Thailand Diabetes Registry Project: Prevalence and Risk Factors of Stroke in Thai Diabetic Patients

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Objective: *To determine the prevalence of stroke and its risk factors in Thai diabetic patients who attended the diabetes clinics of university and tertiary-care hospitals.*
Material and Method: *A cross-sectional, multi-center, hospital-based diabetes registry was carried out at diabetes clinics of 11 university and tertiary-care hospitals. Demographic data, clinical characteristics, common drugs used and laboratory parameters were analyzed for prevalence and risk factors associated with stroke.*
Results: *The prevalence of stroke in the patients studied was 3.5%. Most of the patients were type 2 diabetes and had ischemic stroke. One of the risk factors associated with stroke was age greater than 60 years, and the risk appeared to be highest if the patients' age was greater than 70 years (adjust OR = 3.29, p = 0.012). Other risk factors included male sex, systolic blood pressure of $\geq$ 140 mmHg, use of oral hypoglycemic agents, lipid lowering agents and aspirin. There was no association between stroke and duration of diabetes, occupation, educational level, BMI, smoking, alcohol drinking, diastolic blood pressure, use of antihypertensive drugs or insulin, glycemic control, lipid profiles and kidney function.*
Conclusion: *Ischemic stroke was common among Thai patients with diabetes especially in the elderly. The present result emphasizes the relationship between level of systolic blood pressure and the occurrence of stroke. Optimal blood pressure control should be underscored in caring for diabetic patients.*

Keywords: *Diabetes, Diabetes Registry Stroke, Systolic Blood Pressure*

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Stroke is a devastating chronic macrovascular complication of diabetes. The risk of stroke is increased in both type1 and type 2 diabetes mellitus, conferring a two- to threefold greater risk of first event and recurrent stroke[1,2]. Moreover, there is accumulating evidence that even in the state of abnormal glucose homeostasis such as impaired fasting glucose or impaired glucose tolerance, the association with increased stroke risk still exists. A meta-analysis of several studies indicated that there is a progressive relationship between glucose levels and overall cardiovascular risk. Interestingly, this risk extends beyond diabetes and impaired glucose tolerance into "normal" plasma glucose range[3].

Cerebral infarction and primary intracerebral hemorrhage are responsible for up to 80% and 15% of first stroke in diabetic patients, respectively[4]. Thrombosis is more common (29-44%) than cardioembolism (20-25%) in ischemic stroke[5]. Diabetes also increases the risk of thrombosis of a small artery or "lacunar stroke", especially in posterior circulation[6]. The mechanisms that increase the risk of stroke may be accelerated by atherosclerosis of carotid arteries[7]. This is predisposing to intracranial atheroma of large, medium and smaller vessels[8]. It also increases oxidative stress and formation of advanced glycation end-products (AGEs) in the vessel wall. It increases co-existing diseases such as hypertension[9] and dyslipidemia. Since the expense of diabetic management is exceptionally high in most countries across all continents[10-12], knowledge of the prevalence and risk factors associated with stroke in Thai diabetic patients may facilitate prevention, early diagnosis and better treatment of this condition and thus reducing the cost of medical care.

Material and Method

A cross-sectional, multi-center, hospital-based diabetes registry was carried out from April 2003 to December 2003. Registered patients were from diabetes clinics of 11 tertiary centers. The method of registration and data collection was described in detail in a previous section of this issue. The study was approved by the ethics committee of each participating hospital. Signed informed consent was obtained from all participants. Stroke was divided into three categories: ischemic, hemorrhagic and both ischemic and hemorrhagic. Data were expressed as mean $\pm$ SD. Statistical analyses were performed using STATA version 8.0 (STATA Corporation, College Station TX, US). Comparisons among the groups were analysed by t-test, Chi-square test or Fisher's exact test, where appropriate.

Results

The present analysis included 9,330 diabetic patients. The prevalence of stroke was 3.5% and the ischemic form was the most common. The majority of patients had type 2 diabetes. Table 1 shows clinical characteristics of patients with and without stroke. By using multivariate analysis; age, male sex, systolic blood pressure, use of oral hypoglycemic agents, lipid lowering agents and acetyl salisylic acid (ASA) were independently associated with stroke (Table 2). The risk increased with age and reached statistical significance level at age 60 years or greater (adjust OR = 2.65, p = 0.040). Patients who were greater than 70 years old were at highest risk of stroke (adjust OR = 3.29, p = 0.012).

