



## Incidence of Stroke and Associated Risk Factors in Bogor, Indonesia: A Nested Case-Control Study

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### Abstract

The increasing number of stroke cases and their risk factors is a crisis that needs to be addressed. This study aimed to determine the number of new stroke cases in Bogor, Indonesia, and its risk factors. We conducted a nested case-control study from the Study of Non-Communicable Disease (NCD) Risk Factors of the National Health Institute of Research and Development, Ministry of Health, Indonesia, in 2018. A deep analysis was conducted on 1.210 respondents based on the subset of baseline this data. Data was collected by interview method on permanent residents in Bogor City, Indonesia in 2018. Diagnosis of stroke was based on the anamnesis of a neurologist and a neurological examination. Independent variables include sociodemographic characteristics, metabolic syndrome, and risky behaviors. The data was analyzed with a dual logistic regression test. The incidence of stroke during 2018 amounted to 48 cases (3.9%). The main determinants of stroke in this population include diabetes mellitus and systolic blood pressure being the main factors for stroke, with each p-value, AOR, and (95% CI) being 0,000, 0,222 (0,122-0,405), 0,003, 0,291 (0,128-0,662). There was no significant difference in metabolic syndrome outcomes one year before the diagnosis of stroke and the year when the stroke was diagnosed. Special attention is needed in DM patients with high blood pressure to prevent stroke.

### Introduction

The cause-specific death rate of stroke reaches 5.5 million deaths, and more than 116 million stroke patients with complications including disability each year (Kim et al., 2020; Lindsay et al., 2019; World Stroke Organization, 2019). More than 80 million people had a history of stroke in 2016, and more than 13.7 million new cases each year (Kim et al., 2020). Globally, it is estimated that one in four people over the age of 25 will have a stroke during their lifetime. Over the past four decades, the incidence of stroke in lower-middle-income countries has more than doubled (Johnson et al., 2016), worldwide stroke deaths have most occurred in developing countries, such as Indonesia, which contributes 75.2% of all deaths (Feigin et al.,

2014; Kim et al., 2020; Thomas et al., 2018).

The prevalence of Stroke in Indonesia increased from 7% in 2013 to 10.9% or estimated as many as 2,120,362 people had strokes in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). It is becoming the first cause of death in Indonesia [8,9], with 21.1% of deaths in Indonesia caused by stroke. The non-communicable diseases (NCD) cohort study in Kebon Kelapa, Bogor, showed that stroke became a disease with the first fatality rate (Kemenkes RI, 2018). Despite its enormous impact on the socio-economic development of the country, this growing crisis, stroke has lack of attention to date (Johnson et al., 2016).

The metabolic risk factors of stroke are hypertension, obesity, and diabetes mellitus

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(Boehme et al., 2017; Hasnah, 2020; Lee et al., 2018; Setyopranoto et al., 2019; WHO, 2018). Indonesia's basic health research (riset kesehatan dasar=RISKESDAS) report shows that the prevalence of these risk factors has increased. The prevalence of hypertension for people aged >18-years-old increases from 25.8% to 34.1%. The prevalence of obesity in the >18-year-old increases from 14.8% to 21.8%. And diabetes mellitus in the  $\geq 15$ -year-old increases from 6.9% to 10.9% (Badan Penelitian dan Pengembangan Kesehatan, 2018). This study aimed to find the number of new cases during 2018 and their risk factors based on the data from NCD risk factors cohorts conducted by the National Health Institute of Research and Development, the Ministry of Health of the Republic of Indonesia.

## Methods

This study was a secondary data analysis that used research data of the NCD Risk Factor Cohort Study in Bogor City in 2017-2018 from the Ministry of Health of the Republic of Indonesia and was a community-based prospective cohort study. Respondents registered in the cohort study in 2017-2018 amounted to 3,784 respondents. Of it, 1,210 respondents had carried out stroke confirmation examinations. Dependent variables are strokes categorized into strokes and not strokes based on the results of neurological studies and confirmation of stroke by a neurologist. The independent variables that were potentially associated with stroke were age, gender, and education level (categorized into low education for junior school or lower, and higher education for high school up to college). Type of job by private employees/entrepreneurs and civil servants. Respondents' incomes are categorized as  $< \text{UMK}$  and  $\geq \text{UMK}$ . Health insurance has and does not. Smoking status in the past year as smoking and not smoking; The age of smoking started by  $\leq 15$  years and  $> 15$  years. Alcohol consumption. Physical activity by strenuous

