Microalbuminuria Prevalence Study (MAPS) in hypertensive Patients with Type 2 Diabetes in Thailand

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Background: *Microalbuminuria represents the earliest clinical evidence of diabetic nephropathy, and is a marker of increased cardiovascular (CV) morbidity and mortality.*
Objectives: *This analysis of Thai data from the Microalbuminuria Prevalence Study (MAPS) assessed the prevalence of macroalbuminuria and microalbuminuria in hypertensive patients with type 2 diabetes.*
Design: *Cross-sectional clinic-based epidemiological study.*
Material and Method: *A total of 100 patients were enrolled, of which 97 patients constituted the per-protocol population (patients with bacteriuria and haematuria were excluded). Patients attended one study visit with no follow-up.*
Results: *Overall, the prevalence of diabetic kidney disease was high, with macroalbuminuria contributing 13.4% [9.9-16.9; 95% confidence interval (CI)] and microalbuminuria contributing 43.3% [38.3-48.3; 95%CI].*
Conclusion: *Annual screening for microalbuminuria is recommended for all patients with type 2 diabetes, as early treatment is critical for reducing CV risks. Clinical studies have shown that renin-angiotensin system inhibitors can slow the progression of diabetic nephropathy.*

Keywords: *Diabetic nephropathy, Hypertension, Albuminuria, Renin-angiotensin system, Thailand*

J Med Assoc Thai 2005; 88 (11): 1624-9
Full text. e-Journal: *http://www.medassocthai.org/journal*

Patients with type 2 diabetes are at least twice as likely to have hypertension as the nondiabetic population[1]. The presence of hypertension increases the risk of atherosclerotic vascular disease and microvascular complications, such as retinopathy and nephropathy, in patients with diabetes[1]. The higher the systolic blood pressure (SBP), the greater the absolute excess cardiovascular (CV) risk for patients. This indicates the potential for prevention of CV death among patients with diabetes by controlling elevated blood pressure[2]. The aging population and an increase in obesity and sedentary lifestyle has contributed to a steady increase in the prevalence of diabetes, particularly in Asia[3]. The International Collaborative Study of Cardiovascular Disease in Asia estimated that the national prevalence of diabetes in Thai adults older than 35 years was 9.6% in 2000[4].

Because of the adverse impact of microalbuminuria and proteinuria on survival in these patients[5-7], screening and intervention programmes should be implemented as early as possible. Annual screening for microalbuminuria is recommended by the American Diabetes Association[8], the use of a semi-quantitative dipstick test is easy, and provides immediate and accurate results[9].

There have been few studies in Asian populations on the prevalence of microalbuminuria[10-12]. 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

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the prevalence of microalbuminuria and macroalbuminuria in patients with both type 2 diabetes and hypertension[13]. The present study was a subgroup of MAPS, which included only Thai patients.

The primary study objective was to assess the prevalence rate of macroalbuminuria and microalbuminuria. Secondary objectives aimed to assess levels of glycaemic and blood pressure control.

Material and Method

The study design and methods of MAPS have been previously described[13], and a brief outline is presented 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 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 [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. 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 centres in Thailand. All patients with confirmed onset dates of hypertension and type 2 diabetes constituted the analysed population. Patients with positive leukocytes and nitrites, 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).

Results

Thai patients constituted 1% of the overall enrolments in MAPS. A total of 100 patients were recruited from medical centres in Rajavithi, Ramathibodi and Siriraj, from October 2002 to November 2002. Patients with bacteriuria, and/or haematuria, on the Nephur7Test (Roche Diagnostics GmbH, Mannheim, Germany), were excluded from the per-protocol analysis (Fig. 1). Demographic data of the per-protocol population (n = 97) are shown in Table 1. A family history of hypertension, diabetes, CV and kidney disease was reported in 44.33%, 57.73%, 17.53% and 5.15% of patients, respectively. Overall, 11.34% had at least one CV complication: previous transient ischaemic attack (2.06%), previous stroke (5.15%), angina pectoris (5.15%), myocardial infarction (MI) (1.03%), heart

