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RESEARCH

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Clinical risk factors related to post-stroke epilepsy patients in Indonesia: a hospital-based study

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Abstract

Background Stroke had been accounted to cause almost 50% of epilepsy in the elderly and may lead to poor functional outcomes. Many studies examining the risk factors have been conducted despite showing inconsistent results and currently still difficult to predict the occurrence of post-stroke epilepsy. The study aimed to determine risk factors related to post-stroke epilepsy that influence clinical seizure, electroencephalography (EEG), and functional outcome of patients. Analytic retrospective case–control study was conducted with a total sampling of 62 samples of post-stroke epilepsy and 62 samples of control from all stroke patients in the Neurology Clinic from January 2019 to December 2021. Epilepsy was classified according to the criteria of the International League Against Epilepsy (ILAE) in 2017. The relevant demographic and clinical data were collected.

Result The study involved 62 patients in the case group (average age of onset = 57.69; 42 men, 20 women; 51 ischemic stroke, 11 hemorrhagic stroke) and 62 patients in the control group (average age of onset = 56.90; 24 men, 38 women; 52 ischemic stroke, 10 hemorrhagic stroke). We found that 31 patients had focal-to-bilateral seizures, 26 patients had generalized seizures and 5 patients had focal seizures. Men ($p = 0.001$; OR 3.325) and NIHSS Score ($p = 0.027$; OR 5.094) had significant correlations with post-stroke epilepsy. Ischemic stroke had a significant correlation ($p = 0.008$) with seizure onset. Women also had a significant correlation ($p = 0.012$) with EEG abnormalities. The study found that 59 of 62 post-stroke epilepsy patients had poor functional outcomes (mRS > 2).

Conclusion Our study confirmed that most patients had focal-to-bilateral seizure patterns that occurred in 1–2 years after stroke, and had poor functional outcomes. Men had 3.325 times more likely to develop post-stroke epilepsy than women. Also, NIHSS score ≥ 15 correlated and 5.094 times more likely to develop post-stroke epilepsy. Ischemic stroke had a peak of epilepsy onset at 1–2 years after stroke and women had significant showing abnormalities on EEG recording than men.

Keywords Post-stroke epilepsy, Electroencephalography, Gender, NIHSS score, Seizure onset

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Background

Stroke is still the second leading cause of death with annual mortality rate of about 5.5 million, and is also the first cause of disability (50%) worldwide. Generally, ischemic strokes account for about 80% of stroke cases while hemorrhagic stroke accounts for 20% of cases [1, 2]. Stroke had accounted to be the cause of epilepsy in the elderly while 30–50% of patients diagnosed with epilepsy after stroke [3, 4]. The incidence of epilepsy in post-stroke patients varied based on several studies. As many as 3–30% of stroke patients will develop post-stroke epilepsy and had negative effects on the prognosis also the quality of life of the patients [3].

In 2014, International League Against Epilepsy (ILAE) defined epilepsy as which at least 2 unprovoked or reflex seizures occurred more than 24 h or 1 unprovoked or reflex seizure in which the probability of having two seizures was at least 60% over the next 10 years, or had been diagnosed of the epilepsy syndrome [5]. Seizures after stroke were divided into early seizures and late seizures. There was no consensus on an agreed time limit to distinguish these two types of post-stroke seizures. The study showed that the risk of recurring seizures after 10 years in early post-stroke seizures was 33%, while in late post-stroke seizures was 71.5%, so 1 late post-stroke seizure (> 7 days) can be defined as post-stroke epilepsy caused by a high risk of recurring seizure [6, 7].

Classification of seizure onset showed the different basic pathogenesis while early seizure occurred by acute changes of vascular and neurons due to ischemic or hemorrhagic stroke. Meanwhile, late seizures occurred by epileptogenesis that was complex structural and physiological changes in neuron and synaptic plasticity, gliotic scarring, and chronic inflammation that caused hyperexcitability and synchronization to induce abnormal spontaneous seizures [3, 7, 8].

