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An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study

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Abstract *Aim/hypothesis:* Microalbuminuria represents the earliest clinical evidence of diabetic nephropathy and is a marker of increased cardiovascular morbidity and mortality. Its early detection allows the implementation of individualised and aggressive intervention programmes to reduce cardiovascular risk factors. There is limited information on the prevalence of microalbuminuria among hypertensive type 2 diabetic patients in Asia. *Methods:* This cross-sectional epidemiological study aimed to assess the prevalence of microalbuminuria and macroalbuminuria among consecutively screened hypertensive type 2 diabetic adult patients in 103 centres in 10 Asian countries or regions. Predictive factors for microalbuminuria and macroalbuminuria were characterised using a stepwise logistic regression model. *Results:* A total of 6,801 patients were enrolled and 5,549 patients constituted the per-protocol population (patients with bacteriuria and haematuria were excluded). The prevalence of microalbuminuria was 39.8% (39.2–40.5; 95% CI) and the prevalence of macroalbuminuria was 18.8% (18.2–19.3; 95% CI). Only 11.6% of the patients had systolic and diastolic blood pressure below the 130/80 mm Hg target. In the multivariate analyses, the predictive factors for the presence of microalbuminuria were age, BMI, systolic blood pressure and ethnic origin. The highlighted predictive factors for the presence of macroalbuminuria were age, sex, ethnic origin, BMI, duration of diabetes, presence of diabetic complications, intake of diuretics, intake of calcium channel blockers, diastolic and systolic blood pressure. *Conclusions/interpretation:* The high prevalence (58.6%) of micro or macroalbuminuria observed in these patients is alarming and indicates an impending pandemic of diabetic cardiovascular and renal diseases in Asia with its potential economic consequences.

Keywords Asia · Diabetic nephropathy · Hypertension · Macroalbuminuria · Microalbuminuria · Prevalence

Abbreviations ADA: American Diabetes Association · ARB: angiotensin receptor blocker · MAPS: MicroAlbuminuria Prevalence Study · MAU: microalbuminuria

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Introduction

Hypertension is common among patients with type 2 diabetes, with a prevalence approximately twice that of the nondiabetic population, and may precede the onset of diabetes [1]. The prevalence of hypertension is further increased in patients with type 2 diabetes mellitus and elevated AER, compared with patients with type 2 diabetes mellitus and no evidence of renal involvement. The higher the systolic blood pressure, the greater the absolute excess cardiovascular risk for diabetic patients, indicating a greater potential for preventing cardiovascular death by control of elevated blood pressure [2]. Ageing of the population and an increasing prevalence of obesity and sedentary life habits are leading to an greater prevalence of diabetes, particularly in Asia [3]. By 2025, the World Health Organization predicts that the number of patients with the disease worldwide will increase to 300 million. Half will be Asian. Southeast Asia will have the highest rate of diabetes worldwide [4].

Because of the adverse impact of microalbuminuria (MAU) on survival in patients with type 2 diabetes mellitus and the renal risk of macroalbuminuria [5–8], screening and intervention programmes should be implemented early, at the stage of microalbuminuria. Annual screening for microalbuminuria is recommended by the American Diabetes Association (ADA) [9], as a high proportion of patients with type 2 diabetes are found to have MAU or overt nephropathy shortly after diagnosis of their diabetes. Screening by means of a semiquantitative dipstick test is easy, immediate and accurate [10].

To date there have been few studies in Asian populations on the prevalence of MAU [11–14]. These studies have only explored the percentage of MAU in diabetic or hypertensive patients. The MicroAlbuminuria Prevalence Study (MAPS) is the first large study to evaluate the prevalence of micro and macroalbuminuria in high-risk patients with type 2 diabetes mellitus and hypertension.

Subjects and methods

Patients and study design Outpatients who were above the age of 18, from different Asian ethnic subgroups, and had previously diagnosed hypertension (treated or untreated) and type 2 diabetes mellitus (treated or untreated) were consecutively screened at each participating centre. Previously diagnosed hypertension and diabetes were historically defined as mentioned in the patient medical record and verified during monitoring visits. The only exclusion criterion was previously known macroalbuminuria. Patient data included ethnic origin; past medical and family history; onset dates of hypertension and diabetes; current diabetes status with known complications such as retinopathy, peripheral neuropathy, cardiovascular disease as reported during the interview, as well as glycaemic control (latest values of fasting blood glucose and HbA_1c if available); current hypertensive status (mean of two consecutive measurements of office supine systolic and diastolic blood pressure) and current therapy; and dyslipidaemic status (known or previously diagnosed dyslipidaemia), with latest blood tests results if available, and use of lipid-lowering agents. A single urine specimen was collected in disposable plastic vessels.

