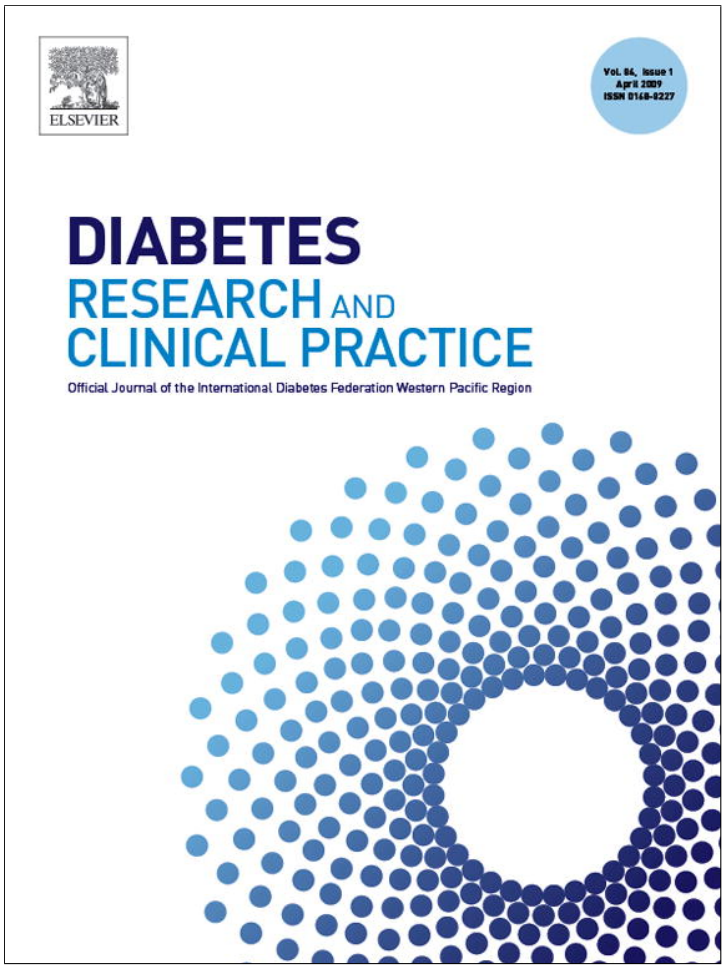

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Microalbuminuria and metabolic risk factors in patients with type 2 diabetes in primary care setting in Thailand

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ABSTRACT

Objective: To determine the prevalence of microalbuminuria and associated risk factors in patients with type 2 diabetes in primary care.

Methods: Clinical information of diabetic patients in 70 primary care units in Thailand was collected in a cross-sectional survey. Multinomial logistic regression model was used to examine several clinical risk factors with microalbuminuria and macroalbuminuria.

Results: A total of 4162 patients were included. The prevalence of microalbuminuria was 39.12% and macroalbumninuria was 7.83%. The proportion of patients with HbA1c $< 7\%$ was 37.9%. Independent risk factors for microalbuminuria and macroalbuminuria included HbA1c (adjusted OR 1.54, 95%CI 1.30–1.83 and 2.06, 95%CI 1.49–2.84 per unit increase in HbA1c, respectively), triglyceride $\geq$1.7 mmol/L (1.31, 1.11–1.56 and 1.44, 1.06–1.98), hypertension (1.31, 1.10–1.54 and 1.64, 1.23–2.20), and duration of diabetes $\geq$5 years (1.31, 1.11–1.55 and 2.39, 1.74–3.28). Metabolic syndrome was associated with macroalbuminuria (OR 1.36, 95%CI 1.01–1.84).

Conclusion: The high prevalence of microabuminuria and suboptimal glycemic control for the diabetic patients were found to highlight the need to improve in control of glycemia and metabolic risk factors.

