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Stroke in Indonesia: Risk Factors and Predispositions in Young Adults

Woro Riyadina[1], Julianty Pradono[1], Dewi Kristanti [1], Yuda Turana [2*]
[1]National Institute of Health Research and Development, Ministry of Health, Republic of Indonesia
[2]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia
**Correspondence Author: Yuda Turana, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia. Jl. Pluit Raya No.1, Jakarta Utara, 14440, Email: yuda.turana@atmajaya.ac.id*

ABSTRACT

Background: Stroke remains to be the main cause of death and disability in Indonesia where the incidence of stroke has been increasing despite the implementation of control programs. This study aims to investigate the predictors of stroke in the adult population through a prospective study in Bogor, Indonesia.

Methods: A cohort prospective study was conducted. A total of 5605 stroke-free subjects over 25 years of age participated in the data collection for the "Cohort Study of Non-Communicable Risk Factors." Data was collected through interviews using structured questionnaires, physical measurements thrice a year, and laboratory examinations every 2 years through 6 years of follow-up (2011-2017).

Results: During the 6-year observation, the incidence of stroke was found to be 330 person-years per 100,000 population (95% CI 130-670). The incidence of stroke among younger adults below 55 years was found to be 27 cases (0.7%) whereas the incidence of stroke among adults ≥ 55 years was 51 (2.7%). After adjusting for age, hypertension and high total cholesterol were found to be predictors of stroke (Hazard Ratio: 2.8 (95% CI 1.8-4.5) vs 1.8 (95% CI 1.1-2.8), respectively).

Conclusion: The incidence of stroke among younger adults aged 25-54 years old was found to be 27 cases (0.7%) and increases with age. Hypertension is the strongest predictor of stroke incidence.

Keywords: Incidence, Indonesia, Stroke

Correspondence:
Yuda Turana
School of Medicine and Health Sciences
Atma Jaya Catholic University of Indonesia
Jakarta Utara
E-mail Address: yuda.turana@atmajaya.ac.id

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INTRODUCTION

Stroke is the most common cardiovascular and neurologic disease in Asia.[1] The incidence rate of stroke varies notably among countries: 120.42 per 100,000 person-years (95% CI 26.17 - 214.67) in China and 200 per 100,000 person-years in Australia.[2] The incidence of stroke in East Asian countries is 247.53 – 347.78 per 100,000 person-years, a rate significantly higher than the United State and the United Kingdom which has a case rate of 220.66 100,000 person-years and 141.97 per 100,000 person-years, respectively.[3] Mortality aside, disability due to stroke adds an economic burden on families and weighs emotional and mental burdens that interfere with the productivity of other family members.[4]

It is estimated that 10% of all incidences of stroke occurs at a young age.[5] In Indonesia, stroke is the leading cause of death and neurological disabilities. The prevalence of stroke in Indonesia is 10.9% and has remained stable at a rate of 120 per 100,000 person-years since 2013.[6,7] Approximately 0.6-14.2% of those cases occur during the ages of 15-54.[6] Additionally, stroke causes an economic strain on Indonesian households, costing higher than other diseases with an estimate of 10.7% of the household income. Presently no longitudinal studies regarding stroke using a large number of subjects have been conducted in Indonesia. This is the first study to do so and it aims to determine the incidence and predictors of new stroke cases during 6 years of observation.

MATERIALS AND METHODS

This prospective stroke cohort study was carried out through the "Cohort Study of Non-Communicable Risk Factors", beginning in 2011 and followed up for 6 years with consecutive 2–year measurement intervals. The sample of the stroke cohort consisted of subjects aged ≥ 25 years from an urban village in Central Bogor. Data was collected through the WHO STEPS method and included interviews, physical measurements, and laboratory tests.[9] The total sample consisted of 5606 subjects who were stroke-free at the start of the study. The incidence of stroke was marked as an 'event' status (hazard) and a stroke diagnosed at any point of the study was continually documented as a stroke event for the rest of the study duration. The inclusion criteria for this study were subjects who were stroke-free at the start of the study, aged 25 years or older, and performed periodic checks at least twice during the 6-year follow-up. The sample recruitment flow is depicted in chart 1.

