The Association Between Risk Factors for Ischemic Stroke and Microalbuminuria

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Objective: To determine the relationship between the risk factors for ischemic stroke and microalbuminuria.
Material and Method: We enrolled 173 patients older than 25 years who had at least two risk factors for stroke. The patients were assessed by questionnaire, blood pressure, microalbuminuria, height and weight measurement. The patients were given health education.
Results: The common risk factors were hypertension (80.3%), dyslipidemia (56.6%), and multiple cerebral infarction (39.9%). The hyptertensive patients had 5 times risk of microalbuminuria 5.0 compared to normotensive patients (95% CI, 1.13-21.90; p-value < 0.05). Among diabetes patients had risk of microalbuminuria 27.1 times compared to non-diabetic patients (95% CI, 9.58-76.82; p-value < 0.01). However, the patients who had dyslipidemia had risk of microalbuminuria 1.784 times of who did not, but no statistically significant (95% CI, 0.79-4.03; p-value > 0.05).
Conclusion: Diabetes mellitus and hypertension are significantly risk factor of ischemic stroke related to microalbuminuria.

Keywords: Microalbuminuria, Risk factors, Stroke

Stroke or cerebrovascular disease (CVD) is the clinical designation for a rapidly developing loss of brain function due to a disturbance in the blood vessels supplying blood to the brain. This phenomenon can be due to ischemia (lack of blood supply) caused by thrombosis or embolism or due to a hemorrhage[1]. Microalbuminuria is the excretion of greater than 30 mg and less than 300 mg a day of albumin in the urine. The normal urinary albumin is less than 30 mg per 24 hours.

Stroke is a medical emergency and can cause permanent neurological damage, complications and death if not promptly diagnosed and treated. It is the third leading cause of death and the leading cause of serious disability[2], with major societal consequences. Risk factors for stroke include advanced age, hypertension (high blood pressure), previous stroke or transient ischaemic attack (TIA), diabetes mellitus, high cholesterol, cigarette smoking, atrial fibrillation,

migraine with aura, and thrombophilia (a tendency to thrombosis). Although microalbuminuria is associated with clinical risk factors for stroke, there is surprisingly little information regarding it as an independent risk factor for stroke or as a predictor of stroke outcome. A large prospective study[3] has reported that microalbuminuria is a risk factor for stroke in men, and a limited case-control study[4] found that the highest quintile of microalbuminuria values was associated with a 13-fold increased risk for stroke. The goal of this study is designed, therefore, to determine its relationship to risk factors for stroke.

Material and Method

A cross-sectional study was carried out at neurologic division, department of medicine, Phramongkutklao Hospital during October 2007-January 2008. The protocol was approved by the Royal Thai Army Medical Department Institutional review boards.

Eligibility criteria were ischemic stroke survivors age more than 25 years who have at least two risk factors of stroke (male, family history, previous stroke, diabetes, high cholesterol, cigarette smoking,

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hypertension (high blood pressure), heart disease). The patients were assessed by questionnaire, blood pressure, microalbuminuria, height and weight measurement.

Assessment of urine albumin

Microalbuminuria was tested by micral test (Roche diagnostic manufacturer, Ltd). This test is also based on the color shift of a monoclonal antibody to human albumin after binding of urinary albumin to antibody. It is a semi-quantitative screening tool and the results of this test were read as 0 mg/L, 20 mg/L, 50 mg/L and 100 mg/L. A reading of 20 mg/L or more was considered positive, according to manufacturer's recommendation.

Definition

Microalbuminuria refers to urinary albumin excretion that exceeds the normal range (20-200 mg/min or > 20 mg/L) but is below the minimum level of detection by standard dipstick (300 mg/L)[5]

Statistical analysis

The continuous data were assessed by mean, range and standard deviation (SD). The discrete data were assessed in number and percent. Chi-square test or Fisher's Exact test was used for determining the relationship between hypertension, diabetes, dyslipidemia and microalbuminuria. P-value (2-sided) < 0.05 represented statistical significance. Statistical analysis was assessed by statistic program, SPSS version 15.0.