1. Introduction

The epidemic of type 2 diabetes is one of the major public health concerns worldwide due to its high prevalence and its serious complications. Diabetes currently affects approximately 170 million people throughout the world [1] and 3 million people in Thailand [2]. Diabetes is a major cause of chronic kidney disease and end stage renal diseases. Albuminuria is a well-known predictor of renal disease in patients with diabetes [3,4]. The American Diabetes Association recommends screening for microalbuminuria in all type 2 diabetic patients annually [5]. Identification of those patients with microalbuminuria would enable an appropriate and timely management for the patients. Previous studies have shown a high prevalence of microalbuminuria (39.8%) among Asian patients with diabetes [6], including in Thai patients (43.3%) [7]. However, the study used only screening test for microalbuminuria and the sample size of Thai patients was relatively small.

Studies have consistently shown the association of metabolic syndrome and some of its components including hypertension, hyperglycemia and obesity with an increased

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risk of microalbuminuria and chronic kidney disease in diabetes patients [8–12]. However, the association between albuminuria and dyslipidemia especially triglyceride were less consistent [11–17]. The present study was aimed to re-evaluate the prevalence of microalbuminuria and its association with metabolic risk factors in patients with diabetes of primary care clinics in a nationwide survey of diabetes management in Thailand.

2. Methods

We conducted a baseline survey of diabetes management in primary care level in 8 provinces including 8 units in general hospitals, 9 units in community hospitals, and 53 units in health care centers. In general, diabetes patients were initially diagnosed and treated at a community hospital, and/or general hospital. After the initial treatment, patients who reside in rural areas and are on oral antiglycemic medication are usually referred to follow up at the health care centers. For those who live in urban area are usually followed up at primary care clinics at the community hospitals or general hospitals. At the health care centers, patients were primarily taken care by well-trained nurses. Some health care centers have a visiting physician from the community or general hospital come to care for the patients at the primary care unit (PCU) once a week on a regular basis. Overall, patients in all community hospitals and general hospitals were treated by general practitioners. The study was approved by the Ethical Review Committee for Research in Human subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

3. Study population

The study involved a multi-center cross-sectional study. The survey team contacted a number of general hospitals, community hospitals and health care centers and invited them to participate in the study. Eligible subjects were type 2 diabetic patients who attended the outpatient care of the participating centers irrespective of age, duration of diabetes, and treatment. In each center, diabetic patients were randomly sampled from the diabetes patients who visited the primary care clinics during 1-month period. Each center was asked to systematically random sample about 10% of its diabetes patients with at least a total of 30 patients. All the selected patients were informed about the study and all of them agreed to participate in the study. Patients were enrolled between January and September 2006.

4. Data collection

Data related to medical history were reviewed from the medical records of each selected patient. Clinical information of the last visit within 3 months was abstracted by the participating physicians and reported. Prior to the study, physicians and nurses of the participating hospitals and health care centers were trained for data collection methods and anthropometric measurement. The anthropometric measurements including weight, height, and waist circumference were obtained from the last visit. Waist circumference was measured from the horizontal plane at one centimeter (1 cm) above the navel. Measurement was made with a participant standing erect, abdomen relaxed, arms at the side, and feet together with weight equally divided over both legs. Participants were told to breathe normally and to breathe out gently at the time of measurement and not to hold in their abdomen or hold their breath. Laboratory data were collected at the latest visit. Biochemical data included total cholesterol, triglyceride, high density lipoprotein (HDL) and HbA1c were collected. All biochemical specimens were transferred to a central laboratory in Bangkok. A spot urine was collected and urine albumin was measured by immunoturbidimetric assay (Tina-quant albumin, Roche Diagnostics). Urine creatinine was measured by Jaffe rate blake and compensate method (Hitachi 917, Roche). Cholesterol and triglyceride were analyzed by enzymatic coloricmetric method (Hitachi, 917, Roche). HDL-C was measured by direct homogeneous enzymatic method. HbA1C was measured by a standardized method according to IFCC by immunoturbidmetric (Integra 400, Roche). Urinary albumin to creatinine ratio (ACR) was calculated by dividing urinary albumin with urinary creatinine.