The covariate determinants of stroke used in this study included subject characteristics (age, sex, ethnicity, education, occupation, and economic status), health status (obesity, hypertension, lipid profile, blood glucose) and risk behaviors (smoking, physical activity, nutrient intake inclusive of carbohydrates, fats, and sodium). Age was categorized into 3 groups according to the distribution of the stroke cohort sample data (age 35-44 years, 45-54 years and ≥ 55 years). Categories for education status were divided into low education (did not receive a formal education or only attended primary school), medium education (graduated from junior high and high school), and higher education (graduated from D3 and Bachelor's). Occupation was categorized into "non-work"

(unemployed), student, civil servant, and private worker. The level of family economic status was the total income of all family members divided by the number of household members and categorized as poor (quintiles 1 and 2) and not poor (quintiles 3, 4, and 5).[10]

Obesity was categorized according to the Body Mass Index (BMI) classification of the Asian population: underweight (BMI <18.5), normal (18.5-22.9), overweight (23-24.9) and obese (≥ 25).[11] Central obesity was determined using the National Cholesterol Education Program classification, i.e. central obesity was identified if abdominal circumference was ≥ 90 cm for males and ≥ 80 cm for females.[12] Lipid profiles included total blood cholesterol, LDL, HDL and triglycerides levels. Lipid profile was marked as abnormal when levels were as follows; total blood cholesterol ≥ 200 mg/dL, LDL ≥ 100 mg/dL, HDL ≥ 40 for men and ≥ 50 for women, and triglycerides ≥ 150 mg/dL. Subjects were classified as having diabetes mellitus type 2 if postprandial blood sugar levels were ≥ 200 mg/dL.[13]

Classification of risk behaviors that contribute to the incidence of stroke included smoking, lack of physical activity, emotional disturbance (stress) and nutrient intake.[12] Physical activity was calculated based on the WHO Steps classification of 2004, i.e. the amount of daily physical activity during work, on the way, and at leisure in Metabolic Equivalent Turnover (MET) units and categorized into less (<600 MET) and sufficient (≥ 600 MET).[14] Smoking behavior was classified based on the Brinkman Index of cigarettes smoked during life, and subjects were categorized as heavy smokers (> 600 cigarettes/year), medium smokers (200-60

0 cigarettes/year) and non-smokers.[15] The consumption of nutrients associated with the incidence of stroke include carbohydrate, fat and sodium intake. The intake of these nutrients was measured by a 2-hour recall method and categorized into nutrient intake percentage (Southeast Asian Food & Agricultural Science and Technology).[16] Nutrient intake was marked as excessive if a subject's daily intake consisted of ≥ 60% carbohydrate, ≥ 25% fat, and ≥ 2000 mg of sodium.[17] Emotional distress (stress) was identified through interviews using the Self-instrument Reporting Questionnaire (SRQ). Stress was identified if a subject answered at least 6 out of 20 symptoms.[18]

Data were analyzed using the SPSS program with a bivariate test and Cox regression to account for the difference of proportion in each covariate variable. The Cox proportional hazard regression model was used to determine the primary hazard ratio of stroke incidence (hazard) by controlling other covariates. The data source is part of a cohort study that focused on monitoring subjects over a period of 6 years (2011-2017) and had received ethical clearance from the Ethics Committee of National Institute of Health Research and Development, Ministry of Health, Republic of Indonesia.

RESULTS

During the 6-year period, 78 (1.6%) cases of new stroke events (incident) were found, out of which 28 cases (35.9%) were found among men and 50 cases (64.1%) among women. The monitoring interval every 2 years shows the total number of new cases (incidents) cumulatively, and the number of cases classified by gender as in graph 2.

An increase in the incidence of stroke was observed in every successive 2-year follow-up. A total of 41 cases were detected in the first follow-up, 24 cases in the second follow-up, and 13 cases in the third follow-up. Hence, the total number of stroke cases in each follow up was 41 cases, 65 cases, and 78 cases consecutively. The hazard ratio of the 6-year follow-up period was calculated to find a stroke incidence rate of 330 person-years per 100,000 population with a 95% confidence interval (CI): 130-670. This figure means the rate of new stroke cases was 330 person-years per 100,000 population during the 6 year observation period.

