Relationship between Microalbuminuria and Dyslipidaemia in Type - 2 Diabetes Mellitus Patients

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Abstract

Background: *It is widely reported that dyslipidaemia is a common feature of type 2 diabetes mellitus and is often associated with a higher risk of diabetic complications.*

Objectives: *Lipid profile and microalbuminuria were examined in all type 2 diabetes mellitus patients. The prevalence of dyslipidaemia was determined and comparison was made amongst the normotensive and hypertensive diabetic patients presenting with microalbuminuria and normotensive diabetes without microalbuminuria.*

Patients and methods: *Ninety- five (95) type 2 diabetes mellitus patients and 20 healthy controls were randomly selected and studied. Seventeen (17) of them were normotensive diabetics with microalbuminuria, forty (40) were hypertensive diabetics with microalbuminuria and thirty-eight (38) were normotensive diabetics without microalbuminuria. The weight, height and blood pressure of the patients were measured and their blood and urine samples were obtained for plasma lipid profile and albumin-creatinine ratio respectively.*

Results: *The mean total cholesterol and low density lipoprotein cholesterol was highest in normotensive DM presenting with microalbuminuria 5.4(1.87) mmol/l and 3.74(1.71) mmol/l, compared to hypertensive DM with microalbuminuria 5.28(1.38)mmol/l and 3.67(1.33)mmol/l and lowest in the normotensive DM without microalbuminuria 5.1(1.32)mmol/l and 3.36(1.15)mmol/l $p<0.05$. A high proportion of diabetic patients presenting with microalbuminuria (normotensive (65%) and hypertensive (67%) had high total cholesterol, this was similar to the diabetics without microalbuminuria (63%) whereas a lower proportion (30%) of the control(non diabetics) has high TC value p=0.0001. Similarly high proportions of the DM patients 47%,57% and 50% respectively had high low density lipoprotein values compared to controls(non-diabetics) (30%) p=0.0012.*

Conclusion: *These findings draw specific attention to the need to screening for microalbuminuria in patients with dyslipidaemia as this will reduce the risk or slow down the progress of cardiovascular complications.*

Keywords: *Microalbuminuria, Dyslipidaemia, Type 2 DM, Normotensive diabetics, Hypertensive Diabetics*

Introduction

Microalbuminuria represents an abnormally elevated urine albumin level below the sensitivity of the conventional semi quantitative test strip[1]. It is defined as the urine excretion rate of >30-300mg/24hr or albumin-creatinine ratio (ACR) >30mg/g. It predicts the worsening of renal disease due to overt diabetic nephropathy. The major clinical objective in the management of DM is to control

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hyperglycaemia and the specific long term objectives are to prevent microvascular and macro vascular complications[2] Diabetic dyslipidaemia is characterised by a triad of lipoprotein abnormalities: high very low density lipoprotein(hypertriglyceridemia), elevated levels of small dense low-density lipoprotein particles (LDL-c) and low levels of high density lipoprotein (HDL-C). The lipid triad is a prominent feature of type 2 DM population and a major risk factor for coronary heart disease[3]. Most DM patients with dyslipidaemia are insulin resistant hence it is a component of insulin resistant syndrome also called metabolic syndrome[4]. The well known components of metabolic syndrome which include impaired glucose tolerance, hyperlipidaemia,insulin resistance and increased blood pressure describes a combination of previously reported risk factor for coronary heart disease[5].whereas, cardiovascular disease is the most prevalent macrovascular com plication which accounts for severe morbidity and mortality in type 2 DM, the microvascular complications such as nephropathy and retinopathy frequently contribute to the disease burden[5].