5. Definition

Type 2 diabetes is defined as fasting plasma glucose of $\geq$7 mmol/L or use of diabetes medication or previously diagnosed diabetes. Hypertension is defined according to the WHO guidelines as systolic blood pressure (SBP) $\geq$ 140 mm Hg and/or diastolic blood pressure (DBP) $\geq$ 90 mm Hg, and/or use of antihypertensive medication. Low high density-lipoprotein cholesterol (low HDL-C) is defined as HDL-C $<$ 1.03 mmol/L for men and $<$ 1.29 mmol/L for women. Elevated low-density lipoprotein cholesterol (LDL-C) is defined as LDL-C $\geq$ 4.1 mmol/L. Hypertriglyceridemia is defined as serum triglyceride (HTG) $\geq$ 1.7 mmol/L. Albuminuria was categorized into microalbuminuria where the spot urine ACR ranged from 30 to 299 μg/mg creatinine and macroalbuminuria as the urine ACR $\geq$ 300 μg/mg creatinine. Metabolic syndrome was defined according to the modified ATP III criteria [18]. Since all of the subjects had diabetes, the criteria for metabolic syndrome would be met if the patient had at least two of the following; abdominal obesity (waist $\geq$ 80 cm for women and $\geq$90 cm for men), triglyceride $\geq$1.7 mmol/L or on drug treatment for elevated triglyceride (fibrates or nicotinic acid), HDL-C $<$ 1.03 mmol/L for men and $<$1.29 mmol/L for women or on fibrates or nicotinic acid and blood pressure $>$130/85 mm Hg (or on treatment of hypertension).

6. Statistical analysis

Patient characteristics and outcomes as categorical variables were compared using Chi-squared test, and those for continuous variables were compared using *F*-test for normally distributed data and Mann–Whitney *U*-test for non-normal.

The comparison of patients' characteristics were done among microalbuminuria, macroalbuminuria and normoalbuminuria and among different clinical settings. Variables that were significantly associated with outcome of normoalbuminuria, microabuminuria and macroalbuminuria in univariate analysis were then entered into the multinomial logistic regression model to determine the adjusted odds ratio for independent predictors of micoroalbuminuria and macroalbuminuria. The independent variables included age, sex, duration of disease (<5, ≥5 years), trigylceride ≥1.7 mmol/L, LDL-C categories (<2.6, 2.6–4.0, and ≥4.1 mmol/L), low HDL-C, BMI, HbA1c, hypertension, smoking status and clinical setting (general hospital, community hospital and primary care center). Additional analysis was performed to determine the association between the condition of metabolic syndrome and albuminuria. In the analysis, those independent variables that were components of metabolic syndrome including abdominal obesity, high triglyceride, hypertension, low HDL were replaced by a variables indicating with or without metabolic syndrome. All the statistical tests were performed using Stata statistical package version 9.

7. Results

Overall, a total of 4162 patients with diabetes were enrolled in the study, of these 566 were recruited in general hospitals, 1142 in community hospitals and 2454 in primary care units. Table 1 shows the patients' characteristics according to the treatment setting. In general, the characteristics of the patients in 3 settings were relatively similar in age, duration of diabetes (years), BMI, waist circumference and HbA1c level. Albuminuria was slightly higher in patients from general hospitals compared to the others, but not significantly different. A higher level of triglyceride and lower level of HDL-C were observed in those in community hospitals. Overall, median HbA1c and albuminuria level were 7.2% and 25.0 μg/mg creatinine, respectively. Nearly two-third of the patients (62%) did not receive adequate glycemic control (HbA1c ≥ 7). Proportion of patient with HbA1c < 7 and with satisfactory lipid profiles were better in the general hospitals. Half of the patients were classified as having metabolic syndrome.

Overall, 39.12% of the patients with diabetes had microalbuminuria and 7.83% had macroalbuminuria. The characteristics of patients by albuminuria category are shown in Table 2. Those with microalbuminuria and macroalbuminuria had higher levels of triglyceride, higher levels of HbA1c, and longer duration of follow-up, but had lower levels of HDL-C compared to those having normoalbulinuria. The prevalence for patients with poor glycemic control (HbA1c ≥ 7) or hypertension were progressively higher in the microalbuminuria and macroalbuminuria groups compared to the normoalbuminuria group. Metabolic syndrome were also more prevalent in the albuminuria groups (Table 2).

