



Association between serum uric acid level and microalbuminuria to chronic vascular complications in Thai patients with type 2 diabetes ☆,☆☆

Somlak Chuengsamarn ^{a,*}, Suthee Rattanamongkolgul ^b, Siwanon Jirawatnotai ^c

^a Division of Endocrinology and Metabolism, Faculty of Medicine, HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Nakornnayok, Thailand

^b Department of Preventive and Social Medicine, Faculty of Medicine, HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, Nakornnayok, Thailand

^c Department of Pharmacology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

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ABSTRACT

Aims: To investigate an association between serum uric acid/microalbuminuria and chronic micro/macro-vascular complications in type 2 diabetic patients.

Methods: This cross-sectional study enrolled 608 patients with type 2 diabetes. All subjects were examined and basic information on health of the subjects was recorded for inclusion criteria. Several chemical parameters (fasting plasma glucose, triglyceride, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid, and microalbuminuria), and related chronic vascular complications were measured and recorded in data forms.

Results: Logistic regressions were used to analyse odds ratios between uric acid/microalbuminuria levels and several chronic vascular complications. Prevalence of chronic vascular complications in T2DM patients, namely coronary arterial disease, cerebrovascular disease, diabetic nephropathy, diabetic retinopathy, and diabetic peripheral neuropathy was significantly correlated with increase of uric acid level [2.29 (1.01–5.2), 16.01 (4.74–54.09), 9.99 (4.4–22.8), 4.43 (1.3–15.1), 4.37 (1.5–12.9)], and of microalbuminuria level [7.0 (3.6–13.8), 3.2 (1.2–8.7), NA, 14.7 (5.1–42.7), 7.2 (2.9–17.7)].

Conclusion: Both elevated uric acid and microalbuminuria levels were significantly associated with diabetic chronic micro/macro-vascular complications. Monitoring of uric acid and microalbuminuria levels provides a predictive value for a presence of chronic micro/macro-vascular complications in patients with type 2 diabetes.

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1. Introduction

Chronic vascular complications in type 2 diabetes (T2DM) are the deteriorating conditions underlined by inflammation (Ceriello & Motz, 2004). The chronic vascular complications in diabetes mellitus (DM) are classified by vascular size into macro- and microvascular diseases. The chronic vascular complications are a serious problem, since they generally yield devastating outcomes for the T2DM patients, which include coronary arterial disease (CAD), cerebrovascular disease (CVD), peripheral arterial disease (PAD), diabetic nephropathy (DN), diabetic retinopathy (DR), and diabetic peripheral neuropathy (PN) (Alberti & Zimmet, 1998).

Elevated levels of uric acid and microalbuminuria are commonly found in patients with severe cardiovascular diseases, such as stroke, and ischemic heart disease (Fukui et al., 2008; Hayden & Tyagi, 2004; Klausen, Scharling, Jensen, & Jensen, 2005; Redon, 2006). The elevated levels correlate with the severity of the conditions, namely, the higher the levels, the more severe the conditions (Kanellis & Kang, 2005; Kim et al., 2011; Newman et al., 2005; Tai et al., 1990). Although it is still unclear, the heightened levels are presumably a result of an up-regulation of inflammatory cytokines, such as interleukin-6 (IL-6), C-reactive protein (CRP), and increased oxidative stress (Ceriello & Motz, 2004; Deckert et al., 1992; Giacco & Brownlee, 2010; Koenig & Meisinger, 2008; Newman et al., 2005).

High levels of inflammation are regularly found in patients with T2DM. This observation is accompanied by the findings that there are correlations between increase of the serum uric acid level/microalbuminuria and severity of the insulin resistance and metabolic profiles (Costa, Iguala, Bedini, Quinto, & Conget, 2002; Dehghan, Van Hoek, Sijbrands, Hofman, & Witteman, 2008; Festa et al., 2000; Hsu et al., 2011; Kodama et al., 2009). It is not known; whether the inflammation associated with T2DM contributes to the elevated levels of serum uric acid and microalbuminuria, and whether or not there is a relationship

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* Corresponding author at: Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, HRH Princess Maha Chakri Sirindhorn Medical Center, Srinakharinwirot University, 63 M 7 Rungsit-Nakornnayok Rd., Ongkarak, Nakornnayok, Thailand. 26120. Tel.: +66 37 395085 6x11001; fax: +66 37 395085 6x11003.

E-mail address: somluc@swu.ac.th (S. Chuengsamarn).

between uric acid/microalbuminuria, and the inflammatory-driven chronic vascular conditions found in the T2DM patients.

In the hope of identifying a reliable parameter that will allow an early detection of the micro- and macro-vascular complications in T2DM population, we investigated the relationships between levels of serum uric acid/ microalbuminuria, and the chronic vascular conditions in a T2DM population through a cross-sectional observation. The study also took into the consideration the information on other indicative parameters, such as duration of diabetes, hypertension status, smoking status, history of CAD, history of CVD, dyslipidemia status, uric acid, microalbuminuria (MAU), fasting plasma glucose (FPG), and hemoglobin A_{1c} (HbA_{1c}).

2. Patients and methods

2.1. Subjects and designed study

This study was a cross-sectional study by design. It included all patients who attended diabetic clinic in the outpatient unit of the Internal Medicine Department at HRH Princess Mahachakri Sirindhorn Medical Center, Faculty of Medicine, Srinakharinwirot University during the years 2007–2008. Inclusion criteria were type 2 diabetes aged of 35 or more. Type 2 diabetes was diagnosed according to the Report of the expert committee on the diagnosis and classification of diabetes mellitus (2003). We excluded patients taking any medications that might affect serum uric acid concentrations such as, thiazides, salicylates, pyrazinamide, ethambutol, nicotinic acid, and cyclosporine. Patients with advanced renal dysfunction by serum creatinine more than 2.0 mg/dl or urinary tract infection were excluded. The subjects were checked for blood chemistry profiles and examined for diabetic micro and macro-vascular complications by endocrinologists after the details of the project were explained to them and after they signed the consent form.

