

Prevalence and risk factors of microalbuminuria in Thai nondiabetic hypertensive patients

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Purpose: To assess the prevalence and risk factors of microalbuminuria in nondiabetic hypertensive patients in Thailand.

Patients and methods: A cross-sectional study was performed during January to December 2007 at outpatients departments of Bhumibol Adulyadej hospital. Nondiabetic hypertensive patients without a history of pre-existing kidney diseases participated in this study. A questionnaire was used for collecting information on demographics, lifestyle, and family history of cardiovascular and kidney disease. Spot morning urine samples were collected for albuminuria estimation. Albuminuria thresholds were evaluated and defined using albumin-creatinine ratio (ACR).

Results: A total of 559 hypertensive patients (283 males, 276 females), aged 58.0 ± 11.6 years were enrolled in this study. Microalbuminuria (ACR 17 to 299 mg/g in males and 25 to 299 mg/g in females) was found in 93 cases (16.6%) [15.0%–18.2%]. The independent determinants of elevated urinary albumin excretion in a multiple logistic regression model were; body mass index ≥ 30 (odds ratio (OR) = 2.24, 95% confidence intervals (CI): 1.33–3.76) and dihydropyridine calcium channel blockers (DCCB) use (OR = 1.92, 95% CI: 1.22–3.02).

Conclusion: In Thai nondiabetic hypertensive patients, microalbuminuria was not uncommon. Obesity and use of dihydropyridine calcium channel blocker were found to be the important predictors. Prognostic value of the occurrence of microalbuminuria in this population remains to be determined in prospective cohort studies.

Keywords: microalbuminuria, hypertension, obesity, calcium channel blocker, metabolic syndrome

Introduction

Microalbuminuria has been shown to be associated with an increased risk of cardiovascular^{1,2} and progressive kidney disease^{3–6} not only in diabetes but also in nondiabetic subjects. In addition, treatment aimed to reduce albuminuria levels have been shown to reduce the risk for cardiovascular events⁷ as well as kidney disease progression.⁸ In hypertensive subjects, microalbuminuria has now been considered as an essential component in the assessment of subclinical organ damage because its detection is easy and relatively inexpensive.⁹ In Thailand, however, reliable data about epidemiology of microalbuminuria in nondiabetic hypertensive patients and its association with cardiovascular and renal morbidity are limited. Previous study by Buranakitjaroen et al, included 505 Thai hypertensive subjects who attended the hypertension clinic at Siriraj Hospital, had reported the prevalence of microalbuminuria and its associated factors.¹⁰ However, the population in this study was the patients who were cared for by hypertensive specialists and might not represent the

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whole hypertensive population of Thailand. Furthermore, the diagnostic test from this study was based on antibody-based dipstick rather than quantitative measuring of albuminuria. The aim of our study, therefore, was to assess the prevalence of microalbuminuria in hypertensive patients who attend general medical clinics. The screening method was antibody-based dipstick, but these were confirmed by urinary albumin creatinine ratio (ACR) in subjects who had tested positive with primary screening. The results from this study will provide us with a precise prevalence of microalbuminuria as well as associated factors and could demonstrate a value of screening for microalbuminuria in this population.

Material and methods

Study population

A cross-sectional study was performed from January to December 2007 at 3 out-patient departments of directorate of medical services, Royal Thai Air Force including: (1) Department of preventive medicine, (2) Department of medicine, Bhumibol Adulyadej hospital, and (3) Primary care unit, Bhumibol Adulyadej hospital. Nondiabetic hypertensive patients, age ≥ 18 years, without a history of pre-existing kidney diseases participated in this study. The major inclusion criteria were patients with hypertension (defined by sitting blood pressure (BP) $\geq 140/90$ mmHg in those not previously diagnosed with hypertension or those who were previously diagnosed with hypertension and reported current use of antihypertensive medications). Exclusion criteria were those with previously diagnosed diabetes mellitus or fasting blood glucose ≥ 126 mg/dL, impaired kidney function (serum creatinine >1.4 mg/dL in male, or >1.2 mg/dL in female), or history associated with false positive albuminuria (fever, menstruation, urinary tract infection and post exercise). All participants gave written informed consent. This study was approved by Bhumibol Adulyadej hospital ethics committee.