The factors related to microalbuminuria are shown in Table 3. In the multinomial logistic regression models, the factors independently associated with microalbuminiuria and macroalbuminuria included male gender, older age, longer duration of disease (≥5 years), poor glycemic control, triglyceride ≥1.7 mmol/L, LDL level ≥4.1 mmol/L. Those treated in primary care clinic of general hospitals were less likely to have microalbuminuria but more likely to have macroalbuminuria. Each unit of HbA1c was associated with 1.54 times of having microalbuminuria and 2.06 times of macroalbuminuria (95%CI 1.49–2.84). Patients with duration of diabetes ≥5 years were 1.31 times more likely to have microalbuminuria and 2.39 times to have macroalbuminuria compared those with duration <5 years. Those patients with triglyceride ≥1.7 mmol/L were more likely to have microablbuminria (OR 1.31) and macroalbuminuria (1.44). No significant association of obesity indices (either waist circumference or BMI) with albuminuria was found. Table 4

Table 1 – Patients' characteristics by treatment settings.

	Total	General hospital	Community hospital	Health care center	*p*-Value
N	4162	566	1142	2454	
Age (years)	58.67 (10.86)	58.35 (10.72)	58.23 (10.43)	58.93 (11.07)	0.13
Male (%)	29.28	30.42	32.15	27.79	0.01
Diabetes duration (years)	6.43 (5.86)	6.81 (5.94)	6.38 (5.62)	6.43 (5.97)	0.37
Hypertension (%)	36.30	40.46	41.33	33.27	<0.01
Waist circumference (cm)	83.52 (10.09)	83.72 (10.73)	83.08 (10.05)	83.71 (9.95)	0.20
BMI (kg/m^2)	25.32 (4.13)	25.68 (4.24)	25.24 (4.08)	25.29 (4.13)	0.14
Triglyceride (mmol/L)	2.22 (1.30)	1.97 (1.10)	2.41 (1.38)	2.19 (1.30)	<0.001
Total cholesterol (mmol/L)	5.22 (1.15)	5.06 (1.22)	5.21 (1.08)	5.25 (1.16)	<0.001
HDL-C (mmol/L)	1.19 (0.29)	1.27 (0.30)	1.15 (0.27)	1.20 (0.28)	<0.001
Low HDL <1.03 in male, female <1.29 mmol/L in female (%)	56.57	46.95	62.53	55.95	<0.001
HbA1c (%)	7.84 (1.82)	7.84 (1.94)	7.90 (1.80)	7.81 (1.80)	0.36
HbAc <7% (%)	37.90	42.88	35.59	37.83	<0.01
LDL-C (mmol/L) (%)	3.03 (0.98)	2.89 (1.06)	3.0 (0.93)	3.08 (0.98)	<0.001
Albuminuria (μg/mg Cr)	88.00 (163.20)	95.96 (181.63)	90.95 (169.39)	84.79 (155.58)	0.26
Smoke (%)	9.23	7.62	11.29	8.54	0.01
Metabolic syndrome (%)	51.56	56.46	50.04	51.03	0.02

Data presented as mean (S.D.) unless otherwise indicated.

Table 2 – Characteristics of patients by albuminuria categories.

	Normoalbuminuria	Microalbuminuria	Macroalbuminuria	*p*-Value
N	2208	1628	326	
Age (years)	58.2 (10.5)	58.6 (11.1)	60.7 (10.2)	<0.001
Male (%)	25.2	32.1	34.1	<0.001
Diabetes duration (years)	5.6 (5.3)	6.6 (5.7)	9.3 (7.5)	<0.001
Waist circumference (cm)	82.98(10.18)	83.78 (10.18)	84.24 (9.69)	0.04
BMI (kg/m^2)	25.3 (4.2)	25.2 (4.0)	25.5 (4.1)	0.61
Triglyceride (mmol/L)	2.05 (1.16)	2.34 (1.40)	2.51 (1.42)	<0.001
Total cholesterol (mmol/L)	5.15 (1.13)	5.23 (1.13)	5.39 (1.25)	0.001
HDL (mmol/L)	1.21 (0.29)	1.17 (0.28)	1.14 (0.27)	<0.001
LDL (mmol/L)	3.01 (0.96)	3.04 (0.99)	3.03 (0.97)	0.79
HbA1c (%)	7.5 (1.7)	8.1 (1.9)	8.5 (2.0)	<0.001
HbA1c > 7% (%)	56.34	66.56	74.07	<0.001
ACR (μg/mg Cr)	11.1 (7.9)	94.6 (67.0)	576.1 (196.7)	<0.001
Hypertension (%)	31.79	36.67	43.87	<0.001
Smoke (%)	8.16	10.74	11.20	0.03
Metabolic syndrome (%)	50.79	54.74	56.63	0.023
General hospital (%)	56.0	34.1	9.89	<0.01
Community hospital (%)	51.4	40.8	7.8	
Health care center (%)_	53.1	39.5	7.4	

