Combined Effects of Hypertension and Diabetes Mellitus with Stroke among Thais in the Central Region of Thailand: A Cross-Sectional Study

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Objective: *To determine associations of individual and combined effects of hypertension and diabetes with stroke among Thais aged 55 years and older.*

Material and Method: *Cross-sectional data from national screening program for metabolic syndrome in Thailand for the year 2010 among participants who lived in central region of Thailand were used. The number of participants was 13,268 in the analysis.*

Results: *The prevalence of stroke was 0.9%. Associations between hypertension and diabetes found among participants who had hypertension only, diabetes only, and both hypertension and diabetes were: 8.99 (95% CI 4.63-17.43), 3.72 (95% CI 1.03-13.37), 10.48 (95% CI 4.54-24.20) among males and 5.16 (95% CI 2.29-11.53), 6.55 (95% CI 2.19-19.55), and 9.29 (95% CI 3.81-22.68) among females, respectively.*

Conclusion: *The present study suggested dramatically the strong effects of the association of combined hypertension and diabetes with stroke. Strengthening health promotion programs for the prevention of hypertension, diabetes, especially having both diseases after screening, is important among Thai population.*

Keywords: *Hypertension, Diabetes mellitus, Stroke, National screening program, Thais*

The incidence of stroke is usually high in many counties all over the world, especially in developing countries. In Thailand, morbidity and mortality of stroke increased from 216.58 per 1,000 to 307.93 per 1,000, and from 276.83 per 1,000 to 397.24 per 1,000 between 2008 and 2010, respectively[1]. Stroke is known to be a disease of blood vessels in the brain, and usually occurs in association with other chronic conditions, such as hypertension, diabetes, high cholesterol levels and heart diseases[2-4]. Having hypertension for a long period of time can strain and damage the blood vessels of heart and brain and become a strong risk factor for stroke, especially in the subject with high diastolic blood pressure[5]. Diabetes, most being ischemic stroke events in diabetes patients, are due to the occlusion of paramedial penetration of arteries. The occlusion causes small infracts within the white matter of brain. Diabetic neuropathy may contribute to the development of these cerebrovascular diseases[6].

Hypertension and type II diabetes are commonly known as associated conditions[5]. Both hypertension and diabetes are 2 among 5 important components of in metabolic syndrome. The cluster of metabolic abnormalities, occurring in the same person, appears to confer a substantial, additional cerebrovascular risk over and above the sum of the risk associated with each abnormality[7]. Prospective study among Finnish subjects reported hypertension and type 2 diabetes increased stroke risk independently, and their combination increases the risk dramatically[8]. Moreover, the highest risk of an occurrence of stroke event was found within the subjects who had had both hypertension and diabetes with an elevated level of inflammation[9,10]. Hypertension and diabetes are already known to be important risk factors for all types of stroke among Thais[4,11]. Many Thais adults and the elderly have both hypertension and diabetes type 2 at the same time, but there was a rare number of studies to assess individual and combined effects of hypertension and diabetes to stroke occurrence, not only

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cardiovascular diseases, among Thais.

This analysis aimed to persuade in assessing strength of associations of hypertension and diabetes, both independent and combined of their effects regarding stroke morbidity by using cross-sectional data from screening programs among Thais who lived in the central region off Thailand.

Material and Method
Study population

The present study is based on cross-sectional data from National Screening program for metabolic syndrome by the National Health Security Office (NHSO) of the Ministry of Public Health, Thailand. The screening program was conducted from October 1, 2009 to July 31, 2010 among Thais who reached the age of 15 and above. There were 673,950 participants within 21 provinces of the central region of Thailand. Some 30,303 participants met inclusion criteria for analysis of these studies by the age of 55 to 75 years, and having plausible and complete data. Participants were randomly selected by using a computer program with simple random sampling in 40% of which 13,268 were included in the analysis.

