ORIGINAL ARTICLE

Microalbuminuria Prevalence Study in Hypertensive Type 2 Diabetic Patients in Malaysia

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Summary

Microalbuminuria is the earliest indicator of diabetic kidney disease and generalised vascular endothelial dysfunction. The Microalbuminuria Prevalence (MAP) Study was carried out to assess the prevalence of macroalbuminuria, microalbuminuria and normoalbuminuria in Asian hypertensive patients with type 2 diabetes on usual care. This paper presents a subanalysis of data from patients in Malaysia. In 733 analysed patients, the prevalence of macroalbuminuria and microalbuminuria was 15.7% and 39.7%, respectively. The high prevalence of diabetic nephropathy in these high-risk patients is a cause for concern, and the Malaysian Health Care system should be prepared for a pandemic of end-stage renal disease due to diabetic nephropathy.

Key Words: Diabetes Mellitus, Type II, Diabetic nephropathy, Hypertension, Albuminuria, Proteinuria

Introduction

Patients with type 2 diabetes are almost twice as likely to have hypertension as the nondiabetic population[1]. The prevalence of hypertension is further increased in patients with type 2 diabetes and renal disease as manifested by elevated urinary albumin excretion rates compared with patients with type 2 diabetes and no evidence of renal involvement[2]. The higher the systolic blood pressure (SBP), the greater the absolute excess cardiovascular (CV) risk for patients[3]. This indicates a greater potential for prevention of CV death among patients with diabetes by optimising blood pressure control[2,3]. Because of the aging population, an increase in obesity and sedentary lifestyle, the prevalence of diabetes is growing, particularly in Asia[2]. Currently, Malaysia has the fourth highest rate of diabetes in Asia[2]. As occurs elsewhere, diabetes is the leading and an increasing cause of end stage renal disease (ESRD) in Malaysia. Diabetics constitute 30% of all new ESRD patients starting dialysis in 1996, 45% in 2000 and 51% in 2003 respectively[4].

Because of the adverse impact of microalbuminuria and proteinuria on survival in patients with diabetes[5-7] screening and intervention programmes should be implemented early[8,9]. Annual screening for microalbuminuria is recommended by the American Diabetes Association[10], since a high proportion of patients with type 2 diabetes are found to have microalbuminuria or overt nephropathy shortly after diagnosis of their diabetes. Screening using a semi-quantitative dipstick test is simple, and provides immediate and accurate results[11].

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There have been few reported studies in Asian populations on the prevalence of microalbuminuria in this high risk population[12-17]. These studies have only explored the percentage of microalbuminuria in either patients with diabetes or patients with hypertension. The MicroAlbuminuria Prevalence (MAP) Study was the first multicentre study to evaluate the prevalences of microalbuminuria and new-onset macroalbuminuria in Asian patients with type 2 diabetes and hypertension[18].

Materials and Methods

The study design and methods of the MAP study have been previously described by Wu AYT and Kong NCT et al in Diabetologia (2005)[18] and are dealt with briefly here. Outpatients from different Asian ethnic subgroups, 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. Microalbuminuria is defined as urinary albumin excretion > 30< 300 mg/24 hours (equivalent to 20-200 µg/min on a timed specimen or 30 mg/gm creatinine on a random morning urine sample). Macroalbuminuria is defined as urinary albumin excretion ≥ 300 mg/24 hours. Previously diagnosed hypertension and diabetes were historically defined as mentioned in the patient medical record 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 systolic blood pressure [SBP] and diastolic blood pressure [DBP], current treatment) and dyslipidaemic status (known or previously diagnosed dyslipidaemia and/or use of lipid-lowering agents).

