Original Paper

Cerebrovascular Diseases

Cerebrovasc Dis 2005;19:18–22
DOI: 10.1159/000081907

Received: September 1, 2003
Accepted: Mai 19, 2004
Published online: November 3, 2004

Risk Factors for Stroke among Urbanised Indonesian Women of Reproductive Age: A Hospital-Based Case-Control Study

J. Kisjanto[a] L. Bonneux[b] J. Prihartono[c] T.A.S. Ranakusuma[d]
D.E. Grobbee[b]

Departments of [a]Medicine, [b]Community Medicine and [c]Neurology, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia; [d]Julius Center for Health Sciences and Primary Care, Utrecht Medical Center, Utrecht, The Netherlands

Key Words
Stroke · Risk factors · Women · Adult · South-East Asia

Abstract
Background: Stroke is a major cause of death in South-East Asia, but few empirical data exist on its risks in Asian populations. ***Methods:*** 235 cases and 682 age-matched controls of women of reproductive age (20–44 years) were recruited in 14 hospitals in Jakarta, Indonesia, between 1989 and 1993. Medical history was collected by a structured interview. In subsamples, glucosuria, serum cholesterol level and body mass index (BMI) were assessed. ***Results:*** In these young and lean Muslim women, with few users of tobacco, alcohol or oral contraceptives, risk factors related to increased weight were strongly related to stroke occurrence. A history of hypertension or diabetes or increased serum cholesterol level showed odds ratios (ORs) of 13.9, 7.4 and 3.7, respectively. A BMI >27 (unadjusted for its potential consequences) caused an OR of 2.9. High social class and higher level of education (both OR 0.7) were associated with a lower risk of stroke, but levels of risk factors were higher in higher socio-economic classes. ***Conclusion:*** The expected transition in lifestyle, characterised by a higher intake of calories and less physical activity, will increase stroke risks in Indonesian women. Increasing wealth should go together with raising levels of health education on nutrition and physical activity.

One of the merits of the Global Burden of Disease project was to draw attention to chronic diseases and more particularly to cardiovascular disease [1]. Age-adjusted stroke mortality is thought to be 60% higher in South-East Asia than in European populations [2]. Ageing, caused by the ongoing decrease of mortality in the large historical birth cohorts, will inevitably increase cardiovascular disease [3, 4].

However, while stroke is a major public health problem, quantitative information on risk factors for stroke in Asian populations in transition are scarce [5]. Lowering infectious disease mortality often goes together with a nutritional transition from low- to high-calory diets and a decrease in physical activity [6]. South-Eastern Asian populations are more vulnerable to the development of obesity and insulin resistance than Caucasian populations [3, 7]. The transition to a more affluent lifestyle will therefore impose a higher cardiovascular disease burden on Asian populations.

KARGER

Fax + 41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1015–9770/05/0191–0018$22.00/0

Accessible online at:
www.karger.com/ced

Luc Bonneux
Federaal Kenniscentrum voor de Gezondheidszorg (KCE)
Residence Palace 10de verdieping
Wetstraat 155, BE–1040 Brussels (Belgium)
Tel. +32 2 287 3325, Fax +32 2 287 3385, E-Mail luc.bonneux@kenniscentrum.fgov.be

Table 1. Distribution of risk factors among cases and controls in complete dataset

	Controls			Cases			Odds ratio	p value
	total	n	%	total	n	%		
Age group	682			235			matching variable	
20–24		58	8.5		19	8.1		
25–29		92	13.5		26	11.1		
30–34		126	18.5		47	20.0		
35–39		216	31.7		60	25.5		
40–44		190	27.9		83	35.3		
Medical history								
Use of hormones	682	9	1.3	235	2	0.9	0.65 (0.14–3.13)	0.59
History of hypertension	682	33	4.8	235	95	40.4	13.85 (8.34–23.00)	<0.01
Use of antihypertensives	682	14	2.1	235	35	14.9	8.83 (4.47–17.4)	<0.01
History of diabetes	682	6	0.9	235	11	4.7	7.42 (2.33–23.6)	<0.01
Glucosuria	544	17	3.1	191	22	11.5	3.61 (1.78–7.31)	<0.01
History or glucosuria	544	19	3.5	191	26	13.6	4.12 (2.12–8.03)	<0.01
Recent history of smoking	682	38	5.6	235	16	6.8	1.26 (0.68–2.32)	0.46
Alcohol use	682	12	1.8	235	9	3.8	2.42 (0.97–6.02)	0.06
Social history								
Social class	682			235				
Lower class		151	22.1		59	25.1	reference	
Middle class		266	39.0		104	44.3	0.95 (0.62–1.45)	0.81
Higher class		265	38.9		72	30.6	0.65 (0.41–1.03)	0.06
Secondary or higher education	682	434	63.6	235	132	56.2	0.72 (0.52–0.99)	0.04
Being single	682	152	22.3	235	42	19.9	0.73 (0.48–1.09)	0.13

Figures in parentheses indicate 95% CIs.