Methods of data collection

Data collection in National Screening program for metabolic syndrome was performed mainly by trained health officers at primary care units of health care centers and health promotion hospital in the villages, under the supervision of provincial health officers.

Interviewing

A questionnaire was used for interviewing those diagnosed or taking drugs through a physician for important chronic diseases, with variable outcomes such as "stroke", heart disease, and hypercholesterolemia. Other lifestyle habits such as cigarette smoking, alcohol drinking, and daily exercise were also in interviewing.

Blood test

Blood sample was taken from vein of the subject in the morning after at least 8 hours overnight fasting for fasting plasma glucose (FPG) level, which was measured by standardized enzymatic method.

Physical examination

Blood pressure was measured by using sphygmomanometer or digital blood pressure monitor

(Omron). Each participant was asked to stop smoking, drinking alcohol, or drinking caffeine substances and exercises for at least 30 minutes before the measurement. Blood pressure was measured in a sitting position for three times at 1-2 minutes apart, and the average of the three readings was recorded. Body weight was measured by using a balanced beam scale, while the height was measured without wearing shoes, using a wall-mounted stadiometer. Body mass index (BMI) was calculated in weight in kilograms, divided by height in meters squared (kg/m^2)[12].

Definition of terms

When the level of FPG was $\geq$126 mg/dl, the result confirmed having diabetes[12]. The cutoff point for having hypertension was when systolic and diastolic blood pressure were greater than 140 and 90 mmHg respectively or a current use of antihypertensive medication[12]. The BMI for Asian people was used to classify participants as underweight if BMI was <18.5, as normal if BMI was 18.5-22.9, as overweight if BMI was 23.0-24.9, as obese I if BMI was 25.0-29.9, and as obese II if BMI was $\geq$30[13].

Statistical analysis

Multiple logistic regression analysis was used when stratified by gender because of the heterogeneity of the results between genders. There was significant interaction term by additive model between hypertension and diabetes on stroke risk (but not significant of multiplicative term of hypertension* diabetes). So hypertension and diabetes were combined and created into four categories, 1) no hypertension and no diabetes, 2) having diabetes only, 3) having hypertension only, and 4) having both hypertension and diabetes. Adjusted odds ratio and 95% confidence interval (OR; 95% CI) for strength of associations between hypertension and diabetes and other existing chronic conditions with stroke were calculated with additional adjustment for effect of covariates simultaneously. The dependent variable was having stroke (yes/no), and independent variables were no hypertension and no diabetes (yes/no), having diabetes only (yes/no), having hypertension only (yes/ no), having both hypertension and diabetes (yes/no), having heart disease (yes/no), and having high cholesterol (yes/no). The covariates were age in years, cigarette smoking (only in male participants), alcohol drinking, exercise, and body mass index. Detection of colinearity between variables was performed before putting in the model with the method of enters with the

level of significance at 0.05.

(Table 1).

Results

Characteristics and lifestyle of study population

Total study population included in analysis was 13,268 (males = 5,265, females = 8,003). They had age between 55 years to 75 years, and average age was 63.3±5.8 years. By lifestyle factors, the prevalence of current and former smokers was the same which were 21.1% and 9.0% among males, and quite rare in 2.2% and 0.6% among females, respectively. The prevalence of current and former alcohol drinkers among males were 21.1% and 5.9% and among females were 3.7% and 2.4, respectively. The prevalence of those, who never exercise were 22.7% and 25.1% among males and females, respectively. In addition, the prevalence of those, who usually had exercised more than 3 times a week and every day were 11.4% and 11.0% among males and 10.1% and 9.6% among females, which were quite low. The prevalence of overweight and obesity among these groups of study population was 20.1% and 26% among males, and 19.4% and 37.5% among females

Prevalence of hypertension, type 2 diabetes, and stroke

The overall prevalence of stroke by self-report and diagnosed by a physician among this group of study population was 0.9%, while the prevalence of stroke among male participants was 1.4%, and that of female participants was 0.6% (Table 2). The prevalence of having hypertension only, diabetes only, and both hypertension and diabetes among male participants were 16.5%, 3.5%, and 5.2%, and among female participants were 21.5%, 4.9% and 8.4%, respectively. The prevalence of heart disease, and hypercholesterolemia, were 2.7% and 6.2% among male participants, and 4.2% and 10.4%, respectively (Table 2).