For the current analysis, we restricted data to include only those patients recruited from study centers in Malaysia. All patients with confirmed onset dates of hypertension and type 2 diabetes constituted the analyzed population. A single urine specimen was collected in disposable plastic vessels on the same morning (up to noon) as the screening visit, and screened for macroalbuminuria using the Nephur7Test® (Roche Diagnostics GmbH, Mannheim, Germany). Patients whose urine tested positive for 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 analyzed population to constitute the per-protocol population. Negative urine samples were then screened for microalbuminuria using the Micral-test® (Roche Diagnostics GmbH, Mannheim, Germany), a semi-quantitative urine test strip.

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 not included in the calculation of percentages. No statistical tests were performed on the albuminuric subgroups. Prevalence rates were calculated with a two-sided 95% confidence interval (CI). The significance level was fixed at 5%. Analyses were performed using Statistical Analysis System software version 8.02.

Results

Malaysia constituted 15% of the overall enrolment in the Asian MAP Study conducted from February 2002 to October 2002. A total of 999 patients were recruited from six medical centres in Kuala Lumpur, Kota Bharu, Kuching and Kota Kinabalu. Patients with bacteriuria and/or haematuria on the Nephur7Test® were excluded from the per-protocol analysis (Figure 1). Patient demographics of the per-protocol population (N = 733) are described in Table I. The majority of patients were Malay (41.2%) or Chinese (41.5%). The mean age was 58.6 ± 10 years, and 69% of patients were aged between 49 and 70 years. A total of 63% of patients had a family history of hypertension, diabetes, CV or kidney disease. Most patients (76%) were non-smokers, 6% were current smokers and 18% were previous smokers.

Characteristics of type 2 diabetes in the per-protocol population are described in Table II. The mean duration of diabetes was 7.1 ± 6.9 years, and the mean age when diabetes was first diagnosed was 51.8 ± 11 years. Measures of glycaemic control revealed a mean serum HbA1C level of 8.0 ±1.9% (NR 4.0-6.4%) and a mean serum creatinine level of 92.8 ± 31.8 µmol/L (NR 64-133). Diabetic complications were more common in the macroalbuminuric subgroup (31.3% had at least one diabetic complication), compared with the microalbuminuric subgroup (21.3%) and

normoalbuminuria subgroup (18.4%) (Table II). Current methods of diabetes management included: dietary control in 80.6% of patients, regular physical exercise in 50.1%, oral hypoglycaemic agents in 89.9% and insulin therapy in 7.1%. Twenty-two per cent of patients had at least one known CV complication, including previous transient ischaemic attack, previous stroke, angina pectoris, myocardial infarction, heart failure and peripheral arterial disease.

The mean duration of hypertension was 8.1 ± 7.9 years, and mean blood pressure was 150.3 ± 19.6/ 89.2 ± 9.6 mmHg. The mean SBP was higher in patients with macroalbuminuria (158.1 ± 22.7 mmHg) than for patients with microalbuminuria or normoalbuminuria (Table III). Most patients (96.9%) were receiving antihypertensive therapy, with 42.5% of those patients on monotherapy and 57.5% on combination therapy. The distribution of therapy was: angiotensin-converting enzyme (ACE) inhibitors (59.2% of patients), calcium channel blockers (28.9%), angiotensin receptor blockers (ARB) (10.0%), beta-blockers (46.8%), diuretics (27.8%), or alpha-blockers (5.1%). Only 13.2% of patients had their SBP/DBP blood pressure below the target of 130/80 mmHg. The distribution of blood pressure levels is shown in Table III.

A high proportion of patients (70.1%) had known dyslipidaemia: 56.2% with hypertriglyceridaemia (TG), 59.7% with hypercholesterolaemia, 29.2% with high low-density lipoprotein (LDL) cholesterol and 26.3% with low high-density lipoprotein (HDL) cholesterol. 55% of the per-protocol patients were on lipid-lowering drugs; 75.2% of these patients were taking statins and 26.6% were taking fibrates. The overall prevalence of new-onset macroalbuminuria was 15.7% [14.3–17.0; 95% CI] and that of microalbuminuria was 39.7% [37.9–41.5; 95% CI]. These figures are essentially similar to those obtained for the larger Asian MAPS cohort (Table IV).