Data collection and evaluation

The two page questionnaire was used for collecting information on demographics, lifestyle, current medical illness, and family history of cardiovascular and kidney disease. Duration of hypertension and data about antihypertensive medications were collected from medical records. All participants have their BP measured after a 5 minutes rest with a calibrated digital BP monitor. Systolic and diastolic BP measurements were calculated as the mean of the last two visits. Participants were also measured for weight, height,

and waist circumference. Data about blood chemistry (fasting plasma glucose (FPG), creatinine (Cr), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and uric acid (UA)) were collected from medical record within last 6 months.

Glomerular filtration rate (GFR) was estimated from the Modification of Diet in Renal Disease (MDRD) study equation as follows:¹¹

$$\text{Estimated GFR (mL/min/1.73 m}^2\text{)} = 186.3 * (\text{serum creatinine by Jaffe})^{-1.154} * \text{age}^{-0.203} \\ (*0.742 \text{ for woman}).$$

Definitions

Obesity and overweight were defined according to World Health Organization (WHO) guidelines.¹² Subjects were classified as having impaired fasting glucose if fasting glucose ≥ 100 mg/dL.¹³ Metabolic syndrome was defined according to the International Diabetes Federation (IDF) worldwide definition of metabolic syndrome (IDF 2005 guidelines)¹⁴ that requires the presence of abdominal obesity according to ethnic-specific cutoff waist circumference (waist circumferences >90 cm. for men, or >80 cm. for women) plus any two or more of the following: (1) high TG (TG ≥ 150 mg/dL or treatment for this abnormality), (2) low HDL-c (HDL-c < 40 mg/dL in male subjects and < 50 mg/dL in female subjects or treatment for this abnormality), (3) high BP (systolic BP ≥ 130 or diastolic BP ≥ 85 mmHg or treatment of hypertension), (4) high fasting glucose (FPG ≥ 100 mg/dL or previously diagnosed type 2 diabetes). High serum uric acid was defined as serum uric acid >8.0 mg/dL for men, and >7.0 mg/dL for women. High cholesterol was defined as taking cholesterol lowering medications, or serum cholesterol >240 mg/dL. Subjects were classified as smokers if they reported smoking or having smoked cigarettes during the previous 5 years. A family history of cardiovascular disease and kidney disease was considered present if at least one first degree relative had documented the diseases.

Urinary albumin measurements

All participants gave a spot morning urine sample for analysis. Screening for elevated urinary albumin excretion (UAE) was tested by antibody-based dipstick: Micral test strips (Roche Diagnostics, Basel, Switzerland) and reported as negative or positive (at least 20 mg/L). Urine sample from participants who report positive from Micral test will be sent for quantitative measurement for albuminuria by using

ACR. Albuminuria measured as urine albumin concentration (UAC) by the method of immunoturbidimetric technique with MODULAR ANALYTICS P 800 module analyzer (Roche Diagnostics, Mannheim, USA). Urine creatinine was measured using the modified Kinetic Jaffé (KJ) method using the same analyzer for albumin. Elevated UAE was defined if ACR was more than 17 mg/g creatinine in males and 25 mg/g creatinine in female as per standard guideline.¹⁵ Microalbuminuria was defined as ACR more than gender specific cutoff levels but less than 300 mg/g creatinine. Macroalbuminuria was defined as ACR more than 300 mg/g creatinine.