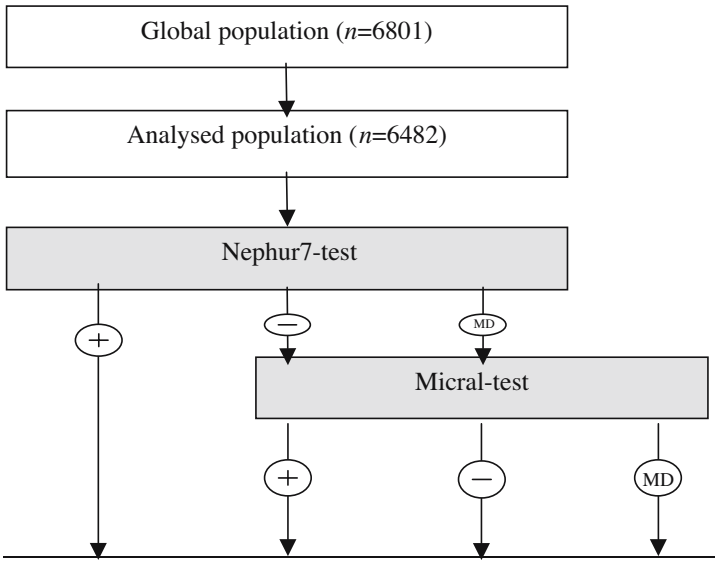
The primary study objective was to assess the prevalence of microalbuminuria and macroalbuminuria. Secondary objectives aimed to assess the routine blood pressure control level, to collect the associated cardiovascular risk factors and diabetic complications, and to characterise the predictive factors for micro and macroalbuminuria.

Informed consent was obtained from all participants. The protocol was approved by the Ethics Committees in countries where it was required by the regulatory bodies. The study was supervised by a multidisciplinary steering committee. The committee designed the study, interpreted the data and wrote the article.

Assays A two-step MAU screening process was conducted. First, the detection of macroalbuminuria was carried out by trained personnel on fresh urine (first morning or random morning specimens) using a visual colorimetric semiquantitative urine test strip (Nephur 7 Test, Roche Diagnostics, Mannheim, Germany). The test strip also allowed quantification of pH, urine glucose, ketones bodies, leucocytes, nitrites, and blood. If specimens were negative for albumin, detection of microalbuminuria was performed on the same urine with a second specific semiquantitative urine test strip (Micral-test, Roche Diagnostics). The intensity of the colour produced was visually compared with the reference chart on the Micral-test bottle (0, 20, 50, 100 mg/l, >100 mg/l). A measurement of 20 mg/l or above was considered positive. Specificity, sensitivity, positive and negative predictive values of the second test strip were determined according to the manufacturer's evaluation report and with a cutoff point set at 20 mg/l. Results were: sensitivity 90.1%, specificity 87.2%, positive predictive value 0.82, negative predictive value 0.93.

Populations Between January 2002 and December 2002 we recruited 6,801 patients from 103 medical centres (30 general practitioner and primary care clinics, 19 general hospital outpatient clinics, 40 diabetic centres, and 14 cardiology or nephrology centres) throughout ten Asian countries or regions (China, Hong Kong, Indonesia, Malaysia, Pakistan, Philippines, Singapore, South Korea, Taiwan and Thailand).

The analysed population (n=6,482) consisted of all patients with confirmed onset dates for hypertension and type 2 diabetes mellitus. Most patients (n=3,070, 47%) were enrolled by diabetologists, whereas 1,429 (22%), 1,236 (19%) and 747 patients (12%) were enrolled by general practitioners, hospital outpatient clinic physicians and specialists (cardiologists or nephrologists), respectively. Patients with positive leucocytes and nitrites, which are indicative of significant bacteriuria, and patients with erythrocytes or haemoglobin equal to or above 25 counts per microlitre, which is indicative of significant haematuria (false positives), were excluded from the analysed



Macroalbuminuric patients	Microalbuminuric patients	Normoalbuminuric[a]	Missing data		*n* (%)
1429	2568	2475	10	Analysed population	6482 (95.3%)
388	357	178	10	Excluded from per-protocol population	933
1041	2211	2297	0	Per-protocol population	5549 (81.6%)

[a] Patients with negative or missing albumin Nephur7-test and negative Micral-test

Fig. 1 Patients' disposition and urinary screening results

population leaving the per-protocol population (Fig. 1). Further to the two-step screening, three albuminuric subgroups were defined: macroalbuminuric, microalbuminuric, normoalbuminuric.