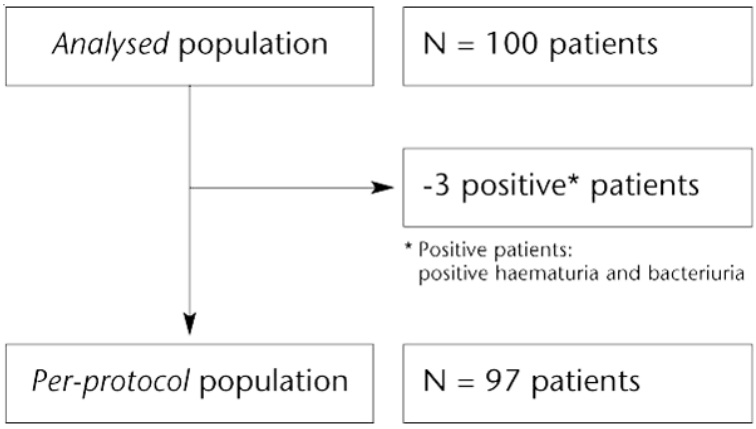

Fig. 1 Patient classification

Table 1. Patient characteristics*

	Macroalbuminuric (n = 13)	Microalbuminuric (n = 42)	Normal (n = 42)	Total (n = 97)
Gender				
Male n (%)	5 (38.46)	11 (26.19)	13 (30.95)	29 (29.90)
Female n (%)	8 (61.54)	31 (73.81)	29 (69.05)	68 (70.10)
Age (years)	60.38±10.20	62.60±11.02	59.74±9.64	61.06±10.31
Height (cm)	156.69±7.38	155.35±7.72	157.98±8.13	156.66±7.87
Weight (kg)	68.51±9.75	66.68±13.20	66.16±10.48	66.70±11.57
Body mass index (kg/m^2)	27.81±2.73	27.66±5.48	26.44±3.15	27.15±4.29
Waist/hip ratio	0.94±0.10	0.91±0.11	0.90±0.07	0.91±0.09
SBP (mmHg)	141.15±16.49	140.55±16.14	137.08±15.22	139.13±15.73
DBP (mmHg)	83.46±10.00	80.93±8.83	81.25±6.42	81.41±8.00
Blood glucose (mmol/L)	7.80±2.21	7.95±1.81	7.53±2.23	7.74±2.04
Duration of hypertension (years)	6.92±6.09	7.12±6.43	4.83±3.95	6.10±5.50
Duration of diabetes (years)	9.23±8.27	7.88±6.17	7.26±6.53	7.79±6.59

* Per-protocol population. All values given are means ± standard deviation (with the exception of gender)
SBP, systolic blood pressure; DBP, diastolic blood pressure

Table 2. Dyslipidaemia in hypertensive patients with type 2 diabetes*

	Macroalbuminuria (n = 13) %	Microalbuminuria (n = 35) %	Normal (n = 39) %	Total (n = 87) %
Hypertriglyceridaemia	76.92	60.00	48.72	57.47
High total cholesterol	92.31	91.43	92.31	91.95
High LDL cholesterol	53.85	62.86	69.23	64.37
Low HDL cholesterol	53.85	48.57	35.90	43.68

* Hyperlipidaemic population (n = 87). LDL, low-density lipoprotein, HDL, high-density lipoprotein. Numbers given are percentage of patients within each subgroup with the given category of dyslipidaemia

failure (1.03%) and peripheral arterial disease (1.03%). Dyslipidaemia was present in 55 (89.69%) patients (Table 2), and 63.22% were using lipid-lowering drugs (76.36% were taking statins and 29.09% were taking fibrates).

The mean duration of diabetes was 7.79 ± 6.59 years, with a mean age of onset of 53.37 ± 10.39 years. Measures of glycaemic control revealed a mean glycosylated haemoglobin (HbA1c) level of 7.68 ± 1.20% and a mean creatinine level of 86.75 ± 25.69 mmol/L. Current methods of diabetes management included dietary control in 100% of patients, regular physical exercise in 32.99%, oral hyperglycaemic agents in 94.85%, and insulin therapy in 10.31%. Twenty-four per cent of patients had at least one diabetic complication, with diabetic retinopathy and peripheral neuropathy present in 19.59% and 14.43%, respectively.

