Profile Of Cardiovascular Disease Risk Factors In Normoalbuminuric Nigerian Diabetic Patients.

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Abstract

BackgroundNephropathy in patients with Diabetes Mellitus is usually progressive, commencing with microalbuminuria and progressing to macroalbuminuria with subsequent development of progressive reduction of glomerular filtration rate. The development of microalbuminuria also substantially increases the risk of cardiovascular morbidity and mortality in the diabetic patients. Recent studies have indicated that substantial cardiovascular risk may exist in patients having proteinuria in the range currently considered to be normal. This risk appears to increase as the level of albuminuria increases in this setting. However, racial and genetic influences on these observations are not known.MethodsThis cross-sectional study, describes the profile of cardiovascular risk factors in 150 normoalbuminuric African diabetic patients with regular clinic attendance at the diabetic clinic of a Teaching Hospital in Lagos, Nigeria. ResultsOne hundred and thirty (86.67%) of the 150 studied subjects had one or more cardiovascular risk factors that did not correlate with the degree of albumin excretion. 50% of the studied subjects were hypertensive, 37.3% were obese, hypercholesterolaemia occurred in 13.3%, elevated LDL in 20% and low HDL in 35.3% of the subjects. Mean duration of diabetes was 6.8yrs.ConclusionsIt was concluded that there is a high background prevalence of Cardiovascular Disease risk factors in these normoalbuminuric Diabetic subjects with short duration of diabetes. This finding is a reflection of the huge Cardiovascular Disease burden in this population of patients.

BACKGROUND

Diabetes Mellitus is an important cardiovascular disease risk factor and various studies have shown an increased prevalence of cardiovascular diseases such as coronary artery disease, stroke, peripheral vascular disease and congestive cardiac failure in diabetic patients.[1,2,3] Apart from cardiovascular diseases, diabetic patients also have a substantial risk of developing Chronic Kidney Disease (CKD).[4,5] Reports from renal registries of many developed countries have indicated Diabetic Nephropathy as the most common cause of End Stage Renal Disease in these countries, [6,7] and the trend is evolving in many developing countries in view of the world wide growing prevalence of diabetes mellitus.[8,9]

The evolution of CKD in many diabetic subjects develops from a stage of microalbuminuria defined as Albumin Creatinine Ratio (ACR) between 30 to 300mg/g, to the stage of macroalbuminuria (ACR > 300mg/24hr) with development of hypertension and progressive decline in glomerular filtration rate.[5]

Most studies on Cardiovascular Diseases in Diabetic patients focused on the diabetics as a group without stratification in respect of presence or absence of nephropathy, making estimation of the contribution of nephropathy to the estimated Cardiovascular Disease burden in these studies difficult .[2] Microalbuminuria apart from being an important predictor of progression of nephropathy in diabetic patients, has also been noted to be a good marker of generalized endothelial dysfunction both in diabetic and non diabetic nephropathies.[10,11] The development of microalbuminuria substantially increases the risk of cardiovascular morbidity and mortality in diabetic as well as non diabetic patients.

Recent studies have indicated that substantial cardiovascular risk may exist in patients having proteinuria in the range currently considered to be normal.[12,13,14] This risk appears to increase as the level of albuminuria increases in this setting.[14]

However, most of the studies were done in the developed countries and little is known about the pattern of cardiovascular risk factors in normoalbuminuric diabetic subjects in developing countries. Hence the effect of racial and genetic influences on risk factors for diabetic nephropathy in the developing regions is largely unknown.

This cross-sectional study, describes the profile of cardiovascular risk factors in normoalbuminuric diabetic patients attending the diabetic clinic of a Teaching Hospital in Nigeria.

AIMS AND OBJECTIVES

Determine the prevalence of hypertension, obesity and dyslipidaemia in normoalbuminuric diabetic patients.

Determine the degree of association between these CVD risk factors and albuminuria in the normoalbuminuric range.