Our study found that 8 cases (0.4%) of stroke occurred during the ages of 25-44 years and 19 cases (1.1%) occurred at the ages of 45-54 years. Cumulatively we found that 27 stroke incidents (0.7%) occurred at a young age, and the incidence increases with age— 51 cases (2.7%) occurred above the age of 55 years. Characteristics of subjects at the baseline showed sociodemographic variances and differences in the comorbidity of diseases between the two groups of stroke outcomes. These characteristics include age, education, occupation, history of coronary heart disease (CHD), and diabetes mellitus (DM) ($p < 0.05$). (Table 1)

The incidence of stroke proportions increased with age, with subjects aged 55 years and older having the greatest proportion. New stroke sufferers were more likely to have received low education and had an unemployment status. New cases of stroke were more likely to occur among patients suffering from comorbidities such as CHD and DM.

Biological health risk factors that related significantly ($p < 0.05$) with stroke incidence during the 6-year monitoring period were hypertension, obesity, stress and lipid profile (total cholesterol, LDL, triglycerides). The proportions of abnormal total cholesterol, LDL, and triglyceride levels were higher in new stroke patients compared to those without stroke. Behavioural risk factors such as physical activity, smoking, high intake of sodium, carbohydrates, and fats were found to have no significance ($p > 0.05$) between stroke and non-stroke groups. (Table 1) Predictors of new cases of stroke during the 6-year monitoring period (multivariate analysis) were found to be hypertension and cholesterol (after adjusting for age). (Table 2) Hypertension was a stronger predictor for the incidence of stroke than total cholesterol levels. Among subjects with hypertension, stroke incidence appeared 2.8 times faster and the likelihood of having a stroke was as high as 73.7% after adjusting for age during the 6-year monitoring period.

DISCUSSION

Results from our study found that the incidence of stroke among younger adults (< 55 years) was 27 cases (0.7%). This finding is in line with the results from other studies. A study by Ekker et al. found an increase in stroke cases among the young, with the incidence of stroke among 18-44-year-olds being higher among women, along with an overall 23% increase of ischemic stroke cases among younger adults in the last 10 years.[19] Another study had observed that 61% of stroke cases at a younger age were caused by ischemic

strokes, whereas 17% of cases were due to intracerebral hemorrhage, and 22% of cases were due to subarachnoid hemorrhage.[20]

The findings of this study also showed a higher stroke incidence at age ≥ 55 years. This result is consistent with the findings of previous epidemiological studies in Indonesia, wherein the mean age of stroke patients is 58.8 years with a prevalence of 0.8%.[21] The risk of re-stroke and death of stroke patients was associated with increased age.[22]

This study found a significant relationship between education status and unemployment with cases of stroke. The relationship between the level of education and the incidence of stroke is still controversial. Studies in the United States and Europe have observed an association between educational levels and stroke events, whereas Japanese studies do not show such associations.[23,24] Status of unemployment was found to cause a higher risk of stroke according to a study by Grimaud O et al, in other words, the unemployed were exposed to a higher risk of stroke relative to the employed.[25]

Results from our study portrayed a significant association between CHD and DM with stroke ($p < 0.05$). Result from Basic Health Survey showed that the prevalence of obesity in Indonesia has increased over time, from 15.4% in 2013 to 21.8% in 2018. Additionally, the study also found that the proportion of the population with borderline LDL levels was still above 20%.[6,7] In the Framingham cohort study, diabetes and metabolic syndrome were found to be strong risk factors for ischemic stroke.[26]