Statistical analysis

An overall prevalence and specific population prevalence of microalbuminuria were estimated along with their 95% confidence interval (CI). Categorical variables were summarized using frequency and percentages \pm standard error (SE) while continuous variables were summarized using mean \pm standard deviations (SD) unless otherwise indicated. Descriptive statistics were used to compare the presence of elevated UAE with comparisons evaluated using t-tests for continuous variables and chi-square tests for categorical variables. The relationship between an elevation of UAE and covariates were assessed using a simple logistic regression model and reported as crude odds ratios (OR) with 95% confident intervals (CI). Multiple logistic regression was then used to examine if the presence of elevated UAE was associated with obesity (BMI \geq 30), metabolic syndrome, abdominal obesity, high blood pressure (BP \geq 130/85 mmHg), and the usage of calcium channel blockade medication. Results are presented as adjusted ORs with upper and lower 95% CIs. *P* values were two sided, and *P* < 0.05 was considered to indicate statistical significance. All analyses were performed using SPSS statistical package version 15.0 (SPSS Inc, Chicago, IL, USA).

Results

Demographic and clinical characteristics

A total of 559 hypertensive patients, aged 58.0 ± 11.6 years were enrolled in this study. Demographic and baseline clinical characteristics of studied subjects were shown in Tables 1 and 2 respectively. Two hundred and eighty three were males and 276 were females. The mean duration of hypertension was 60.3 ± 58.3 months. Mean body mass index (BMI) was 26.1 ± 6.9 kg/m² with ninety-seven patients (17.4%) were found to be obesity (BMI \geq 30 kg/m²). Mean BMI of patients

Table 1 Demographic data of study subjects

| Characteristics | Number n = 559 | Percent \pm SE |
|-----------------------------------|-------------------|------------------|
| Age, year, mean \pm SD | | 58.0 \pm 11.6 |
| Gender | | |
| Male | 283 | 50.6 \pm 2.1 |
| Female | 276 | 49.4 \pm 2.1 |
| Site | | |
| 1 Preventive medicine | 169 | 30.2 \pm 1.9 |
| 2 Medicine | 276 | 49.4 \pm 2.1 |
| 3 Primary care unit | 114 | 20.4 \pm 1.7 |
| Region of origin (n = 552) | | |
| Bangkok | 207 | 37 \pm 2.0 |
| Central | 218 | 39 \pm 2.0 |
| Northern | 41 | 7.3 \pm 1.1 |
| North-eastern | 40 | 7.2 \pm 1.1 |
| Eastern | 31 | 5.5 \pm 1.0 |
| Southern | 15 | 2.7 \pm 0.6 |
| Educational level (n = 532) | | |
| High school | 432 | 81.2 \pm 1.7 |
| University | 94 | 17.7 \pm 1.6 |
| Post-graduate | 6 | 1.1 \pm 0.4 |
| Cardiovascular disease (n = 556) | | |
| Yes | 31 | 5.6 \pm 1.0 |
| No | 525 | 94.4 \pm 1.0 |
| Cerebrovascular disease (n = 556) | | |
| Yes | 18 | 3.2 \pm 0.7 |
| No | 538 | 96.8 \pm 0.7 |
| Family history of CVD (n = 514) | | |
| Yes | 54 | 10.5 \pm 1.4 |
| No | 460 | 89.5 \pm 1.4 |
| Family history of CKD (n = 514) | | |
| Yes | 34 | 6.6 \pm 1.1 |
| No | 480 | 93.4 \pm 1.1 |
| Smoking (n = 537) | | |
| Yes | 57 | 10.6 \pm 1.3 |
| No | 480 | 89.4 \pm 1.3 |

Abbreviations: CVD, cardiovascular disease; CKD, chronic kidney disease.

in the macroalbuminuria and microalbuminuria groups were significantly higher than those in the normoalbuminuria group (*P* = 0.04 and *P* = 0.03, respectively). Mean estimated GFR in males and females were 77.7 ± 16.8 mL/min/1.73 m² and 80.8 ± 19.2 mL/min/1.73 m², respectively. Majority of subjects were not currently smokers (89.8.1%). Underlying disease was also described. Prevalence of metabolic syndrome was about 41.3% whereas the prevalence of high cholesterol and impaired fasting glucose (IFG) were as high as 59.9% and 36.8%. However, history of cardiovascular disease and cerebrovascular disease (CVA) were quite rare, ie, 5.6%, and 3.2%, respectively. Family history of cardiovascular disease and kidney disease were found in 10.5% and 6.6%.