The study we present here formed the Indonesian part of a WHO multicentre case-control study of cardiovascular disease and oral contraceptive use [8–10]. Because of the very low prevalence of hormone users (1%), the data have never been published. This has been a sad omission as data on stroke risks in Asian populations living in Asia are scarce. Information is restricted to adult women of reproductive age, but that information allows valuable insights into the epidemiology of stroke in the large urbanised population of modern Indonesia.

Methods

Two hundred and thirty-five cases and 682 controls were recruited after receiving informed consent in 14 hospitals in Jakarta, Indonesia, between January 1, 1989 and June 1, 1993. Cases were women aged 20–44 years admitted with first-time stroke. The diagnosis of stroke, based on rapidly developing clinical signs of cerebral dysfunction lasting more than 24 h, was made by a neurologist and confirmed by the WHO coordinating centre [8–10]. As few imaging data were available, no subtype-specific analysis was performed (table 1).

Control subjects were randomly selected women without cardiovascular disease admitted to a randomly selected ward in the same period as the cases. All controls were matched within the same 5-year age band (e.g. 20–24 and 25–29 years) as the cases. For each case, 3 age-matched controls were selected. Cases and controls were interviewed using a standardised questionnaire, if possible. If not (38% of cases), a close relative was interviewed; the information from these proxy interviews has been shown to be reliable [11].

Cigarette smoking, oral contraceptive use, alcohol use, a history of diabetes, a history of hypertension and the use of antihypertensives were recorded during the interview. In subsamples, urine was tested for the presence of glucose (191 cases and 544 controls), total cholesterol was determined in fasting venous blood (173 cases and 226 controls) and height and weight determined (73 cases and 263 controls). An elevated cholesterol level was defined as a value ≥ 6.5 mm/l (>250 mg/dl). Overweight was defined as a body mass index (BMI) >23 and obesity as a BMI >27.

Socio-economic status was defined by a score based on information of income, type of housing and common luxury household items, according to the methods used by the Indonesian bureau of statistics [12]. Subjects were classified in three groups: low class, middle class and high class. Level of education was defined by two classes: illiterate or elementary schooling vs. secondary education or higher.

In the matched study, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by conditional logistic regression (STATA 7.0). Multivariate regression was assessed for confounding. In the subsample containing cholesterol measurements and BMI, ORs and confidence limits were calculated by unconditional logistic regression.

Table 2. Distribution of risk factors among cases and controls in subsamples

	Controls			Cases			Odds ratio	p value
	total	n	%	total	n	%		
Cholesterol >6.5 mmol/l	226	14	6.2	173	34	19.7	3.70 (1.92–7.15)	0.000
BMI categories	263			73				
<23		175	66.5		38	52.1	reference	
23–27		64	24.3		20	27.4	1.44 (0.78–2.66)	0.244
≥27		24	9.1		15	20.5	2.88 (1.38–6.00)	0.005
mean ± SD	21.7 ± 3.6			23.1 ± 4.0			1.10 (1.03–1.18)[1]	0.008

Figures in parentheses indicate 95% CIs.
[1] Per BMI unit.

Table 3. Distribution of risk factors by social class

Social class	Weight[1], kg		BMI >27[1], %		Alcohol use, %		Hypertension, %		Hypercholesterolemia[2], %		Diabetes, %	
	controls	cases	controls	cases	controls	cases	controls	cases	controls	cases	controls	cases
Higher	54.2	57.3	10.5	28.1	1.5	8.3	3.0	47.2	8.3	23.3	4.9	14.5
Middle	50.5	54.7	8.6	17.9	2.3	1.9	8.3	42.3	2.7	17.3	2.0	13.3
Lower	50.0	52.4	6.1	7.7	1.3	1.7	2.0	28.8	6.3	18.4	3.3	13.0

[1] Measured in 363 persons (table 2).
[2] Measured in 399 persons (table 2).

