AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 33 NUMBER 1 MARCH 2004

ISSN 1116—4077

Afr. J. Med. med. Sci (2004) 33, 19-22

Prevalence of microalbuminuria in newly diagnosed Type 2 diabetic patients in Jos Nigeria

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Summary
Diabetic nephropathy contributes significantly to end- stage renal disease in Nigeria. The earliest clinically detectable stage is that of microalbuminuria when interventions could halt or retard the progression to end- stage renal disease. To investigate the prevalence of microalbuminuria in newly diagnosed type 2 diabetic patients and its clinical correlates in Jos, consecutive patients with newly diagnosed type 2 diabetes attending two large hospitals in Jos were evaluated at three different occasions of monthly intervals for microalbuminuria using Micral test strips II. Patients with proteinuria, positive nitrite test/ urine microbial culture, acute illnesses or cardiac decompensation were excluded. Out of a total of 99 patients recruited, only 65 completed the study. Microalbuminuria was present in 32(49.2%) of the patients, and was significantly associated with mean arterial pressure, systemic hypertension and diabetic retinopathy ($P < 0.05$). Microalbuminuria is common in newly diagnosed patients with type 2 diabetes mellitus. Our finding supports routine screening for microalbuminuria as part of the initial evaluation of these patients.

Keywords: *Diabetes, diabetic nephropathy, microalbuminuria*

Résumé
Le diabéte néphropathique contribue signicativement a l'étape finale de la chute des riens aux nigérians. La detection clinique précose est celle du taux de microalbuminurie car les interventions pouraient retardé la progression a l'étape finale de cette maladie. Pour investiguer ce taux des patients diabétiques type 2 diagostiqués , ayant le microalbuminurie et les correlations dans 2 hopitaux dans la Ville de Jos a trios differents occasion par mois utilisant le test de micral strips II. Les patients ayant la proténurie ,le test de nitrite était positif a la culture microbiénne de l'urine, les patients ayant les maladies acute ou la décompensation cardiaque étaient exclu. Soixante cinq (65) des 99 paients recruités completaient l'étude. La microalbiuminurie était present chez 32 patients (49.2%) et était significativement associés avec la tension arterielle moyenne, l'hypertension systemique et la rétinopathie diabétique ($P<0.05$). En conclusion, la microalbuminurie est commune chez les patients récemment diagnostiqués ayant le diabéte mellitus type II. Ce résultat supporte le test routine pour la micoalbuminurie comme partie de l'évaluation initiale de ces patients.

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Introduction

Diabetic nephropathy is the third leading cause of end stage renal disease (ESRD) in Nigeria [1]. The earliest clinically detectable stage of this disease is that of microalbuminuria [excretion of albumin in urine in amounts greater than 30mg/24hour (20 µg/min) but less than or equal to 300mg/24hour (200 µg/min) [2]. This stage is characterized by an increased risk of developing some complications of diabetes mellitus (DM), especially overt nephropathy and retinopathy. It is also the stage when interventions could halt the progression and/or the development of these complications [3,4].

Microalbuminuria occurs in 14- 19% of newly diagnosed patients with type 2 DM in the Western world [5-7], although it has been reported to predate the onset of hyperglycaemia and symptoms of DM in some cases [8]. Though scanty, available data suggests that microalbuminuria occurs frequently in Nigerians with type 2 DM. While Adebisi *et al* [9] reported a frequency of 25% in Ilorin; we recently reported a figure of 41.7% in Jos [10]. However, none of these studies was in newly diagnosed patients. We therefore, report the prevalence of microalbuminuria in Nigerians with newly diagnosed type 2 DM and its clinical correlates using Micral test strips, a relatively cheap and available method of detecting microalbuminuria.

Material and methods

Study design

This is a five-year cross-sectional study of newly diagnosed type 2 diabetic patients [11] seen at the medical out patient clinics of the Jos University Teaching Hospital (JUTH) and Our Lady of Apostle Hospital Jos. Evaluation of patients was carried out within five months of diagnosis.