Microalbuminuria may also be a marker of dyslipoproteinaemia[6] in DM patients. The most consistent lipoprotein abnormalities are; a reduction in the concentration of HDL, apolipoprotein A1 and changes in the composition of triglyceride rich lipoprotein in DM and non-DM with microalbuminuria. The earliest course of diabetic nephropathy is the appearance of microalbuminuria (incipient nephropathy) which without intervention progresses rapidly to overt nephropathy and subsequently renal failure in adults in the western world and a major cause of end stage renal disease (ESRD) in Nigeria[7]. Hypertension is common among type 2 DM patients and as such in the presence of microalbuminuria it further predicts a more rapid downhill progression of renal impairment by increasing intraglomerular pressure leading to ESRD[8].Therefore to reduce diabetic complications, the management of DM should be reappraised from time to time. Measures aimed at influencing and reducing any known modifiable risk factors that interact with complications should be employed. We therefore examined lipid profile patterns in type 2 DM (normotensive and hypertensive) patients presenting with or without microalbuminuria. The prevalence was also determined in these groups of patients.

Patients and Methods

A total 95 type 2 DM patients aged between 25-70 years were randomly selected from the registered diabetic patients attending the medical outpatient department of the University of Benin Teaching Hospital, Benin-city. The patients were classified into four groups using the urine Albumin: Creatinine Ratio (ACR) levels and blood pressure. Subjects with urine ACR>30mg/g and ACR<30mg/g were assumed to have microalbuminuria and normal albuminuria respectively.Groups:

(A)Normotensive Diabetes presenting with microalbuminuria (NDM), n=17 patients.

(B) Hypertensive Diabetics with microalbuminuria (HDM) n=40

(C) Normotensive Diabetics without microalbuminuria (ND), n=38.

(D) Non-Diabetics normotensive (controls) without microalbuminuria, n=20,they were of same age range as the patients and were drawn from the hospital staff.

All participants gave written consent after due explanation by the researchers. Ethical clearance was sought and obtained from the hospital research and ethics committee. The health parameters such as, body weight (kg), height (m) and blood pressure (mmHg) were obtained. Heights were measured to 0.1cm free standing against a marked wooden ruler in (cm). Weights were measured to 0.1kg without shoes and minimal clothing using a flat weighing scale (Hop- on-Hanson model). Blood pressure was measured using a mercury sphygmomanometer and hypertension was

defined as BP>140/90mmHg. Body mass index (BMI) was calculated using the formula:

BMI = wt (kg)/ht (m2). BMI <19 = Underweight, 19-25 =normal weight, 25-30 = overweight, >30= obesity[9]. Fasting plasma samples were obtained for blood glucose and plasma lipid profile. The total cholesterol was determined using the enzymatic method[10], HDL-c was determined using precipitation method[11], triglyceride by enzymatic method[12] and LDL-c was calculated based on Friedwald's formula[13]. Albumin was determined by Folin-Lowry method [14] and creatinine by modified Jaffe method[15]. Aibumin-Creatinine ratio was then calculated

Statistical Analysis

Data obtained from this study was grouped and analysed by tables using SPSS version 13.0.0. Means and standard deviations were determined for quantitative data and frequency determined for categorical variables. Student's t-test was used to test for significant association between two means, ANOVA was used to compare multiple means, while chi-squared test was used to analyse group differences for categorical variables. All tests were carried out at 5% probability levels.

Table 1.

Physical characteristics of diabetics with complications and controls

	NDM(n=17) mean(SD)	HDM(n=40) mean(SD)	ND(n=38) mean(SD)	Control(n=20) mean(SD)	p-value
Age(yrs)	57.4(10.05)	56.8(9.24)	53.8(9.80)	50.2(10.2)	0.0546
BMI(Kg/m2)	25.6(4.27)	26.9(5.65)	25.3(4.22)	25.4(4.73)	0.3832
SBP(mmHg)	133.5(26.4)	158.4(16.7)	121.2(11.6)	118.0(8.33)	0.0001
DBP(mmHg)	81.2(12.7)	92.0(8.30)	78.7(9.05)	75.0(6.88)	0.0001

The DM patients with microalbuminuria are more in the older age group than those without microalbuminuria
KEY: NDM=Normotensive Diabetic with microalbuminuria, HDM=Hypertensive Diabetic with microalbuminuria, ND=Normotensive diabetic without microalbuminuria, controls=healthy non-diabetic.