and light. Diabetes Mellitus. Emotional distress status (stress) was classified as stress if the respondents experienced at least 6 out of 20 symptoms in the Instrument Self Reporting Questionnaire (SRQ). Metabolic syndrome factors include fasting blood glucose levels, post-loading blood glucose, total cholesterol, LDL, HDL, triglyceride, systolic blood pressure, diastolic blood pressure, and body mass index (BMI). Risk categories include fasting blood glucose  $\geq 125$  mg/dL, postprandial blood glucose  $\geq 180$  mg/dL, total cholesterol  $\geq 200$  mg/dL, LDL  $\geq 100$  mg/dL, HDL  $< 40$  for men and  $< 50$  for women and triglycerides  $\geq 150$  mg/dL, systolic blood pressure  $\leq 120$  mmHg, diastolic blood pressure  $\leq 80$  mmHg, and BMI classified as normal and obese ( $\geq 27$ ).

Data were presented as frequencies and percentages based on variable categories. Bivariate analysis is used to identify risk factors associated with stroke incidence. In the absence of collinearity, all variables were included in the logistic regression model using a gradual method to determine the associated variable ( $p < 0.05$ ). Odds ratio (OR) with a confidence interval of 95% (CI) was calculated as a measure of association. In addition, the Mann-Whitney test was conducted to find out the difference in risk factors for metabolic syndrome years before the stroke was diagnosed with the year of the stroke diagnosis. All analyses were conducted by SPSS 22.0 (IBM Corporation, NY, USA). This cohort data source had received updated ethical approval every year from the Health Research Ethics Commission, Health Research and Development Agency, Ministry of Health of the Republic of Indonesia. Research ethics permit in 2017 number LB.02.01/5.2/KE.108/ 2017. No further ethical permission was required for the analysis of secondary data.

## Results and Discussion

Based on the research that has been done, the following results were obtained:

Table 1. Characteristics of Research Respondents

<b>Variable</b>	<b>Frequency</b>	<b>Percent</b>
<b>Age (mean; SD)</b>	43.3; 10.14	
<b>Gender</b>		
Male	419	34.6
Female	791	65.4
<b>Education</b>		
Low (Not School - Junior school)	734	60.7
High (high school - college)	476	39.3
<b>Type of work</b>		
Private employee/entrepreneur	1182	97.7
Civil Servants	28	2.3
<b>Income (UMK = Rp 3, 557. 146)</b>		
< city minimum wage	1154	95.4
≥ city minimum wage	56	4.6
<b>Ownership of Health Insurance</b>		
It doesn't have	424	35.0
Have	786	65.0
<b>Smoking Status</b>		
Smoke	665	55.0
No smoking	545	45.0
<b>Age to Start Smoking</b>		
≤ 15 years	267	22.1
> 15 years	943	77.9
<b>Alcohol Consumption</b>		
Yes	255	21.1
Not	955	78.9
<b>Physical Activity</b>		
Heavy	64	5.3
Light	1146	94.7
<b>Diabetes Mellitus</b>		
Positive	181	15.0
Negative	1029	85.0
<b>Emotional Mental Disorders</b>		
Annoyed	160	13.2
Normal	1050	86.8
<b>Fasting Blood Sugar Levels</b>		
Risky	271	22.4
Normal	939	77.6
<b>Fasting Blood Sugar Levels Post-Loading</b>		
Risky	460	38.0
Normal	750	62.0
<b>Total Cholesterol Levels</b>		
Risky	565	46.7
Normal	645	53.3
<b>Triglyceride Levels</b>		
Risky	295	24.4
Normal	915	75.6
<b>LDL levels</b>		
Risky	935	77.3
Normal	275	22.7

Variable	Frequency	Percent
<b>HDL levels</b>		
Risky	424	35.0
Normal	786	65.0
<b>Systolic Blood Pressure</b>		
Risky	715	59.1
Normal	495	40.9
<b>Diastolic Blood Pressure</b>		
Risky	687	56.8
Normal	523	43.2
<b>BMI</b>		
Obesity	429	35.5
Normal	781	64.5

**Source:** Secondary Data of the NCD Risk Factor Cohort Study in Bogor City in 2017-2018 from the MoH RI

Table 1 shows that the average age of respondents was 43.3 years. The majority of respondents were female (65.4%) with low level of education (60.7%) and income below the city minimum wage in Bogor City (95.4%). The majority of respondents had normal metabolic syndrome test results, only on systolic blood pressure measurements (59.1%) and diastolic (56.8%) with risky outcomes.