Data presented as mean (S.D.) unless otherwise indicated.

Table 3 – Adjusted odds ratio (95%CI) for microalbuminuria and macroalbuminuria with components of metabolic factors.

Parameters	Microalbuminuria	Macroalbuminuria
Sex (female = 0)	1.43 (1.14–1.79)	1.33 (0.90–1.97)
Age (10 years)	1.06 (0.97–1.14)	1.17 (1.01–1.35)
HbAlc (%)	1.54 (1.30–1.83)	2.06 (1.49–2.84)
Duration of diabetes (≥5 vs. <5 years)	1.31 (1.11–1.55)	2.39 (1.74–3.28)
Smoking (yes vs. no)	1.06 (0.83–1.34)	1.84 (1.24–2.74)
Hypertiglyceridemia (≥1.7 vs. <1.7 mmol/L)	1.31 (1.10–1.56)	1.44 (1.06–1.98)
Hypertension	1.31 (1.10–1.54)	1.64 (1.23–2.20)
BMI ≥ 25 kg/m^2	1.10 (0.93–1.29)	1.06 (0.79–1.42)
LDL < 2.6 mmol/L	1	1
LDL 2.6–4.0 mmol/L	0.98 (0.79–1.21)	1.05 (0.70–1.52)
LDL ≥ 4.1 mmol/L	1.28 (1.01–1.61)	1.44 (1.01–2.06)
Low HDL[a]	1.04 (0.88–1.24)	1.36 (1.00–1.87)
General hospital	1	1
Community hospital	1.23 (0.91–1.68)	0.52 (0.33–0.83)
Health care centers	1.20 (0.89–1.61)	0.55 (0.36–0.85)

[a] Low HDL; HDL < 1.03 mmol/L in male and <1.29 mmol/L in female.

shows the association between metabolic syndrome and albuminuria. Diabetes patients with metabolic syndrome were more likely to have microalbuminuria (OR 1.10) and macroalbuminuria (1.36) compared to those without the metabolic syndrome.

8. Discussion

This study supports the evidence of high prevalence of microalbuminuria (39.12%) and macroalbiuminuria (7.83%)

Table 4 – Adjusted odds ratio (95%CI) for microalbuminuria and macroalbuminuria with metabolic syndrome.

Parameters	Microalbuminuria	Macroalbuminuria
Sex (female = 0)	1.47 (1.18–1.84)	1.25 (0.84–1.87)
Age (10 years)	1.07 (0.99–1.16)	1.21 (1.05–1.40)
HbAlc (%)	1.17 (1.11–1.23)	1.30 (1.20–1.40)
Duration of diabetes (≥5 vs. <5 years)	1.24 (1.05–1.47)	2.35 (1.70–3.23)
Smoking (yes vs. no)	1.05 (0.83–1.33)	2.01 (1.35–2.99)
Metabolic syndrome	1.10 (0.94–1.30)	1.36 (1.01–1.84)
General hospital	1	1
Community hospital	1.31 (0.99–1.75)	0.71 (0.45–1.12)
Primary care	1.20 (0.91–1.57)	0.70 (0.45–1.08)

among patients with diabetes in primary care settings in Thailand. We found an association of albuminuria with poor glycemic control (as measured by HbA1c), elevated triglyceride, elevated LDL-C, hypertension and metabolic syndrome. Over half of the patients had suboptimal glycemic control at a target level of HbA1c at 7% and were found in both normoalbuminria and albuminurian patients. These findings underscore the need to intensify the glycemic control among these patients in all primary care settings.