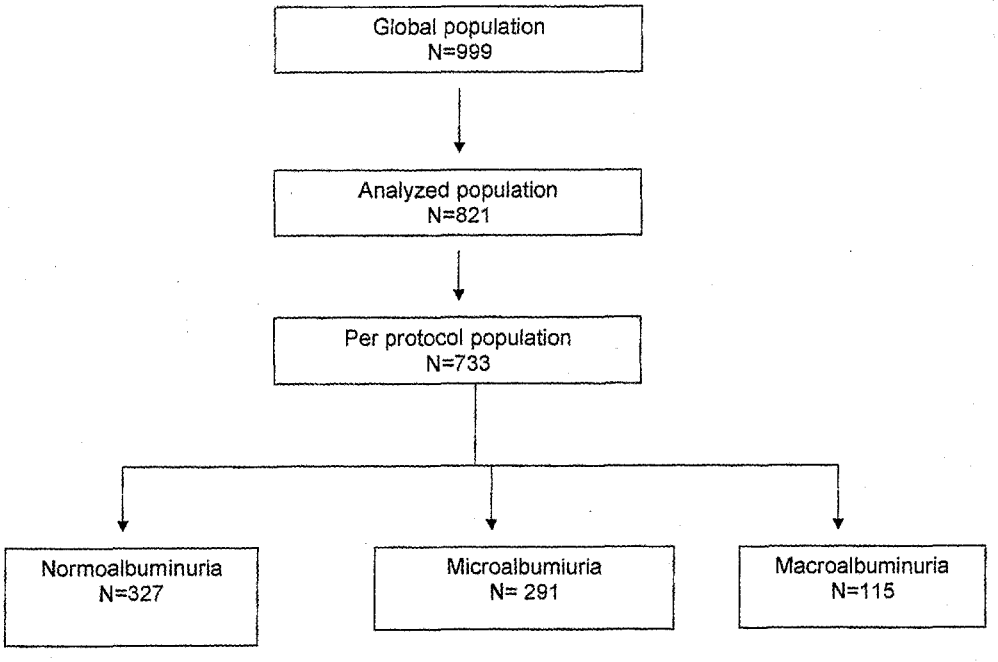

Fig. 1: Patients' disposition and urinary screening results

NB: 999 patients were enrolled. 178 were excluded (unconfirmed dates of onset of diabetes) resulting in the analyzed population of 821. A further 88 patients were excluded due to suspected urinary tract infection or significant haematuria; resulting in the protocol population of 733.

Table I: Patient characteristics*

	Macroalbuminuric (n = 115)	Microalbuminuric (n = 291)	Normal (n = 327)	Total (n = 733)
Age (years)				
Mean	60.8±10	57.8±10.5	58.5±9.5	58.6±10
Gender				
Male N (%)	60 (52.2)	120 (41.2)	144 (44.0)	324 (44.2)
Female N (%)	55 (47.8)	171 (58.8)	183 (56)	409 (55.8)
Mean height (cm)	157.7±8.7	157.3±8.7	158.7±8.8	158±8.8
Mean weight (kg)	67.5±13.6	67.6±14.6	66.8±12.7	67.2±13.6
Mean body mass index (kg/m^2)	27.1±4.4	27.2±4.7	26.5±4.1	26.9±4.4
Waist/hip ratio	0.9±0.1	0.9±0.1	0.9±0.1	0.9±0.1
Ethnicity (%)				
Chinese	39.1	38.1	45.3	41.5
Malay	47.8	45.0	35.5	41.2
Indian	7.8	12.0	11.9	11.3
Caucasian	–	0.3	–	0.1
Other	5.2	4.1	7.3	5.7
Family history				
History of diabetes	54 (47%)	136 (46.7%)	179 (54.7%)	369 (50.3%)
History of hypertension	55 (47.8%)	133 (45.7%)	156 (47.7%)	344 (46.9%)
History of cardiovascular disease	16 (13.9%)	41 (14.1%)	55 (16.8%)	112 (15.3%)
History of kidney disease	5 (4.4%)	13 (4.5%)	11 (3.4%)	29 (4%)