Table 2 Clinical characteristics of study subjects

| Characteristics | All (n = 559) | Normo-albuminuria (n = 449) | Micro-albuminuria (n = 93) | Macro-albuminuria (n = 17) |
|--------------------------------------|------------------|--------------------------------|-------------------------------|-------------------------------|
| Age (years) | 58.0 ± 11.6 | 58.2 ± 11.0 | 57.3 ± 13.7 | 55.5 ± 15.4 |
| Male gender (%) | 50.6 ± 2.1 | 51.2 ± 2.4 | 50.5 ± 5.2 | 35.3 ± 11.6 |
| Weight (kg) | 67.2 ± 13.7 | 66.6 ± 13.4 | 69.4 ± 14.8 | 69.2 ± 16.1 |
| BMI (kg/m ²) | 26.1 ± 6.9 | 25.9 ± 7.2 | 26.9 ± 5.1 | 28.0 ± 5.9 |
| Obesity (%) | 17.4 ± 1.6 | 14.3 ± 1.7 | 26.9 ± 4.6* | 47.1 ± 12.1** |
| Smoker (%) | 10.2 ± 1.2 | 9.4 ± 1.4 | 16.1 ± 3.8 | 0 |
| Systolic BP (mmHg) | 140.6 ± 16.3 | 139.0 ± 15.2 | 147.1 ± 19.1** | 148.5 ± 15.8* |
| Diastolic BP (mmHg) | 80.9 ± 11.4 | 80.4 ± 11.4 | 82.9 ± 11.0 | 84.3 ± 10.9 |
| Duration of HT (months) | 60.3 ± 58.3 | 57.3 ± 55.7 | 70.9 ± 63.4 | 80.1 ± 83.6 |
| FPG (mg/dL) | 99.1 ± 24.1 | 97.4 ± 14.7 | 106.7 ± 48.2* | 103.5 ± 12.0 |
| IFG (%) | 36.8 ± 2.1 | 34.9 ± 2.3 | 48.2 ± 5.2 | 56.3 ± 12.4 |
| eGFR (ml/min/1.73 m ²) | 79.3 ± 17.8 | 79.1 ± 16.7 | 79.4 ± 21.2 | 86.3 ± 23.0 |
| Uric acid (mg/dL) | 6.3 ± 3.0 | 6.4 ± 3.3 | 6.2 ± 1.6 | 6.4 ± 1.7 |
| Total cholesterol (mg/dL) | 198.7 ± 39.5 | 198.5 ± 39.4 | 198.1 ± 40.7 | 206.2 ± 39.3 |
| High cholesterol (%) | 59.9 ± 2.1 | 59.4 ± 2.3 | 58.1 ± 5.1 | 82.4 ± 9.2 |
| Triglyceride (mg/dL) | 144.5 ± 97.4 | 141.2 ± 102.4 | 158.6 ± 69.7 | 153.8 ± 88.2 |
| HDL-c (mg/dL) | 57.1 ± 15.0 | 57.6 ± 15.3 | 55.1 ± 13.7 | 56.3 ± 14.4 |
| Uncontrolled BP (%) | 52.8 ± 2.1 | 49.2 ± 2.4 | 66.7 ± 4.9* | 70.6 ± 11.0 |
| Number of antihypertensive drug used | 1.64 ± 0.98 | 1.62 ± 0.97 | 1.7 ± 0.98 | 1.94 ± 1.03 |
| METS-IDF (%) | 41.3 ± 2.1 | 38.1 ± 2.3 | 54.8 ± 5.2* | 52.9 ± 12.1 |

Abbreviations: BMI, body mass index; BP, blood pressure; HT, hypertension; FPG, fasting plasma glucose; IFG, impaired fasting glucose; eGFR, estimated glomerular filtration rate; HDL-c, high density lipoprotein cholesterol; METS-IDF, metabolic syndrome by IDF criteria.

