigeria. Our study found that dyslipidaemia is common among T2DM patients andit also showed that the prevalence of hypercholesterolemia and low density lipoproteinaemia were significantly higher among study participants who developed DKD than those without DKD. Among our study participants, patients with DKD had lower levels HDL as compared to those without DKD.

The mean age of patients who developed DKD in our study is similar to that of study conducted in Southeastern Nigeria by Jisieike-Onuigbo et al [19]. However the mean age of patients who develop DKD is higher in developed countries [6]. These differences may be due to better care received by diabetic patients in developed countries give them longer life expectancy.

Our study found disproportionately larger number of women who developed DKD than men. This difference is consistent with report from other parts of Nigeria [19], but Kajingulu et al. [20] in Uganda showed that more men with T2DM had albuminuria than women. The preponderance of women developing DKD in our cohort may due to higher prevalence of DKD risk factors among women [21].

Dyslipidaemia has an pathogenic relationship with T2DM, although our study did not find significant difference in the mean serum cholesterol between patients with DKD and those without. The prevalence of dyslipidemia among DKD patients in our studyis 50% and it is significantly higher than that of patients without DKD. This finding is consistent with studies conducted by Jisieike-Onuigbo et al. [11] in south-eastern Nigeria. However Kajingulu et al [20] found prevalence lower (36%) than that of the index study among Ugandans. The lower prevalence in their study may have resulted from the lower duration of diabetes among their study participants. It is also possible that life style differences and genetic factors may underlie such differences. This can be inferred from the findings of Sarfaz et al [22] who found the prevalence of dyslipidemia among Parkistani diabetic patients to be 97.18%.A study by Okaka et al found a prevalence of dyslipidaemia of 31% among non diabetic rural dwellers in southern Nigeria [23]. Their finding is similar to the prevalence of dyslipidaemia among diabetic patients without DKD in this study, suggests that dyslipidaemia may have an aetiologic link to DKD among diabetic patients in north eastern Nigeria.

The prevalence of poor glycemic control is was found to be significantly higher among participants who had DKD and dyslipidemia. Dyslipidemia and poor glycemic control share a common pathogenic pathway through insulin resistance and hyperinsulinemia [23]. Yan et al [23] in their study of Chinese T2DM patients found that patients who have normal lipid levels have better glycemic control. Studies have shown that, dyslipidemia is associated with commencement of renal replacement therapy and rapid progression of renal disease in CKD patients [24,25].

Although the present study found higher prevalence of low HDL among DKD patients compared to those without it, its overall prevalence was found to be low. This probably underscores the lower prevalence of atherosclerotic cardiovascular diseases among Africans.

This study is limited by the cross sectional study design which will preclude establishing a temporal relationship between the variables of interest. It is also limited by the lack of investigating behavioral, dietary and environmental factors that may be associated with dyslipidaemia among patients with diabetes mellitus.

5. CONCLUSION

The present study showed that lipid abnormalities are common among DKD patients in northeastern Nigeria. Identification and aggressive management of these disorders will help in slowing down the progression chronic kidney disease and prevention of other cardiovascular diseases.

CONSENT AND ETHICAL APPROVAL

Ethical approval was sought and obtained from the University of Maiduguri Teaching Hospital's research and ethics committee. Consent from the patients was also sought before the recruiting subjects for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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