ABSTRACT

**Aim:** to assess the prevalence of macroalbuminuria and microalbuminuria in hypertensive patients with type 2 diabetes in 10 Asian countries.

**Methods:** this cross-sectional clinic-based epidemiological study is a subanalysis of data collected from patients attending three medical centres in Indonesia from May 2002 to October 2002. A total of 207 patients were enrolled, of which 177 patients constituted the per protocol population (patients with bacteriuria and haematuria were excluded).

**Results:** overall, the prevalence of diabetic kidney disease was high, with macroalbuminuria comprising 44.7% [41.2–48.1; 95% confidence interval] and microalbuminuria comprising 33.0% (29.7–36.3; 95% confidence interval). While the majority (91.53%) of patients were receiving treatment for hypertension, only 6.21% of the patients had systolic/diastolic blood pressures below the 130/85 mmHg target.

**Conclusion:** the prevalence of microalbuminuria and macroalbuminuria was high in hypertensive patients with type 2 diabetes in Indonesia, which is indicative of an impending pandemic of diabetic cardiovascular and renal diseases in the region.

**Key words:** diabetic nephropathies, hypertension, albuminuria, renin-angiotensin system.

INTRODUCTION

Patients with type 2 diabetes are at least twice likely to have hypertension compared to nondiabetic patients. The presence of hypertension increases the risk of atherosclerotic vascular disease and microvascular complications such as retinopathy and nephropathy in patients with diabetes. The higher the systolic blood pressure (SBP), the greater the absolute excess cardiovascular (CV) risk for patients. This indicates a greater potential for prevention of CV death among patients with diabetes by controlling elevated blood pressure. Because of the ageing population and an increase in obesity and sedentary lifestyle, the prevalence of diabetes is growing, particularly in Asia. Indonesia has an estimated prevalence of 1.2–2.3% among people over 15 years, but higher rates have been reported in urban areas. In Jakarta, the prevalence of diabetes in urban areas increased from 1.63% in 1982 to 5.7% in 1995.

Microalbuminuria represents the earliest clinical evidence of diabetic nephropathy and is a marker of increased CV morbidity and mortality. Because of the adverse impact of microalbuminuria and proteinuria on survival, screening and intervention programmes should be implemented early. Annual screening for microalbuminuria is recommended by the American Diabetes Association, and the use of a semi-quantitative dipstick test is easy, and provides immediate and accurate results.

There have been few studies in Asian populations on the prevalence of microalbuminuria, and these studies have only explored the percentage of microalbuminuria in either patients with diabetes or patients with hypertension. The microalbuminuria prevalence study (MAPS) is the first study to evaluate the prevalence of microalbuminuria and macroalbuminuria in patients with type 2 diabetes and hypertension. The primary objective of MAPS was to assess the
prevalence rate of macroalbuminuria and microalbuminuria. Secondary objectives was assessment levels of glycaemic and blood pressure control.

METHODS

The study design and methods of MAPS have been previously described, and are dealt with briefly here. Outpatients of 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. 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 SBP and diastolic blood pressure/DBP, 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.

For the current analysis, we restricted data to include only those patients recruited from three study centres in Indonesia. All patients with confirmed onset time of hypertension and type 2 diabetes constituted the analysed population. Patients with positive leukocytes and nitrates, indicative of significant bacteriuria, and patients with erythrocytes or haemoglobin equal or above 25/microL, 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. No statistical tests were performed on the albuminuric subgroups. Prevalence rates were calculated with a two-sided 95% confidence interval (CI). For the multivariate analysis, links between two qualitative criteria were assessed by a Chi-squared test or Fisher’s exact test if the assumptions of the Chi-squared test were not fulfilled. The best global model of prediction was assessed by a stepwise logistical regression. The significance level was fixed at 5%. All analyses were performed using statistical analysis system (SAS) software version 8.02.

RESULTS

Indonesia constituted 3% of the overall enrolment in MAPS. A total of 207 patients were recruited from three medical centres in Indonesia, from May 2002 to October
2002. Patients with bacteriuria, and/or haematuria, on the Nephur7Test® (Roche Diagnostics GmbH, Mannheim, Germany), were excluded from the per-protocol analysis (Figure 1). Patient characteristics of the per-protocol population (N = 177) are shown in Table I. All participants were Malay. A total of 69.49% had a family history of the following conditions: hypertension (40.68%), diabetes (49.72%), CV disease (15.25%) and kidney disease (3.95%). Of the patients enrolled, 8.47% were current smokers and 6.21% were ex-smokers.