Statistical analysis Quantitative variables were described by their means, standard deviations, and counts. Median and quartiles 1 and 3 were reported when appropriate. Qualitative variables were described by counts and percentages, missing data were included in the calculation of percentages. The three albuminuric subgroups were compared by one-way ANOVA for quantitative variables and by a chi square test for sex. The significance level was fixed at 5%. Prevalence rates were calculated with a two-sided 95% CI. A two-step logistic regression analysis was performed on the per-protocol population. First, a univariate analysis determined the links between microalbuminuria (Yes/No) or macroalbuminuria (Yes/No) and the following 17 variables: ethnic subgroup, sex, age group, BMI, duration of diabetes classes, duration of hypertension classes, systolic blood pressure by class (high normal/mild/moderate/severe/very severe) based on the 1999 WHO/ISH classification [15], diastolic blood pressure by class, cardiovascular complications (Yes/No), diabetic complications (Yes/No), smoking (Yes/No), diuretic intake (Yes/No), α blocker (Yes/No), β blocker (Yes/No), calcium channel blocker (Yes/No), ACE inhibitor (Yes/No), and angiotensin II receptor blockers (ARB) intake (Yes/No). A link between two variables was considered significant if the *p* value test was 0.25 or less. Then, a stepwise logistic regression that only included the significant variables determined the best model to predict microalbuminuria or macroalbuminuria. All analyses were performed using SAS software version 8.02.

Results

Patient characteristics Patient characteristics of the per-protocol population (*n*=5,549, 81.6% of the enrolled population) are described in Table 1. No clinically significant difference in body weight and BMI was noted among the three subgroups. The duration of diabetes was significantly higher in the macroalbuminuric subgroup (8.0 years) than in the microalbuminuric (6.8 years) or normoalbuminuric (6.3 years) subgroups ($p<0.0001$; Table 2). The mean age at diagnosis of diabetes was similar (54.6 years) among the three subgroups. The mean HbA_1c level was significantly higher in the macroalbuminuric subgroup (8.2%; documented results available in 541 patients, which corresponds to 52.0% of this population) than in the microalbuminuric subgroup (7.9%; *n*=1,297, 58.7% of microalbuminuria population) and the normoalbuminuric subgroup (7.6%; *n*=1,466, 63.8% of normoalbuminuric population). Diabetic complications were particularly observed in macroalbuminuric patients

Table 1 Patient characteristics and family history in the per-protocol population

	Macroalbuminuric (*n*=1,041)		Microalbuminuric (*n*=2,211)		Normoalbuminuric (*n*=2,297)		Total (*n*=5,549)		*p* value
Men, *n* (%)	466 (44.8)		918 (41.5)		968 (42.1)		2,352 (42.4)		0.2073[a]
Women, *n* (%)	575 (55.2)		1,293 (58.5)		1,329 (57.9)		3,197 (57.6)		
Mean age in years (SD)	62.3 (10.8), *n*=1,041		61.3 (10.6), *n*=2,210		60.3 (10.1), *n*=2,296		61.1 (10.4), *n*=5,547		<0.0001
Ethnic group	*n*	%	*n*	%	*n*	%	*n*	%	
Chinese	615	59.1	1,420	64.2	1,515	66.0	3,550	64.0	
Malay	142	13.6	212	9.6	165	7.2	519	9.4	
Filipino	213	20.5	228	10.3	285	12.4	726	13.1	
Indian	14	1.3	55	2.5	52	2.3	121	2.2	
Korean	31	3.0	212	9.6	135	5.9	378	6.8	
Other	24	2.3	81	3.7	130	5.7	235	4.2	
Mean height in cm (SD)	159.8 (8.2), *n*=1,033		160.0 (8.8), *n*=2,206		160.0 (8.5), *n*=2,289		160.0 (8.5), *n*=5,528		0.7264
Mean weight in kg (SD)	65. 5 (12.4), *n*=1,038		65.9 (12.4), *n*=2,209		64.6 (11.4), *n*=2,291		65.3 (12.0), *n*=5,538		0.0011
Mean BMI in kg/m^2 (SD)	25.6 (4.2), *n*=1,032		25.7 (4.0), *n*=2,204		25.2 (3.7), *n*=2,285		25.5 (3.9), *n*=5,521		<0.0001
Family history	*n*	%	*n*	%	*n*	%	*n*	%	
History of diabetes	465	44.7	950	43.0	1,007	43.8	2,422	43.7	
History of hypertension	498	47.8	1,043	47.2	1,073	46.7	2,614	47.1	
History of cardiovascular disease	197	18.9	383	17.3	449	19.6	1,029	18.5	

