MICROALBUMINURIA PREVALENCE STUDY IN HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETES IN PAKISTAN

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Background: Microalbuminuria is a renal marker of general vascular endothelial damage and early atherosclerosis with adverse prognostic implications. It is associated with diabetes, insulin resistance, central adiposity and hypertension **Objective:** The Microalbuminuria Prevalence Study (MAPS) aimed to assess the prevalence of microalbuminuria in consecutively-screened hypertensive adult patients with type 2 diabetes mellitus in 103 centres of ten Asian countries. **Design:** Cross-sectional clinic-based epidemiological study. **Methods:** This is the sub-analysis of data collected from patients attending the OPD of Baqai Institute of Diabetology and Endocrinology in Pakistan. Patients attended one study visit with no follow-up. Patients with bacteriuria and haematuria were excluded. **Results:** A total of 99 subjects were studied out of which 56.3% were females. Mean age was 49.9±10.8 years. The prevalence of macroalbuminuria and microalbuminuria was 9.09% and 24.2% respectively. **Conclusion:** In Pakistan the prevalence of diabetic kidney disease was high in diabetic hypertensive subjects which is alarming and indicates an impending pandemic of diabetic renal and cardiovascular disease in the region.

Keywords: MAPS, Pakistan, Diabetes, Hypertension, Microalbuminuria

INTRODUCTION

Microalbuminuria is a renal marker of general vascular endothelial damage and early atherosclerosis with adverse prognostic implications. It is associated with diabetes, insulin resistance, central adiposity and hypertension.[1] Microalbuminuria is defined as a urinary albumin excretion rate of 30 to 300 mg in 24 hour urine collection or as a urinary albumin excretion rate of 20 to 200 mg/min in a timed overnight urine collection. It is undetectable by conventional tests, however, these values are currently detectable by semi-quantitative dipstick tests, and can be accurately measured by several widely available sensitive methods such as ELISA, RIA, and nephelometry.

In healthy adult subjects, the mean concentration of urinary albumin is found to be 5.1 mg/L, regardless of the time of collection with 95% of samples having a concentration of less than 29.6 mg/L. Although a 24-hour urine collection is the most appropriate method for the measurement of protienuria, there are limitations. Since exercise and erect posture increase albumin excretion, an overnight urine collection is suggested as the most representative sample to detect and evaluate microalbuminuria.

Association of factors such as age, duration and type of diabetes, blood glucose levels with microalbuminuria is well known.[2] It has been shown to be a strong predictor of renal dysfunction and reflects vascular abnormalities such as atherosclerosis, retinopathy, probably nephropathy and is independently associated with renal and cardiovascular risks.[3,4]

Since the early 80s, it has been recognized that microalbuminuria predicts the onset of protienuria and chronic renal failure in both insulin and non-insulin-dependent diabetes mellitus.[5,6] Moreover, non-insulin-dependent diabetic patients with microalbuminuria have an increased mortality rate, especially from cardiovascular disease.[6,7] Also, these patients usually have overt hypertension when microalbuminuria is first detected.[8] This finding however is usually absent in patients with type 1 diabetes and in incipient nephropathy.[9] Although a very recent study suggests that an increase in systolic blood pressure during sleep precedes the development of microalbuminuria.[10,11] Our study aimed to see the prevalence of microalbuminuria in consecutively-screened hypertensive adult patients with type 2 diabetes mellitus.

MATERIAL AND METHODS

The study design and methods of MAPS have been previously described[13], and a brief outline is presented here. Outpatients older than 18 years of age, with previously diagnosed hypertension (treated or untreated) and type 2 diabetes (treated or untreated) were consecutively screened at each participating centre. Previously diagnosed hypertension and diabetes were historically defined as mentioned in the patients' medical records and verified during monitoring visits. Patients with known (previously diagnosed) macroalbuminuria were excluded. Patient data included demographic information, past medical history, dates of onset of hypertension and diabetes, current diabetes status (complications such as retinopathy, peripheral neuropathy, as well as CV disease, glycaemic

control, current therapy), current hypertensive status (mean of two consecutive measurements of office supine SBP and diastolic blood pressure, current treatment), and dyslipidaemic status (known or previously diagnosed dyslipidaemia, use of lipid-lowering agents). A single urine specimen was collected in disposable plastic vessels on the same day as the screening visit. Micral-Test from Roche Diagnostics was used in screening for microalbuminuria.