The mean duration of hypertension was 6.02±5.89 years, with an average age of onset of 55.31±10.41 years. Mean blood pressure was 152.66±18.44/91.04±8.97 mmHg. Only 11 of 177 (6.21%) patients had SBP/DBP below the 130/85 mmHg target. Blood pressure was normal in 5.33%, 5.00% and 9.52% of macroalbuminuric, microalbuminuric and normoalbuminuric patients, respectively. Ninety-two per cent of patients were receiving treatment for their hypertension: 73.46% and 26.54% were on monotherapy and combination therapy, respectively. The distribution of therapy was: angiotensin-converting enzyme (ACE) inhibitors (90.12% of patients), angiotensin receptor blockers (ARB) (0.62%), calcium channel blockers (14.81%), beta-blockers (5.56%), diuretics (17.28%), and alpha-blockers (1.23%). Hyperlipidaemia was present in 70 patients (39.55%) (Table 2), but only 17 (24.29%) of these patients were receiving lipid lowering drugs: 76.47% statins, 23.53% fibrates.

**Primary Endpoint**

The overall prevalence of albuminuria was 77.7%. The prevalence of macroalbuminuria was 44.7% (41.2–48.1;95%CI) and 33.0% (29.7–36.3;95%CI) for microalbuminuria.

**DISCUSSION**

MAPS is the first large multicentre epidemiological study conducted in Asia to determine the prevalence of microalbuminuria and macroalbuminuria in patients with hypertension and type 2 diabetes. This subanalysis of data from Indonesia showed that a high proportion of patients had evidence of proteinuria. The prevalence of macroalbuminuria was higher than rates of 17–21% reported from Western population-based studies in patients with diabetes. The relatively high prevalence of macroalbuminuria (44.7%) indicates that it is a common and poorly managed condition. Screening and more aggressive treatment management of patients with albuminuria should be undertaken as a priority to reduce the prevalence of the condition and progression of nephropathy.

Although the majority of patients (92%) were receiving antihypertensive therapy, blood pressure control was particularly poor. Only 6.21% of patients achieved the target recommended by the American Diabetes Association for adequate blood pressure control (<130/85 mmHg). The mean blood pressure of
patients was 152.66±18.44/91.04±8.97 mmHg. This may in part be explained by the relatively low use of combination therapy in this cohort. Only 26.54% of patients were receiving two or more antihypertensive agents, even though a number of clinical trials have confirmed that multi-drug therapies are required for the majority of patients with diabetes to reach target blood pressure.15–17

The benefits of reducing blood pressure to the recommended goal of <130/85 mmHg in patients with diabetes are well established.16,18 In the United Kingdom Prospective Diabetes Study 38 (UKPDS 38),16 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 MI, a 13% reduction in risk for microvascular complications and a 12% reduction in risk for any diabetes-related complications. In the Hypertension Optimal Treatment (HOT) study,17 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. 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.19

Previous studies have suggested that effective treatment of dyslipidaemia may slow the progression of nephropathy in patients with type 2 diabetes.20,21 In this study, 39.55% of the per-protocol population had a known dyslipidaemia. It is of concern that only 24.29% of patients with dyslipidemia were using lipid lowering drugs. Hyperglycaemia is an important determinant for the development of proteinuria in patients with type 2 diabetes. Effective glycaemic control has been shown to prevent the development of nephropathy and reverse established pathology. A national audit of diabetes