Discussion

It is estimated that in North America and the United Kingdom, cerebrovascular disease is the third major cause of death, the major cause of severe disability in the community and the single most expensive medical disorder, consuming up to 6% of the total clinical budgets[13]. Stroke is primarily a disease of the elderly with the peak incidence occurring in those of 75 years or older[14]. Diabetes is also an important risk factor of stroke[1,2]. The present result confirmed these findings, as risk of this complication increased with age and appeared as early as the age of 40 years, although it did not reach the level of statistical significance until the age of 60 years or older. Hypertension is perhaps the most important risk factor for stroke. Observational studies have shown that the levels of systolic and diastolic blood pressure are directly and continuously associated with the risk of both cerebral infarction and hemorrhage[15,16]. Treatment of hypertension even in patients without preexisting cerebrovascular disease has been shown to reduce the risk of stroke by approximately one third, with no large differences being apparent among the main drug classes[17]. Recently, the American Diabetes Association and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) had issued guidelines[18,19] advocating the target blood pressure of less than 130/80 mm Hg for people with diabetes. According to Bunnag et al[20], only 14% of hypertensive diabetic patients in this registry achieved this target. Moreover, patients with diabetes have multiple risk factors for stroke. Taken together it could explain the rather high prevalence of this macrovascular complication. In accordance with the United Kingdom

Table 1. Baseline characteristics of diabetic patients with and without stroke (data in mean ± SD)

Characteristics	Subjects without stroke	Subjects with stroke	p value
Age (years)	59.1 ± 13.6	65.6 ± 10.3	<0.001
Sex (% male)	33.7	42.6	0.001
Sex (% female)	66.3	57.4	0.001
Duration of diabetes (years)	10.3 ± 7.6	12.9 ± 8.1	<0.001
Body mass index (kg/m^2)	25.5 ± 4.4	25.1 ± 4.7	0.058
HbA_{1c} (%)	8.1 ± 1.8	8.2 ± 2.0	NS
Non-smoking (%)	80.2	74.2	0.009
Current and ex-smoking (%)	19.9	25.8	0.009
Non-alcoholic drinking (%)	81.6	75.5	0.005
Abstinence and current drinking (%)	18.4	24.5	0.005
Fasting plasma glucose (mg/dl)	153.6 ± 56.7	151.5 ± 54.2	NS
HbA1C (%)	8.2 ± 1.9	8.1 ± 1.9	NS
Creatinine (mg/dl)	1.2 ± 0.9	1.2 ± 0.6	NS
Total Cholesterol (mg/dl)	197.2 ± 42.5	195.8 ± 42.2	NS
Triglyceride (mg/dl)	150.7 ± 106.3	151.8 ± 80.8	NS
HDL-C (mg/dl)	53.9 ± 15.3	52.1 ± 16.1	NS
LDL-C (mg/dl)	114.6 ± 35.8	112.9 ± 34.2	NS
Systolic blood pressure (mmHg)	142.0 ± 22.9	149.8 ± 23.7	<0.001
Diastolic blood pressure (mmHg)	78.7 ± 11.3	79.2 ± 12.0	NS

NS = Not statistically significant

Prospective Diabetes Study[21], the present result did not show any relation between level of glycemic control and risk of stroke. Moreover, there was no relationship between stroke risk and dyslipidemia in the present study which is in agreement with data from the meta-analysis of a large epidemiological study[16]. The findings that more patients with this macrovascular complication were put on lipid lowering agents and acetylsalicylic acid may be due to the fact that more aggressive management is needed in treating this high risk group[22]. Interestingly, it was not clear at this time why patients with stroke were prescribed less oral hypoglycemic agents than those without. More studies are needed to clarify this issue.