Results

173 ischemic stroke survivors who met inclusion criteria were enrolled. The mean age was 66.1 years (range 28-90 years, SD 12.7). The mean body mass index was 25.1 (range 15.2-37.5, SD 4.0). The mean systolic blood pressure was 140.8 mmHg (range 83-217 mmHg, SD 24.1). The mean diastolic blood pressure

was 79.9 mmHg (range 47-113 mmHg, SD 12.7). The mean stroke risk assessment was 13.3 (range 0-57) (Table 1).

Of 173 patients, there were 98 female (56.6%) and 75 male(43.3%). Forty five patients had the history of coronary artery disease (27.6%), 69 patients had the history of multiple cerebral infarction (39.9%), 18 patients were smokers (10.4%), 98 patients had dyslipidemia (56.6%), 55 patients had diabetes (31.8%), 35 patients had microalbuminuria (20.2%), 139 patients had hypertension and were on treatment (80.3%). The common risk factors were hypertension (80.3%), dyslipidemia (56.6%), and multiple cerebral infarction (39.9%) (Table 2).

Thirty two patients had neither hypertension nor albuminuria, 2 patients had only albuminuria, 106 patients had only hypertension and 33 patients had either hypertension or albuminuria, 113 patients had neither diabetes nor albuminuria, 25 patients had only diabetes, 5 patients had only albuminuria and 30 patients had either diabetes or albuminuria. For 163 patients, 55 patients had neither dyslipidemia nor albuminuria, 74 patients had only dyslipidemia, 10 patients had only albuminuria and 24 patients had either dyslipidemia or albuminuria (Table 3).

The patients who had hypertension will have risk of microalbuminuria 5.0 times of the patients who did not have hypertension. It's statistically significant (95% CI, 1.1-21.9; p-value < 0.05). Among the patients who had diabetes will have risk for microalbuminuria 27.1 times of those who did not and is statistically significant (95% CI, 9.6-76.8; p-value < 0.05). The patients who had dyslipidemia will have the risk for microalbuminuria of 1.8 times of those who did not, but it has no statistic significance (95% CI, 0.8-4.0; p-value > 0.05).

Discussion

The common risk factors of stroke were hypertension, dyslipidemia and multiple cerebral

Table 1. Summary of demographic data of ischemic stroke patients

	n	Minimum	Maximum	Mean	Std. Deviation
Age	173	28	90	66.1	12.7
body mass index	165	15.2	37.5	25.1	4.0
systolic blood pressure	173	83	217	140.8	24.1
diastolic blood pressure	173	47	113	79.9	12.7
stroke risk assessment	171	0	57	13.3	11.2

infarction. Microalbuminuria could be detected in patients with diabetes, hypertension and dyslipidemia. Of 139 hypertensive patients, 33 had microalbuminuria (23.74%), of 55 diabetic patients, 30 had microalbuminuria (54.55%) and of 98 patients with dyslipidemia, 24 had microalbuminuria (24.49%). The patients who had diabetes mellitus will have 27.1 times the risk for developing microalbuminuria. Microalbuminuria was closely related to diabetes.

Although previous studies had shown proteinuria as an independent predictor of stroke outcomes in the general population[3,6], none have examined the possible association between microalbuminuria and the incident of stroke. In the general population, microalbuminuria has a prognostic significance in patients with stroke, independently predicting recurrent strokes and mortality[7]. Microalbuminuria was independently associated with carotid artery intima-media thickness in non-diabetic individuals in the Insulin Resistance and Atherosclerosis Study, USA[8]. Carotid intima-media thickness is a risk factor for stroke and coronary heart disease[9]. Prospective studies have observed that microalbuminuria predicts allcause and cardiovascular mortality in the general population[10-14]. The EPIC-Norfolk Study is the first report evaluating the prospective relationship between microalbuminuria and incidence of fatal and nonfatal cerebrovascular disease in the general population[15]. The mechanism of the association between albuminuria and CVD is still largely unknown and a focus of research and debate. Several explanations have been suggested: albuminuria may reflect universal endothelial dysfunction that might enhance the penetration of atherogenic lipoproteins into the arterial wall[16]; albuminuria is a marker of established CVD[17], such that albuminuria and cerebrovascular disease are not causally related but rather reflect common determinants[18,16].