Table 2. Associated Risk Factors of Stroke

Variable	Stroke		Not		P-Value	OR	CI 95%
	n	%	n	%			
<b>Gender</b>							
Male	18	4.30	401	95.70	0.670	1.139	0.627 – 2.068
Female	30	3.79	761	96.21			
<b>Education</b>							
Low (Not School - Junior school)	35	4.77	699	95.23	0.076	1.783	0.933 – 3.407
High (high school - college)	13	2.73	463	97.27			
<b>Type of work</b>							
Private employee/entrepreneur	46	3.89	1136	96.11	0.384	0.526	0.121 – 2.285
Civil Servants	2	7.14	26	92.86			
<b>Income</b>							
<b>(City minimum wage = Rp 3,557,146)</b>							
< city minimum wage	45	3.90	1109	96.10	0.585	0.717	0.216 – 2.382
≥ city minimum wage	3	5.36	53	94.64			
<b>Ownership of Health Insurance</b>							
It doesn't have	15	3.54	409	96.46	0.574	0.837	0.449 – 1.559
Have	33	4.20	753	95.80			
<b>Smoking Status</b>							
Smoke	32	4.81	633	95.19	0.096	1.6771	0.907 – 3.080
No smoking	16	2.94	529	97.06			
<b>Age to Start Smoking</b>							
≤ 15 years	9	3.37	258	96.63	0.572	0.809	0.387 – 1.691
> 15 years	39	4.14	904	95.86			
<b>Alcohol Consumption</b>							
Yes	13	5.10	242	94.90	0.298	1.412	0.736 – 2.711
Not	35	3.66	920	96.34			
<b>Physical Activity</b>							

Variable	Stroke		Not		P-Value	OR	CI 95%
	n	%	n	%			
Heavy	3	4.69	61	95.31	0.762	1.203	0.364 – 0.364
Light	45	3.93	1101	96.07			
<b>Diabetes Mellitus</b>							
Positive	22	12.15	159	87.85	0.000	5.338	2.953 – 9.647
Negative	26	2.53	1003	97.47			
<b>Emotional Mental Disorders</b>							
Annoyed	6	3.75	154	96.25	0.880	0.935	0.391 – 2.236
Usual	42	4.00	1008	96.00			
<b>Fasting Blood Sugar Levels</b>							
Risky	19	7.01	252	92.99	0.004	2.366	1.305 – 4.290
Usual	29	3.09	910	96.91			
<b>Fasting Blood Sugar Levels Post-Loading</b>							
Risky	23	5.00	437	95.00	0.149	1.526	0.856 – 2.722
Usual	25	3.33	725	96.67			
<b>Total Cholesterol Levels</b>							
Risky	31	5.49	534	94.51	0.011	2.145	1.174 – 3.918
Usual	17	2.64	628	97.36			
<b>Triglyceride Levels</b>							
Risky	17	5.76	278	94.24	0.069	1.744	0.951 – 3.199
Usual	31	3.39	884	96.61			
<b>LDL levels</b>							
Risky	42	4.49	893	95.51	0.084	2.109	0.887 – 5.014
Usual	6	2.18	269	97.82			
<b>HDL levels</b>							
Risky	15	3.54	409	96.46	0.574	0.837	0.449 – 1.559
Usual	33	4.20	753	95.80			
<b>Systolic Blood Pressure</b>							
Risky	41	5.73	674	94.27	0.000	4.241	1.887 – 9.533
Usual	7	1.41	488	98.59			
<b>Diastolic Blood Pressure</b>							
Risky	36	5.24	651	94.76	0.009	2.355	1.213 – 4.572
Usual	12	2.29	511	97.71			
<b>BMI</b>							
Obesity	22	5.13	407	94.87	0.125	1.570	0.878 – 2.805
Usual	26	3.33	755	96.67			

Source: Secondary Data of the NCD Risk Factor Cohort Study in Bogor City in 2017-2018 from the MoH RI

Table 2 shows the results of cross-tabulation of stroke factors with the incidence of stroke that diabetes mellitus (p = 0.000; OR=5,338; CI 95%=2,953-9,647), systolic blood pressure (p=0.000; OR=4.241; CI 95%=1,887-9,533), total cholesterol (p=0.011; OR=2,145, CI 95%=1,174-3,918), diastolic blood pressure (p=0.009; OR=2,355; CI 95%=1,213-4,572), and fasting blood sugar levels (P=0.149; OR=1,526, CI 95%=0.856-2,722) is a variable related to stroke incidence in Bogor City in 2018.