Associations between hypertension, diabetes with stroke

Results from multiple logistic regression stratified by gender demonstrated significant associations between hypertension and diabetes with stroke in both genders (model fitness by p-value from

Table 1. Demographic characteristics of study population

Variables	All (n = 13,268)	Males (n = 5,265)	Females (n = 8,003)	p-value
Age (years)				
55-65	8,468 (63.8%)	3,295 (62.6%)	5,173 (64.6%)	0.008*
66-75	4,800 (36.2%)	1,970 (37.4%)	2,830 (35.4%)	
Mean of age	63.3±5.8	63.4±5.9	63.3±5.8	
Smoking				
Never	11,533 (87.6%)	3,817 (73.0%)	7,716 (97.2%)	<0.001*
Current	1,275 (9.7%)	1,104 (21.1%)	171 (2.2%)	
Ex	361 (2.7%)	307 (5.9%)	54 (0.6%)	
Alcohol drinking				
Never	11,157 (84.7%)	3,696 (70.6%)	7,461 (93.9%)	<0.001*
Current	1,358 (10.3%)	1,066 (20.4%)	292 (3.7%)	
Ex	665 (5.0%)	472 (9.0%)	93 (2.4%)	
Exercise				
Never	3,166 (24.1%)	1,178 (22.7%)	1,988 (25.1%)	0.001*
<3 times a day	4,768 (36.4%)	1,872 (36.0%)	2,896 (36.6%)	
= 3 times a day	2,453 (18.7%)	984 (18.9%)	1,469 (18.6%)	
>3 times a day	1,389 (10.6%)	591 (11.4%)	798 (10.1%)	
Everyday	1,336 (10.2%)	573 (11.0%)	763 (9.6%)	
Body mass index				
Normal	5,204 (40.1%)	2,329 (45.2%)	2,875 (36.8%)	<0.001*
Underweight	949 (7.3%)	454 (8.8%)	495 (6.3%)	
Overweight	2,553 (19.7%)	1,035 (20.1%)	1,518 (19.4%)	
Obese I	3,417 (26.3%)	1,138 (22.1%)	2,279 (29.2%)	
Obese II	853 (6.6%)	202 (3.9%)	651 (8.3%)	

* = Statistically significant

Hosmer and Lemeshow test = 0.255 and 0.055, respectively). The significant effects among male participants, who had hypertension only, had diabetes only, had both hypertension and diabetes were 8.99 (95% CI 4.63-17.43, p-value <0.001), 3.72 (95% CI 1.03-13.37, p-value = 0.044), and 10.48 (95% CI 4.54-24.20, p-value <0.001), respectively, when compared to those did not have both hypertension and diabetes (Table 3). While the significant effects among female participants, who had hypertension only, had diabetes only, had both hypertension and diabetes, were 5.16 (95% CI 2.29-11.53, p-value <0.001), 6.55 (95% CI 2.19-19.55, p-value = 0.001), and 9.28; 95% CI 3.81-22.68, p-value <0.001) when it was compared to those who did not have both hypertension and diabetes (Table 4). Besides, there was significant association of having heart

disease with stroke (Adjusted OR = 2.82; 95% CI 1.30-6.11, p-value = 0.009) among male participants, but not among female participants, when compared to those, who did not have a heart disease (Table 3, 4).