Data collection

Each consecutive patient was interviewed and physically examined. Blood pressure (BP) was measured on the right arm using standard sphygmomanometer (ACCOUSON; cuff 12 x 15cm) supine and erect; diastolic BP recorded at phase V Korotkoff sounds. Nervous system examination included fundoscopy, deep tendon reflexes, and sensory and motor functions. Each patient's early morning first void (mid-stream) urine sample was tested for clinical proteinuria using multi-stix and negative samples tested for microalbuminuria using Micral test II strips (Boehringer Mannheim UK, batch number 28662631). This procedure was done on at least three occasions of one monthly interval. Urine culture and glycaemic assessment using a mean of three fasting blood glucose values were done for all the subjects. Glomerular filtration rate (GFR) was estimated by the Cockcroft and Gault formula [12]. Patients with acute illnesses, cardiac decompensation, clini

cal grade proteinuria, positive Nitrite test and/ or urinary microbial culture were excluded from the study.

Definitions

1. Microalbuminuria was defined as present if at least two of the urine samples produced a reaction colour corresponding to 20mg/L albumin or more.
2. Hypertension: previous treatment for hypertension and/ or BP ≥ 140/90mmhg [13] on at least three different occasions of monthly intervals.
3. Retinopathy: Background retinopathy as micro-aneurysms, dot and blot hemorrhages, hard exudates and proliferative retinopathy as new vessel formation [14].
4. Peripheral neuropathy: failure to elicit the knee and/ or ankle reflexes after reinforcement with or without symptoms of neuropathy or gross sensory disturbance in both feet [15].

Statistics

Statistical analysis was performed using EPI Info 2000 version 1.1.2a [16]. Results are expressed in means (SD). The Student "t" test was used to compare means and Chi- Square to test the significance of associations. The non- parametric test, Kruskal- Wallis, however was used to analyze the mean arterial pressure (MAP), as the values were not uniformly distributed. Probability values < 0.05 were considered significant.

Results

A total of 99 patients were recruited for the study, 14 were excluded because of positive proteinuria on diagnosis while 20 were lost to follow-up, hence 65 patients completed the study. There were 28 males (43%) and 37 females (57%) giving a male to female ratio of 1:1.3. The mean age of the study subjects was 51.53 ± 10.14 years. Microalbuminuria was present in 32 (49.2%) of the patients with a preponderance of females (59.4%).

The mean age of patients with and without microalbuminuria were similar, being 50.90 ± 9.69 and 51.78 ± 8.73 years respectively, p = 0.7 (Table 1). Similarly, the means of body weight and body mass index (BMI) were not different between the patients with or without microalbuminuria. Diabetic retinopathy (background) occurred in 62.5% of subjects with microalbuminuria compared to 36.4% of those without ($P < 0.0004$). Peripheral neuropathy was however not associated with microalbuminuria ($p > 0.05$). The presence of hypertension was significantly associated with microalbuminuria, being present in 37.5% subjects with microalbuminuria compared to15.1% of those without ($P = 0.004$). Although the mean systolic and diastolic blood pressures were similar for both groups, the mean arterial blood pressure (MAP) was significantly associated with microalbuminuria (103.34 ± 11.61 mmHg versus 97.39 ± 17.21 mmHg, Kruskal- Wallis H = 4.52, $P = 0.03$).

The mean fasting blood glucose level was higher in patients with microalbuminuria compared to those without, although the difference was not statistically significant (8.80 ± 2.89 vs. 8.29 ± 3.75 mmol/L; p = 0.7). The mean total cholesterol and high- density lipoprotein (HDL) levels were lower in patients with microalbuminuria compared to those without (3.95 ± 0.92 Vs. 4.04 ± 1.00 mmol/L and 0.93 ± 0.22 Vs. 1.02 ± 0.33 mmol/L respectively). These differences were however not statistically significant ($P = 0.7$ and 0.2 respectively). The mean triglyceride and low-density (LDL) lipoprotein were on the contrary, higher in patients with microalbuminuria compared with those without (1.25 ± 0.57 Vs. 1.19 ± 0.63 mmol/L and 2.88 ± 3.16 vs. 2.42 ± 1.06 mmol/L respectively), although these were not statistically significant ($P = 0.7$ and 0.4 respectively). Correspondingly, the LDL/ HDL ratio, an index of atherogenicity was higher in patients with microalbuminuria compared to those without, being 3.23 ± 3.53 and 2.73 ± 2.42 mmol/L respectively. This difference was however not statistically significant (P 0.5)

Table 1: Clinical charateristics of newly diagnosed diabetics with microalbuminuria in Jos