This study was approved by the Ethic Committee of Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand (serial number: SWUEC 9/2550) in accordance with the Declaration of Helsinki. Participants were informed, and gave their consent before participation.

2.2. Data collection

Basic information of patients and factors associated with increased diabetic complications were collected using case record form containing information of age, sex, weight, height, waist circumference, duration of diabetes, hypertension status, smoking status, history of CAD, and history of CVD, dyslipidemia status, uric acid, fasting plasma glucose (FPG), and haemoglobin A_{1c} (HbA_{1c}). The circumferences of the waist were measured at the level of the iliac crest. Blood samples were collected after a 12 h overnight fasting. Serum uric acid concentrations in our reference range (2.6–7.2 mg/dl) were assessed using enzyme colorimetric method. Plasma fasting glucose was assessed using standard enzymatic method. Serum total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride concentrations were measured by standard enzymatic methods. The high-performance liquid chromatography was used for assay in HbA_{1c} level.

2.3. Metabolic syndrome and chronic vascular complications

Metabolic syndrome criteria were defined by the joint criteria (2009) (Alberti et al., 2009). Patients have metabolic syndrome, if they have central obesity by waist circumference (WC) ≥ 90 cm in men, or ≥ 80 cm in women (according to the recommendation by the joint criteria (2009) for Asian population), and any two of the following: elevated triglyceride (≥ 150 mg/dl), low High-density

lipoprotein cholesterol (<40 mg/dl in men, <50 mg/dl in women), hypertension ($\geq 130/85$ mm/Hg), impaired fasting glucose (FPG ≥ 100 mg/dl).

DN is defined by abnormalities in albumin excretion; the level of microalbuminuria (MAU) is ≥ 30 mg/g Cr, and the subject has positive results twice, consecutively (Klausen et al., 2005; Redon, 2006). The MAU was used by measurement of the albumin-to-creatinine ratio in an early morning spot urine, by the immunoassay method (Silver, Dawnay, Landon, & Cattell, 1986). MAU was classified into three groups; normal, microalbuminuria and macroalbuminuria as the following value of <30 , 30 – 299 , ≥ 300 mg/g Cr, respectively (Klausen et al., 2005). Urinary infections were diagnosed by positive test of nitrites or leucocytes ≥ 250 leucocytes/ml in the urine sample.

Table 1

Characteristics of subjects in the study.

Characteristics	Total	Number (Mean)	Percent (S.D.)
Age (total, mean, SD.)	608	(57.8)	(13.4)
Sex	608		
- Male		180	29.6
- Female		428	70.4
Smoking status	607		
- Current Smoking		33	5.4
- Ex-Smoking		60	9.9
- Non-Smoking		514	84.7
Serum creatinine (mg/dL) mean	608	1.1	0.6
MDRD-GFR (ml/min per 1.73m ²) (total, mean, SD.)	608	70.2	26.3
Insulin user (%)	608	187	30.8
ACEI user (%)	608	302	49.7
ARB user (%)	608	80	13.2
Statin user (%)	608	473	77.8
History of hypertension (%)	605	445	73.6
Body mass index (kg/m ²) (total, mean, SD.)	608	27.1	5.6
Waist circumference (cm.)	608	90.9	13.1
Systolic blood pressure (mmHg)	601	131.7	18.9
Diastolic blood pressure (mmHg)	601	81.0	7.2
Duration of diabetes (years) (total, mean, SD.)	460	7.85	8.1
Fasting plasma glucose (mg/dL) (total, mean, SD.)	608	138.9	52.6
Total cholesterol (mg/dL) (total, mean, SD.)	607	217.3	48.2
Low-density lipoprotein cholesterol (mg/dL) (total, mean, SD.)	607	128.1	46.8
High-density lipoprotein cholesterol (mg/dL) (total, mean, SD.)	607	43.9	9.7
Triglyceride (mg/dL) (total, mean, SD.)	607	175.0	73.3
Uric acid (mg/dL) (total, mean, SD.)	608	6.6	2.1
Microalbuminuria (mg/g Cr.) (total, mean, SD.)	586	75.3	97.5
Chronic vascular complications			
Coronary arterial disease	607	112	18.5
Cerebrovascular disease	608	37	6.1
Diabetic nephropathy	608	264	43.4
Diabetic retinopathy	606	154	25.4
Diabetic peripheral neuropathy	608	102	16.8
Number of chronic vascular complications			
0 chronic vascular complication	608	334	54.9
1 chronic vascular complication	608	74	12.2
2 chronic vascular complications	608	76	12.5
3 chronic vascular complications	608	58	9.5
4 chronic vascular complications	608	61	10.0
5 chronic vascular complications	608	5	0.8
Metabolic components			
- Waist circumference (IDF)	607	446	73.4
- Triglyceride (IDF)	607	384	63.2
- High-density lipoprotein cholesterol (IDF)	607	422	69.4
- Blood pressure (IDF)	603	446	73.4
- Fasting plasma glucose (IDF)	608	455	74.8
- Body mass index (WHO)	608	485	79.8
- Microalbuminuria (WHO)	575	296	48.7
- Uric acid	608	286	47.0

MDRD-GFR, Modification of Diet in Renal Disease-glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers.

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