[a]Comparison of men/women ratio among the three subgroups

Table 2 Description of type 2 diabetes mellitus in the per-protocol population

	Macroalbuminuric (*n*=1,041)		Microalbuminuric (*n*=2,211)		Normoalbuminuric (*n*=2,297)		Total (*n*=5,549)		*p* value
Duration of diabetes (years)									
Mean (SD)	8.0 (7.1)		6.8 (6.7)		6.3 (6.1)		6.9 (6.6)		<0.0001
Median	6.0		5.0		5.0		5.0		
Q1	2.0		2.0		1.0		2.0		
Q3	12.0		10.0		10.0		10.0		
	n	%	*n*	%	*n*	%	*n*	%	
≤1 year	195	18.7	487	22.0	576	25.1	1,258	22.7	
>1–5 years	274	26.3	704	31.8	724	31.5	1,702	30.7	
>5–10 years	260	25.0	530	24.0	515	22.4	1,305	23.5	
>10 years	312	30.0	490	22.2	482	21.0	1,284	23.1	
Known complications	*n*	%	*n*	%	*n*	%	*n*	%	
At least 1 diabetic complication	367	35.3	624	28.2	604	26.3	1,595	28.7	
Retinopathy	213	20.5	323	14.6	321	14.0	857	15.4	
Peripheral neuropathy	247	23.7	431	19.5	401	17.5	1,079	19.4	
Other neuropathy	18	1.7	32	1.5	14	0.6	64	1.2	
Known cardiovascular complications	*n*	%	*n*	%	*n*	%	*n*	%	
At least 1 cardiovascular complication	306	29.4	542	24.5	535	23.3	1,383	24.9	
Previous stroke	111	10.7	171	7.7	165	7.2	447	8.1	
Myocardial infarction	45	4.3	68	3.1	58	2.5	171	3.1	
Congestive heart failure	37	3.6	57	2.6	21	0.9	115	2.1	
Mean fasting blood glucose in mmol/l (SD)	8.9 (3.4), *n*=937		8.5 (3.1), *n*=2,013		8.1 (2.9), *n*=2,128		8.4 (3.1), *n*=5,078		<0.0001
Mean HbA_1c values in % (SD)	8.2 (1.9), *n*=541		7.9 (1.8), *n*=1,297		7.6 (1.8), *n*=1,466		7.8 (1.8), *n*=3,304		<0.0001
Mean serum creatinine in μmol/l (SD)	103.7 (49.9), *n*=707		85.3 (26.9), *n*=1,554		83.4 (25.2), *n*=1,723		87.7 (32.5), *n*=3,984		<0.0001

(35.3%), while the percentage of complications observed in microalbuminuric patients was close to that in normoalbuminuric patients (28.2% and 26.3%, respectively; Table 2). Likewise, cardiovascular complications were more prevalent in macroalbuminuric patients (29.4%), whereas percentages of cardiovascular complications in microalbuminuric and normoalbuminuric patients were similar (24.5% and 23.3%, respectively; Table 2).

The mean duration of hypertension (8.5 years) was similar among the subgroups (Table 3). Mean systolic and diastolic blood pressure were significantly higher in macroalbuminuric patients (148.3/85.0 mm Hg) than in microalbuminuric and normoalbuminuric patients (142.9/83.3 and 140.0/82.0 mm Hg, respectively). Only 11.6% of the patients had their systolic and diastolic blood pressure below the 130/80 mm Hg target. The proportion of patients receiving an antihypertensive treatment (89.0%) was homogeneous among the three subgroups, with 57.1% of them on monotherapy and 42.9% on combination therapy. Previously diagnosed lipid metabolism anomalies were observed in 48.8% of the patients, but less than 40% of them were receiving a lipid-lowering agent.