Table 2. Risk factors of stroke and microalbuminuria

		Frequency	Percent
Sex	M	75	43.4
	F	98	56.6
History of CAD	Yes	45	26.0
	No	118	68.2
Multiple cerebral	Yes	69	39.9
infarction	No	104	60.1
Smoking	Yes	18	10.4
	No	155	89.6
Dyslipidemia	Yes	98	56.6
	No	65	37.6
Diabetes	Yes	55	31.8
	No	118	68.2
Hypertension	Yes	139	80.3
	No	34	19.7
On treatment HT	Yes	139	80.3
	No	34	19.7
Microalbuminuria		35	20.2

Conclusion

Microalbuminuria is thought to be a marker for vascular endothelial damage due to the severity and/or duration of numerous pathophysiological insults, especially the injurious effects of poorly controlled diabetes and hypertension. The results of this study show that diabetes is the factor most closely related to microalbuminuria with statistic significance.

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Table 3. relationship of hypertension, diabetes and dyslipidemia with microalbuminuria

		Microalbuminuria		Odds ratio (95% CI)	p-value
		No	Yes		
Hypertension	No	32	2	5.0 (1.1-21.9)	0.018
	Yes	106	33		
Diabetes	No	113	5	27.1 (9.6-76.8)	<0.001
	Yes	25	30		
Dyslipidemia	No	55	10	1.8 (0.8-4.0)	0.175
	Yes	74	24		

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ความสัมพันธ์ระหว่างปัจจัยเสี่ยงของโรคหลอดเลือดสมองกับอัลบูมินในปัสสาวะ

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วัตถุประสงค์: เพื่อหาความสัมพันธ์ระหว่างปัจจัยเสี่ยงของโรคหลอดเลือดสมองกับอัลบูมินในปัสสาวะ

วัสดุและวิธีการ: การศึกษาแบบตัดขวางในผู้ป่วยโรคหลอดเลือดสมองตีบที่มีอายุตั้งแต่ 25 ปี ขึ้นไปที่มีปัจจัยเสี่ยงของโรคหลอดเลือดสมองตีบ 2 ปัจจัยขึ้นไป ทำแบบสอบถาม, วัดความดันโลหิต น้ำหนัก ส่วนสูง ตรวจอัลบูมินในปัสสาวะ

ผลการศึกษา: ผู้ป่วยโรคหลอดเลือดสมองตีบจำนวน 173 ราย พบว่าปัจจัยเสี่ยงที่พบบ่อยคือ ความดันโลหิตสูง (80.3%), ไขมันในเลือดสูง (56.6%) และเป็นโรคหลอดเลือดสมองตีบหลายครั้ง (39.9%) ผู้ป่วยที่มีภาวะความดันโลหิตสูงจะตรวจพบอัลบูมินในปัสสาวะมากกว่าคนปกติ 5.0 เท่า และมีนัยสำคัญทางสถิติผู้ป่วยเบาหวานจะตรวจพบอัลบูมินในปัสสาวะมากกว่าคนปกติ 27.1 เท่า และมีนัยสำคัญทางสถิติสำหรับผู้ป่วยที่มีภาวะไขมันในเลือดสูงจะตรวจพบอัลบูมินในปัสสาวะมากกว่าคนปกติ 1.784 เท่า แต่ไม่มีนัยสำคัญทางสถิติ

สรุป: โรคเบาหวาน และความดันโลหิตสูงเป็นภาวะเสี่ยงของโรคหลอดเลือดสมองตีบที่มีความสัมพันธ์กับอัลบูมินในปัสสาวะเป็นอย่างมีนัยสำคัญ