The mean duration of hypertension was 6.10 ± 5.50 years, with an average age of onset of 55.06 ± 10.31 years. Mean blood pressure was 139.13 ± 15.73/81.41 ± 8.00 mmHg. Overall, 32.99% of patients achieved the target blood pressure of 130/85 mmHg (the target level recommended by the American Diabetes Association for adequate blood pressure control at the time of study initiation[14]). Blood pressure was normalised in 7.69%, 33.33% and 40.48% of macroalbuminuric, microalbuminuric and normoalbuminuric patients, respectively. 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% of patients), 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%).

Primary endpoint

The overall prevalence of albuminuria was 56.7%. The prevalence of macroalbuminuria and microalbuminuria was 13.4% [9.9-16.9; 95%CI] and 43.3% [38.3-48.3; 95%CI], respectively.

Secondary endpoint

Only 32.99% (32 of 97) of patients achieved blood pressure readings below the target blood pressure of 130/85 mmHg.

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[13]. This subanalysis of data from Thailand indicates that 13.4% of the per-protocol population had macroalbuminuria and 43.3% had microalbuminuria. The prevalence of microalbuminuria was much higher than rates of 17-21% reported from patients with diabetes in Western population-based studies[15], and slightly higher than the mean of 39.8% reported from the overall Asian MAPS cohort[13].

Almost one-third of Thai patients achieved the target blood pressure of < 130/85 mmHg, recommended by the American Diabetes Association for adequate blood pressure control at the time of study initiation[14]. This rate of blood pressure control is similar to rates that have been reported from many Western countries[16].

The benefits of reducing blood pressure to below 130/85 mmHg in patients with diabetes are well established[17,18]. In the United Kingdom Prospective Diabetes Study 38 (UKPDS 38)[18], 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[19], a 51% reduction in CV events was observed in patients with diabetes randomised to a group with target DBP of ≤ 80 mmHg compared with those randomised 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 a higher risk for renal complications and stroke compared with Caucasian patients[20].

Previous studies have suggested that effective treatment of dyslipidaemia may slow the progression of nephropathy in patients with type 2 diabetes[21,22]. In the present study, 89.69% of patients had known dyslipidaemia, and 63.22% of patients 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. However, as evidenced by the mean HbA1c of 7.68% (range 5.3%-10.6%), the majority of patients in the present study did not achieve optimal glycaemic control.

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 who were 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]. Additionally, the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) and Irbesartan in Diabetic Nephropathy (IDNT) trials have conclusively demonstrated the advantage of ARB therapy[24,25]. When used as part of a multi-drug strategy to lower blood pressure, losartan 100 mg or irbesartan 300 mg have been shown to prevent doubling of serum creatinine, ESRD or death in hypertensive patients with type 2 diabetes and macroalbuminuria[24,25]. In the present study, ACE inhibitors and ARB were used in 52.63% and 6.32% of Thai patients, respectively.

Despite its complications, diabetes is largely a preventable and treatable disease. Annual screening for microalbuminuria in all patients with type 2 diabetes is recommended[8], as early treatment with inhibitors of the renin-angiotensin system can help slow the progression of diabetic nephropathy[23].

In conclusion, this subanalysis of data from the Thai cohort of MAPS demonstrated a 43.3% 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. Furthermore, the advantages of lowering blood pressure and blockade of the renin-angiotensin system have been clearly demonstrated in clinical trials.

Acknowledgements

The authors wish to thank the investigators and the Monitoring Teams of the participating centres in Thailand for their contribution to the study. This work was supported by a grant from Sanofi~Aventis.