Results

A total of 95 type 2 DM patients and 20 healthy controls (non-diabetics) were studied. The patients constituted of 62(65.3%) of females and 33(34.7) males giving a female to male ratio of 1.8:1.0. the study participants were in four groups, as shown in the method section.

Table 2.

Mean lipid values in DM complications and controls

Lipid type	NDM	HDM	ND	Controls	p-value
TC (mmol/l)	5.4(1.87)	5.28(1.38)	5.1(1.32)	4.0(1.22)	0.0058
TG (mmol/l)	1.59(0.78)	1.26(0.47)	1.37(0.60)	1.19(0.40)	0.127
HDL-c(mmol/l)	0.95(0.35)	1.05(0.39)	1.11(0.57)	1.07(0.24)	0.627
LDL-c(mmol/l)	3.74(1.71)	3.67(1.33)	3.36(1.15)	2.39(1.12)	0.0028

Normotensive and hypertensive diabetics have more severe dyslipidaemia (TC and LDL-c) than normotensive DM without micoalbuminuria.

Key: *TC=total cholesterol TG = triglyceride, LDL-c =low density lipoprotein cholesterol, HDL-c= high density lipoprotein cholesterol.*

Table 1 shows some physical characteristics of patients and controls. The mean age in years of the patients were 57.4(10.05) for the normotensive DM with microalbuminuria, 56.8(9.24) for hypertensive DM with microalbuminuria, 53.8(9.80) for normotensive DM without microalbuminuria and that of controls is 50.2(10.2) compared with controls' age did not show statistically significant difference, p=0.0546. The mean BMI was highest in the hypertensive DM with microalbuminuria 26.9(5.65)kg/m2 and least in the normotensive without microalbuminuria 25.3 (4.22) kg/m2, p = 0.3832 (ANOV A).

hypertensive DM with microalbuminuria 5.28(1.38) mmol/l , lower in the normotensive without microalbuminuria 5.1(1.32)mmol/l and least in the healthy controls 4.0(1.22), this was found to be statistically significant (p=0.0058). The mean LDL-C value also was higher in the normotensive DM with microalbuminuria 3.74(1.71)mmol/l and lower in the DM normotensive without microalbuminuria and the controls (3.36(1.15) mmol/l and 2.39(1.12) mmol/l respectively (P=0.0028). The mean HDL was higher (more favourable) in the respondents without microalbuminuria 1.11(0.57) mmol/l and 1.07(0.24)mmol/l than those with microalbuminuria 0.95(0.35) and 1.05(0.39)

Table 3.

ATP III Classification of categories of risk based on lipoprotein levels in adults

Risk category	TC mmol/dl	mmol/l	LDL-c mg/dl	mmol/l	HDL-cmg/dl	mmol/l	TG mg/dl	mmol/l
High	>240	>6.2	>130	>3.4	<40	<1.0	>150	>1.7
Low	<240	<6.2	<130	<3.4	>40	>1.0	<150	<1.7

Table 4.

Percentage distribution of low and high atherogenic risk levels in complicated DM patients and controls based on ATP III criteria

Disease type/ control	TC low n (%)	High n(%)	TG Low n(%)	High n(%)	HDL- c Low n(%)	High n(%)	LDL-c Low n(%)	High n(%)
ND	14(37)	24(63)	9(24)	29(76)	16(42)	22(58)	19(50)	19(50)
HDM	13(33)	27(67)	11(28)	29(72)	18(45)	22(55)	17(43)	23(57)
NDM	6(35)	11(65)	4(23)	13(77)	6(35)	11(65)	9(53)	8(47)
control	14(70)	6(30)	7(35)	13(65)	12(60)	8(40)	14(70)	6(30)
÷2(p-value)	37.66	(0.0001)	4.46	(0.2155)	13.43	(0.0038)	15.86	(0.0012)

All the diabetics with or without microalbuminuria had high degrees of atherogenic risk when compared with the controls. However, a higher proportion is seen in the diabetic groups with microalbuminuria than those without microalbuminuria. KEY: ÷ 2= Chi-squared value, p-value <0.05 is statistically significant.