Discussion

This cross-sectional study suggested additive interaction in combined effect of hypertension and diabetes to stroke risk, which was consistent with that of the cohort study of the impact of hypertension and diabetes to the incidence of stroke in Finnish study[8]. The present study also confirmed significantly high effects of hypertension to stroke risk among non-diabetes and diabetes participants from a screening program as indicated in a study among Thailand diabetes registry projects concerning risk factors of

Table 2. Prevalence of hypertension, diabetes type 2 and stroke by gender

Chronic diseases	All (n = 13,268)		Males (n = 5,265)		Females (n = 8,003)	
	n	%	n	%	n	%
Stroke	122	0.9	73	1.4	49	0.6
Hypertension only	2,587	19.5	870	16.5	1,717	21.5
Diabetes type 2 only	576	4.3	185	3.5	391	4.9
Both hypertension and diabetes	676	7.1	272	5.2	676	8.4
Heart diseases	447	3.6	133	2.7	314	4.2
Hyperlipidimia	1,160	8.8	327	6.2	833	10.4

Table 3. Crude and adjusted association (OR: 95% CI) between diabetes mellitus, hypertension, heart diseases and stroke among male participants

Variables	Stroke (n/%)	Non-stroke (n/%)	Crude Odds ratio (95% CI)	Adjusted* Odds ratio (95% CI)	p-value
Hypertension and diabetes					
No hypertension and no diabetes	17 (23.3)	3,905 (75.2)	1**	1**	
Hypertension without diabetes	36 (49.3)	834 (16.4)	9.91 (5.54-17.73)	8.99 (4.63-17.43)	<0.001***
Diabetes without hypertension	4 (5.5)	181 (3.5)	5.07 (1.69-15.24)	3.72 (1.03-13.37)	0.044***
Hypertension and diabetes	15 (20.5)	257 (4.9)	15.31 (1.91-122.52)	10.48 (4.54-24.20)	<0.001***
Having heart diseases					
No	53 (84.1)	4,752 (97.5)	1**	1**	0.009***
Yes	10 (15.9)	123 (2.5)	7.28 (3.62-14.66)	2.82 (1.30-6.11)	
Having high cholesterol					
No	45 (61.6)	4,541 (87.6)	1**	1**	0.095***
Yes	16 (21.9)	311 (6.0)	5.19 (2.90-9.29)	1.78 (0.90-3.50)	

Table 4. Adjusted association (OR: 95% CI) between diabetes mellitus, hypertension, heart diseases and stroke among female participants

Variables	Stroke (n/%)	Non-stroke (n/%)	Crude Odds ratio (95% CI)	Adjusted Odds ratio* (95% CI)[a]	p-value
Hypertension and diabetes					
No hypertension and no diabetes	11 (22.4)	5,193 (65.3)	1**	1**	
Hypertension without diabetes	19 (38.8)	1,698 (21.3)	5.28 (2.50-11.12)	5.16 (2.29-11.53)	<0.001***
Diabetes without hypertension	5 (10.2)	386 (4.9)	6.11 (2.11-17.68)	6.55 (2.19-19.55)	0.001***
Hypertension and diabetes	14 (28.6)	662 (8.5)	9.98 (4.51-22.08)	9.29 (3.81-22.68)	<0.001***
Having heart diseases					
No	42 (87.5)	7,200 (95.9)	1**	1**	0.254
Yes	6 (12.5)	308 (4.1)	3.34 (1.40-7.91)	1.69 (0.68-4.16)	
Having high cholesterol					
No	34 (69.4)	6,659 (83.9)	1**	1**	0.293
Yes	14 (28.6)	819 (10.3)	3.34 (1.78-6.26)	1.45 (0.72-2.95)	

* = Adjusted by all variables in table and age in years, smoking, alcohol drinking, exercise, and body mass index
** = Reference group
*** = Statistically significant

stroke among Thai diabetes patients[4].

Although, treatment of hypertension is known to reduce risk of stroke for long periods of time[14], there have been studies that demonstrated the use of some drugs in the treatment of hypertension for reducing cardiovascular events appeared to increase the risk of subsequent development of diabetes by its effect on insulin sensitivity. However, it was still inconsistent with the limitation for conclusion, and needs a longer term study[15,16].