Primary endpoint The prevalence of microalbuminuria was 39.8% (39.2–40.5; 95% CI) and the prevalence of macroalbuminuria was 18.8% (18.2–19.3; 95% CI). The highest prevalence of microalbuminuria was observed in Korea (56.5%) and the lowest in Pakistan (24.2%) (Fig. 2). When analysed 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]). For prevalence of macroalbuminuria, the opposite was observed, with the highest prevalence found in patients attending polyclinics/hospital outpatient clinics (26.9% [25.5–28.3, 95% CI]) and the lowest in patients attended by cardiology or nephrology specialists (13.2% [11.9–14.6, 95% CI]).

In the multivariate analyses, the predictive factors for the presence of microalbuminuria were age greater than 59 years, elevated BMI, systolic blood pressure level greater than 139 mm Hg, and ethnic origin (Table 4). The statistically significant predictive factors for the presence of macroalbuminuria were age greater than 70 years, male sex, ethnic origin, elevated BMI, duration of diabetes

Table 3 Description of hypertension in the per-protocol population

	Macroalbuminuric (*n*=1,041)		Microalbuminuric (*n*=2,211)		Normoalbuminuric (*n*=2,297)		Total (*n*=5,549)		*p* value
Duration of hypertension (years)									
Mean (SD)	9.0 (9.7)		8.7 (9.5)		8.1 (9.0)		8.5 (9.3)		0.0080
Median	6.0		5.0		5.0		5.0		
Q1	2.0		2.0		2.0		2.0		
Q3	12.0		12.0		11.0		12.0		
	n	%	*n*	%	*n*	%	*n*	%	
≤1 year	211	20.3	503	22.8	521	22.7	1,235	22.3	
>1–5 years	301	28.9	644	29.1	724	31.5	1,669	30.1	
>5–10 years	222	21.3	419	19.0	465	20.2	1,106	19.9	
>10 years	307	29.5	645	29.2	587	25.6	1,539	27.7	
Mean systolic blood pressure in mm Hg (SD)	148.3 (21.0), *n*=1,040		142.9 (17.9), *n*=2,206		140.0 (17.6), *n*=2,292		142.7 (18.7), *n*=5,538		<0.0001
Systolic blood pressure by class	*n*	%	*n*	%	*n*	%	*n*	%	
≤130 mm Hg (normal)	224	21.5	640	29.0	809	35.2	1,673	30.2	
>130–139 (high normal)	111	10.7	276	12.5	307	13.4	694	12.5	
>139–159 (mild)	400	38.4	857	38.8	847	36.9	2,104	37.9	
>159–179 (moderate)	220	21.1	341	15.4	270	11.8	831	14.5	
>179–209 (severe)	72	6.9	90	4.1	55	2.4	217	3.9	
>209 (very severe)	13	1.3	2	0.1	4	0.2	19	0.3	
Mean diastolic blood pressure in mm Hg (SD)	85.0 (10.9), *n*=1,040		83.3 (10.2), *n*=2,206		82.0 (9.9), *n*=2,291		83.1 (10.3), *n*=5,537		<0.0001
Diastolic blood pressure by class	*n*	%	*n*	%	*n*	%	*n*	%	
≤85 mm Hg (normal)	572	55.0	1,359	61.5	1,510	65.7	3,441	62.0	
>85–89 (high normal)	45	4.3	139	6.3	146	6.4	330	6.0	
>89–99 (mild)	300	28.8	528	23.9	489	21.3	1,317	23.7	
>99–109 (moderate)	100	9.6	153	6.9	130	5.7	383	6.9	
>109–119 (severe)	16	1.5	18	0.8	15	0.7	49	0.9	
>119 (very severe)	7	0.7	9	0.4	1	0.0	17	0.3	
Systolic/diastolic blood pressure	*n*	%	*n*	%	*n*	%	*n*	%	
<130/80 mm Hg	85	8.2	234	10.6	326	14.2	645	11.6	<0.0001

longer than 5 years, presence of diabetic complications, diuretics intake, calcium channel blockers intake, diastolic and systolic blood pressure levels (Table 5).