METHODS

One hundred and fifty normoalbuminuric diabetic patients with regular clinic attendance at the diabetic clinic of the Lagos State University Teaching Hospital Ikeja, were studied. Patients were screened for microalbuminuria in accordance with the American Diabetic Association guideline. [5]

Acutely ill patients, patients recently discharged from the hospital and pregnant women were excluded from the study.

Patient was taken to be normoalbuminuric if the Albumin Creatinine Ratio (ACR) as at time of study was below 30mg/g with no previous record of elevated ACR within the last 3-6 months prior to study evaluation.

To evaluate the cardiovascular disease risk profile within the normoalbuminuric range, the patients were grouped into three categories based on their Albumin Creatinine Ratio.

These are: (1) Low normal ACR group with ACR less than 7.5mg/g, (2) middle normal ACR group with ACR of 7.5 to less than 15mg/g and (3) high normal ACR group with ACR greater than 15mg/g but less than 30mg/g.

Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or and/or concomitant use of antihypertensive medications according to the WHO/ISH guidelines.[15]

The body mass index (BMI) was calculated from the measured weight (in kilograms) and height (in metres). Obesity was defined according to the 1999 WHO criteria. Cut off points for BMI were: overweight (BMI 25.0 – 29.99kg/m2), obesity (BMI 30 kg/m2).[16]

Dyslipidaemia was categorized using the NICEP III criteria.[17]

STATISTICAL ANALYSIS

All data were analysed using the SPSS version 17 statistics software. Results are presented as numbers and percentages or mean ± SD. Chi-square statistics was used to compare categorical variables and ANOVA for the continuous variables. The degree of association between albuminuria and cardiovascular risk factors was evaluated using Pearson's correlation coefficient. A p-value <0.05 is considered as being statistically significant.

RESULTS

One hundred and fifty type 2 diabetic subjects attending the diabetic clinic of the Lagos State University Teaching Hospital between 1 st of January and 30 th June 2009 were recruited in the study. There were 46(30.7%) males and 104 (69.3%) females. M:F = 1:2.3. Mean age was 58.04 ± 10.9yrs, range 32 -85yrs. [Table 1]. Mean duration of diabetes mellitus was 6.8 ± 6.5yrs, range 0.5 – 28yrs.

The frequency distribution of Albumin Creatinine Ratio in the sample population is shown in Figure 1. Eighty two patients (54.67%) had ACR levels below 7.5mg/g, 48(32%) had levels between 7.5mg/g and 15mg/g, while 20(13.33%) had ACR values above 15mg/g.

CARDIOVASCULAR DISEASE RISK FACTORS

One hundred and thirty (86.67%) patients had one or more cardiovascular risk factors present irrespective of duration of diabetes and level of microalbuminuria. Only 20(13.33%) patients had no risk factor demonstrable.

HYPERTENSION

Prevalence of hypertension in our studied patients was 50%. There were 21 (14%) males while the remaining 54 (36%) were females. There was no statistical difference in the proportion of hypertensive males compared with that of the females. $X^2 = 0.502$, p=0.48.

The correlation between hypertension and the degree of albuminuria in the normoalbuminuric range of proteinuria was not statistically significant r = -0.081, p>0.05 for systolic blood pressure, and r = -0.072, p>0.05 for diastolic blood pressure.

There was also no statistically significant difference in the occurrence of elevated blood pressure when the three ACR groups were compared. F=1.058, p>0.05 and F =0.541, p>0.05 for systolic and diastolic blood pressures respectively. [Table II]

However, compared to the general population of the country, with a prevalence rate of hypertension of about 25%,[18,19,20] a significant difference was observed using chi-square test of goodness of fit. $X^2 = 46.552$, $p<0.0001$.

ANTHROPOMETRIC INDICES AND ALBUMINURIA

BODY MASS INDEX

Four (2.7%) patients were underweight (BMI < 18.5 Kg/m^2), 37(24.7%) had normal weight with BMI between 18.5 – 24.9 Kg/m^2, 53(35.3%) Kg/m^2 were overweight (BMI 25 – 29.9 Kg/m^2), while 56(37.3%) were obese (BMI ≥ 30 Kg/m^2).

