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Mental emotional disorder is a predictor of stroke incidence in adults: Ten year results of the Bogor Cohort Study on Non−Communicable Disease Risk Factors in Indonesia

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ABSTRACT

Objective: To determine the stroke predictors for the 10-year of follow-up in Bogor City, Indonesia.

Methods: The prospective study analyzed the data of 4445 stroke-free subjects aged 25 years and above that was part of "the Bogor Cohort Study on Non-Communicable Disease Risk Factors". Data were collected by interview method with structured questionnaires, physical measurements three times a year, and laboratory examination every two years during a 10-year follow-up (2011-2021, without examination in 2020). The incidence of stroke is based on anamnesis results and examination by a neurologist. Other stroke predictor variables include characteristics, biological conditions, and risk behavior. We analysed 4445 stroke-free samples with Cox proportional hazard regression test.

Results: During the 10-year observation, stroke incidence was 440 person-years per 100000 population (95% *CI* 370-530). During the follow-up of ten years, the main predictor of stroke was mental-emotional disorders with *HR* 4.2 (95% *CI* 2.8-6.3) after adjustment by age, hypertension, obesity, abdominal obesity, and high LDL-cholesterol levels.

Conclusions: Mental-emotional disorders are the strongest predictor of stroke incidence. Hence, psychological factors must be controlled in a stroke prevention program.

KEYWORDS: Adult; Cohort; Mental-emotional disorder; Stroke predictor

1. Introduction

Stroke is the most common cardiovascular and neurologic disease in Asian countries[1]. Aside from being a cause of death, disability due to stroke puts an economic burden on the family and the mental-emotional burden that interferes with the productivity of other family members[2]. In Indonesia, stroke is ranked first as the leading cause of death and neurological disability. The prevalence of stroke remains consistent at a rate of 120 per 100000 person-years in 2018, and in Bogor, 110 per 100000 people/years[3,4]. In other population, the stroke incidence rate is 120.42 per 100000 person-years (95% *CI* 26.17-214.67) in China[5], and the incidence is slightly higher at 200 per 100000 person-years in Australia[6]. The irreversible risk factors of stroke include age, sex, and ethnicity. The modifiable risk factors include diet (salt), cholesterol, hypertension, obesity, lack of physical activity, alcohol consumption, smoking, diabetes mellitus, atrial fibrillation, sleep apnea, and mental emotional disorders[7,8].

Significance

The aims of this study were to determine the stroke predictors for the 10-year of follow-up in Bogor City, Indonesia. Stroke is one of the main causes of death in Indonesia, our study found that the subjects with mental-emotional disorders have a higher risk of stroke 4-fold higher rather than those without mental-emotional disorders. These results underscore the critical need for targeted prevention and control of mental-emotional disorders in stroke prevention programs.

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The factor of mental-emotional disorder as a predictor of stroke incidence remains unexplored in longitudinal studies with large sample especially in Indonesia. Most of studies link the opposite condition to a much greater risk of mental disorders after stroke[9-11], or the mechanism influences changes in emotional neural circuits after stroke[12].

A longitudinal study linked the incidence of mental disorders and psychiatric disorders as a risk factor for vascular disease, reported by Jackson *et al.* found, retrospectively the risk increased 2 to 2.5 times among people with psychiatric disorders[13]. Patients with obsessive-compulsive disorder [hazard ratio (*HR*)], 3.02 (95% *CI* 1.91-4.77)[14], psychiatric disorders (*HR* 1.88, 95% *CI* 1.79-1.98)][15]. Determining how these associations are affected longitudinally by controlling for risk factors could deepen our understanding of the relationship between mental disorders and stroke incidence, as well as increase implications for cardiovascular disease prevention. Therefore, the aim of this study was to determine the stroke predictors for the 10-year of follow-up in Bogor City, Indonesia.

2. Subjects and methods

The prospective stroke cohort study was part of "the Bogor Cohort Study on Non-Communicable Disease Risk Factors" that began in 2011 and followed up for ten years, with a period of measurement every 2-year interval. The sample of the stroke cohort is permanent residents aged 25 years and over in the urban village of Central Bogor. Data collected by the World Health Organization (WHO) STEPS method included interviews, physical measurements, and laboratory tests[16]. The sample size was comprised of 4 445 subjects who were stroke-free at the start of the study (Figure 1).

2.1. Stroke assessment

The dependent variable is a stroke incident (hazard), based on the results of stroke confirmation examination (history and the presence of sequelae) by a neurologist. The incidence of stroke as an 'event' status (hazard) was the first stroke diagnosed and remained a stroke until the end of the observation (10 years), the proportion of lost to follow up for 6 years observation was 9.3%. Inclusion criteria includes: stroke-free subjects at the start of the study; aged 32 and older, and performed periodic check-ups at least twice during the follow-up of 10 years. The amount of data analyzed is shown in Figure 1.