Many studies had conducted to find the risk factors of post-stroke epilepsy despite showing inconsistent results and still difficult to predict until now. Some studies showed many risk factors that correlated with the higher incidence of post-stroke epilepsy including hemorrhagic stroke, cortical involvement, wide infarction, the severity of stroke, decreased of consciousness, and vascular risk factors. The severity of stroke was correlated and became the major risk factor for epileptogenesis [3, 8, 9].

The study aimed to retrospectively evaluate the risk factors of post-stroke epilepsy and their influence on clinical seizure, electroencephalography, and functional outcome of patients.

Methods

This study was designed as a retrospective analytical case–control study with non-probability total sampling from patients diagnosed with stroke in the Neurology Clinic from January 2019 to December 2021. This study had conducted in the period of May–July, 2022. Post-stroke epilepsy was classified according to the International League Against Epilepsy (ILAE) criteria that seizures occurred after 7 days of onset. Stroke was diagnosed according to WHO Criteria by an expert stroke neurologist and proven by a head non-contrast computerized tomography scan reviewed by an expert neuroradiologist.

Population of the study was derived from outpatients who come to our neurology clinic that have an established history of stroke and had gone through acute care phase at hospital. Patients who experienced clinical seizure after 7 days of stroke onset will be included for post-stroke epilepsy samples. Patients with seizure or diagnosis of epilepsy before the onset of stroke, acute symptomatic seizure, had other complications that influenced the clinical condition of stroke, intracranial lesion beside of stroke, and passed away during acute stroke treatment were excluded to ensure that epileptogenesis occurred due to stroke. The control samples were taken from stroke patients without clinical seizures during the period of study.

We retrospectively analyzed the medical histories of 62 post-stroke epilepsy patients and 62 control patients. Demographical and clinical data including the age of stroke onset, gender, type of stroke, location of the stroke, the severity of stroke based on NIHSS, history of hypertension, and history of diabetes mellitus were collected. From 62 post-stroke epilepsy patients, clinical data including the onset of seizure, seizure pattern, EEG recording, and functional outcome based on mRS were also collected.

Stroke location was categorized by cortical, subcortical, and wide lesions involved in both. Seizure onset was categorized by < 1 month, 1–6 months, 6–12 months, 1–2 years, and > 2 years after stroke. The seizure patterns were categorized as focal, generalized, and focal-to-bilateral seizures as ILAE criteria [10]. EEG recordings were classified as Normal EEG, and Abnormal EEG Type I, II, and III. Referred to as Normal EEG if there is no abnormality in the EEG features. The degree of EEG abnormalities is divided into Abnormal I, II, and III. EEG categories depend on the clinical significance of the findings and correlate with either the severity of cerebral dysfunction or the specificity of the abnormalities [11].

All statistical analysis were performed with SPSS 25.0 at a significance level of $\alpha = 0.05$, $p < 0.05$, confidence interval 95%. Parametrical analysis of numerical factors

with Independent *T*-test was used if normal distribution criteria had been met. Analysis of categorical factors was conducted with the X^2 test and spearman correlation test. Mean standard deviation is used to represent continuous variables (Age of Onset) whereas number percentage is used to represent categorical variables (gender, stroke type, location of stroke, stroke severity, vascular risk factor, seizure onset, seizure pattern, EEG recording, and functional outcome).

Results

The study involved 62 patients case group (average age of onset = 57.69) which consist of 42 Men and 20 Women, also 62 patients control group (average age of onset = 56.90) which consist of 24 Men and 38 Women. This study consists of 51 patients with ischemic stroke, 11 patients with hemorrhagic stroke in the case group, also 52 patients with ischemic stroke, and 10 patients with hemorrhagic stroke in the control group. Subcortical lesions were the predominant finding in both groups, followed by wide lesions including cortical and subcortical lesions, and the remainder being cortical lesions. Moderate stroke as indicated by NIHSS 5–14 was found in 85.48% of the case group and 96.77% of the control group, then followed by severe stroke in both groups. Hypertension as a vascular risk factor was the predominant finding in both groups. Table 1 presents the detailed characteristics of the study group.