The finding that nearly 40% of patients had microalbuminuria is comparable to the microalbuminuria prevalence study (MAPS) [6,7]. In that study, the prevalence of albuminuria in Thai and other Asian population was about 39.8% for microalbuminuria and 18.8% for macroalbuminuria. However, those studies used a semiquantitative urine test to detect albuminuria. The prevalence of microalbuminuria in the present study was higher than that of the western population, but lower than that of the Pima Indians and a population in middle East [19,20]. The variation might be due to the difference in duration of diseases, laboratory technique and possibly the genetic factor [21].

Our study supports the evidence that poor glycemic control as measured by HbA1c was associated with microalbuminuria [22]. The positive association of hypertension, hypertriglyceridemia with microalbuminuria was consistent with several studies [8–10,22–24]. The findings of several risk factors for albuminuria including age, male, duration of diseases, and smoking were also consistent with those studies [8,10,24]. Although there was inconsistent evidence with regard to the association of triglyceride with microalbuminuria, the observed association with high triglyceride was consistent with some recent studies [8,22,23] and a clinical study using fenofibrate to decrease the progression of microalbuminuria [25]. In addition, the findings that high LDL-C and low HDL-C were independently associated with microalbuminuria and macroalbuminuria are consistent with studies in different populations [17,24,26]. We found LDL-C at the level of greater than 4.1 mmol/L and low HDL ($<$1.03 mmol/L in male and $<$1.29 mmol/L in female) was associated with albuminuria. Note that, the present study also found that patients with metabolic syndrome were more likely to have albuminuria and this is consistent with other studies [27,28]. It is possible that condition of dyslipidemia and obesity, as marker of insulin resistance, induces the deterioration of renal function and microalbuminuria [29]. Further clinical study to clarify whether the effect of preventing and treating metabolic components such as healthy eating and lipid lowering drug and weight loss will result in improved renal prognosis is warranted.

The present study did not find the associations of BMI and waist circumference with microalbuminuria. The lack of association were also found in a study in Taiwanese diabetes male patients and other cross-sectional studies [20,30]. A recent study in Japan demonstrates that decrease in BMI is an independent risk factor for proteinuria and chronic kidney disease in diabetes patients. [31]. The lack of association in the present study could possibly be due to the nature of cross-sectional design which limits the inference of causal relationship. It is not clear whether other factors such as genetic, hormonal, stage of disease or lifestyle might contribute to this observation. Further prospective study is warranted to investigate this relation in this population.

Currently, in Thailand, the incidence of ERSD patient, who need renal replacement therapy is estimated to be 10,000 cases per year [32]. It is expected that the number of renal impairment associated with diabetes is increasing due to the high prevalence of diabetes [33]. Without any proactive intervention to prevent the diabetes incidence and to properly manage diabetes to prevent renal complication it is likely that the number of ESRD will increase. A recent study also indicates that diabetic patients with microalbuminuria and metabolic syndrome have an increased risk of cardiovascular diseases [34].

The present study has its strength as it includes a large sample size of diabetic patients from a country wide distributed primary care units. Some limitations of the study should be noted. We did not have complete data on use of hypoglycemic drugs and ACE inhibitors in this study. Note that this study also could not evaluate the adequacy of blood pressure control due to the incomplete data in some of the medical records. However, previous study indicated that poor blood pressure control was observed [7,35]. Further prospective study to evaluate quality of care in terms of blood pressure control, comorbidity and other complications among diabetic patients in primary care are needed. It is also difficult to determine the real difference in quality of care across the settings. Long term follow up of the patients could further help shed light on the difference of the care quality given at different settings. Other factors such as betel nut chewing and high uric acid had been reported to be associated with increased risk of microalbuminuria; unfortunately, however, such data were not collected in this study [36,37]. Finally, the cross-sectional design limits the inference of cause–effect relationship of the risk factors and the outcome of microalbuminuria.

In conclusion, this study underscores the high prevalence of microalbuminuria and its association with glycemic control and metabolic factors among diabetic patients. There is an urgent need to implement a more effective glycemic control and treatment of metabolic risk factors in these patients.

Conflict of interest

The authors declare that they have no conflict of interest.

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