This study found hypertension as a risk factor for stroke. Results from Basic health Survey found that the prevalence of hypertension among 18-54-year-olds in 2013 was 8.7-35.6% and increased to 13-45% in the year 2018. .[6,7] Hypertension is the main determinant of stroke.[27] Research from Bangladesh has shown similar results wherein hypertension was found to be a major risk factor for stroke (63%) and most stroke patients (42.85%) either did not seek treatment or only sought treatment irregularly.[28] Hypertension is a major predictor of stroke incidence.[29] Studies from Asian countries, particularly China, Japan and the Republic of Korea, have reported a higher risk of stroke associated with hypertension compared to western countries.[30] Research on the global magnitude of disease problems indicates that high systolic blood pressure affects stroke problems in eastern Asian countries, with an attributable risk of 52-73% stroke-related DALYs.[28]Increased systolic blood pressure (≥ 160 mmHg) and diastolic blood pressure (≥ 90 mmHg) along with atrial fibrillation are risk factors for the incidence of stroke among the elderly population.[30] The relationship between total cholesterol levels and stroke remains controversial.[31]

Our study also showed that obesity is associated with the incidence of stroke. Obesity is an independent risk factor for stroke and an increased BMI is associated with the cause of death in the general population.[32] Increased weight changes by 2.7% for a prolonged period (since 25 years of age) are associated with an increased risk of stroke.[33] BMI and risk of ischemic stroke are linear and comparable between males and females and between races.[34]

This study found that subjects experiencing stress are more likely to be affected by stroke. Subjects experiencing mental disorders are almost twice (OR: 1.96; 95% CI 1.20 - 3.48) as likely to have a stroke compared to subjects without mental disorders. Further analysis of the Indonesian basic health survey from 2007 showed that the number of subjects with stroke who experienced mental health problems amounted to 43.7%. [21]

Based on the results of the lipid profile measurements, subjects with high total cholesterol and LDL levels had a significantly increased incidence of stroke at age 25 years and over. This finding is consistent with previous studies showing that the increased incidence of stroke is associated with the increase of blood total cholesterol levels.[35,36] A study by Laloux et al. found that high total cholesterol levels are associated with the risk of small vessel disease and large vessel disease.[37] Moreover, Biswas et al. reported that high LDL levels are a risk factor for ischemic stroke. [38]

The strengths of this study include the use of a prospective cohort design on a large sample. Additionally, our sample starts at age 25 years hence allowing for the monitoring of subjects before entering the degenerative age. The weakness of the study is that the diagnosis of stroke was made mainly based on results from history taking and confirmation of the presence or absence of residual symptoms by a neurologist and not through a brain scan examination.

CONCLUSION

The incidence of stroke among younger adults aged 25-54 years old was found to be 27 cases (0.7%) and increases with age. Hypertension is the strongest predictor of stroke incidence.

DATA AVAILABILITY

The data used to support the findings of this study is available from the corresponding author upon request.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest regarding the publication of this paper.

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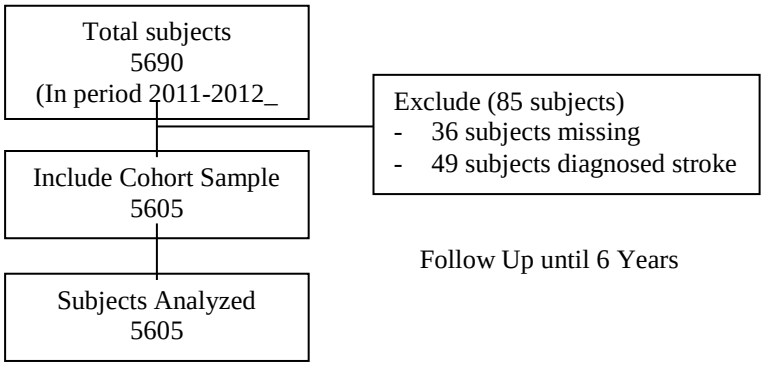

