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Evaluation of Dyslipidemia, Lipid Ratios and Atherogenic Indices in Elderly Type 2 Diabetes Mellitus Patients

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ABSTRACT

Cardiovascular risk is high in elderly type 2 diabetes mellitus (DM). The combination of DM and aging has impact on dyslipidemia, lipid ratios and atherogenic indices in the elderly which increases their cardiovascular risk. This study assessed the prevalence of lipid abnormalities, lipid ratios and atherogenic indices among elderly type 2 DM patients in a tertiary hospital in Southwest Nigeria. It was a cross-sectional study that involved 92 elderly type 2 DM patients and 92 elderly controls without DM. The lipid profile, lipid ratios and atherogenic indices were assessed and compared in both groups. P-value<0.05 was taken as significant. The mean ages of the diabetic and control groups were 66.73±5.18 years and 66.78±5.25 years, respectively. The overall prevalence of dyslipidaemia in the elderly DM group versus control group were (94[97.9%]vs 86[89.6%]), P=<0.001). The mean values of TC and LDL-C and median values of TC/HDL-C, LDL-C/HDL-C,TG/HDL-C, atherogenic index of plasma and atherogenic coefficient were significantly higher among elderly DM group than controls (P=<0.001). The median value of HDL-c was significantly lower among elderly DM group (P= 0.001). The prevalence rates of elevated lipid fractions among the elderly DM group vs control were elevated TC (54[56.3%]vs0[0%];P=<0.001); elevated LDL-C(47[49%]vs0[0%]; P=<0.001), elevated TG (58[60.4%]vs21[21.9%]; P=<0.001) and reduced HDL-C (88[91.7%]vs84[87.5%]; P=0.240). The elderly DM group had more mixed lipid abnormalities compared to controls (P=<0.001). Dyslipidaemia and atherogenic risk were high among the elderly DM patients. Lipid ratios should be used to assess cardiovascular risk in these patients. Statins should be used in those with increased cardiovascular risk based on lipid assessment.

Key words: Atherogenic risk, Dyslipidaemia, Elderly, lipid fraction, Lipid ratio. Type 2 diabetes mellitus

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INTRODUCTION

There is an increase in the aging population globally and this trend has been projected to continue even in the low and middle-income countries (LMIC). [1,2] Cardiovascular disease (CVD) is among the leading causes of death in the elderly[3,4] and aging is an established independent cardiovascular risk factor.[5] The aging process is characterized by increase in oxidative stress and pro-inflammatory mediators which predisposes to accelerated CVD.[6] Both stress and inflammation have also been implicated in the pathogenesis of obesity, diabetes mellitus (DM) and frailty in aging, thereby further contributing to the process of CVD.[6] Also, aging is usually associated with other risk factors for CVD such as hypertension and DM. Hence, the elderly patients are at higher risk of CVD.[6-8] Diabetes mellitus is common in the elderly population and this may partly account for the higher CVD burden observed in them.[8] In the past, DM was regarded as a CVD risk equivalent however, recent evidence suggests that cardiovascular risk is not entirely similar in the diabetic patients and patients with prior CVD.[9,10] There is need to risk stratify patients to identify those that have high cardiovascular risks and will require aggressive management in order to reduce CVD burden.[9] Dyslipidemia is common in DM because of the effect of insulin resistance in increasing hepatic very low lipoprotein (VLDL) production which subsequently predisposes to impairment in lipid metabolism.[11] Similarly, aging has significant effect on alteration of lipid metabolism through insulin resistance caused by changes in hormones such as growth hormone; androgens; changes in the hepatic sinusoidal endothelium; and changes in the expression and activity of peroxisome proliferator-activated receptor-α (PPAR-α).[12] The combination of DM and aging undoubtedly has huge impact on dyslipidemia and ultimately heightens cardiovascular risk in the elderly population.

Studies have shown that various lipoprotein ratios provide more clinical information in predicting and preventing CVD than individual lipid fractions.[13-18] There is growing evidence supporting the importance of the utility of these lipid ratios in routine practice.[13-18] These ratios are also easy to calculate and may serve as cheap and readily available alternatives to other lipid fractions such as apolipoproteins and other cardiovascular risk markers. Despite the potential adverse cardiovascular effects of DM and abnormal lipid fractions as well as ratio in the elderly, there is paucity of data in this aspect of endocrinology in Africa, including Nigeria. The objective of this study therefore was to assess the prevalence of lipid abnormalities, atherogenic lipid ratios and indices among elderly diabetics patients attending a tertiary hospital in Southwest Nigeria. The information from this study may help provide the justification for clinicians to assess cardiovascular risk in elderly diabetic patients using lipid fractions and ratios and to overcome the inertia of not using lipid lowering medications in individuals whom it may be beneficial.