**P < 0.005, *P < 0.05 compared with normoalbuminuria group.

Blood pressure control and antihypertensive medication

Table 3 shows the extent of BP control achieved in study subjects. There were 306 (47.2%) patients whose systolic BP and diastolic BP were both well controlled (<140/<90 mmHg), while normalization rates of either systolic BP (<140 mmHg) or diastolic BP (<90 mmHg) were 50.8% and 77.6%, respectively. The presence of poorly controlled BP was seen more frequently in subjects with increased levels of albuminuria (Table 2). The mean number of antihypertensive agents was 1.64 ± 0.98 and 54.9% of subjects were prescribed with combination therapy. Dihydropyridine calcium channel blockers (DCCB) were prescribed in 36.5% of patients, followed by a thiazide type diuretic (34.3%) and ACE-I (33.3%). Antihypertensive medications in study subjects according to albuminuria are shown in Table 4. Patients who were prescribed with DCCB have a significantly higher percentage of having microalbuminuria and macroalbuminuria compared with other classes of drugs.

Prevalence of microalbuminuria

Overall, the frequency of an elevated UAE by antibody-based dipstick of 559 screened population was 183 (32.7%). However, 110 subjects who were test positive by antibody-based dipstick were confirmed by increased albumin-creatinine ratio, giving a prevalence of 19.6% (95% CI: 14.4%–18.8%). After excluding 17 persons with macroalbuminuria, microalbuminuria was found in 93 cases (16.6%) [15.0%–18.2%]. The prevalence was similar in males and females, ie 16.6% (95% CI: 14.4%–18.8%) and 16.7% (95% CI: 14.4%–18.9%), respectively. The gender-specific prevalences of albuminuria are shown in Table 5.

Factors associated with elevated urinary albumin excretion

Microalbuminuria and macroalbuminuria were combined and compared with the normoalbuminuria group for this analysis. Odds of having elevated UAE was estimated for those 13 factors (ie, age, sex, smoking status, BMI, waist circumference, duration of hypertension, BP control,

Table 3 Antihypertensive medications used by study subjects categorized by blood pressure control

| Antihypertensive medication | <140/<90 mmHg (n = 264) | ≥140/≥90 mmHg (n = 105) | ≥140/<90 mmHg (n = 170) | <140/≥90 mmHg (n = 20) |
|---|----------------------------|----------------------------|----------------------------|---------------------------|
| Total (n = 559) | 264 (47.2%) | 105 (18.8%) | 170 (30.4%) | 20 (3.6%) |
| ACE-I (n = 186, 33.3%) | 86 (32.6%) | 32 (30.5%) | 62 (36.5%) | 6 (30.0%) |
| ARB (n = 137, 24.5%) | 50 (18.9%) | 35 (33.3%)* | 48 (28.2%)* | 4 (20.0%) |
| Thiazide (n = 192, 34.3%) | 92 (34.8%) | 37 (35.2%) | 56 (32.9%) | 7 (35.0%) |
| DCCB (n = 204, 36.5%) | 88 (33.3%) | 44 (41.9%) | 66 (38.8%) | 6 (30.0%) |
| β-Blocker (n = 178, 31.8%) | 81 (30.7%) | 27 (25.7%) | 65 (38.2%) | 5 (25.0%) |
| On 0–1 class of drugs (n = 252, 45.1%) | 128 (48.5%) | 45 (42.9%) | 68 (40.0%) | 11 (55.0%) |
| On 2 classes of drugs (n = 204, 36.3%) | 93 (35.2%) | 42 (40.0%) | 61 (35.9%) | 8 (40.0%) |
| On ≥3 classes of drugs (n = 103, 18.6%) | 43 (16.3%) | 18 (17.1%) | 41 (24.1%)* | 1 (5.0%) |

Abbreviations: ACE-I, angiotensin converting enzyme-inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker.