Table 2 shows the mean lipid values in DM patients with and without microalbuminuria and controls. The mean total cholesterol was highest in the normotensive DM 5.4(1.87)mmol/l when compared with mmol/l mmol/l for groups A and B respectively (p=0.627). The mean triglyceride was elevated in all diabetics but more marked in patients with microalbuminuria with the highest value in normotensive DM with microalbuminuria

1.59(0.78) mmol/l mmol/l and lowest value in the controls 1.19(0.40) mmol/l but this was not significant (p=0.127).

We analysed the frequency of dyslipidaemia based on low and high atherogenic risk according to the criteria laid down by Adult Treatment Panel (ATP III) of the American Medical Association[16] as shown in table 3 Table 4 shows a comparison of the frequency of degree of atherogenic risk in the DM patients presenting with or without microalbuminuria using the ATPIII classification. A high proportion of the normotensive and hypertensive DM with microalbuminuria were at higher atherogenic risk as evidenced by elevated levels of total cholesterol and LDL-c levels ÷2 =37.66(p=0.0001) and ÷2 =15.86(p=0.0012) respectively. Similar to this were their findings characterised by low HDL-c values compared with the controls (÷2=13.43, p=0.0038).

Discussion

This present study reveals the occurence of combinedhyperlipidaemia, hypercholesterol-aemiaand hypertriglyceridaemia more especially in the DM with microalbuminuria. These findings are similar to previous reports amongst the Saudi type-2 DM patients[17]. The cause of lipid alteration among these patients is due to defects in insulin distribution and lipoprotein lipase enzyme which depends on insulin for its actions. The resultant effect is an increase in very low density lipoprotein and triglyceride due to hyperinsulinaemia[17].

The higher mean BMI, which is another determinant of lipid abnormality in the DM patients with microalbuminuria supports the fact that lipid abnormalities are related to obesity probably due to insulin resistance. This was in keeping with the findings of Idogun *et al* [18]who studied BMI in type-2 DM with complications and concluded that the consequences of overweight and obesity are increased free fatty acid promoting dyslipidaemia and increased risk of end stage renal disease in diabetics.

The reported higher mean values for triglyceride, total cholesterol and low density lipoprotein in the diabetics with microalbuminuria than those without microalbuminuria in this study, is comparable to dyslipidaemia in type 2 DM with and without metabolic syndrome as documented by Adediran *et al*[19] where it was observed that those with metabolic syndrome had higher mean values. The severe dyslipidaemia in normotensive and hypertensive dyslipidaemia with microalbuminuria may be due to reduced metabolic processes and impaired excretion of metabolic waste products. It is also worthy of note that hypertension even in the absence of DM is known to cause insulin resistance[20] and the consequent hyperglycaemia leads to increased lipolysis with a resultant elevated lipids in plasma.

We also found dyslipidaemia in a higher proportion of normotensive DM and hypertensive DM patients with microalbuminuria when compared with those without and least in the controls (non diabetics) 30%.Using the ATP III classification, a high proportion of the diabetics, had hypercholesterolemia 63-67% but the highest proportion is amongst those with microalbuminuria. This finding is in keeping with other reports that documented the incidence of dyslipidaemia among type 2 DM to vary from 23.6-77.1%[21] and closely approximates 25-60% reported in yet another study[22]. These reports are comparable because we employed the same strict criteria of abnormality as the ATP III classification [16]. The higher percentage seen for total cholesterol and LDL-c levels, is in line with the NCEP guidelines for treatment where LDL-c is the major target of cardiovascular disease prevention. The highest proportion of patients with hypertriglyceridaemia was also noted amongst DM with microalbuminuria.

Conclusion

A significant number of subjects presented with high lipid levels in this study and these values were higher in subjects with microalbuminuria when compared with normoalbuminuric subjects. This suggest the need for early screening for microalbuminuria in type 2 DM patients who present with hyperlipidaemia in addition to regular lipid screening as this will reduce the risk or slow the progress of cardiovascular complications.

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