For the current analysis, the authors restricted data to include only those patients recruited from study centre in Pakistan. Patients with positive leukocytes and nitrites, indicative of significant bacteriuria, and patients with erythrocytes or haemoglobin equal or above 25/µL, indicative of significant haematuria, were excluded from the analysed population to constitute the per-protocol population.

Quantitative variables were described by their mean, standard deviation, count and number of missing values. Qualitative variables were described by the counts and percentages of each response choice, missing data were included in the calculation of percentages.

RESULTS

Pakistani patients constituted 1% of the overall enrolments in MAPS. Basic clinical characteristics of the per-protocol population (n=99) are shown in Table-1.

A family history of hypertension, diabetes and CV disease was reported in 16%, 72% and 2% of patients, respectively. Overall, 46% had at least one CV complication: previous transient ischaemic attack (2%), previous stroke (3%), angina pectoris (11%), myocardial infarction (9%), heart failure (0%) and peripheral arterial disease (30%). Dyslipidaemia was present in 23% patients, and 17% were using lipid-lowering drugs, all of them were taking statins. The mean duration of diabetes was 9.13±6.86 years, with a mean age of onset of 53.14±10.61 years. Measures of glycaemic control revealed mean glycosylated haemoglobin (HbA1c) level of 9.32±2.14% while a mean creatinine level was 1.19±1.38. Current methods of diabetes management included dietary control in 80% of the total patients while 40% of the patients were having regular physical exercise. Oral hyperglycaemic agents were used by 79% and combination therapy of insulin and oral hypoglucemic agents was used by 21% patients. Sixty eight per cent of patients had at least one diabetic complication, with diabetic retinopathy and peripheral neuropathy present in 20% and 66%, respectively. The mean duration of hypertension was 9.20±7.33 years, with an average age of onset of 44.01±10.93 years. Mean blood pressure was 144.19±19.90/ 79.64±10.69 mm Hg. Overall, 37.3% of patients were on the target blood pressure of 130/85 mm Hg (the target level recommended by the American Diabetes Association for adequate blood pressure control at the time of study initiation (14). Only 9.09% of macroalbuminuric, 24.2% of microalbuminuric and 66.66% of normoalbuminuric patients were on the target blood pressure.

Mean values of BMI were not found significantly different in three groups (normoalbuminuric, microalbuminuric and macroalbuminuric subjects) (*p*-value=0.266) (Table-1). The majority of patients (97.94%) were receiving treatment for their hypertension: 28.42% and 71.58% were receiving monotherapy and combination therapy respectively. The distribution of antihypertensive therapy was as follows: diuretics (55.79%), alpha blockers (10.53%), beta blockers (49.47%), calcium channel blockers (34.74%), ACE inhibitors (52.63%) and angiotensin II receptor blockers (ARB) (6.32%).

The prevalence of macroalbuminuria and microalbuminuria was 9.09 and 24.2% respectively shown in Table-2.

Only 37.3% of patients achieved blood pressure readings below the target blood pressure of 130/85 mm Hg.

Table-1: Basic clinical characteristics of the per protocol population.

	Macroalbuminuric (n=9)	Microalbuminuric (n=24)	Normal (n=66)	P value	Total (n=99)
Male n (%)	3 (6.81%)	15 (34.09%)	26 (59.09%)	0.000	44 (44.4)
Female n (%)	6 (10.9%)	9 (16.36%)	40 (72.72%)	0.000	55 (55.6)
Mean Age (years)	55.67±13.73	53.08±13.27	52.78±9.13	0.755	53.12±10.66
Mean BMI (kg/m^2)	30.176±6.25	27.377±4.29	28.46±3.92	0.266	28.35±4.25
Waist/Hip ratio	1.008±0.298	0.9305±.077	0.9243±.082	0.019	0.9345±0.11
Mean SBP (mmHg)	131.11±13.64	141.32±23.22	147.06±18.60	0.054	144.19±19.9
Mean DBP (mmHg)	77.22±9.718	78.36±8.27	80.47±11.6	0.548	79.65±10.67
Plasma Glucose(mg/dl)	130.33±24.2	160.52±68.86	161.31±52.98	0.293	57.79±55.83
Duration of Diabetes(yr)	8.7±9.1305	9.32±7.24	9.09±6.68	0.948	9.32±6.87