Chart 1: **Sample Recruitment**

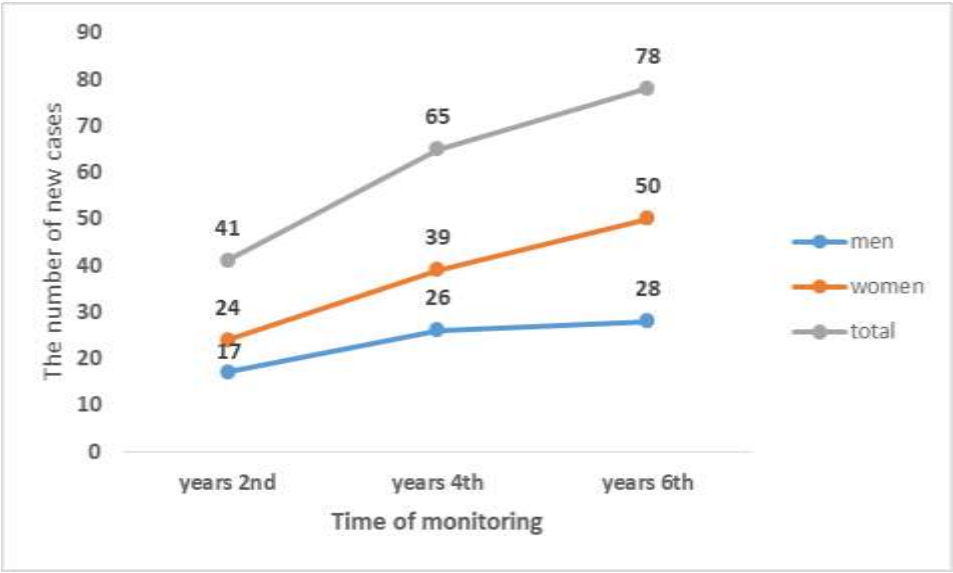

Figure 2: **The cumulative number of stroke incidents during the 6-year monitoring at 2-year intervals.**

Table 1: **Characteristics of stroke cohort samples**

Characteristics	Total n (%)	Stroke Yes (n=78)	No(n=5527)	p
Socio-demography				
Age				
25-44 y.o	1965(35.2)	8(0.4)	1957(99.6)	<0.001
45-54 y.o	1734(30.9)	19(1.1)	1715(98.9)	

≥ 55 y.o	1896(33.9)	51(2.7)	1845(97.3)	
Women	3631(64.9)	50 (1.4)	3581(98.6)	0.982
Low education	1928(34.4)	40(2.1)	1888(97.9)	0.006
Not working	1928(34.5)	40 (2.1)	1888(97.9)	0.002
Low economic status	2945(52.5)	44(1.5)	2901(98.5)	0.351
Comorbidity				
CHD *	815(14.5)	24(2.9)	791(97.1)	<0.001
Diabetes	395(7.1)	15(3.8)	383(96.2)	<0.001
Biological risk				
Hypertension	27.2(1525)	54(3.5)	1471(96.5)	<0.001
Obesity	2432(43.4)	47(1.9)	2385(98.1)	0.004
Stress	1482(26.4)	31(2.1)	1451(97.9)	0.011
Higher cholesterol	2598(46.4)	51(2.0)	2547(98.0)	0.001
High LDL	78(76.5)	73(1.7)	4214 (98.3)	0.001
Low HDL	3511(37.4)	41(1.2)	3470(98.8)	0.083
High triglycerides	989(17.6)	24(2.4)	965(97.6)	0.004
Behavior risk				
Lack of physical activity	2794(49.8)	32(1.1)	2762(98.9)	0.146
Heavy Smoker	129(2.3)	4(3.1)	125(96.9)	0.176
High intake of carbohydrates	2555(52.6)	35(1.4)	2520(98.6)	0.417
High intake of sodium	2121(43.7)	24(1.1)	2097(98.9)	0.064
High intake of fat	1616(33.4)	27(1.7)	1589(98.3)	0.600

*) CHD: coronary heart disease, sig (p <0.05)

Table 2: Predictors of Stroke Incidence on monitoring for 6 years

Predictors	*Hazard Ratio* (HR)	95% Confidence Interval (CI)
Age		
45 - 54 years old	1.722	0.744 - 3.985
≥ 55 years old	3.967	1.847 – 8.521
Hypertension	2.813	1.753 – 4.513
Higher cholesterol levels	1.759	1.090 – 2.838

*) HR: Hazard Ratio, CI: confidence Interval

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