Table 3. Logistic Regression Risk Factors of Stroke

Risk Factors	P	Model 1	P	Model 2	P	Model 3	P	Model 4
		AOR (95% C.I)		AOR (95% C.I)		AOR (95% C.I)		AOR (95% C.I)
Diabetes Mellitus	0,000	0.249 (0.124-0.502)	0.000	0.237 (0.129-0.435)	0.000	0.238 (0.130-0.436)	0.000	0.222 (0.122-0.405)
Systolic Blood Pressure	0.333	0.333 (0.127-0.876)	0.025	0.331 (0.126-0.868)	0.005	0.308 (0.135-0.702)	0.003	0.291 (0.128-0.662)
Total Cholesterol	0.116	0.608 (0.327-1.131)	0.114	0.606 (0.326-1.127)	0.110	0.604 (0.325-1.122)		
Diastolic Blood Pressure	0.883	0.333 (0.397-1.962)	0.782	0.894 (0.404-1.978)				
Fasting Blood Sugar Levels	0.774	0.901 (0.443-1.833)						
Constant	0.000	117.326	0.000	115.277	0.000	112.855	0.000	90.648

Notes. Model 4: Hosmer and Lemeshow test:  $\chi^2 = 38,281$ ,  $P = 0.000$ , Nagelkerke  $R^2 = 11\%$ ;

Source: Secondary Data of the NCD Risk Factor Cohort Study in Bogor City in 2017-2018 from the MoH RI

The results of the logistic regression test for stroke with p-value, AOR, and (95% C.I) in table 4 showed that diabetes mellitus and systolic blood pressure were the main factors respectively at 0.000, 0.222. (0.122-0.405), 0.003, 0.291 (0.128-0.662).

Table 4. Differences in Biomarkers of Metabolic Syndrome a Year Before Being Diagnosed with Stroke

Biomarkers of Metabolic Syndrome	2017	2018	Z; p-value
	Mean; $\pm$ SD	Mean; $\pm$ SD	
Fasting blood sugar levels (mg/dL)	101.13; $\pm$ 10:70 p.m.	129.08; $\pm$ 68.52	-2,163; 0.031
Post-loading blood sugar levels (mg/dL)	146.69; $\pm$ 67.98	183.08; $\pm$ 110.17	-1.07; 0.285
Total Cholesterol Levels (mg/dL)	211.77; $\pm$ 37.22	216.88; $\pm$ 40.02	-0.612; 0.541
Triglyceride Levels (mg/dL)	119.02; $\pm$ 61.25	159.21; $\pm$ 106.14	-1.8; 0.058
LDL (mg/dL)	142.67; $\pm$ 32.74	138.58; $\pm$ 35.64	-0.608; 0.543
HDL (mg/dL)	49.19; $\pm$ 11.95	49.83; $\pm$ 11:00	-0.458; 0.647
Systolic Blood Pressure (mmHg)	157.31; $\pm$ 36.12	140.69; $\pm$ 10:15 p.m.	-2,177; 0.029
Diastolic Blood Pressure (mmHg)	95.19; $\pm$ 6:57 p.m.	90.31; $\pm$ 13.78	-1,389; 0.165
IMT	27.13; $\pm$ 4.09	27.42; $\pm$ 4.66	-0.166; 0.869

*Mann-Whitney Test*

Source: Secondary Data of the NCD Risk Factor Cohort Study in Bogor City in 2017-2018 from the MoH RI

The average biomarker of metabolic syndrome a year before the diagnosis of stroke and the year when diagnosed with stroke showed results that did not differ significantly, only fasting blood sugar levels and systolic blood pressure, where fasting blood sugar levels in the year diagnosed stroke were higher than the year before the stroke was diagnosed, while the average systolic blood pressure in the year before diagnosis was higher, p-values 0.031, and 0.029, respectively.

The incidence of stroke during 2018 amounted to 48 cases (3.9%). Based on this study, the most vital risk factors for stroke in

this population of diabetes mellitus and systolic blood pressure, especially in male patients with an average age of 43 years, a 2013 study in the same population showed that stroke was found at 49 (2.6%) of the people from 1912 subjects studied (Riyadina & Rahajeng, 2013). It is a 1.3% increase over five years. While the incidence of stroke nationally in 2018 reached 10.9% (Badan Penelitian dan Pengembangan Kesehatan, 2018).

The proportion of strokes in this population was more common in men Zhang Y et al. (Y. Zhang et al., 2012). The incidence of Stroke in the United States, England, France,

Germany, Italy, and Spain increased with age, greater in men than women. Stroke is already present in the young age group of 15-24 years with a prevalence of 0.3% and 25 - 34 years by 0.4%, increasing sharply at 45 years and above. The National Health and Nutrition Examination Survey 2009-2012 in the United States found the prevalence of stroke in women ages 20-39 at 0.2% and men at 0.7% (Mozaffarian et al., 2015). Stroke was higher in groups with low education (not high school). It was closely related to less knowledge due to poor education, so less knowing the consequences of the improper lifestyle, such as eating high-fat and others will facilitate the onset of degenerative diseases (Meschia et al., 2014). It is necessary to counsel stroke prevention methods for a poorly educated specificity society. The appearance of stroke at a young age indicates that stroke prevention interventions should begin early.