Results

Forty per cent (95/235) of cases declared to have had hypertension and 15% used antihypertensives. Among controls, this was 5% (33/682) and 2% (14/682), respectively, showing ORs for a history of hypertension of 13.9 (95% CI 8.3–23.0) and of antihypertensive use of 8.8 (95% CI 4.5–17.4). A history of diabetes was declared by 5% (11/235) of cases and 12% (22/191) had traces of glucosuria. Among controls, this was 1% (6/682) and 3% (17/544), respectively, yielding ORs for a history of diabetes of 7.4 (95% CI 2.3–23.6) and of glucosuria of 3.6 (95% CI 1.8–7.3). Only 6% of women smoked, with no notable differences between cases and controls. Four per cent (9/235) of cases and 2% (12/682) of controls declared the use of alcohol. The OR was 2.4 (95% CI 0.97–6.0); the excess risk of alcohol use was limited exclusively to the more privileged social class (table 3).

Women of a higher social class (OR 0.65, 95% CI 0.41–1.03) and level of education (OR 0.72, 95 CI 0.52–0.99) showed lower risks. Higher socio-economic class showed consistently higher prevalences of all risk factors (table 3). Multivariate modelling showed no confounding.

In the subsamples, an increased serum cholesterol level was an important risk factor: 20% (34/173) of cases and 6% (14/226) of controls showed a cholesterol level ≥6.5 mmol/l (table 2), yielding an OR of 3.7 (95% CI 1.9–7.2). The BMI was related to stroke risk, even among these lean and young Javanese women. Risk increased by 10% (95% CI 3–18) per BMI unit, with an OR of 2.9 (95% CI 1.4–6.0) for a BMI >27. Overweight (BMI between 23 and 27) increased risk by 44%, but by lack of power, it did not reach statistical significance. Women of the highest social class were 2 cm taller and 4 kg heavier than women of lower classes.

Discussion

This case-control study is a carefully controlled study of stroke risks in young women from Jakarta, an urbanised South-East Asian population living in a transitional

country. The epidemiological characteristics of this population are very different from Western populations, as very few were users of tobacco, alcohol or oral contraceptives. Even in these young and lean women (on average 52 kg for 1.55 m), BMI, diabetes, hypercholesterolaemia and a history of hypertension were positively correlated with stroke. Low socio-economic class and low levels of education predispose to stroke, while the prevalence of risk factors was highest in the higher socio-economic classes (table 3).

The control population reflects hospitalised persons; the distribution of socio-economic classes was comparable to that published by the Indonesian bureau of statistics [12]. By choosing both controls and cases from the hospital, the study matches for the use of hospital services [8]. In various health care settings, various health care filters apply. The aim of this design was to obtain estimates not conditional on health care use by subjecting cases and controls to the same health care filter. Smoking, alcohol use and oral contraceptive use were uncommon in this group of young Muslim women. Blood pressure before stroke was determined by the medical history and use of antihypertensives [9, 13]. The measured blood pressure after stroke correlated well with that history, but the measured levels were considered insufficiently reliable. A history of hypertension conferred the highest relative risk (OR 14), while users of antihypertensives have a slightly lower risk (OR 9).

These very large relative risks have to be interpreted against the background of very low absolute risks in a young female population. A relative risk of 14 for a history of hypertension and 9 for a history of antihypertensive use is comparable to these of a large study of Asian populations, documenting a 13-fold risk between the highest (mean 97 mm Hg) and lowest (mean 76 mm Hg) diastolic blood pressure group [14]. The high relative risk of a history of diabetes mellitus (OR 7.4) can be compared to the relative risk conferred by glucose in the urine (OR 3.6); the prevalence of 3.1% for glucosuria observed in this young female (hospitalised) population shows the potential extent of insulin resistance in Indonesian populations.

Serum cholesterol level was measured in a subsample only, but results differed little from the complete data (data on file). Not all hospitals had sufficient laboratory capacity or budget. The data on BMI should be interpreted with more caution, as they were not collected according to the matched protocol and only available in smaller subsamples. It is likely that the available BMI data in stroke cases reflect a selection of less disabled patients. The lack of BMI data in controls testifies to the lack of clinical importance attached to such a 'cheap' measurement of weight and height and is observed in other Asian studies [6]. However, it is hard to imagine how selection in BMI assessment could have biased the observed risks: the data can be seen as an unmatched case-control study. We included the data on BMI, as they show the potential consequences of an opulent lifestyle. The lower relative risks should not detract from the relevant attributable risks: as prevalence of overweight and obesity is higher, the attributable risks are in the same order of magnitude as the other risk factors.