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**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Macroalbuminuric</th>
<th>Microalbuminuric</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.69±8.36</td>
<td>60.63±9.91</td>
<td>60.24±8.16</td>
<td>60.99±8.85</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male N (%)</td>
<td>27 (36.00)</td>
<td>17 (28.33)</td>
<td>16 (38.10)</td>
<td>60 (33.90)</td>
</tr>
<tr>
<td>Female N (%)</td>
<td>48 (64.00)</td>
<td>43 (71.67)</td>
<td>26 (61.90)</td>
<td>117 (66.10)</td>
</tr>
<tr>
<td>Mean height (cm)</td>
<td>156.74±7.74</td>
<td>156.00±8.29</td>
<td>155.40±7.14</td>
<td>156.17±7.77</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>59.83±9.84</td>
<td>60.52±10.69</td>
<td>59.47±9.86</td>
<td>59.98±10.09</td>
</tr>
<tr>
<td>Mean body mass index (kg/m²)</td>
<td>24.29±3.26</td>
<td>24.83±3.58</td>
<td>24.56±3.56</td>
<td>24.54±3.43</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.93±0.07</td>
<td>0.90±0.06</td>
<td>0.89±0.06</td>
<td>0.91±0.07</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>155.90±17.28</td>
<td>153.38±19.96</td>
<td>145.83±16.71</td>
<td>152.66±18.44</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>91.50±10.10</td>
<td>92.00±8.48</td>
<td>90.38±7.49</td>
<td>91.40±8.97</td>
</tr>
<tr>
<td>Blood glucose (mmol/L)</td>
<td>8.40±3.16</td>
<td>9.01±3.70</td>
<td>8.71±3.84</td>
<td>8.68±3.50</td>
</tr>
<tr>
<td>Mean duration of hypertension (years)</td>
<td>6.67±6.46</td>
<td>5.50±5.32</td>
<td>5.62±5.61</td>
<td>6.02±5.89</td>
</tr>
<tr>
<td>Mean duration of diabetes (years)</td>
<td>8.17±6.13</td>
<td>5.48±4.68</td>
<td>6.14±5.56</td>
<td>6.78±5.64</td>
</tr>
</tbody>
</table>

*Per-protocol population (N = 177)

**Table 2. Dyslipidaemia in Hypertensive Patients with Type 2 Diabetes**

<table>
<thead>
<tr>
<th></th>
<th>Macroalbuminuria (n=32)</th>
<th>Microalbuminuria (n=23)</th>
<th>Normal (n=15)</th>
<th>Total (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertriglyceridaemia</td>
<td>59.38</td>
<td>56.52</td>
<td>53.33</td>
<td>57.14</td>
</tr>
<tr>
<td>High total cholesterol</td>
<td>90.63</td>
<td>91.30</td>
<td>73.33</td>
<td>87.14</td>
</tr>
<tr>
<td>High LDL chole sterol</td>
<td>28.13</td>
<td>39.13</td>
<td>40.00</td>
<td>34.29</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>15.63</td>
<td>4.35</td>
<td>6.67</td>
<td>10.00</td>
</tr>
</tbody>
</table>

*Hyperlipidaemic population (N = 70). LDL = low-density lipoprotein, HDL = high-density lipoprotein.
control conducted in 2001 indicated that glycaemic control is poor in Indonesia; the mean HbA1c in patients with type 2 diabetes was 8.5 ± 2.1%, and more than half (53%) had values exceeding 8%.22

It is widely established that optimal blood pressure, tight glycaemic control and pharmacological blockade of the renin-angiotensin system with ACE inhibitors or ARB can decrease urinary albumin excretion (UAE) rates and, subsequently, slow the progression from incipient to overt nephropathy.23 For example, in the IRMA 2 (irbesartan microalbuminuria type 2 diabetes mellitus in hypertensive patients) study, hypertensive patients with type 2 diabetes and 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.23,24,25 When used as part of a multi-drug strategy to lower blood pressure, irbesartan 300 mg has been shown to prevent doubling of serum creatinine, end-stage renal disease (ESRD) or death in hypertensive patients with type 2 diabetes and microalbuminuria.25 In this study, ACE inhibitors were used by 90.12% of patients, but only 0.62% were receiving ARBs.

Despite its complications, diabetes is largely a preventable and treatable disease. Microalbuminuria is the first clinical sign of diabetic damage to the kidney and is an indication of progressive kidney damage, MI and CV death.2 Annual screening for microalbuminuria is recommended by the American Diabetes Association,8 as early treatment with inhibitors of the renin-angiotensin system can slow the progression of diabetic nephropathy.23

**CONCLUSION**

This subanalysis of data from the Indonesia cohort of MAPS demonstrated a high prevalence of diabetic kidney disease in hypertensive patients with type 2 diabetes. This study also showed a particularly low level of optimal blood pressure control in Indonesian Patients. The advantages of lowering blood pressure targets and the benefits of the blockade of the renin-angiotensin system have been clearly demonstrated in clinical trials. Improvements in management of diabetes and hypertension are urgently needed to contain the epidemic of ESRD due to diabetic nephropathy in Indonesia.

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