The results show that DM was a significant factor in the occurrence of stroke, though statistically multivariate shows a negative direction, but some previous studies have proven a lot. DM increases the risk of stroke because excess glucose in the blood causes vasculopathy, making it more likely to develop hypertension and atherosclerosis. In addition, diabetes increases the risk of blood clots, which can lead to heart attacks and strokes (Azam et al., 2017; Sofiana et al., 2019). Excess sugar in the blood has a direct effect on the walls of blood vessels, binding to and changing the structure of proteins and molecules lining blood vessels, making it thicker, less elastic, and more likely to trigger thrombosis. Thicker, less elastic blood vessels mean that blood has a harder time flowing through narrower gaps and must do so at higher pressures. These changes cause tissue damage called final organ damage. A smaller space for blood to flow means a greater likelihood that clots can completely block blood vessels, causing a stroke or heart attack (Chaturvedi et al., 2020; Sofiana & Rahmawati, 2019; Sorgun et al., 2018). DM was a significant risk factor for cardiovascular disease, including stroke. It is also an independent risk factor in which 20% of diabetic patients will die from stroke (Lau et al., 2019; Mohiuddin, 2019; Shang et al., 2020).

Systolic blood pressure was shown to be a risk factor for stroke although an increase

in systolic blood pressure had a higher effect on outcomes, both systolic and diastolic hypertension independently affected the risk of adverse cardiovascular events, regardless of the definition of hypertension ( $\geq 120$  mmHg and  $\geq 80$  mmHg (Flint et al., 2019), including Recurrent Stroke (Ovbiagele et al., 2011), and is the leading cause of cardiovascular death (Itoga et al., 2021; Paultre & Mosca, 2005). The association of hypertension with stroke has been widely explained by many studies. One study by O'Donnell et al. (2010), identified as many as 3,000 cases of stroke with the results of an OR analysis of 2.64. These results can be concluded that people diagnosed with hypertension have a risk of 2.64 times the incidence of stroke compared to people who are not diagnosed with hypertension (O'Donnell et al., 2010). Research by Chen et al. (2014), showed Asians were at 2.84 times the risk of having a stroke with hypertension as a risk factor (Chen et al., 2014). Another study by Zhang et al. (2004), also stated that hypertension is the most dominant risk factor that causes stroke incidence in Asians (X.-F. Zhang et al., 2004). The significant association between stroke and other hypertension in the Asian region is evidenced in a study conducted by Burke and Venketasubramanian (2006), with OR 9.03 (95% CI, 5.25–15.5) in Taiwan (Burke & Venketasubramanian, 2006). Research related to isolated systolic blood pressure in Indonesia said that the prevalence of stroke in ISH reached 8.3%. Women with smoking habits, experiencing mental and physical stress, urban living, and being poorly educated were associated with stroke status in ISH subjects in Indonesia (Pamelasari et al., 2021).

Stroke prevention strategies in this population should include early detection and immediate treatment. It is vital to control risk factors to reduce the burden of stroke. Both primary prevention and secondary prevention. Such as quitting smoking, doing exercise at least 150 minutes/week, a high-fiber diet, fruit and vegetable intake and low in sugar and salt, regulating weight, and pharmacotherapy to control hypertension and blood glucose. This research has some drawbacks. This study only covers one city area in West Java Province, so it has not been able to represent other regions

with different characteristics; this study does not consider the subtypes of ischemic stroke, as well as several other risk factors such as other accompanying diseases not yet included. More research needs to be done to overcome these limitations. Hospital-based research on stroke and the risk factors associated with it should also be conducted in comparison to the results of this community-based study.

## Conclusions

Strokes found in the community in the Kebon Kalapa village, Bogor City, based on the Study of NCD Risk Factors of the National Health Institute of Research and Development, MoH RI in 2018, amounted to 48 cases (3.9%). The main determinants of stroke in this population include diabetes mellitus and systolic blood pressure being the main factors for stroke, with each p-value, AOR, and (95% C.I.) being 0.000, 0.222 (0.122-0.405), 0.003, 0.291 (0.128-0.662). There was no significant difference in metabolic syndrome outcomes one year before the diagnosis of stroke and the year when the stroke was diagnosed. Special attention is needed in D.M. patients who have high blood pressure to prevent.

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