*Per-protocol population (N = 733)

Table II: Type 2 diabetic complications in the various categories

Variable	Macroalbuminuric (n = 115)	Microalbuminuric (n = 291)	Normal (n = 327)	Total (n = 733)
Mean duration of diabetes (years)	8.5±7.8	7.2±6.8	6.6±6.5	7.11±6.9
Mean age of onset of diabetes (years)	52.6±11.2	51±11.1	52.3±10.7	51.81±11
Known diabetic complications				
At least one complication	36 (31.3%)	62 (21.3%)	60 (18.4%)	158 (21.6%)
Retinopathy	16 (13.9%)	32 (11%)	23 (7.0%)	71 (10%)
Peripheral neuropathy	23 (20%)	37 (12.7%)	49 (15%)	109 (14.9%)
Other neuropathy	9 (7.8%)	11 (3.8%)	1 (0.3%)	21 (2.9%)
Known cardiovascular complications				
At least one complication	38 (33%)	63 (21.7%)	62 (19%)	163 (22.2%)
Previous transient ischaemic attack	3 (2.6%)	7 (2.4%)	3 (0.9%)	13 (1.8%)
Previous stroke	14 (12.2%)	18 (6.2%)	14 (4.3%)	46 (6.3%)
Angina pectoris	19 (16.5%)	33 (11.3%)	39 (12%)	91 (12.4%)
Myocardial infarction	7 (6.1%)	7 (2.4%)	4 (1.2%)	18 (2.5%)
Congestive heart failure	6 (5.2%)	11 (3.8%)	7 (2.1%)	24 (3.3%)
Peripheral arterial disease	4 (3.5%)	3 (1%)	4 (1.2%)	11 (1.5%)
Blood glucose (mmol/L)	8.9±3.6	8.8±3.2	8.5±3.2	8.7±3.2
HbA1C value (%)	8.4±2.2	8±2	7.8±1.6	8±1.9
Creatinine value	112.5±48.2	89±26.5	89.4±26.4	92.8±31.8

Table III: Hypertension in the per-protocol population

Variable		Macroalbuminuric (n = 115)	Microalbuminuric (n = 291)	Normal (n = 327)	Total (n = 733)
Mean duration of hypertension (years)		8.9±8.2	8.1±7.5	7.9±8.1	8.1±7.9
Systolic blood pressure					
Mean		158.1±22.7	151.1±19.2	146.8±17.9	150.3±19.6
Normal [≤130 mmHg]		13 (11.3%)	39 (13.4%)	68 (20.8%)	120 (16.4%)
High normal	[130–139 mmHg]	8 (7%)	29 (10%)	45 (13.8%)	82 (11.2%)
S1 (mild)	[139–159 mmHg]	42 (36.5%)	130 (44.7%)	141 (43.1%)	313 (42.7%)
S2 (moderate)	[159–179 mmHg]	28 (24.4%)	66 (22.7%)	57 (17.4%)	151 (20.6%)
S3 (severe)	[179–200 mmHg]	22 (19.1%)	26 (8.9%)	14 (4.3%)	62 (8.5%)
S4 (very severe)	[>209 mmHg]	2 (1.7%)	1 (0.3%)	2 (0.6%)	5 (0.7%)
Diastolic blood pressure					
Mean		89.2±9.6	86.2±12.1	85.6±10.1	86.4±10.9
Normal	[≤85 mmHg]	39 (33.9%)	129 (44.3%)	162 (49.5%)	330 (45%)
High normal	[>85-89 mmHg]	9 (7.8%)	28 (9.6%)	32 (9.8%)	69 (9.4%)
S1 (mild)	[>89-99 mmHg]	45 (39.1%)	90 (31%)	99 (30.3%)	234 (31.9%)
S2 (moderate)	[>99-109 mmHg]	20 (17.4%)	34 (11.7%)	29 (8.9%)	83 (11.3%)
S3 (severe)	[>109-119 mmHg]	2 (1.7%)	6 (2.1%)	4 (1.2%)	12 (1.6%)
S4 (very severe)	[>119 mmHg]	-	4 (1.4%)	1 (0.3%)	5 (0.7%)