From 62 post-stroke epilepsy in the case group, we collected data about the clinical seizure, EEG recording, and functional outcome based on the modified Rankin Scale (mRS). The peak of seizure onset occurred in 1–2 years after stroke, also we found 31 patients had focal-to-bilateral seizures, 26 patients had generalized seizures and 5 patients had focal seizures. From EEG recording we found 33 patients had normal results, 3 patients had abnormal I, 11 patients had abnormal II, and 15 patients had abnormal III. The study found that 59 patients had poor functional outcomes (mRS > 2), and only 3 patients had good functional outcomes (mRS ≤ 2). Tables 2, 3, 4 and 5 present seizure onset, seizure pattern, EEG recording, and functional outcome characteristics of the study and its correlation with demographic variables.

We analyzed the age of onset with the Kolmogorov–Smirnov test and we found $p = 0.200$ which showed normal distribution. Post-stroke epilepsy was found to be linked with gender ($p = 0.001$; OR 3.325) and severity of stroke based on NIHSS ($p = 0.027$; OR 5.094). Ischemic stroke also had a significant correlation ($p = 0.008$) with seizure onset in the time onset peak in 1–2 years after stroke. Women also had a significant correlation ($p = 0.012$) with EEG abnormalities.

Table 1 Detailed demographic and clinical data of the groups

Variables	Case group	Control group	*p*-value
Age of stroke onset (mean ± SD)	57.69 ± 9.51	56.90 ± 10.38	0.659[a]
Gender (frequency)			**0.001**[b]
Male	42 (67.74%)	24 (38.71%)	**OR 3.325 (95% CI 1.59–6.96)**
Female	20 (32.26%)	38 (61.29%)	
Stroke type (frequency)			0.811[b]
Ischemic stroke	51 (82.26%)	52 (83.87%)	
Hemorrhage stroke	11 (17.74%)	10 (16.13%)	
Location of stroke (frequency)			0.573[b]
Cortical	1 (1.61%)	0 (0%)	
Subcortical	40 (64.52%)	41 (66.13%)	
Cortical-subcortical (wide)	21 (33.87%)	21 (33.87%)	
Stroke severity (frequency)			**0.027**[b]
Moderate (NIHSS 5–14)	53 (85.48%)	60 (96.77%)	**OR 5.094 (95% CI 1.05–24.64)**
Severe (NIHSS 15–21)	9 (14.52%)	2 (3.23%)	
Hypertension (frequency)			0.243[b]
Hypertension (+)	57 (91.94%)	60 (96.77%)	
Hypertension (−)	5 (8.06%)	2 (3.23%)	
Diabetes mellitus (frequency)			0.567[b]
Diabetes mellitus (+)	22 (35.48%)	19 (30.65%)	
Diabetes mellitus (−)	40 (64.52%)	43 (69.35%)	

[a] Analyzed with independent *T*-test

[b] Analyzed with X^2; bold: statistically significant ($p < 0.05$)