Thirty men (20%) were either obese 8(5.3%) or overweight 22(14.67%), compared with 79(52.67%) women out of which 48(32%) were obese with 31(20.67%) overweight. This is statistically significant X^2=11.345, $p<0.05$.

A non-significant negative correlation was found between BMI and the degree of albuminuria in the normoalbuminuric range of proteinuria r = -0.85, p>0.05. There was also no statistically significant difference in the BMI distribution, when the three ACR groups were compared. F =0.542,p>0.05. These results are shown in Table II.

WAIST CIRCUMFERENCE (WC)

Waist circumference was assessed in 148 patients. 8(5.4%) males had WC greater than 102cm while WC was less than 102cm in the remaining 36(24.3%) male patients. In females, WC greater than 88cm was observed in 77(52.0%) while WC less than 88cm was seen in 27(18.3%) patients. This was statistically significant X^2= 39.458, $p<0.05$. Waist circumference was not assessed in 2 male patients.

A non-significant negative correlation was found between waist circumference and the degree of albuminuria in the normoalbuminuric range of proteinuria r = -0.071, p>0.05.

There was no statistically significant difference in distribution of central obesity, when the three ACR groups were compared. F =0.452, p>0.05. [Table II]

GLYCAEMIC CONTROL AND ALBUMINURIA

One hundred and six (70.7%) had good glycaemic control with HbA1c levels below 7%. While the remaining 44 (29.3%) had poor glycaemic control with HbA1c levels above 7%.

There was no statistically significant difference in glycaemic control, when glycosylated haemoglobin levels were compared in the three ACR groups. F =2.209, p>0.05. [Table II]

DYSLIPIDAEMIA

Hypercholesterolaemia was found in 20(13.3%) of the patients, while ninety (60%) patients had normal Total Cholesterol (TC) levels. Forty (26.7%) patients had borderline values. Eighty three (55.3%) patients had normal Low Density Lipoprotein (LDL-C) levels while 37(24.7%) had borderline values. Elevated LDL-C level was found in 30(20.0%) of the patients. Low High Density Lipoprotein (HDL) level was found in 53(35.3%) while 97(64.7%) had normal HDL values.

One hundred and eighteen (78.7%) patients had normal triglyceride levels while 17(11.3%) had borderline values. Hypertriglyceridaemia was found in 15(10.0%) of the patients.

Multiple lipid abnormalities were found in 18(12%) subjects with 13(8.67%) patients having a combination of high TC and LDL-C, 1(0.67%) patient had high LDL-C and low HDL. The combination of a high LDL-C and high TG was seen in 1(0.67%) patient. One (0.67%) of the patients had a combination of three abnormalities; high TC with high LDL-C and low HDL. In 2(1.33%) patients, all 4 evaluated lipid abnormalities were present.

There was no statistically significant difference in the frequency of occurrences of dyslipidaemia, when the three ACR groups were compared. Table II

Figure 1

Table 1 Baseline characteristics of the studied subjects in relationship to the duration of diabetes mellitus

	Less than 5yrs	5years to less than 10years	More than 10years	Total
	GENDER			
Male	22 (14.7%)	12 (8.0%)	12 (8.0%)	46 (30.7%)
Female	65 (43.3%)	21 (14.0%)	18 (12.0%)	104 (69.3%)
Total	**87(58%)**	**33(22%)**	**30(20%)**	**150 (100%)**
	AGE GROUP (years)			
20 - 39	9 (6%)	0 (0%)	0 (0%)	9 (6%)
40 - 59	39(26%)	17(11.3%)	9 (6%)	65 (43.3%)
60 - 79	37(24.7%)	15 (10%)	20 (13.3%)	72(48%)
≥80	2 (1.3%)	1 (0.7%)	1 (0.7%)	4(2.7%)
Total	**87(58%)**	**33(22%)**	**30(20%)**	**150(100%)**