Table IV: Comparison of the proteinuria status in Malaysian patients versus the Asian cohort. *Adapted from Wu AYT *et al.* An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. Diabetologia 2005; 48: 17-26 (Ref 18)

	Malaysia	Asia*
Total screened	999	6801
Per Protocol Population	733	5549
Normoalbuminuria	327 (44.6%)	2297 (41.4%)
Microalbuminuria	291 (39.7%)	2211 (39.8%)
Macroalbuminuria	115 (15.7%)	1041 (18.8%)

Discussion

The MicroAlbuminuria Prevalence (MAP) Study was the first large multicentre epidemiological study conducted in Asia to determine the prevalence of microalbuminuria and new-onset macroalbuminuria in hypertensive type 2 diabetic patients[18]. This sub-analysis of data from Malaysia indicates that 39.7% of the 733 per psotocol patients had microalbuminuria and 15.7% had new-onset macroalbuminuria. Malay patients were more likely to present with macroalbuminuria and microalbuminuria than Chinese or Indian patients. In a review of 1031 diabetic patients treated at a rural, government clinic in Sarawak, Wong JS had reported the prevalences of hypertension to be 75%, microalbuminuria 16% and overt proteinuria a whopping 48% respectively[16]. Mafauzy M reported on the Diabase-Asia project in Malaysia which screened 438 diabetic (96.5% with type 2) patients attending 49 primary private healthcare clinics[17]. Glycaemic, lipaemic and blood pressure control were poor and diabetic complications were prevalent – neuropathy in 30.1% of patients, background retinopathy in 23.5%, macroalbuminuria in 22.9% and microalbuminuria in 20.4%[17]. The prevalence of microalbuminuria in our study was also significantly higher than rates of 17–21% reported from Western population-based studies in patients with diabetes[19].

As the objective of the MAP Study was to seek out microalbuminuria and new-onset macroalbuminuria in hypertensive type 2 diabetics attending academic or general hospital diabetic clinics, we did not expect to report similar prevalence rates as the other studies. Microalbuminuria, being an earlier stage of diabetic kidney disease, is more amenable to aggressive treatment. Nonetheless, the high prevalence rate for microalbumiuria and the fewer new-onset macroalbuminuric patients reported by us may reflect more patients being treated with ACE-inhibitors (59.2%) and/or angiotensin receptor blockers (ARBs – 10%) at these healthcare facilities as there would be greater awareness of their benefits and greater availability of these drugs for patient care.

In this sub-analysis of the MAP Study data from Malaysia, the mean blood pressure of patients was 150.3 ±19.6 /89.2 ± 9.6 mmHg and the mean duration of hypertension was 8.1 ± 7.9 years. The severity of proteinuria correlated with duration and severity of hypertension, with macroalbuminuric patients having the greatest mean SBP and duration of hypertension. Although a high proportion of patients in this sub-analysis (96.9%) were receiving antihypertensive therapy, only 13.2% had achieved the recommended target blood pressure (130/80 mmHg)[20]. The lowest level of blood pressure control was observed in the macroalbuminuric subgroup (8.7%). In this study, only 57% of patients were receiving combination therapy.