Table 2 Factors analysis related to seizure onset

Clinical variables	Seizure onset	*n* (%)	*p*-value
Age of stroke onset (mean ± SD)			0.833[a]
57.69 ± 9.51	7 days–1 month	2 (3.22%)	
	1–6 months	23 (37.07%)	
	6–12 months	6 (9.68%)	
	1–2 years	25 (40.32%)	
	> 2 years	6 (9.68%)	
Gender (frequency)			0.448[b]
Male (*n* = 42)	7 days–1 month	1 (2.38%)	
	1–6 months	18 (42.86%)	
	6–12 months	5 (11.90%)	
	1–2 years	14 (33.33%)	
	> 2 years	4 (9.52%)	
Female (*n* = 20)	7 days–1 month	1 (5.00%)	
	1–6 months	5 (25.00%)	
	6–12 months	1 (5.00%)	
	1–2 years	11 (55.00%)	
	> 2 years	2 (10.00%)	
Stroke type (frequency)			**0.008[b]**
Ischemic stroke (*n* = 51)	7 days–1 month	1 (1.96%)	
	1–6 months	21 (41.18%)	
	6–12 months	6 (11.76%)	
	1–2 years	21 (41.18%)	
	> 2 years	2 (3.92%)	
Hemorrhage stroke (*n* = 11)	7 days–1 month	1 (9.09%)	
	1–6 months	2 (18.18%)	
	6–12 months	0 (0.00%)	
	1–2 years	4 (36.36%)	
	> 2 years	4 (36.36%)	
Location of stroke (frequency)			0.576[b]
Cortical (*n* = 1)	7 days–1 month	0 (0.00%)	
	1–6 months	0 (0.00%)	
	6–12 months	0 (0.00%)	
	1–2 years	1 (100%)	
	> 2 years	0 (0.00%)	
Subcortical (*n* = 42)	7 days–1 month	2 (4.76%)	
	1–6 months	16 (38.10%)	
	6–12 months	3 (7.14%)	
	1–2 years	15 (35.71%)	
	> 2 years	6 (14.29%)	
Cortical–subcortical (wide) (*n* = 19)	7 days–1 month	0 (0.00%)	
	1–6 months	7 (36.84%)	
	6–12 months	3 (15.79%)	
	1–2 years	9 (47.37%)	
	> 2 years	0 (0.00%)	
Stroke severity (frequency)			0.614[a]
Moderate (NIHSS 5–14) (*n* = 53)	7 days–1 month	2 (3.77%)	
	1–6 months	20 (37.74%)	
	6–12 months	3 (5.66%)	
	1–2 years	22 (41.51%)	
	> 2 years	6 (11.32%)	
Severe (NIHSS 15–21) (*n* = 9)	7 days–1 month	0 (0.00%)	
	1–6 months	3 (33.33%)	
	6–12 months	3 (33.33%)	
	1–2 years	3 (33.33%)	
	> 2 years	0 (0.00%)	
Hypertension (frequency)			0.576[b]
Hypertension (+) (*n* = 57)	7 days–1 month	2 (3.50%)	
	1–6 months	22 (38.60%)	
	6–12 months	4 (7.02%)	
	1–2 years	23 (40.35%)	
	> 2 years	6 (10.53%)	
Hypertension (−) (*n* = 5)	7 days–1 month	0 (0.00%)	
	1–6 months	1 (20.00%)	
	6–12 months	2 (40.00%)	
	1–2 years	2 (40.00%)	
	> 2 years	0 (0.00%)	
Diabetes mellitus (frequency)			0.709[b]
Diabetes mellitus (+) (*n* = 22)	7 days–1 month	0 (0.00%)	
	1–6 months	7 (31.82%)	
	6–12 months	3 (13.64%)	
	1–2 years	10 (45.45%)	
	> 2 years	2 (9.09%)	
Diabetes mellitus (−) (*n* = 40)	7 days–1 month	2 (5.00%)	
	1–6 months	16 (40.00%)	
	6–12 months	3 (7.50%)	
	1–2 years	15 (37.50%)	
	> 2 years	4 (10.00%)	

[a] Analysed with Spearman correlation

[b] Analysed with X^2; bold: statistically significant ($p < 0.05$)

Discussion

The prevalence of stroke globally in 2020, stroke affects over 101 million people with a ratio of women (56%) and men (44%). There are over 12.2 million of new stroke each year, which one in four people over 25 years