metabolic syndrome, FPG, cholesterol, triglyceride, HDL, and uric acid) that were suspected to be associated with elevated UAE (Table 6). In addition, data about current medication use (ie, renin angiotensin system (RAS) blockade, DCCB, number of antihypertensive medications, and statin) were also assessed. In univariate analysis, elevated UAE was associated with increased BMI, abdominal obesity, poor blood pressure control, metabolic syndrome, and the using of DCCB. These 5 factors were therefore considered simultaneously in the multivariate logistic model. After adjusting for confounding effects, the independent determinants of elevated UAE were; body mass index ≥30 (OR = 2.24, 95% CI: 1.33–3.76) and DCCB use (OR = 1.92, 95% CI: 1.22–3.02). Subjects who had metabolic syndrome were

about 20% higher risk (OR = 1.2, 95% CI: 1.0–1.4) of having elevated UAE than subjects who did not. However, this risk was only borderline significant.

Discussion

Microalbuminuria is common in Thai nondiabetic hypertensive patients with a prevalence of 16.6% and independently associated with obesity and certain classes of antihypertensive medication. A number of previous studies evaluated the prevalence of microalbuminuria in hypertensive patients has been published, which is varied from 16% in the USA,¹⁶ 11.5% to 30% in Europe,^{17–21} and 14.4 to 26.2% in Asian populations.^{22–24} This varying might be due to type of study-base (ie, community versus hospital-base), patient

Table 4 Antihypertensive medications used by study subjects according to albuminuria levels

| | All (n = 559) | Normo-albuminuria (n = 449) | Micro-albuminuria (n = 93) | Macro-albuminuria (n = 17) |
|------------------------|------------------|--------------------------------|-------------------------------|-------------------------------|
| ACE-I | 186 (33.3%) | 142 (31.6%) | 35 (37.6%) | 9 (52.9%) |
| ARB | 137 (24.5%) | 116 (25.8%) | 19 (20.4%) | 2 (11.8%) |
| DCCB | 204 (36.5%) | 147 (32.7%) | 46 (49.5%)* | 11 (64.7%)* |
| NDCCB | 8 (1.4%) | 7 (1.6%) | 1 (1.1%) | 0 (0%) |
| Thiazide diuretics | 192 (34.3%) | 164 (36.5%) | 25 (59.5%) | 5 (29.4%) |
| Loop diuretics | 10 (1.8%) | 7 (1.6%) | 3 (3.2%) | 0 (0%) |
| β-Blocker | 178 (31.8%) | 141 (31.4%) | 31 (33.3%) | 6 (35.3%) |
| On 0–1 class of drugs | 252 (45.1%) | 204 (45.4%) | 43 (46.2%) | 5 (29.4%) |
| On 2 classes of drugs | 204 (36.3%) | 168 (37.4%) | 30 (32.3%) | 6 (35.3%) |
| On ≥3 classes of drugs | 103 (18.6%) | 77 (17.1%) | 20 (21.5%) | 6 (35.3%) |

Abbreviations: ACE-I, angiotensin converting enzyme-inhibitor; ARB, angiotensin receptor blocker; DCCB, dihydropyridine calcium channel blocker; NDCCB, nondihydropyridine calcium channel blocker.

*P < 0.05 compared with other classes.

Table 5 Prevalence of albuminuria according to gender

| Gender | n | Normoalbuminuria | | Microalbuminuria | | Macroalbuminuria | |
|---------|-----|------------------|----------------|------------------|----------------|------------------|----------------|
| | | n | Prevalence (%) | n | Prevalence (%) | n | Prevalence (%) |
| Male | 283 | 230 | 81.3 ± 2.3 | 47 | 16.6 ± 2.2 | 6 | 2.1 ± 0.8 |
| Female | 276 | 219 | 79.3 ± 2.4 | 46 | 16.7 ± 2.2 | 11 | 4.0 ± 0.8 |
| Overall | 559 | 449 | 80.3 ± 1.7 | 93 | 16.6 ± 1.6 | 17 | 3.0 ± 0.7 |