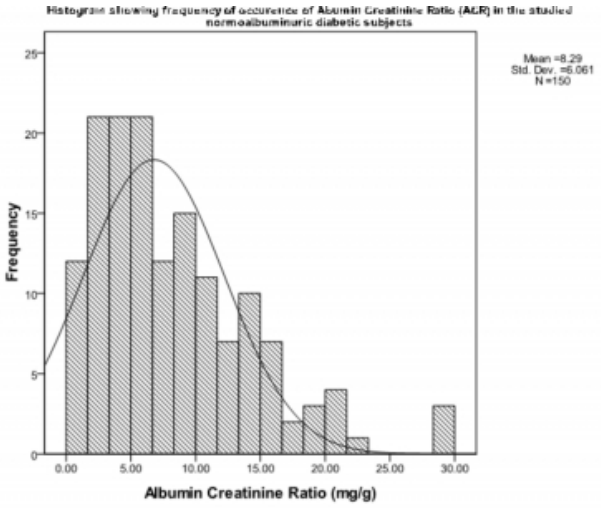
Figure 2

Table 2 Cardiovascular risk profile in the three ACR groups in the studied subjects

	ACR Less than 7.5mg/g N =82	ACR ≥ 7.5mg/g but < 15mg/g N =46	ACR ≥ 15mg/g N = 22	Remarks
Age (yrs)± SD	59.28± 12.12	56.26±10.21	55.35± 11.47	F=1.552,p=0.22
Sex (M/F)	28/54	10/36	6/14	X^2 = 2.17, p =0.34
DM duration (yrs) [mean ± SD]	7.28 ± 6.60	5.84± 6.24	7.4 ± 6.88	F = 0.786, p=0.46
HbA1c [mean ± SD]	6.07 ± 2.23	6.82 ± 2.56	7.12 ± 3.14	F = 2.209, p=0.11
FBS [mean ± SD]	161.87 ± 67.41	172.96 ± 71.97	157.85 ± 84.32	F = 0.466, p= 0.63
ACR [mean ± SD]	3.94 ± 2.05	10.88 ± 2.03	19.91 ± 4.41	F = 369.3 , p=0.001
SBP (mmHg) ± SD	141.16 ± 23.70	135.43 ± 19.9	137.5 ± 17.7	F=1.058, p=0.35
DBP (mmHg) ± SD	83.34 ± 23.70	83.93 ± 11.4	80.5 ± 10.5	F=0.541, p =0.58
WC [mean ± SD]	93.68 ± 13.70	91.81±12.4	91.30 ± 11.4	F = 0.452, p=0.64
BMI [mean ± SD]	29.16 ± 6.79	28.58 ± 6.25	25.52 ± 4.08	F = 0.542, p=0.58
T. Cholesterol [mean ± SD]	199.52 ± 67.41	187.54 ± 41.0	189.90 ± 39.70	F = 1.242, p= 0.29
Triglyceride [mean ± SD]	120.00 ± 53.10	119.83 ± 55.4	96.10 ± 44.3	F =1.787, p=0.17
HDL [mean ± SD]	42.74 ± 14.1	43.10 ±17.60	38.25 ±13.70	F = 0.806, p= 0.45
LDL [mean ± SD]	110.05 ± 38.40	124.43 ± 43.30	133.30 ± 33.60	F = 1.728, p= 0.18

Figure 3

Figure 1 Histogram showing frequency of Albumin Creatinine Ratio (ACR) in the studied normoalbuminuric diabetic subjects



DISCUSSION

Our findings demonstrate a high background prevalence of cardiovascular risk factors in normoalbuminuric diabetic subjects (86.67% of the studied subjects) that are not associated with the degree of albumin excretion. This has clinical relevance, as the population studied consists of diabetic patients with relatively short duration of diabetes (Duration of diabetes was less than 5 years in 58% of the patients, with a mean of 6.8yrs).

The impact of this early presence of multiple cardiovascular risk factors (many of them also risk factors for the development of CKD) on future development of diabetic nephropathy in the patients would require further evaluation.