MATERIALS AND METHODS

This was a cross-sectional study that was conducted over a 6-month period between December, 2016 and May 2017 at the Federal Medical Centre, Owo, Ondo State, Southern Nigeria.

Study Participants

A total of 96 elderly type 2 DM patients presenting at the endocrinology outpatient clinic of the Federal Medical Centre, Owo and 96 age and sex matched non-diabetic elderly men and women from the general outpatient department of the hospital who fulfilled inclusion criteria were recruited as controls.

Sample Size Calculation

Fisher's formula was used to calculate the sample size;[19] using 6% as prevalence of DM in elderly from a

previous study;[20] and 5% as the absolute precision limit. The minimum sample size was 87; however, a total of 96 patients were recruited to include 10% attrition rate.

Inclusion criteria were consenting type 2 DM patients who were 60 years and above,[21] diabetic for a minimum of 6 months, without chronic illness such as human immunodeficiency virus, heart failure, thyroid disorders and chronic obstructive pulmonary disease. Inclusion criteria for control were consenting individuals who were 60 years and above who do not have DM, glucose intolerance or chronic diseases.

Five mls of fasting venous blood was taken for lipid profile. The total cholesterol (TC) and triglyceride (TG) were estimated by enzymatic method. High density lipoprotein-cholesterol (HDL-C) estimation was done by precipitation method while low density lipoprotein-cholesterol (LDL-C) was derived using Friedewald's equation.[22]

Definition of Variables

Elevated total cholesterol was defined as value >5.17mmol/l. Elevated LDL was defined as LDL-C >3.36mmol/l, HDL-C <1.03 mmol/l in men or <1.3mmol/dl in women, TG >1.7mmol/l.[23]

The atherogenic index of plasma (AIP) was defined as the logarithm of the ratio TG and HDL-C (log TG/HDL-C). AIP value less than 0.1 is associated with low cardiovascular risk, value between 0.1-0.24 is associated with high cardiovascular risk, and value >0.24 is associated with cardiovascular risk.[1]The Castelli's risk index I (CRI-I) was defined as the ratio of TC to HDL-C. CRI-I greater than 5.0 in males and 4.5 in females were regarded as high.[24] CRI-II was defined as the ratio of LDL-C to HDL-C. CRI-II values density greater than 3.5 in males and 3.0 in females were regarded as high.[13] The atherogenic coefficient (AC) was defined as ratio of the difference of TC and HDL-C and HDL-C. AC greater than 3.0 was regarded as abnormal.[24]

Ethical Approval and Consideration

Ethical approval was obtained from Human Research and Ethical Committee of Federal Medical Centre, Owo. The reference for the ethical approval was FMC/OW/380/VOL.XLII/185. Consent was obtained from all participants in the study. Confidentiality of provided information was ensured throughout the study.

Data Management and Analysis

Data obtained were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 software 9 (IBM-SPSS, Armonk, NY: IBM Corporation). Descriptive data were presented as tables. Categorical variables of the two groups being studied were expressed as percentages. Associations between categorical variables were analyzed using Chi-square while Fisher's exact test was used when the cell count was less than 5. Continuous variables were presented as means and standard deviation for unskewed data and median, interquartile range for skewed data. Student t-test was used to compare mean values of unskewed data while Mann Whitney U was used to compare skewed data. P-value of <0.05 was taken as significant.

RESULTS

There were 192 participants in the study comprising of 96 elderly type 2 DM patients and 96 elderly controls without DM. The mean age of the elderly diabetic group was 66.73±5.18 years while that of the control group was 66.78±5.25 years. The male: female ratio for both groups was 1:1. (Table 1)

The mean values of the lipid fractions among the elderly DM group versus control group were TC (5.32±1.08mmol/l vs 3.76±0.050; P=<0.001). The median values and interquartile range of the lipid fractions among the elderly DM group versus control group were LDL-C (3.32[0.98]mmol/l vs 1.59[0.32] mmol/l; P=<0.001); HDL-C (0.79[0.40]mmol/l vs