In Thailand, costs of medications for treatments for chronic non-communicable diseases, especially treatment for vascular diseases of hypertension and diabetes that the Thai government had to pay yearly was quite high, but incidence of stroke still increased. It was known that to decrease the incidence of stroke is to decrease incidence of hypertension and diabetes. Physician should focuses on standard guidelines for treatments[17,18], and patients should follow strictly what physicians prescribe and order. Improvement of patient's knowledge about prevention and treatment of hypertension and diabetes during the course of life are extremely necessary. Lifestyle change through health promotion programs after screening program for Thais should be strengthened and evaluated yearly.

The result from this analysis also found a significant association between heart disease and stroke but only among male participants. Study demonstrated that arteriosclerosis, atrial fibrillation of heart disease showed its role as important risk factor of ischemic stroke, but there were a few studies with inclusive results of heart diseases in hemorrhagic stroke, and still needed further clarification[16].

However, the main limitation of the present study was the nature of cross-sectional data, which produced association, not the causation. Data from this population-based survey may have some bias in measuring stroke outcome that was assessed by self-reporting and diagnosed by a physician. However, data from screening programs should be used regularly to evaluate effectiveness of national screening and health promotion programs. Further prospective study in subgroups of population who have annual health examinations is suggested to be analyzed not only to confirmed results, but also to identify the inter relationship between hypertension and diabetes which cannot be found in secondary hypertension, including the treatment effect of hypertension among Thais[19].

Conclusion

The present study points out the high,

independent effects of the association of hypertension with stroke than with diabetes. The higher effects were found among participants who had both hypertension and diabetes in both genders.

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Potential conflicts of interest

None.

References
1. Ministry of Public Health, Bureau of Non Communicable Diseases. Public health statistics for morbidity and mortality of non communicable diseases. Nonthaburi: Bureau of Non Communicable Diseases; 2010.
2. Rohr J, Kittner S, Feeser B, Hebel JR, Whyte MG, Weinstein A, et al. Traditional risk factors and ischemic stroke in young adults: the Baltimore-Washington Cooperative Young Stroke Study. Arch Neurol 1996; 53: 603-7.
3. Nightingale AL, Farmer RD. Ischemic stroke in young women: a nested case-control study using the UK General Practice Research Database. Stroke 2004; 35: 1574-8.
4. Plengvidhya N, Leelawatana R, Pratipanawatr T, Deerochanawong C, Krittiyawong S, Bunnag P, et al. Thailand diabetes registry project: prevalence and risk factors of stroke in thai diabetic patients. J Med Assoc Thai 2006; 89 Suppl 1: S49-S53.
5. MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet 1990; 335: 765-74.
6. Megherbi SE, Milan C, Minier D, Couvreur G, Osseby GV, Tilling K, et al. Association between diabetes and stroke subtype on survival and functional outcome 3 months after stroke: data from the European BIOMED Stroke Project. Stroke 2003; 34: 688-94.
7. Golden SH, Folsom AR, Coresh J, Sharrett AR, Szklo M, Brancati F. Risk factor groupings related to insulin resistance and their synergistic effects on subclinical atherosclerosis: the atherosclerosis risk in communities study. Diabetes 2002; 51: 3069-76.
8. Hu G, Sarti C, Jousilahti P, Peltonen M, Qiao Q,