Table-2: Macroalbuminuria and Microalbuminuria of the per-protocol population

	Number (n= 99)	%	95% CI
Macroalbuminaria	9	9.09	3.3–14.7
Microalbiminaria	24	24.2	15.6–32.4
Normalbuminaria	66	66.6	56.6–75.4

DISCUSSION

Microalbuminuria is the first clinical sign of involvement of kidney in patients with type2 diabetes. It also predicts the underlying cardiovascular disease. Hypertension which is often accompanied is itself a risk factor for microalbuminuria. Parving *et al*, in 1974 was the first to report microalbuminuria in hypertensive patients without diabetes.[13] Since then, several studies have shown that microalbuminuria occurs in about 30% of patients with mild or moderate hypertension, ranging from 7% to 40% depending on age and ethnic group.[14,15]

The MAPS is the first large multicentre epidemiological study conducted in Asia to determine the prevalence of microalbuminuria in patients with type 2 diabetes and hypertension. This sub analysis of data from Pakistan indicates that 24.2% of the 99 analysed patients had microalbuminuria. The prevalence of microalbuminuria was slightly higher than the rates of 17% to 21% reported from western population–based studies in patients with diabetes.[16] This is in contrast to another Pakistani study which has shown microalbuminuria to be around 34% in diabetic subjects [17] the likely reason could be the use of antihypertensive drugs that may have affected the results. Overall in this study of ten Asian countries, the prevalence of microalbuminuria was 39.8% and the prevalence of macroalbuminuria was 18.8%. The highest prevalence of microalbuminuria was observed in Korea (56.5%) and the lowest in Pakistan (24.2%).When analyzed by type of practice, the highest prevalence of microalbuminuria was observed in patients attended by cardiology or nephrology specialists (43.8% [41.8–45.7,95% CI]) and the lowest in patients followed by general practitioners (35.0% [33.6–36.4, 95% CI]).[13]

Other epidemiological studies report prevalence of microalbuminuria in type 2 diabetes ranging between 8% to 32%.[6,11] This variation may be due to different criteria used for defining the condition, the stage of the disease, method of assessment and ethnicity[18] while prevalence of microalbuminuria in general population is reported between 5–10%.[3]

Microalbuminuria was more frequent in males (23.8% vs. 9.3%) as compared to females which was observed by others also.[19,20] We have also found significant association of microalbuminuria with obesity in other studies, in contrast to this study, and is now a well known fact that microalbuminuria is associated with metabolic syndrome.[21]

In this study in contrast to other studies[19,22], microalbuminuria was more frequent in younger age group (<50 years) as compared to older age group (p<0.005), this is most probably due to combination of risk factors, i.e., diabetes, obesity and hypertension in younger age group.

There are a few limitations to the study results. Firstly, microalbuminuria detection was based on a single urine spot collection with semi-quantitative dipstick determinations. The ADA guidelines[23] acknowledge that this technique has acceptable sensitivity and specificity, but recommend that positive tests be reconfirmed with more specific methods and, due to the marked day-to-day variability, that several collections should be done in a 3 to 6 month period before designating a patient as having microalbuminuria. Moreover, a within-trial validation of the Micral-test was performed by one of the authors (C.Y. Pan) in China. Micral-test results of 119 consecutive MAPS patients were compared with those obtained by immunochemical assay (DCA 2000+ commercial kit, Bayer Diagnostics, Germany) and 56 samples were compared with immunoturbidimetric determination (Beckman Array 360 system, USA). In comparison with DCA 2000+ (albumin/creatinine ratio), the Micral-test had an overall sensitivity of 91.9% and specificity of 63.4%. In comparison with immunoturbidimetric assay, the overall sensitivity and specificity of the Micral-test was 95% and 80%, respectively.

CONCLUSION

This sub-analysis of data from the Pakistani cohort of MAPS demonstrated a high prevalence of microalbuminuria in hypertensive patients with type 2 diabetes. Screening for microalbuminuria in all patients with type 2 diabetes is recommended, as early treatment with CV risk reduction strategies is critical.

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