0.90[0.30]mmol/l; P=<0.001) and TG(1.89[0.60] mmol/l vs1.00[0.70]mmol/l; P=<0.001).The median values and interquartile range of the lipid ratios were TC/HDL-C (7.00[4.07] vs 4.00[1.67] ;P=<0.001), LDL-C/HDL-C (4.49[2.99] vs1.69[0.60]; P=<0.001), TG/HDL-C (2.44[1.78] vs1.14[0.67]; P=<0.001), AC (6.00[4.07] vs 3.00[1.67]; P=<0.001) and AIP (0.39[0.33] vs 0.06 [0.24]; P=<0.001) (Table 2)

There was no significance difference in the lipid fractions, lipid ratios and atherogenic indices between male and female elderly diabetic groups. Table (3)

The overall prevalence of dyslipidaemia in the elderly DM group versus control group was (94[97.9%] vs 86[89.6%]), P=<0.001). The prevalence rates of elevated lipid fractions among the elderly DM group vs control were elevated TC(54[56.3%] vs 0 [0%] ; P=<0.001); elevated LDL-C (47[49.0%]vs 0[0%]; P=<0.001), elevated TG (58[60.4%] vs 21[21.9%]; P=<0.001) and reduced HDL-C (88[91.7%] vs 84[87.5%]; P=0.240)) (Table 4)

The elderly diabetic group had more mixed lipid abnormalities compared to those without DM (P=<0.001). Among the elderly with type 2 DM, 25(26.4%) had 4 patterns of lipid abnormalities and 26(27.1%) had 3 patterns of lipid abnormalities. (Table 5)

The prevalence of lipid ratios and atherogenic indices among the elderly diabetic group versus control group were high Castelli Risk Index-I (86[89.6%] vs 28[29.2%]; P=<0.001), high Castelli Risk Index-II (71[74%] vs 0[0%] ; P=<0.001), high cardiovascular risk according to atherogenic index of plasma (68[70.8%]vs 18[18.8%]; P=<0.001), and high atherogenic coefficient (90[93.8%] vs 44[45.8%]; P=<0.001). (Table 6)

Table 1: Demographic Information of Study Participants

Demography	Elderly with DM (N = 96) n (%)	Elderly without DM (N= 96) n (%)	P-value
Age in years *(Mean ± SD)*	66.73±5.18	66.78±5.25	0.902
60 – 69	71(74.0%)	70(72.9%)	
70 – 79	22(22.9%)	21(21.9%)	0.767
>79	3(3.1%)	5(5.2%)	
Gender			
Males	48(50.0%)	48(50.0%)	
Females	48(50.0%)	48(50.0%)	1.000

Table 2: Comparison of Lipid Fractions and Ratios between the Elderly with Type 2 diabetes mellitus and the Elderly without Type 2 diabetes mellitus

Lipid Fractions/Ratios	Elderly with DM (N = 96) Mean(SD)/Median(IQR)	Elderly without DM (N = 96) Mean(SD)/Median(IQR)	P-value
**TC (mmol/l)	5.32 (1.08)	3.76 (0.50)	<0.001
*HDL-C (mmol/l)	0.79 (0.40)	0.95 (0.30)	0.001
*LDL-C (mmol/l)	3.32 (0.98)	1.59 (0.32)	<0.001
*TG	1.80 (0.60)	1.00 (0.70)	<0.001
*TC/HDL-C	7.00 (4.07)	4.00 (1.67)	<0.001
*TG/HDL-C	2.44 (1.78)	1.14 (0.67)	<0.001
*LDL/HDL-C	4.49 (2.99)	1.69 (0.60)	<0.001
*AIP	0.39 (0.33)	0.06 (0.24)	<0.001
*AC	6.00(4.07)	3.00(1.67)	<0.001

**(expressed as median [interquartile range]). **(expressed as mean [standard deviation])*
IQR: interquartile range, SD: standard deviation,TC: total cholesterol, HDL -c: high density lipoprotein -cholesterol, LDL -c: low density lipoprotein-cholesterol, TG: triglyceride, AIP: Atherogenic Index of Plasma, AC: Atherogenic Coefficient,

Table 3: Comparison of Lipid Fractions and Ratios between Male and Female Elderly with Type 2 diabetes mellitus