A leftward skew of the albumin Creatinine ratio was observed in this sample of patients [Figure 1]. This may be attributable to the relatively short duration of diabetes mellitus in these patients as nephropathy is a long term complication of diabetes mellitus.

CARDIOVASCULAR DISEASE RISK FACTORS

HYPERTENSION

The prevalence of hypertension in the studied patient population was 50%. There was no statistically significant differences when males were compared with females [X^2 = 0.502, p=0.48]. However, compared with the general population with an estimated prevalence of about 25% [18,19,20] in our country, hypertension was significantly higher in the studied diabetic patients than in the general population [X2 = 46.552, p<0.0001].

Hypertension however, was not found to be significantly associated with the degree of albuminuria in the normoalbuminuric range of proteinuria in this study. Apparently due to the fact that hypertension is a common co-morbid illness independent of Diabetes in type 2 diabetic patients.

Coexistence of hypertension with diabetes have been found to confer greater additive risk of development of cardiovascular disease in diabetic patients, compared with patients having diabetes or hypertension alone.[21,22,23]

OBESITY WITH VISCERAL FAT DISTRIBUTION.

Prevalence of obesity was found to be 37.3% in the studied patients. Obesity was commoner in female subjects compared with males [32% Vs 5.3%. X^2 =11.345, p<0.05]. A similar result was found when visceral fat distribution was assessed using the patients' waist circumference. [52% Vs5.4%. X2 = 39.458, p<0.05]. However, there was no significant correlation between the body mass index and

degree of proteinuria [r= -0.85, p>0.05].

Relationship between body weight and cardiovascular death in the general population is curvilinear. Relative to normal weight, risk of death due to cardiovascular disease increases in overweight and obese individuals. However, it is also higher for individuals who are malnourished.[24]

In the diabetic subjects, obesity has been found to contribute significantly to cardiovascular diseases by many investigators.[25,26,27] The high prevalence of obesity, in our study population with relatively short duration of diabetes mellitus and its coexistence with multiple cardiovascular risk factors portends future high cardiovascular disease burden for the group more especially if nephropathy develops.

GLYCAEMIC CONTROL

Glycaemic control was found to be good in 70.7% of the studied subjects. This is slightly higher than findings by other authors working in other parts of the country.[28] However, residents of Lagos where our hospital is located are generally believed to be more affluent than those living in other parts of the country and are thus able to afford the cost of diabetes care than others living in the other parts of the country.

There was no statistically significant difference in glycaemic control when the three ACR groups were compared. This as noted earlier might be due to the relatively short duration of Diabetes in our group as long term complications of Diabetes such as nephropathy are yet to set in, given the short duration of the patients' illness.

DYSLIPIDAEMIA

The most common lipid abnormality found in our patient group was low High Density Lipoprotein, found in 35.3% of the patients. Elevated LDL-C was found in 20% of the subjects, 13.3% had elevated total Cholesterol while 10% had hypertriglyceridaemia. Multiple lipid abnormality occurred in 18(12%) of the subjects. This observation is similar to findings by other investigators in Nigerian diabetic patients.[29,30,31] There was no significant correlation between the measured lipid abnormalities, and no significant differences exists between the three ACR groups. Table II.

Dyslipidemia is a major underlying risk factor contributing to the excess CVD risk in the general population, and is usually more atherogenic in the presence of diabetes.[32] The finding of a high prevalence of atherogenic lipid profile with a high background prevalence of other Cardiovascular Disease risk factors in our studied normoalbuminuric subjects provide a pointer to the very high burden of Cardiovascular Disease that should be expected in these patients if they develop nephropathy.

CONCLUSIONS

Our study demonstrates a high background prevalence of Cardiovascular Disease risk factors in normoalbuminuric Diabetic subjects with short duration of diabetes. Therefore, physicians working in this environment should appreciate this fact and make active efforts at diagnosing and managing these risk factors early, in order to reduce Cardiovascular Disease morbidity and mortality in our diabetic patients.

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