	Patients with microalbuminuria	Patient without microalbuminuria	P value
Mean age (yrs)	50.90±6.69	51.78± 8.73	0.7
Sex (M/F)	13/19	15/18	
Mean BMI** (Kg/M2)	27.75±6.18	27.16±5.85	0.6
Mean SBP# (mmHg)	133.94±18.54	125±20.16	0.1
Mean DBP## (mmHg)	87.50±11.36	83.03±16.10	0.2
Frequency Hypertension (%)	of 37.5	15.1	0.004
Frequency Retinopathy (%)	of 62.5	36.4	0.0004
Frequency Neuropathy (%)	of 59.4	51.5	0.3

± = Standard deviation of means;
M/F M= Males and F = Females;*
*BMI** = Body Mass Index:*
 # + Systolic Blood Pressure:
= Diastolic Blood Pressure

No difference existed in the level of blood urea in patients with and without microalbuminuria (4.41 ± 1.33 vs. 4.54 ± 1.20 mmol/L respectively; $P = 0.2$). The mean serum creatinine and mean GFR appeared lower in patients with microalbuminuria compared to those without, although these differences were not statistically significant (79.94 ± 20.93 Vs. 86.30 ± 16.63 µmol/L; $P = 0.2$ and 91.03 ± 20.73 Vs. 98.11 ± 20.32 ml/min; p = 0.2 respectively).

Discussion

Nearly half of the patients with newly diagnosed type 2 DM in this study had microalbuminuria. This figure is at least twice the reported figures of 14- 19% in the Western world [5-7]. In this study, we used a convenient and semi-quantitative side room test kit as opposed to the method of radioimmunoassay used in the previous studies. This test kit has a sensitivity of 91% and specificity of 97% and a positive predictive value of 67% when compared to radioimmunoassay but it is cheaper, more readily available and easy to use. It is likely then that this may in part, account for the rather high prevalence in this study.

Another possibility for this high prevalence of microalbuminuria is the problem of late diagnosis of type 2 DM. It has been established that patients with type 2 DM in the western world, have had hyperglycaemia for an average of 6 to 10 years before having a diagnosis made [17,18]. It is very likely then that in resource poor countries like ours where access to health care is not readily available, that the duration of hyperglycaemia before diagnosis would be longer, hence a higher prevalence of target organ damage at diagnosis.

It is however surprising that the prevalence of microalbuminuria in this study is much higher than the 25% reported from Ilorin [9] and the 41.7% previously reported by us [10] in patients with long standing type 2 DM. The difference in prevalence of microalbuminuria could be partly attributed to differences in patient population. The presence of hypertension may also have been contributory as previously reported [2,19]. Further-more, our study demonstrated a significant association between microalbuminuria and mean arterial blood pressure (MAP), a finding that agrees with that of Haneda *et al* [19]. The MAP is an indicator of the pressures to which the end organs are exposed and thus may have contributed to target organ damage in this study. MAP may then be useful in optimising blood pressure control in type 2 diabetics with concomitant hypertension. The association of microalbuminuria with hypertension in this study is consistent with the literature [9,19] and may account in part for the increased cardiovascular risk in type 2 DM [20].

The relatively small number of patients presented in this study however, limits the generalisation of our findings on the prevalence of microalbuminuria. This has been a major problem with most reports on microalbuminuria [9,10] and may influence the true magnitude of the problem.

Microalbuminuria was significantly associated with the presence of diabetic retinopathy in this study as had been demonstrated by previous studies [21,22]. This suggests that microalbuminuria may be highly predictive of diabetic retinopathy. This is not surprising, as microalbuminuria is not specific for nephropathy alone but is considered to reflect generalized vascular damage (the Steno hypothesis) [20]. Microalbuminuria and diabetic retinopathy have common pathogenesis, as they are both microvascular complications of diabetes. Where screening for microalbuminuria in patients with type 2 DM is not possible, the finding of diabetic retinopathy should raise the suspicion of the presence of microalbuminuria.

Conclusion

This report shows that nearly half of the patients with newly diagnosed type 2 DM in Jos, Nigeria have microalbuminuria; therefore routine screening is recommended in ideal circumstances. However since this may not be applicable in resource poor settings, the finding of retinopathy should raise the suspicion of its presence.

Acknowledgements

We wish to thank Drs Chuhwak, Idalu and Achinge in these clinics for allowing us access to their patients.

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Received: 19 June 2003
Accepted: 27 January 2004