Lipid Fractions/Ratios	Elderly Males with Type 2 DM (N=48) Mean(SD)/Median(IQR)	Elderly Female with Type 2 DM(N=48) Mean(SD)/Median(IQR)	P-value
**TC (mmol/l)	5.15(1.14)	5.49(1.01)	0.131
*HDL-C(mmol/l)	0.75(0.30)	0.79(0.50)	0.838
*LDL-C(mmol/l)	3.20(1.05)	3.44(0.91)	0.233
*TG (mmol/l)	1.80(0.60)	1.90(0.60)	0.683
*TC/HDL-C	6.93(3.99)	7.19(4.65)	0.838
*TG/HDL-C	2.51(1.56)	2.42(2.07)	0.838
*LDL-C/HDL-C	4.56(2.91)	4.30(3.12)	0.540
*AIP	0.40(0.30)	0.38(0.37)	0.838
*AC	5.93(3.99)	6.19(4.65)	0.838

**(expressed as median [interquartile range]) **(expressed as mean [standard deviation])*
IQR: interquartile range, SD: standard deviation , TC: total cholesterol, HDL -C: high density lipoprotein -cholesterol, LDL -C: low density lipoprotein-cholesterol, TG: triglyceride, AIP: Atherogenic Index of Plasma, AC: Atherogenic Coefficient

Table 4: Comparison between Prevalence of Lipid Abnormalities between Elderly with type 2 DM and Elderly without type 2DM

	Elderly with Type 2 DM (N = 96) n (%)	Elderly without Type 2 DM (N = 96) n (%)	P-value
Elevated Total Cholesterol			
Present	54(56.3%)	0(0%)	<0.001
Absent	42(43.8%)	96(100.0%)	
Elevated LDL-C			
Present	47(49.0%)	0(0%)	<0.001
Absent	49(51.0%)	96(100.0%)	
Elevated Triglyceride			
Present	58(60.4%)	21(21.9%)	<0.001
Absent	38(39.6%)	75(78.1%)	
Low HDL-C			
Present	88(91.7%)	84(87.5%)	0.24
Absent	8(8.3%)	12(12.5%)	
Dyslipidemia			
Present	94(97.9%)	86(89.6%)	0.016
Absent	2(2.1%)	10(10.4%)	

DM: diabetes mellitus, HDL-C: high density lipoprotein-cholesterol, LDL-C: low density lipoprotein- cholesterol

Table 5: Comparisons of number of Lipid Abnormalities between Elderly with type 2 DM and Elderly without type 2 DM

Number of Lipid Abnormalities	Elderly with type 2 DM (N=96) n (%)	Elderly without type 2 DM (N=96) n (%)	P-value
0	2 (2.1 %)	10 (10.4%)	
1	17 (17.7%)	67 (69.8%)	
2	26 (27.1%)	19 (19.8%)	<0.001
3	26 27.1%)	0 (0.0%)	
4	25 (26.4%)	0 (0.0%)	

Table 6: Comparison of various Lipid Ratios and Atherogenic Indices and Coronary Artery Disease Risk between Elderly with and without Type 2DM

Lipid Ratios and Atherogenic Indices	Elderly with 2 DM DM (N=96) n (%)	Elderly without DM DM (N=96) n (%)	P-value
High CRI-I			
Present	86(89.6)	28(29.2)	<0.001
Absent	10(10.4)	68(70.8)	
High CRI-II			
Present	71(74.0)	0(0)	<0.001
Absent	25(26.0)	96(100)	
AIP			
High Risk	68(70.8)	18(18.8)	<0.001
Low/Medium Risk	28(29.2)	78(81.2)	
High AC			
Present	90(93.8)	44(45.8)	<0.001
Absent	6(6.2)	52(54.2)	

CR: Castelli Risk Index; AIP: Atherogenic Index of Plasma; AC: Atherogenic Coefficient

DISCUSSION

This study determined the prevalence and pattern of dyslipidaemia and atherogenic indices among elderly with and without DM. The study found that the overall prevalence of dyslipidaemia among elderly type 2 DM was 97.5% which was significantly higher than 89.6% found in the age and sex matched elderly controls without DM. The prevalence of dyslipidaemia in our study is higher than 69.9% reported by Odenigbo et al[26] among a population of elderly individuals. The higher prevalence in our study in comparison with that of Odenigbo et al[26] may be due to the fact that while our study participants composed entirely of type 2 DM patients, the study by Odenigbo et al[26] involved a general population of elderly. Similarly, the prevalence of dyslipidaemia in our study is equally higher than 85.4% reported by Sarac et al[27] among elderly with type 2 DM in Turkey. The high prevalence of dyslipidaemia in our study like other studies that involved elderly type 2 DM patients may be attributed to the effect of DM in promoting the development of dyslipideamia. Diabetes mellitus is associated with insulin resistance which leads to hyperlipidemia by increasing VLDL production from the liver.[11,28]