2.2. Mental emotional disorder

Mental-emotional disorder was collected using the Self-instrument Reporting Questionnaire (SRQ) developed by the WHO in Indonesia version. This questionnaire contains 20 items related to symptoms of neurotic disorders such as pain and certain problems[17], which may have bothered the subject in the last 30 days with 2 categories of answer choices (Yes or No). A mental emotional disorder criterion is determined when answering at least six symptoms out of 20 symptoms. For predictors, the analysis has selected mental emotional disorders that occur before the stroke incident[18,19]. Several studies have tested the Indonesian version, SRQ is appropriate for assessing mental disorders[17,20]. The SRQ-20 had good internal consistency and reliability (α=0.82)[19], and indicated that all the questionnaire items related to psychiatric disturbances were reliable.

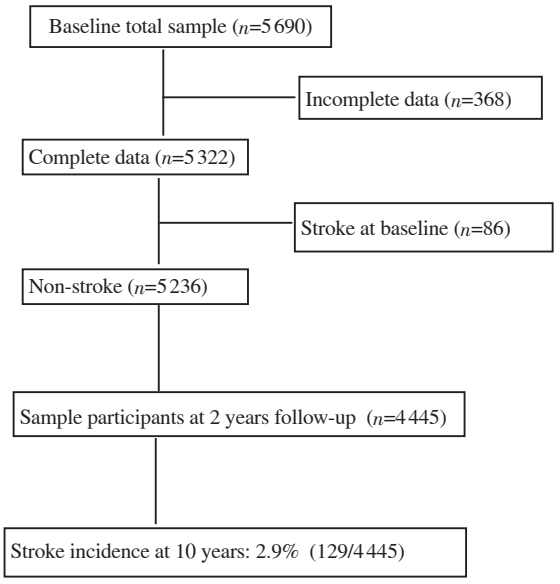

Figure 1. Sample recruitment.

2.3. Covariates variable

Some of the covariates as a determinant of stroke include status characteristics (age, sex, education, occupation, and marital status), health status (hypertension, mental emotional disorders, obesity, abdominal obesity, lipid profile, blood glucose), and risk behaviors: smoking and physical activity.

2.3.1. Characteristics of demography

Characteristics of demography include age, gender, education, and marital status. According to the distribution of stroke cohort sample data *i.e.*, the sample was divided into four age groups; 32-34 years old, 35-44 years old, 45-54 years old and >55 years old. Sex was categorized into male and female. Categories for education are low education (not primary school and primary school), medium education (graduated from junior high and high school), and higher education (graduated from diploma and bachelor's). Marital status was categorized into three groups; single, married, and divorced.

2.3.2. Chronic diseases

Hypertension is categorized according to JNC 8 classification, SBP

140 mmHg or DBP 90 mmHg and over[21]. Obesity is categorized according to the Body Mass Index (BMI) classification of the Asian population (*i.e.*, BMI<18.5), normal (18.5-22.9), overweight (23.0-24.9), and obesity (≥25)[22]. Central obesity is determined by abdominal circumference 90 cm for males and 80 cm for females. The lipid profile includes total cholesterol, low-density lipoprotein. (LDL), high-density lipoprotein (HDL), and triglycerides in the blood. Lipid profile levels are considered abnormal if the total cholesterol level is ≥200 mg/dL, LDL≥100 mg/dL, HDL≤40 mg/dL for males and ≤50 mg/dL for females, and triglycerides ≥150 mg/dL. Type-2 diabetes mellitus is diagnosed if post-prandial blood glucose levels are ≥200 mg/dL[23].

2.3.3. Behavioral risk factors

Risk factors contributing to stroke incidence include smoking and lack of physical activity. Smoking is calculated based on the Brinkman Index of the number of cigarettes smoked during life, categorized as smokers >200 cigarettes/year, smokers 1-200 cigarettes/year and non-smokers[24]. Physical activity is calculated based on the WHO Steps classification of 2004[16], *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)[25].

2.4. Statistical analysis

We analysed the data using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 25.0). Categorical data were presented as frequencies and percentages, the proportion of each characteristic category using crosstabulation with the *Chi*-square test, statistical significance was determined by a P <0.05.

A multivariable analysis using Cox proportional hazard regression test to determine the primary hazard ratio of stroke incidence (hazard) by controlling other covariates. Simple Cox regression analysis assessed the association between each characteristic and stroke incidence. Variables with a P-value <0.25 were selected to enter the multivariate model. After variable selection, the final model is a variable with a change value in the adjusted hazard ratio <10% with statistical significance of P-value <0.05. The main predictor factor is shown through a higher adjusted *HR* value among the variables selected in the final model.