Discussion

MAPS is the first large multicentre epidemiological study in Asia to determine the prevalence of microalbuminuria in type 2 diabetic patients with hypertension. This study indicates that 39.8% of the analysable population of 5,549 patients have microalbuminuria. This is higher than the prevalence rates, reported in population-based studies [16] for Western diabetic patients, which range from 17% to 21%. In another Asian study, microalbuminuria was detected in 36.3% of type 2 diabetics at a diabetes centre in southern India [12]. The wide range in the prevalence of microalbuminuria in type 2 diabetics is probably due to genetic and cardiovascular risk factors (blood pressure, cholesterol, salt intake, etc.). In MAPS, most of the patients were Chinese (64%). Compared to patients of Chinese origin, patients of Korean and Malay ethnic origin were most likely to have microalbuminuria. The high prevalence of microalbuminuria in non-Caucasians has also been observed in the Pima Indians of North America, where type 2 diabetes is very common, and more than 50% develop proteinuria within 20 years [17]. In type 2 diabetes, microalbuminuria is often associated with clustering of cardiovascular risk factors to form the metabolic syndrome [18]. High prevalence of metabolic syndrome has been reported in Asia [19, 20] with early onset of metabolic syndrome and diabetes mellitus in Asian Indians

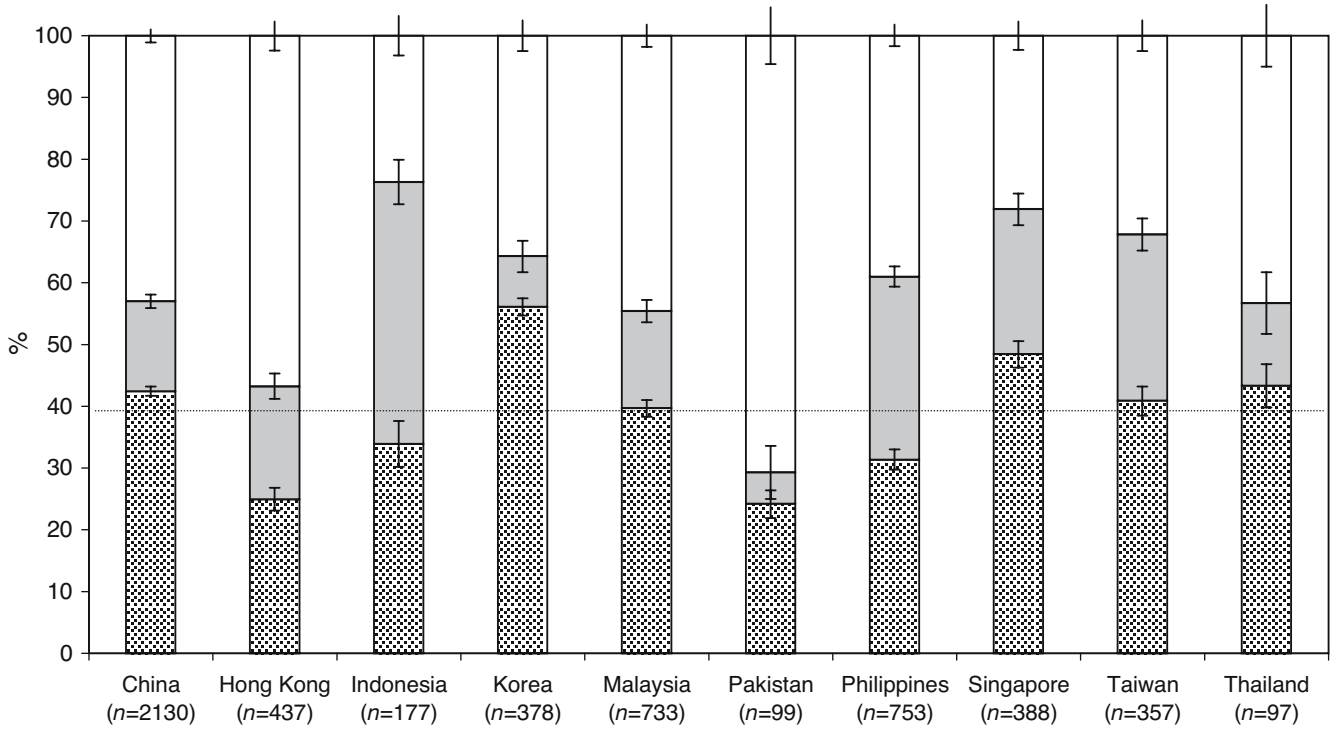


Fig. 2 Prevalence of microalbuminuria and macroalbuminuria (and 95% CI) by country in the per-protocol population. The *dotted line* represents the average prevalence of microalbuminuria (39.8%). *Dotted bars* indicate microalbuminuric; *grey bars* macroalbuminuric; *white bars* normoalbuminuric

[19, 21]. In our study, over 48% of the patients had a known dyslipidaemia. Hypertriglyceridaemia, hypercholesterolaemia, high LDL cholesterol and low HDL cholesterol levels were reported among 58%, 63%, 42%, and 23% of these patients, respectively. Drug therapy of dyslipidaemia was suboptimal as only 40% of patients were receiving a lipid-lowering agent.