The mean and median values of TC, LDL-C, TG was significantly higher in the elderly with type 2 DM compared with the controls. Also, the median value of HDL-C was significantly lower in the elderly with type 2 DM. These findings also corroborated the effect of DM in promoting dyslipidaemia.[11,28]

There was no significant difference in the mean and median values of the various lipid fractions between the male and female elderly diabetics. Our finding is similar to that of Habib et al[29] and Bello-Ovosi et al[30] who also reported no significant gender difference in lipid profile. Expected gender influence on lipid fractions due to the effect of oestrogen are increase in HDL-C; and reduction in LDL-C and TC.[31] However, this pattern was not seen in our study possibly because aging could have attenuated the expected impact of aging on lipid frictions. Oestrogen level in our female study participants is likely to be low since they are postmenopausal.

Elevated triglyceride and reduced HDL-C were the frequent pattern of dyslipidaemia that was seen in our study. This trend is similar to the diabetic dyslipidaemic pattern that has been reported in some previous studies.[11,28] Mixed dyslipidaemia was also significantly more common in the elderly with type 2 DM compared to the control. About 53.5% of elderly type 2 DM in our study had a combination of 3 or 4 lipid parameter abnormalities which was absent amongst the control. This is in keeping with reports of other studies that showed that mixed dyslipidemia is a common finding in DM.[30,32]

The median values of the various lipid ratios such as the CRI-1, CRI-II, AC, AIP were significantly higher among the elderly type 2 DM compared to the control in this study. In the same vein, the proportion of elderly type 2 DM with high lipid ratios and atherogenic indices (CRI-1, CRI-II, AC, AIP) were significantly higher compared to the control. This therefore highly suggests that elderly type 2 DM patients are at a high risk of developing atherosclerotic heart disease and other forms of CVDs. Diabetes mellitus is therefore a risk multiplier for CVD in the elderly as found in our study.

Significantly high cardiovascular risk based on the AIP greater than 2.4 was present in 70.8% of the elderly with type 2 DM compared with 18.8% observed among the control group. The proportion of elevated AIP observed in our study is far higher than that reported by Olamoyegun et al[25] who reported a prevalence of 11% among a general population who were younger.

AIP is easy to calculate and has been validated to be a better predictor of cardiovascular risk than individual lipid fraction.[14] Previous reports have established that AIP is an independent risk factor for development of coronary artery disease and mortality.[17,33]

The proportion of elderly type 2 DM patients with high CRI-1, CRI-II, AC were 89.6% ,74% and 93.8%, respectively. These findings were significantly higher compared to the control group. These percentages were also remarkably higher than that reported by Olamoyegun et al.[25] These ratios are better predictors of coronary heart disease and other CVDs when compared with individual lipid fraction.[13,33,34]

Dyslipidaemia and atherogenicity is notably high in elderly type 2 DM patients. Lifestyle modifications is the first step in the management of dyslipidemia, however, the practicability, sustainability and compliance of this in the elderly population group is a challenge. Combination with pharmacotherapy has been found to be more effective and more likely to achieve a better outcome. However, this is equally not without its challenges: there is under-prescription of statins among elderly in clinical practice even when there is indication for its use.[35,36] This is partly because there are limited clinical trials on safety profile of statins in elderly compared to the younger population.[36] Evidences from some studies that involved significant number of elderly patients have shown the effectiveness of statins in reducing CVD and mortality.[36,37] These studies also showed that the side effects of stains in elderly are comparable to those observed in younger population.[36,37] The clinical advisory report by Pasternak *et al*[36] showed that the adverse effects of statins are less when cautiously used. The advisory encouraged the appropriate use of statins when indicated.[36]

The limitation of this study is that the cross-sectional nature of the study design did not allow those with increase cardiovascular risk to be followed up for a period of time. However, this study has been able to demonstrate that the cardiovascular risk in elderly type 2 DM patient is high and that there is need to take active steps toward risk reduction using combination pharmacotherapy to minimize adverse cardiovascular outcome which is already a challenge in this patient population.

In conclusion, dyslipidaemia and atherogenic risk was found to be high among elderly type 2 DM compared to their aged and sex matched controls. There is need to utilize lipid ratios for better cardiovascular risk stratification in these group of patients. Lifestyle modification and use of statins should be deployed in those with increased cardiovascular risk based on the evaluation of lipid ratios and fractions.

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