Table 3 Factors analysis related to seizure pattern

Clinical variables	Seizure pattern	*n* (%)	*p*-value
Age of stroke onset (mean ± SD)			0.869[a]
57.69 ± 9.51	Focal	5 (8.06%)	
	Generalized	26 (41.94%)	
	Focal to bilateral	31 (50.00%)	
Gender (frequency)			0.815[b]
Male (*n* = 42)	Focal	4 (2.38%)	
	Generalized	17 (42.86%)	
	Focal to bilateral	21 (11.90%)	
Female (*n* = 20)	Focal	1 (25.00%)	
	Generalized	9 (5.00%)	
	Focal to bilateral	10 (55.00%)	
Stroke type (frequency)			0.945[b]
Ischemic stroke (*n* = 51)	Focal	4 (7.84%)	
	Generalized	21 (41.18%)	
	Focal to bilateral	26 (50.98%)	
Hemorrhage stroke (*n* = 11)	Focal	1 (9.10%)	
	Generalized	5 (45.45%)	
	Focal to bilateral	5 (45.45%)	
Location of stroke (frequency)			0.104[b]
Cortical (*n* = 1)	Focal	0 (0.00%)	
	Generalized	0 (0.00%)	
	Focal to bilateral	1 (100%)	
Subcortical (*n* = 42)	Focal	4 (9.52%)	
	Generalized	22 (52.38%)	
	Focal to bilateral	16 (38.10%)	
Cortical–subcortical (wide) (*n* = 19)	Focal	1 (5.26%)	
	Generalized	4 (21.05%)	
	Focal to bilateral	14 (73.68%)	
Stroke severity (frequency)			0.065[a]
Moderate (NIHSS 5–14) (*n* = 53)	Focal	5 (9.44%)	
	Generalized	24 (45.28%)	
	Focal to bilateral	24 (45.28%)	
Severe (NIHSS 15–21) (*n* = 9)	Focal	0 (0.00%)	
	Generalized	2 (22.22%)	
	Focal to bilateral	7 (77.78%)	
Hypertension (frequency)			0.759[b]
Hypertension (+) (*n* = 57)	Focal	5 (8.77%)	
	Generalized	24 (42.11%)	
	Focal to bilateral	28 (49.12%)	
Hypertension (−) (*n* = 5)	Focal	0 (0.00%)	
	Generalized	2 (40.00%)	
	Focal to bilateral	3 (60.00%)	
Diabetes mellitus (frequency)			0.094[b]
Diabetes mellitus (+) (*n* = 22)	Focal	4 (18.18%)	
	Generalized	8 (36.36%)	
	Focal to bilateral	10 (45.45%)	
Diabetes mellitus (−) (*n* = 40)	Focal	1 (2.50%)	
	Generalized	18 (45.00%)	
	Focal to bilateral	21 (52.50%)	

[a] Analyzed with Spearman correlation

[b] Analyzed with X^2

Table 4 Factors analysis related to EEG recording

Clinical variables	EEG recording	*n* (%)	*p*-value
Age of stroke onset (mean ± SD)			0.930[a]
57.69 ± 9.51	Normal	33 (53.23%)	
	Abnormal I	3 (4.84%)	
	Abnormal II	11 (17.74%)	
	Abnormal III	15 (24.19%)	
Gender (frequency)			**0.012[b]**
Male (*n* = 42)	Normal	26 (61.90%)	
	Abnormal I	2 (4.77%)	
	Abnormal II	9 (21.43%)	
	Abnormal III	5 (11.90%)	
Female (*n* = 20)	Normal	7 (35.00%)	
	Abnormal I	1 (5.00%)	
	Abnormal II	2 (10.00%)	
	Abnormal III	10 (50.00%)	
Stroke type (frequency)			0.583[b]
Ischemic stroke (*n* = 51)	Normal	29 (56.86%)	
	Abnormal I	2 (3.92%)	
	Abnormal II	8 (15.69%)	
	Abnormal III	12 (23.53%)	
Hemorrhage stroke (*n* = 11)	Normal	4 (36.36%)	
	Abnormal I	1 (9.10%)	
	Abnormal II	3 (27.27%)	
	Abnormal III	3 (27.27%)	
Location of stroke (frequency)			0.691[b]
Cortical (*n* = 1)	Normal	1 (100%)	
	Abnormal I	0 (0.00%)	
	Abnormal II	0 (0.00%)	
	Abnormal III	0 (0.00%)	
Subcortical (*n* = 42)	Normal	20 (47.62%)	
	Abnormal I	3 (7.14%)	
	Abnormal II	7 (16.67%)	
	Abnormal III	12 (28.57%)	
Cortical–subcortical (wide) (*n* = 19)	Normal	12 (63.16%)	
	Abnormal I	0 (0.00%)	
	Abnormal II	4 (21.05%)	
	Abnormal III	3 (15.79%)	
Stroke severity (frequency)			0.467[a]
Moderate (NIHSS 5–14) (*n* = 53)	Normal	29 (54.72%)	
	Abnormal I	3 (5.66%)	
	Abnormal II	9 (16.98%)	
	Abnormal III	12 (22.64%)	
Severe (NIHSS 15–21) (*n* = 9)	Normal	4 (44.44%)	
	Abnormal I	0 (0.00%)	
	Abnormal II	2 (22.22%)	
	Abnormal III	3 (33.33%)	