Body weight, hypertension, hypercholesterolaemia and diabetes were associated with very high stroke risks; risks were increased in populations with lower education and lower income. The prevalence of all physiological risk factors was often highest in the highest socio-economic class (table 3). Cardiovascular risk increases initially in the more affluent classes and then percolates through the social classes [15]. In other transitional countries such as Hong Kong and India, higher coronary heart disease prevalence is associated with higher socio-economic class [16–19].

Asian populations seem even more vulnerable to the consequences of an opulent lifestyle, in terms of obesity, diabetes and its correlates [7, 20]. Starting from such a low population BMI, the potential for future health problems when living through the epidemiologic and nutritional transition is particularly severe. There is no obvious solution to the increasing weight and decreasing physical activity of populations of developing countries. As standards of living and education increase, health promotion aiming at maintaining weight and encouraging physical activity should be an indelible part of these increasing standards.

Acknowledgements

This study was funded as part of the WHO Collaborative Study of Cardiovascular and Steroid Hormone Contraception. We wish to thank Dr. Anna Peeters for helpful comments and suggestions.

References

1 Murray CJ, Lopez AD: Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997;349:1269–1276.
2 World Health Organization. GBD 2000 version 1 estimates by subregion. http://www3.who.int/whosis/menu.cfm?path=evidence,burden,burden_gbd2000,burden_gbd2000_-subregion&language=english. 2002. Accessed on 23-01-2003.
3 Yusuf S, Reddy S, Ounpuu S, Anand S: Global burden of cardiovascular diseases. 2. Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001;104:2855–2864.
4 Khor GL: Cardiovascular epidemiology in the Asia-Pacific region. Asia Pac J Clin Nutr 2001; 10:76–80.
5 Yusuf S, Ounpuu S: Tackling the growing epidemic of cardiovascular disease in South Asia. J Am Coll Cardiol 2001;38:688–689.
6 Sullivan DR: Cardiovascular risk in the Asia-Pacific region from a nutrition and metabolic point of view: Visceral obesity. Asia Pac J Clin Nutr 2001;10:82–84.
7 McKeigue PM, Shah B, Marmot MG: Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. Lancet 1991;337:382–386.
8 WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception: A multinational case-control study of cardiovascular disease and steroid hormone contraceptives. Description and validation of methods. J Clin Epidemiol 1995;48:1513–1547.
9 WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception: Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: Results of an international, multicentre, case-control study. Lancet 1996;348:505–510.
10 Kisjanto J, Ranakusuma TAS, Kaligis RWM, Tadjudin MK, Valkenburg HA, Grobbee DE: A case-control study of risk factors for stroke in young women in Jakarta, Indonesia: Design and Methods. Med J Christ Univ Indonesia 1995;24:30–36.
11 Poulter NR, Chang CL, Farley TM, Marmot MG: Reliability of data from proxy respondents in an international case- control study of cardiovascular disease and oral contraceptives. J Epidemiol Community Health 1996;50:674–680.
12 Ministry of Health, Republic of Indonesia. Indonesia Health Profile 1994. Jakarta, Centre for Health Data, 1995.
13 WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception: Ischaemic stroke and combined oral contraceptives: Results of an international, multicentre, case-control study. Lancet 1996;348:498–505.
14 Eastern Stroke and Coronary Heart Disease Collaborative Research Group: Blood pressure, cholesterol, and stroke in eastern Asia. Lancet 1998;352:1801–1807.
15 Marmot MG: Socio-economic determinants of CHD mortality. Int J Epidemiol 1989;18: S196–S202.
16 Wannamethee SG, Shaper AG: Socioeconomic status within social class and mortality: A prospective study in middle-aged British men. Int J Epidemiol 1997;26:532–541.
17 Backlund E, Sorlie PD, Johnson NJ: The shape of the relationship between income and mortality in the United States. Evidence from the National Longitudinal Mortality Study. Ann Epidemiol 1996;6:12–20.
18 Singh RB, Sharma JP, Rastogi V, Niaz MA, Ghosh S, Beegom R, et al: Social class and coronary disease in rural population of north India. The Indian Social Class and Heart Survey. Eur Heart J 1997;18:588–595.
19 Wong SL, Donnan SP: Influence of socioeconomic status on cardiovascular diseases in Hong Kong. J Epidemiol Community Health 1992;46:148–150.
20 Kim JS, Jones DW, Kim SJ, Hong YP: Hypertension in Korea: A national survey. Am J Prev Med 1994;10:200–204.