The benefits of reducing blood pressure to the recommended goal of <130/80 mmHg in patients with diabetes are well established[21]. In the United Kingdom Prospective Diabetes Study 38 (UKPDS 38), each decrease of 10 mmHg in mean SBP was associated with a 15% reduction in risk for death related to diabetes, an 11% reduction in risk for myocardial infarction, a 13% reduction in risk for microvascular complications and a 12% reduction in risk for any diabetes-related complications[22]. In the Hypertension Optimal Treatment (HOT) study, a 51% reduction in CV events was observed in patients with diabetes randomized to a group with target DBP of ≤ 80 mmHg compared with those randomized to a target DBP of ≤ 90 mmHg[23]. It is, therefore, important to develop strategies that increase the percentage of patients who achieve optimal blood pressure control as Asian patients with type 2 diabetes have higher risk for renal complications and stroke compared with their Caucasian counterparts[24]. Hence Asian patients with type 2 diabetes and hypertension require even more aggressive antihypertensive and anti-proteinuric treatment to adequately control their blood pressure and slow the progression of nephropathy. To achieve this, multiple antihypertensive drugs are often required as occurred in 57.5% of our study cohort.

Hyperglycaemia is an important determinant for the development of proteinuria in patients with type 2 diabetes. If instituted early and maintained, effective glycaemic control has been shown to prevent the development of nephropathy and may even lead to regression of albuminuria [25-27]. Nevertheless, as evidenced by the mean HbA1C of 8.0 ± 1.9%, the majority of patients in this study did not achieve adequate glycaemic control. The mean HbA1C level was higher in the macroalbuminuric subgroup (8.4%) than in the microalbuminuric subgroup (8.0%) or the normoalbuminuric subgroup (7.8%). Wong JS *et al* had reported better glycaemic control with HbA1C levels ≤ 7.5% in 64% of their 1031 patients from the Sarawak urban clinic[16]. In the Diabcare-Asia (Malaysia) project which surveyed diabetic patients managed in primary private healthcare facilities, Mafauzy M reported that

only 12% of the patients had their HbA1C measured in the preceding 12 months. Of these, only 20% had HbA1C levels <7.0%[17].

Many studies have suggested that effective treatment of dyslipidaemia may slow the progression of nephropathy in patients with type 2 diabetes[28-30]. Despite the fact that more than 50% of patients with known dyslipidaemia in our study were prescribed a lipid-lowering agent (a statin in 75.2% and fibrates in the rest), lipaemic control was suboptimal especially with regards hypertrigylceridaemia (56.2%) and hypercholesterolaemia (59.7%). This may be related to the use of less effective statins (eg lovastatin), failure of patients to purchase the prescribed drug (eg. simvastatin) or take the said medications and poor patient compliance with diet. On the other hand, despite the high prevalence of hypertriglyceridaemia, only 26.6% of these dyslipidaemic patients were prescribed fibrates. This is another vital facet of treatment that requires to be tightened in the overall management of these high risk patients.

Microalbuminuria is the first clinical sign of diabetic vascular damage and is a predictor for progressive kidney damage, myocardial infarction and CV death[3]. Once present, microalbuminuria progresses over 5–10 years to macroalbuminuria in 22–50% of patients[31,32]. The development of macroalbuminuria is usually followed by a further decline in glomerular filtration rate[8-9,31-32].