characteristics, urine sample collection, and the methods of tests used. In Thailand, a study at Siriraj hospital had reported a prevalence of microalbuminuria, assessed by antibody-based dipstick, of 18.6% comparable to our study.¹⁰ However, it should be kept in mind that prevalence of microalbuminuria by dipstick screening in our study was 32.7% using the same cut off value at 20 mg/L. There had been a study showing that screening of microalbuminuria by Micral test strips had a low positive predictive value of 69%.²⁵ Therefore, we could say that our population had much higher prevalence of microalbuminuria. These results could be explained by a difference in population characteristics as following: (1) patients enrolled in Siriraj study were from a hypertension clinic and cared for by a hypertensive specialists; (2) majority of patients taken on combination antihypertensive

medication with a mean number of 2.6 ± 0.8 ; and (3) higher BP normalization rate (BP < 140/90 78.8% compared with 47.2%). Better BP control could explain the lower prevalence of target organ damage.

Various studies have documented risk factors associated with microalbuminuria. Among those factors, obesity has been shown to be important in many studies.^{26–29} To the best of our knowledge, this is the first study to show that increased urinary albumin excretion is associated with obesity in the Thai population. The importance of obesity in the development of albuminuria has been studied in experimental models. It was shown that obesity, by several mechanisms, can lead to glomerular hyperfiltration and subsequently developed early histological changes together with the development of albuminuria.³⁰ Recent

Table 6 Odds ratio and 95% confidence interval for presence of elevated urinary albumin excretion: univariate and multivariate analyses

| Variables | Univariate | 95% CI | P-value | Multivariate | 95% CI | P-value |
|---------------------------------|------------|-----------|---------|--------------|-----------|---------|
| BMI ≥ 30 kg/m ² | 2.58 | 1.59–4.19 | <0.001 | 2.24 | 1.33–3.76 | 0.002 |
| DCCB | 2.20 | 1.44–3.36 | <0.001 | 1.92 | 1.22–3.02 | 0.005 |
| METS-IDF | 1.95 | 1.28–2.97 | 0.002 | 1.65 | 1.02–2.67 | 0.043 |
| Abdominal obesity-Asia | 1.78 | 1.06–2.99 | 0.028 | 1.63 | 0.95–2.80 | 0.077 |
| BP $\geq 130/85$ mmHg | 1.84 | 1.05–3.22 | 0.033 | 1.49 | 0.83–2.67 | 0.182 |
| Age ≥ 60 years | 0.85 | 0.55–1.29 | 0.444 | | | |
| Female gender | 1.13 | 0.74–1.71 | 0.567 | | | |
| Smoking | 1.57 | 0.83–2.96 | 0.163 | | | |
| HT ≥ 10 years | 1.77 | 1.10–2.85 | 0.019 | | | |
| FPG ≥ 100 mg/dL | 1.49 | 0.96–2.29 | 0.073 | | | |
| TG > 150 mg/dL | 1.42 | 0.92–2.18 | 0.110 | | | |
| Low HDL-c | 1.38 | 0.82–2.33 | 0.229 | | | |
| High uric acid | 1.36 | 0.84–2.20 | 0.217 | | | |
| High Cholesterol | 1.02 | 0.56–1.85 | 0.951 | | | |
| ACE-I or ARB | 0.97 | 0.64–1.48 | 0.895 | | | |
| Anti HT ≥ 3 classes | 1.48 | 0.90–2.46 | 0.125 | | | |
| Statins | 1.18 | 0.78–1.80 | 0.437 | | | |

Abbreviations: BMI, body mass index; DCCB, dihydropyridine calcium channel blocker; METS-IDF, metabolic syndrome by IDF criteria; BP, blood pressure; HT, hypertension; FPG, fasting plasma glucose; TG, triglyceride; HDL-c, high density lipoprotein cholesterol; ACE-I, angiotensin converting enzyme-inhibitor; ARB, angiotensin receptor blocker.