Table 2. Risk factors of stroke in diabetic patients by multivariate analysis

	Adjust OR	p-value of Adjust OR
Age (years)		
< 40	1	
40-49.9	1.68	0.309
50-59.9	1.72	0.258
60-69.9	2.65	0.040
> 70	3.29	0.012
Sex		
Male	1.35	0.011
Systolic BP (mmHg)		
< 140	1	
> 140	1.38	0.009
Use of Oral hypoglycemic agents		
Yes	1	
No	1.60	0.002
Use of lipid lowering agents (Statin,fibrate)		
No	1	
Yes	1.52	0.001
Use of Aspirin		
No	1	
Yes	4.18	<0.001

The present study has shown that the elderly diabetic patients are vulnerable to stroke and has emphasized the role of controlling blood pressure to prevent this macrovascular complication.

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โครงการลงทะเบียนผู้ป่วยเบาหวานในประเทศไทย: ความชุกและปัจจัยเสี่ยงของโรคหลอดเลือดสมอง

ณัฐเชษฐ์ เปล่งวิทยา, รัตนา ลีลาวัฒนา, ธงชัย ประฏิภาณวัตร, ชัยชาญ ดีโรจนวงศ์, สิริเนตร กฤติยาวงศ์, พงศ์อมร บุนนาค, ณัฐพงศ์ โฆษชุณหนันท์, สมพงษ์ สุวรรณวลัยกร, ยุพิน เบ็ญจสุรัตน์วงศ์, ธัญญา เชฏฐากุล, ฉัตรประอร งามอุโฆษ, สาธิต วรรณแสง, สิริมา มงคลสัมฤทธิ์, จุฬาลักษณ์ โกมลตรี, เพชร รอดอารีย์

วัตถุประสงค์: *เพื่อศึกษาถึงความชุกและปัจจัยเสี่ยงต่อการเกิดโรคหลอดเลือดสมองในผู้ป่วยเบาหวานชนิดที่ 2 ที่มารับการรักษาที่คลินิกโรคเบาหวานของโรงพยาบาลมหาวิทยาลัยและโรงพยาบาลศูนย์*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาแบบตัดขวางโดยมีการลงทะเบียนผู้ป่วยเบาหวานที่มารับการรักษาที่คลินิกเบาหวานของโรงพยาบาลระดับตติยภูมิจำนวนทั้งสิ้น 11 แห่ง โดยมีการเก็บข้อมูลพื้นฐานของผู้ป่วย, ลักษณะทางคลินิก, ยาที่ผู้ป่วยได้รับตลอดจนผลการตรวจทางห้องปฏิบัติการที่สำคัญเพื่อนำมาวิเคราะห์หาความชุกและปัจจัยเสี่ยงของโรคหลอดเลือดสมอง*

ผลการศึกษา: *ความชุกของโรคหลอดเลือดสมองในผู้ป่วยเบาหวานที่ทำการศึกษามีค่าเท่ากับร้อยละ 3.5 โดยผู้ป่วยส่วนใหญ่ได้รับการวินิจฉัยเป็นโรคเบาหวานชนิดที่ 2 และป่วยเป็นโรคหลอดเลือดสมองชนิดเส้นเลือดในสมองตีบ ปัจจัยเสี่ยงต่อการเกิดโรคแทรกซ้อนดังกล่าว คือ ผู้ป่วยที่มีอายุมากกว่า 60 ปี, เพศชาย, ความดันโลหิตซิสตอลิคมากกว่าหรือเท่ากับ 140/90 มิลลิเมตรปรอท, ผู้ป่วยที่ได้รับการรักษาด้วยยาเม็ดลดน้ำตาลในเลือด, ยาลดไขมันในเลือดและยาแอสไพริน*

สรุป: *โรคหลอดเลือดสมองชนิดเส้นเลือดในสมองตีบเป็นโรคแทรกซ้อนที่พบได้บ่อยในผู้ป่วยเบาหวานโดยเฉพาะอย่างยิ่งในผู้ป่วยสูงอายุ การศึกษานี้ยังเน้นถึงความสัมพันธ์ระหว่างความดันโลหิตต่อการเกิดโรคแทรกซ้อนดังกล่าว ดังนั้นการควบคุมความดันโลหิตในผู้ป่วยเบาหวานจึงมีความจำเป็นอย่างยิ่งเพื่อป้องกันการเกิดโรคหลอดเลือดสมอง*