It is now well established that optimal blood pressure, tight glycaemic control and pharmacologic blockade of the renin-angiotensin system with ACE-inhibitors or ARBs can decrease urinary albumin excretion (UAE) rates and subsequently slow the progression of diabetic kidney disease from incipient to overt nephropathy[33]. In the Irbesartan Microalbuminuria Type 2 Diabetes Mellitus in Hypertensive Patients (IRMA 2) study, hypertensive type 2 diabetic patients with microalbuminuria taking irbesartan 300 mg daily had a significant (70%, p<0.001) relative risk reduction for the development of diabetic nephropathy as measured by the changes in UAE[33]. This can also be interpreted as microalbuminuria regression. Additionally, the Reduction of Endpoints in NIDDM with the Angiotensin II receptor blocker (ARB) Losartan (RENAAL) and Irbesartan in Diabetic Nephropathy (IDNT) trials and many other studies to date have conclusively demonstrated the advantage of ARB therapy[34,35]. When used as part of a multi-drug strategy to lower blood pressure, losartan 100 mg or irbesartan 300mg have been shown to prevent doubling of serum creatinine, end-stage renal disease (ESRD) or death in hypertensive type 2 diabetic patients with macroalbuminuria[34,35]. As inhibitors of the renin-angiotensin system have been shown to reduce proteinuria, independently of their blood pressure lowering effects[36,37], use of ACE inhibitors or ARBs in combination with other antihypertensive agents may provide additional benefits to hypertensive patients with type 2 diabetes. In this Malaysian population, a high proportion (59.2%) of patients was receiving ACE inhibitors but only 10% of patients were receiving ARBs. This is because the MAP Study was conducted back in 2002 when ARBs were still fairly new to the local market and were also more expensive than ACE-inhibitors back then.

Despite its complications, diabetes is largely a preventable and treatable disease. Annual screening for microalbuminuria in all patients with type 2 diabetes is recommended, as early treatment that includes CV risk reduction strategies is critical[10]. The recent availability of microalbuminuria dipstick test strips provides a simple method for primary screening and continued monitoring in patients without overt proteinuria. In those who test positive for microalbuminuria by the dipstick test, quantitative analysis should be carried out to confirm the diagnosis and assist in planning the treatment regimen. The principal strategy is to slow the progression of renal disease with aggressive antihypertensive treatment which should include agents that block the renin-angiotensin system.

In conclusion, this sub-analysis of data from the Malaysia cohort of the MAP Study demonstrated a high prevalence of diabetic kidney disease in hypertensive type 2 diabetic patients. A total of 55.4% of the patients screened had albuminuria (39.7% with microalbuminuria and 15.7% with new-onset macroalbuminuria). This high prevalence is a considerable public health concern and appropriate measures should be taken to contain the likely pandemic of ESRD due to diabetic nephropathy in Malaysia. Although prevention of type 2 diabetes, hypertension, obesity and the cardio-metabolic syndrome should be the ultimate goal, existing patients should be screened for microalbuminuria at the time of diagnosis of type 2 diabetes with/without systemic hypertension and annually thereafter as multiple strategies exist for minimizing CV complications and progression to ESRD in these high risk patients[8-9,38].

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Conflict of Interest Statement

The main author received a travel grant to attend an initial meeting in Singapore with other regional collaborators.