Table 4 Predictive factors for the presence of microalbuminuria (odds ratio and 95% CI)[a]

Variables ($p \leq 0.05$)	Odds ratio	Odds ratio CI
Age (vs. [30, 49] years, *n*=635)		
>59–70 (*n*=1,766)	1.216	[1.005–1.472]
>70 (*n*=786)	1.346	[1.079–1.678]
BMI (kg/m^2)	1.042	[1.026–1.059]
SBP levels (vs. normal, *n*=1,449), mm Hg		
>139–159 (*n*=1,704)	1.261	[1.092–1.457]
>159–179 (*n*=611)	1.619	[1.330–1.969]
>179–209 (*n*=145)	2.165	[1.509–3.105]
Ethnic subgroup (vs. Chinese, *n*=2,935)		
Korean (*n*=347)	1.761	[1.396; 2.221]
Malay (*n*=377)	1.274	[1.019; 1.593]
Other[b] (*n*=209)	0.613	[0.455; 0.824]

SBP systolic blood pressure
[a](*n*=4,508), per-protocol population less the macroalbuminuric patients
[b]Unclassified ethnic subgroup (see Table 1)

In addition to the 39.8% prevalence rate of microalbuminuria, 18.8% of 5,549 patients were found to have macroalbuminuria. As patients with previously known diabetic nephropathy or macroalbuminuria were excluded from screening, this high rate of macroalbuminuria was not anticipated and raises important questions about current screening strategies in diabetic patients.

There are a few limitations to the study results. Firstly, MAU detection was based on a single urine spot collection with semiquantitative dipstick determinations. The ADA guidelines [9] 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 be done in a 3- to 6-month period before designating a patient as having MAU. In this large cross-sectional epidemiological study, the single urine collection and semiquantitative determination was judged adequate for the study objectives. 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 sensitiv-

Table 5 Predictive factors for the presence of macroalbuminuria (odds ratio and 95% CI)[a]

Variables ($p \leq 0.05$)	Odds ratio	Odds ratio CI
Diuretic (Yes vs. No) (n=580/2,758)	1.319	[1.073–1.621]
Calcium channel blocker (Yes vs. No) (n=1,221/2,117)	1.332	[1.126–1.575]
DBP levels (vs. normal, n=2,082)		
>89–99 mm Hg (n=1,317)	1.474	[1.198–1.813]
>119 mm Hg (n=17)	9.260	[1.041–82.361]
Sex (men vs. women) (n=1,434/1,904)	1.315	[1.117–1.548]
Diabetic complication (Yes vs. No) (n=971/2,366)	1.489	[1.248–1.776]
BMI (kg/m^2)	1.051	[1.029–1.074]
Age (vs. [30, 49] years, n=451)		
>70 (n=628)	2.063	[1.519–2.801]
Duration of diabetes subgroups (vs. ≤1 year, n=771)		
>5–10 years (n=776)	1.584	[1.245–2.016]
>10 years (n=793)	1.892	[1.477–2.422]
Ethnic subgroup (vs. Chinese, n=2,130)		
Filipino (n=498)	2.256	[1.800–2.829]
Korean (n=166)	0.594	[0.391–0.903]
Malay (n=307)	1.873	[1.435–2.446]
Other[b] (n=152)	0.374	[0.231–0.606]
SBP levels (vs. normal, n=1,033)		
>130–139 mm Hg (n=418)	1.455	[1.101–1.922]
>139–159 mm Hg (n=1,247)	1.599	[1.295–1.975]
>159–179 mm Hg (n=490)	2.445	[1.868–3.201]
>179–209 mm Hg (n=127)	3.708	[2.388–5.757]
>209 mm Hg (n=17)	7.825	[2.426–25.240]

DBP diastolic blood pressure, *SBP* systolic blood pressure
[a](n=3,338), per-protocol population less the microalbuminuric patients
[b]Unclassified ethnic subgroup (see Table 1)

ity and specificity of the Micral-test was 95% and 80%, respectively.