Antikainen R, et al. The impact of history of hypertension and type 2 diabetes at baseline on the incidence of stroke and stroke mortality. Stroke 2005; 36: 2538-43.
9. Arenillas JF, Moro MA, Davalos A. The metabolic syndrome and stroke: potential treatment approaches. Stroke 2007; 38: 2196-203.
10. Anand AV, Mahikanda R, Begum TN, Kuma KV, Akilandeswari G, Jerline MB, et al. Hypertension, diabetes, metabolic syndrome, inflammation and the risk of stroke. Int J Biol Med Res 2011; 2: 429-32.
11. Bandasak R, Narksawat K, Tangkanakul C, Chinvarun Y, Siri S. Association between hypertension and stroke among young Thai adults in Bangkok, Thailand. Southeast Asian J Trop Med Public Health 2011; 42: 1241-8.
12. National Heart, Lung, and Blood Institute. National Institute of Health. Third report of the National Cholesterol Education Program (NCEP). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. NIH publication number 02-5215. September 2002.
13. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004; 363: 157-63.
14. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450,000 people in 45 prospective cohorts. Prospective studies collaboration. Lancet 1995; 346: 1647-53.
15. Bakris GL, Fonseca V, Katholi RE, McGill JB, Messerli FH, Phillips RA, et al. Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: a randomized controlled trial. JAMA 2004; 292: 2227-36.
16. Gress TW, Nieto FJ, Shahar E, Wofford MR, Brancati FL. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis Risk in Communities Study. N Engl J Med 2000; 342: 905-12.
17. American diabetes Association. Standards of medical care in diabetes—2006. Diabetes Care 2006; 29 (Suppl 1): S4-42.
18. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High

Blood Pressure: the JNC 7 report. JAMA 2003; 289: 2560-72.

19. Sechi LA, Melis A, Tedde R. Insulin hypersecretion: a distinctive feature between essential and secondary hypertension. Metabolism 1992; 41: 1261-6.

อิทธิพลร่วมของการมีโรคความดันโลหิตสูงและเบาหวานต่อการเกิดโรคหลอดเลือดสมองในประชากรภาคกลางของประเทศไทย: การศึกษาภาคตัดขวาง

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วัตถุประสงค์: ศึกษาความสัมพันธ์อิสระและความสัมพันธ์ร่วมของการมีโรคความดันโลหิตสูงและโรคเบาหวาน ต่อการเกิดโรคหลอดเลือดสมองในประชากรภาคกลางของประเทศไทยอายุ 55 ปีขึ้นไป

วัสดุและวิธีการ: วิเคราะห์ข้อมูลทุติยภูมิจากการสำรวจตรวจขัดกรองความเสี่ยงในกลุ่มภาวะโรคเมตาโบลิคที่ดำเนินการในปี พ.ศ. 2553 จำนวน 13,286 ราย

ผลการศึกษา: พบความชุกของการมีโรคหลอดเลือดสมอง ร้อยละ 0.9 ความสัมพันธ์ระหว่าง การเป็นโรคความดันโลหิตสูงอย่างเดียว การเป็นโรคเบาหวานอย่างเดียว และการเป็นทั้งโรคความดันโลหิตสูงและโรคเบาหวาน กับการเกิดโรคหลอดเลือดสมอง เท่ากับ 8.99 เท่า (95% CI 4.63-17.43), 3.72 เท่า (95% CI 1.03-13.37) และ 10.48 เท่า (95% CI 4.54-24.20) ในประชากรเพศผู้ชายและ 5.16 เท่า (95% CI 2.29-11.53), 6.55 เท่า (95% CI 2.19-19.55) และ 9.29 เท่า (95% CI 3.81-22.68) ในประชากรเพศหญิงตามลำดับ

สรุป: ผลการศึกษาแสดงขนาดของความสัมพันธ์ร่วมของการเป็นโรคความดันโลหิตสูงและโรคเบาหวาน ต่อการเกิดโรคหลอดเลือดสมองที่สูงกว่าการมีโรคใดโรคหนึ่งการกำหนดให้มีกิจกรรมการสร้างเสริมสุขภาพ หลังการคัดกรองความเสี่ยงในกลุ่มภาวะโรคเมตาโบลิคที่มีอยู่มีความสำคัญ ที่ควรต้องให้ความสำคัญ และให้การสนับสนุนให้มีความเข้มแข็งและยั่งยืนในการดำเนินการและการเข้าร่วมกิจกรรมของประชาชน ตลอดจนมีการประเมินผลที่ต่อเนื่องและเป็นระบบ