References

1. Epstein M, Sowers JR. Diabetes mellitus and hypertension. Hypertension 1992; 19: 403-18.
2. Diabetes e-Atlas, International Diabetes Foundation website: http://www.idf.org/e-atlas/home/ Accessed 6 January 2004.
3. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993; 16: 434–44.
4. Lim TO and Lim YN (Eds). 11th Annual Report of the Malaysian Renal and Transplantation Registry 2003.
5. Dinneen SF, Gerstein HC. The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus. A systematic overview of the literature. Arch Intern Med 1997; 157: 1413-18.
6. Miettinen H, Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Proteinuria predicts stroke and other atherosclerotic vascular disease events in nondiabetic and non-insulin-dependent diabetic subjects. Stroke 1996; 27: 2039.
7. Wang SL, Head J, Stevens L, Fuller JH. Excess mortality and its relation to hypertension and proteinuria in diabetic patients. The World Health Organization multinational study of vascular disease in diabetes. Diabetes Care 1996; 19: 305-12.
8. Parving HH. Diabetic nephropathy: prevention and treatment. Kidney Int 2001; 60: 2041-55.
9. Gross JL, de Azedevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: Diagnosis, Prevention and Treatment. Diabetes Care 2005; 28: 176-88.
10. American Diabetes Association. Nephropathy in Diabetes. Position Statement. Diabetes Care 2004; 27 (Suppl 1): S79-S83.
11. Spooren PF, Lekkerkerker JF, Vermes I. Micral-Test: a qualitative dipstick test for micro-albuminuria. Diabetes Res Clin Pract 1992; 18: 83- 87.
12. Mather HM, Chaturvedi N, Kehely AM. Comparison of prevalence and risk factors for microalbuminuria in South Asians and Europeans with type 2 diabetes mellitus. Diabet Med 1998; 15: 672-77.
13. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J 2001; 77: 399-402.
14. Tomura S, Kawada K, Saito K *et al.* Prevalence of microalbuminuria and relationship to the risk of cardiovascular disease in the Japanese population. Am J Nephrol 1999; 19: 13-20.
15. Lee WR, Lim HS, Thai AC *et al.* A window on the current status of diabetes mellitus in Singapore - the Diabcare-Singapore 1998 study. Singapore Med J 2001; 42: 501-7.
16. Wong JS. Proteinuria in diabetic patients in a primary health care setting in Sarawak. Med J Malaysia 2005; 60(2): 146-50.
17. Mafauzy M. Diabetes control and complications in private primary healthcare in Malaysia. Med J Malaysia 2005; 60(2): 212-17
18. Wu AYT, Kong NCT, de Leon FA, Pan CY, Tai TY, Yeung VTF *et al* for the MAPS Investigators. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. Diabetologia 2005; 48: 17-26.

19. Parving HH, Osterby R, Ritz E. Diabetic nephropathy. In: Brenner BM, editor. The Kidney, Philadelphia: Saunders, 2000; 1731-73.

20. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289: 2560-72.

21. Ball SG. Benefits of blood pressure reduction in diabetic patients. J Hypertens Suppl 2003; 21 (Suppl 6): S31–S36.

22. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998; 317: 703-13.

23. Hansson L, Zanchetti A, Carruthers SG *et al.* Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998; 351: 1755-62.

24. Morrish NJ, Wang SL, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia 2001; 44 Suppl 2: 14S-21S.

25. UK Prospective Diabetes Study (UKPDS) Group: Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-53.

26. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993; 329: 977-86.

27. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. JAMA 2003; 290: 2159-167.

28. Lam KS, Cheng IK, Janus ED, Pang RW. Cholesterol-lowering therapy may retard the progression of diabetic nephropathy. Diabetologia 1995; 38: 604-9.

29. Smulders YM, van Eeden AE, Stehouwer CD, Weijers RN, Slaats EH, Silberbusch J. Can reduction in hypertriglyceridaemia slow progression of microalbuminuria in patients with non-insulin-dependent diabetes mellitus? Eur J Clin Invest 1997; 27: 997-1002.

30. Fried LF, Orchard TJ, Kasiske BL. Effect of lipid reduction on the progression of renal disease: a meta-analysis. Kidney Int 2001; 59: 260-69.

31. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Engl J Med 1984; 310: 356-60.

32. John L, Rao PS, Kanagasabapathy AS. Rate of progression of albuminuria in type II diabetes. Five-year prospective study from south India. Diabetes Care 1994; 17: 888-90.

33. Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001; 345: 870-78.

34. Brenner BM, Cooper ME, de Zeeuw D *et al.* Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345: 861-69.

35. Lewis EJ, Hunsicker LG, Clarke WR *et al.* Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345: 851-60.

36. Viberti G, Wheeldon NM. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure-independent effect. Circulation 2002; 106: 672-78.

37. Song JH, Lee SW, Suh JH *et al.* The effects of dual blockade of the renin-angiotensin system on urinary protein and transforming growth factor-beta excretion in 2 groups of patients with IgA and diabetic nephropathy. Clin Nephrol 2003; 60: 318-26.

38. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003; 348: 383-93.