studies by Goumenos et al demonstrated histological lesions such as glomerulomegaly as well as focal segmental glomerulosclerosis in patients with morbid obesity even before the appearance of microalbuminuria.³¹ Furthermore, microalbuminuria in nondiabetic subjects might be part of insulin resistance syndrome.^{32,33} Many risk factors associated with microalbuminuria (eg, hypertension, hyperglycemia, obesity, hyperlipidemia) are well-known components of insulin resistance syndrome (metabolic syndrome). Therefore, one could argue that insulin resistance is the key pathophysiologic mechanism to link between all of the above-mentioned risk factors and microalbuminuria.³⁴ Nevertheless, results from our study showed only a borderline association between albuminuria and metabolic syndrome. This finding is similar to a study by Kitiyakara et al showing that metabolic syndrome was not associated with developing chronic kidney disease in the Thai population when using IDF definition with Asian-specific cutoff waist circumference.³⁵

Another finding from this study is the association between certain classes of antihypertensive medication and urinary albumin excretion. In our study, patients currently taking DCCB had a higher prevalence of microalbuminuria compared with other classes. This relation was independent from blood pressure level. In several studies, DCCB were not shown to reduce proteinuria levels and to slow the progression of CKD despite achieving BP goals comparable to that achieved with angiotensin converting enzyme-inhibitor (ACE-I) or angiotensin receptor blocker (ARB).³⁶ Results from animal studies suggested that DCCB markedly attenuate the autoregulatory ability of glomeruli.^{37,38} This would result in an increase in glomerular capillary pressure and albuminuria unless BP was reduced to level below 120 mmHg.³⁹ The result from our study may support this theory since the majority of study subjects did not have good BP control. Nevertheless, this association in our study only showed cross-sectional but not a cause-effect relationship.

It has been accepted that screening for microalbuminuria is cost-effectiveness in the prevention of progressive kidney disease in diabetic patients.^{40,41} However, there is still a debate concerning whether or not that benefit would be the same in other high risk groups such as hypertensive patients. According to the 2007 European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines, microalbuminuria has been considered as a recommended test for risk stratification.⁹ However, this recommendation has not been implemented for

hypertensive care in Thailand. Consequently, physicians and health care providers are still reluctant to screen for microalbuminuria and to follow this screening with appropriate treatment in these populations. Athobari et al have studied the issue of the cost-effectiveness of screening for albuminuria and the subsequent treatment of individuals with microalbuminuria with an ACE inhibitor. Although this approach was not cost-effective in terms of preventing end stage renal disease, it was cost-effective in preventing short term outcomes like cardiovascular events.⁴² Our study reported the prevalence of microalbuminuria in nondiabetic hypertensive patients to be high enough to make screening worthwhile. Moreover, the screening method is easy and with an acceptable cost. Taking these evidences together with the Wilson-Jungner criteria for screening programs,⁴³ we conclude that screening for albuminuria may prove to be useful in early risk assessment and prevention of cardiovascular disease in hypertensive patients in Thailand.

Our study has some limitations. Urinary albumin was measured on only a single occasion. Thus, we cannot exclude the possibility of false positive/negative test. Our study, however, corrected for some potential variability in urine concentrations by measuring for urinary creatinine excretion and used ACR in the analysis. Secondly, a cross-sectional design limits the ability to show any cause-effect relationship between risk factors and albuminuria as well as cardiovascular and renal outcomes. Further longitudinal studies of the natural course of microalbuminuria in nondiabetic hypertensive subjects will answer these questions.

Conclusion

In summary, microalbuminuria is not uncommon in Thai nondiabetic hypertensive subjects. Obesity and the use of dihydropyridine calcium channel blockers were found to be the important predictors. Prognostic value of the occurrence of microalbuminuria in this population remains to be determined in prospective cohort studies.

Acknowledgments

We thank Miss Punnee Amornithikul and Miss Kwanruan Narkkaew for their support in data collection, and acknowledge group captain Traisit Tassanavitate, Chief of the Department of Preventive Medicine, Royal Thai Air Force, for his support during studies in the Department of Preventive Medicine.

Disclosures

No conflicts of interest were declared in relation to this paper.

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