2.5. Ethical statement

The studies involving human participants were reviewed and approved by the Ethical Committee for Health Research, National Institute of Health Research and Development (KE.01.08/EC/485/2011 and KE.01.05/EC/394/2012). The patients/participants provided their written informed consent to participate in this study.

3. Results

3.1. Stroke incidence

Our study found that the incidence of stroke found over ten years was 129 cases (2.9%). During the 10-year observation, stroke incidence was 440 person-years per 100 000 population (95% *CI* 370-530). The incidence was higher in female 79 cases than males 50 cases. The monitoring interval every two years shows the total number of cumulative incidents and the number by sex, as depicted in Figure 2.

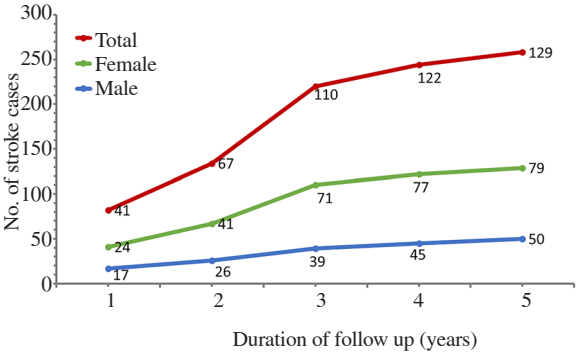

Figure 2. The cumulative incidence of stroke during 10 year monitoring with 2 years intervals.

3.2. Sociodemographic factors

Characteristics of subjects at the baseline showed differences in sociodemographic characteristics between two groups of outcomes stroke. The age of 55 and older, female, middle education and married status has the most significant related with stroke (Table 1).

Table 1. Socio-demography characteristics of stroke cohort samples according to sociodemographic and comorbidity factors [*n* (%)].

Characteristics	Stroke (*n*=129)	No stroke (*n*=4316)	*P*-value
Age, years			<0.001
32-34	0 (0.0)	126 (2.9)	
35-44	6 (4.7)	1240 (28.7)	
45-54	29 (22.4)	1446 (33.6)	
≥55	94 (72.9)	1504 (34.8)	
Sex			0.73
Male	38 (29.5)	1302 (30.2)	
Female	91 (70.5)	3014 (69.8)	
Education			0.23
Low	47 (36.4)	1234(28.6)	
Middle	76 (58.9)	2836(65.7)	
High	6 (4.7)	246(5.7)	
Marital status			0.001
Single	0(0.0)	150(3.5)	
Married	85(65.9)	3445(79.8)	
Divorce	44(34.1)	721 (16.7)	

3.3. Risk factors of stroke

Our study found that the proportion of mental emotional disorders, hypertension, abdominal obesity, abnormal triglyceride, blood glucose, lack of physical activity and smoking >200 cigarettes/years was higher in new stroke patients than in those without stroke. Mental-emotional disorders, hypertension, abdominal obesity, high triglycerides, blood glucose, lack of physical activity and smoking >200 cigarettes/years elated significantly (P<0.05) with stroke incidence during the 10-year monitoring (Table 2).

Table 2. Characteristics of stroke cohort samples according to biological and risks behavior condition [n (%)].

Characteristics	Stroke (n=129)	Non-stroke (n=4316)	P-value
Biological conditions			
Mental emotional disorders	29 (22.5)	232 (5.4)	<0.001
Hypertension	64 (49.6)	1575 (36.5)	<0.001
Obesity	83 (64.3)	2516 (58.3)	0.17
Abdominal obesity	100 (77.5)	2888 (66.9)	<0.001
Cholesterol >200 mg/dL	89 (69.0)	2142 (49.6)	0.05
LDL >100 mg/dL	120 (93.0)	3455 (80.1)	0.07
HDL: M > 40/F >50 mg/dL	59 (45.7)	1864 (43.2)	0.33
Triglycerides >150 mg/dL	49 (38.0)	1135 (26.3)	0.04
Blood glucose ≥200 mg/dL	27 (20.9)	440 (10.2)	0.01
Risk behavior			
Lack of physical activity	87 (67.4)	1898(44.0)	<0.001
Smokers >200 cigarettes/year, (Brinkman Index*)	68 (57.2)	830(19.2)	<0.001

LDL= Low density liporprotein; HDL= High density liporprotein. M: male, F: female,

Table 3. Predictors of stroke incidence on monitoring span of ten years.