Another possible limitation is that this was not a real population-based study. The extrapolation of these findings to the global type 2 diabetic and hypertensive population should be carefully evaluated. Nevertheless, at the study level, all efforts were made to have a balanced distribution between patients enrolled by diabetologists (47%) and by non-diabetes specialists (53%). And, at the country level, only representative physicians experienced in managing type 2 diabetic patients were selected and consecutive patients enrolled.

A third limitation concerns the blood test values as no systematic blood sampling was required per protocol. Only documented previous blood test results were recorded. For glycaemic control, 93.9% and 59.7% of patients had documented values of blood glucose and HbA_1c, respectively. For serum lipids, the available data rate varied between 72.8% (LDL cholesterol) and 81.6% of patients (triglycerides) with previously known dyslipidaemia. Importantly, the rates of available data were similar among the three subgroups.

Hypertension is common among diabetic patients and the prevalence is further increased in the presence of renal disease [22]. In MAPS, the mean blood pressure level was 143/83 mm Hg and the mean duration of hypertension was 8.5 years. Systolic blood pressure was predictive of both microalbuminuria and macroalbuminuria. The presence of diabetic complications, duration of diabetes, and types of antihypertensive agent, i.e., diuretics and calcium channel blockers, were also predictive of macroalbuminuria. Although no conclusions could be drawn from a cross-sectional study, these predictors are probably indicative of more severe underlying blood pressure elevation, and it is consistent with previous reports that dihydropyridine calcium channel blockers are not as effective as ACE inhibitors or ARB in alleviating albuminuria [23, 24]. Only 10.6% of patients with microalbuminuria and 8.2% with macroalbuminuria achieved blood pressure lower than 130/80 mm Hg. Eleven percent of our patients did not receive any antihypertensive therapy. The low control rates observed in this analysis reflect the prescribing habits of doctors in Asia, their perception of target blood pressure levels and the influence of guidelines in managing hypertension. These low control rates are not substantially different from many western countries [25]. As expected, severely elevated systolic blood pressure (>179 mm Hg) was more common in the macroalbuminuric group. It is therefore important to develop strategies that increase the percentage of patients who achieve optimal blood pressure control as Asian type 2 diabetic patients have a higher risk of renal complications and stroke than their Caucasian counterparts [26].

Optimal blood pressure, tight glycaemic control and pharmacological blockade of the renin–angiotensin system with ACE inhibitors or ARB have been shown to decrease AER and decrease progression from incipient to overt nephropathy [23, 27]. In the IRMA 2 study ("Irbesartan microalbuminuria type 2 diabetes mellitus in hypertensive patients"), 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 AER [28]. The RENAAL and IDNT trials have conclusively demonstrated the advantage of ARB therapy (losartan 100 mg or irbesartan 300 mg) as part of a multidrug strategy to lower blood pressure and to prevent doubling of serum creatinine, end-stage renal disease or death in type 2 diabetic patients with hypertension and macroalbuminuria [23, 27]. There is compelling evidence that therapy that negatively modulates the renin–angiotensin system may be especially effective in reducing renal and cardiovascular disease in diabetic patients with hypertension. In the MAPS evaluation, ACE inhibitors and ARB were used in only 43.9% and 19.2% of patients, respectively. Less than 50% of patients were receiving two or more antihypertensive agents, even though a number of clinical trials have confirmed the need for multidrug therapies to reach target blood pressure in diabetes [29, 30].

Glycaemic control has been shown to prevent development of nephropathy and to reverse established pathology [31]. However, the majority of our patients in the microalbuminuric and macroalbuminuric groups did not achieve adequate glycaemic control as evidenced by available mean HbA_1c values of over 7%.

In conclusion, a 39.8% prevalence rate of microalbuminuria was observed in Asian type 2 diabetic and hypertensive patients. This high prevalence is alarming and indicates an impending pandemic of diabetic cardiovascular and renal disease in Asia with its potential economical burden. We strongly recommend implementing screening programmes for microalbuminuria in type 2 diabetic patients. Through cardiovascular risk reduction, lowering of blood pressure, renin–angiotensin system blockade and glycaemic control such early and targeted intervention could significantly reduce the occurrence of cardiovascular and renal complications.

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