References

1. Dodson PM. Hypertension and diabetes. Curr Med Res Opin 2002; 18(Suppl 1): s48-57.
2. 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.
3. Diabetes e-Atlas, International Diabetes Foundation website [ONLINE]. Available at: http://www.idf.org/e-atlas/home. Accessed 6 January 2004.
4. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. Diabetes Care 2003; 26: 2758-63.
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: 1413-8.
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. American Diabetes Association. Diabetic nephropathy. Position Statement. Diabetes Care 2002; 25(Suppl 1): 85S-9S.
9. Spooren PF, Lekkerkerker JF, Vermes I. Micral-test: a qualitative dipstick test for micro-albuminuria. Diabetes Res Clin Pract 1992; 18: 83-7.
10. 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: 672-7.
11. Tomura S, Kawada K, Saito K, Lin YL, Endou K, Hirano C, et al. Prevalence of microalbuminuria and relationship to the risk of cardiovascular disease in the Japanese population. Am J Nephrol 1999; 19: 13-20.
12. Lee WR, Lim HS, Thai AC, Chew WL, Emmanuel S, Goh LG, 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.
13. Wu AY, Kong NC, de Leon FA, Pan CY, Tai TY, Yeung VT, 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.
14. American Diabetes Association. Position statement: standards of medical care for patients with diabetes mellitus. Diabetes Care 1999; 22(Suppl 1): S32-41.
15. Parving HH, Osterby R, Ritz E. Diabetic nephropathy. In: Brenner BM, editor. The kidney. Philadelphia: Saunders, 2000: 1731-73.
16. Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997; 157: 2413-46.
17. Ball SG. Benefits of blood pressure reduction in diabetic patients. J Hypertens Suppl 2003; 21 (Suppl 6): S31-6.
18. 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.
19. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, 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.
20. 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.
21. Lam KS, Cheng IK, Janus ED, Pang RW. Cholesterol-lowering therapy may retard the progression of diabetic nephropathy. Diabetologia 1995; 38: 604-9.
22. 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.
23. 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: 870-8.
24. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345: 861-9.
25. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, 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.

การศึกษาความชุกของไมโครแอลบูมินนูเรียในผู้ป่วยความดันโลหิตสูงร่วมกับเบาหวานชนิดที่ 2 ในประเทศไทย

พีระ บูรณะกิจเจริญ, ชัยชาญ ดีโรจนวงศ์, พงศ์อมร บุนนาค

ไมโครแอลบูมินนูเรียเป็นหลักฐานแรกทางคลินิกที่บ่งชี้ว่าไตเริ่มมีความผิดปกติจากโรคเบาหวาน และยังเป็นมาตรแสดงถึงการเพิ่มขึ้นของอัตราการเกิดโรคและอัตราตายของโรคหัวใจและหลอดเลือด การวิเคราะห์ข้อมูลของคนไทยจากการศึกษาหลักของ The Microalbuminuria Prevalence Study (MAPS) เพื่อดูความชุกของแมคโครแอลบูมินนูเรียและไมโครแอลบูมินนูเรียในผู้ป่วยความดันโลหิตสูงร่วมกับโรคเบาหวานชนิดที่ 2 โดยการศึกษาแบบตัดขวางจากผู้ป่วยทั้งหมด 100 ราย ซึ่งมี 97 รายได้รับการวิเคราะห์ตามเกณฑ์วิธี (ผู้ป่วยที่มีแบคทีเรียและเลือดในปัสสาวะถูกคัดออกไป) ผู้ป่วยมาตามนัดเพียงครั้งเดียวโดยไม่มีการนัดติดตามอีก ผลจากการศึกษาพบว่ามีความชุกของโรคไตในผู้ป่วยเบาหวานมาก, โดยพบแมคโครแอลบูมินนูเรียร้อยละ 13.4 (ร้อยละ 95 ของช่วงความเชื่อมั่นอยู่ระหว่าง 9.9-16.9) และ พบไมโครแอลบูมินนูเรียร้อยละ 43.3 (ร้อยละ 95 ของช่วงความเชื่อมั่นอยู่ระหว่าง 38.3-48.3) กล่าวโดยสรุป, ผู้ป่วยเบาหวานชนิดที่ 2 ควรได้รับการตรวจหาไมโครแอลบูมินนูเรียเป็นประจำทุกปี ทั้งนี้เพราะการรักษาตั้งแต่แรกมีความสำคัญอย่างยิ่งในการลดความเสี่ยงจากโรคหัวใจและหลอดเลือด การศึกษาทางคลินิกพบว่ายาต้านระบบเรนนิน แองจิโอเทนซิน สามารถชะลอการเสื่อมของไตจากโรคเบาหวาน