Predictors	Adjusted HR	95% CI
Age, years		
32-34	1	
35-44	2.36	0.55-10.10
45–54	3.02	0.72-12.59
≥55	4.83	1.17-19.96
Hypertension		
Yes	3.41	1.75-4.51
No	1	
Mental emotional disorders		
Yes	4.21	2.80-6.33
No	1	
Obesity		
Yes	2.28	1.39-3.73
No	1	
Abdominal obesity		
Yes	0.34	0.24-0.61
No	1	
High LDL-cholesterol levels		
Yes	1.96	1.11-3.75
No	1	

LDL= Low density liporprotein.

Predictors of new stroke cases during the span of 10-year monitoring of multivariate analysis of Cox proportional hazard regression, proportional hazards were mental emotional disorders, hypertension, obesity, and LDL cholesterol levels after considering the age factor (Table 3). After considering the age factor, mental emotional disorders were a stronger predictor than hypertension for a new stroke case with an HR score of 4.21 (95% CI 2.80-6.33). During the span of 10-year monitoring and considering the age factor, stroke incidence appeared 4.21 times faster in mental-emotional disorders status than in no-mental emotional disorders people (Table 3).

4. Discussion

This study is the first cohort in Indonesia with a large sample size and long monitoring period. Our study reported stroke incidence was 440 person-years per 100000 population (95% CI 370-530) in the adult population. The finding of cumulative incidence was 2.9% during the ten years of monitoring. Compared with other Asian countries, our findings show a higher incidence rate. Malaysia has the lowest stroke incidence at 67 per 100000 person-years[26], an investigation in China shows the range between 122 per 100000 person-years (1992-1999) to 471.8 per 100000 person-years (2008-2015)[27]. The other study in Japan found crude incidence rates of total stroke (per 100000 person-years) were 225 in the early period (1990-2001) and 187 in the late period (2002-2010)[28]. The high incidence of stroke in Indonesia is possibly due to various stroke risk factors, which still tend to be high in Indonesia[29].

Our longitudinal study showed that the main predictor of stroke incidence in this study population was mental disorder. Mental health is known to be a risk factor or a result of stroke itself[30-33]. Our study reported that the risk of stroke incidence was found to increase four times greater in subjects who experienced mental disorders. Several studies in different populations support our findings; mental health disorders such as depression and stress are associated with an increased risk of stroke[34-36], Zuflacht *et al.*'s research on inpatients with mental health showed an increased risk of stroke, especially 15 days after hospitalization[37]. In a population-based study of the elderly, psychosocial distress was investigated in stroke mortality and stroke incidence over a 6-year follow-up[33].

Mental disorders are known to trigger changes in cells and cause inflammation and oxidative stress, which contribute to the risk of stroke. Kottega *et al.* explained the relationship between acute and chronic mental-emotional disorders and the risk of stroke[38]. Mental emotional disorders can increase the risk of cerebrovascular disease by modulating sympathomimetic activity, affecting blood pressure reactivity, brain endothelium, coagulation, or heart rhythm.

Mental emotional disorders still appear to be underestimated as a neurological practice and research[38,39].

Our study also shows that predictor factors associated with stroke incidence are older age, hypertension, obesity, and high LDL cholesterol. Variations in stroke risk factors were found to be different in Western and Asian populations[40], However, there are still few studies in Indonesia that explain this relationship prospectively. Cross-sectional study reports in Indonesia show a tendency for stroke incidence to be 2-4 times greater in subjects with hypertension[41,42]. The relationship of comorbid risk factors such as obesity, hypertension, and other cholesterol to stroke has also been proven in several studies[43-46], the combination of increasing age and a higher number of pre-existing comorbidities increases the risk of stroke[47]. The mechanism of atherosclerosis, which includes inflammatory and immunological responses, and oxidative stress triggered by hyperlipidemia, diabetes mellitus, or hypertension, underlies neuroinflammation, which plays a significant role in brain tissue damage in stroke[48].

The strength of this study is to use prospective cohort designs on large samples starting at age 25 years before entering the degenerative age. The study's limitation is that the stroke diagnosis was based on history and confirmation of the presence of residual symptoms by the neurologist (without a brain scan). Hence the type of stroke cannot be determined.

In conclusion, the incidence of stroke showed was increased from year to year. Mental-emotional disorder is the strongest predictor of stroke incidence after adjusted other variables. It is important to prevent persons with mental-emotional disorders from developing stroke.

Conflict of interest statement

The authors have no potential conflict of interest to declare.

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Authors' contributions

The authors confirm contribution to the research as followed: WR, ST and YT on study concept, design, and methodology; WR, ASP, ST on data collection; ASP and IS on data analysis and interpretation; WR, YT, ASP, ST, IS writing manuscript; WR, YT, ASP, ST, IS on discussion and revision. All authors approved the final version of the manuscript.

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