Table 4 (continued)

Clinical variables	EEG recording	*n* (%)	*p*-value
Hypertension (frequency)			0.232[b]
Hypertension (+) (*n* = 57)	Normal	31 (54.39%)	
	Abnormal I	2 (3.51%)	
	Abnormal II	11 (19.30%)	
	Abnormal III	13 (22.81%)	
Hypertension (−) (*n* = 5)	Normal	2 (3.50%)	
	Abnormal I	1 (38.60%)	
	Abnormal II	0 (7.02%)	
	Abnormal III	2 (40.35%)	
Diabetes mellitus (frequency)			0.159[b]
Diabetes mellitus (+) (*n* = 22)	Normal	13 (0.00%)	
	Abnormal I	0 (31.82%)	
	Abnormal II	6 (13.64%)	
	Abnormal III	3 (45.45%)	
Diabetes mellitus (−) (*n* = 40)	Normal	20 (9.09%)	
	Abnormal I	3	
	Abnormal II	5	
	Abnormal III	12	

[a] Analyzed with Spearman correlation

[b] Analyzed with X^2; bold: statistically significant ($p < 0.05$)

Table 5 Factors analysis related to functional outcome

Clinical variables	Func. outcome	*n* (%)	*p*-value
Age of stroke onset (mean ± SD)			0.192[a]
57.69 ± 9.51	Good (mRS ≤ 2)	3 (4.84%)	
	Poor (mRS > 2)	59 (95.16%)	
Gender (frequency)			0.967[b]
Male (*n* = 42)	Good (mRS ≤ 2)	2 (2.38%)	
	Poor (mRS > 2)	40 (42.86%)	
Female (*n* = 20)	Good (mRS ≤ 2)	1 (11.90%)	
	Poor (mRS > 2)	19	
Stroke type (frequency)			0.469[b]
Ischemic stroke (*n* = 51)	Good (mRS ≤ 2)	2 (1.96%)	
	Poor (mRS > 2)	49 (41.18%)	
Hemorrhage stroke (*n* = 11)	Good (mRS ≤ 2)	1 (41.18%)	
	Poor (mRS > 2)	10 (3.92%)	
Location of stroke (frequency)			0.971[b]
Cortical (*n* = 1)	Good (mRS ≤ 2)	0 (0.00%)	
	Poor (mRS > 2)	1 (100%)	
Subcortical (*n* = 42)	Good (mRS ≤ 2)	2 (0.00%)	
	Poor (mRS > 2)	40 (100%)	
Cortical–subcortical (wide) (*n* = 19)	Good (mRS ≤ 2)	1 (0.00%)	
	Poor (mRS > 2)	18	
Stroke severity (frequency)			0.464[b]
Moderate (NIHSS 5–14) (*n* = 53)	Good (mRS ≤ 2)	3 (3.77%)	
	Poor (mRS > 2)	50 (37.74%)	
Severe (NIHSS 15–21) (*n* = 9)	Good (mRS ≤ 2)	0 (41.51%)	
	Poor (mRS > 2)	9 (11.32%)	
Hypertension (frequency)			0.099[b]
Hypertension (+) (*n* = 57)	Good (mRS ≤ 2)	2 (3.50%)	
	Poor (mRS > 2)	55 (38.60%)	
Hypertension (−) (*n* = 5)	Good (mRS ≤ 2)	1 (40.35%)	
	Poor (mRS > 2)	4 (10.53%)	
Diabetes mellitus (frequency)			0.188[b]
Diabetes mellitus (+) (*n* = 22)	Good (mRS ≤ 2)	0 (0.00%)	
	Poor (mRS > 2)	22 (31.82%)	
Diabetes mellitus (−) (*n* = 40)	Good (mRS ≤ 2)	3 (45.45%)	
	Poor (mRS > 2)	37 (9.09%)	

[a] Analyzed with independent *T*-test

[b] Analyzed with X^2

old will have a stroke in their lifetime. Each year, 47% of men and 53% of women have a stroke. Stroke is still the second leading cause of death worldwide about 6.5 million of people die annually, of which 6% of all deaths from stroke occur in people in 15–49 years old, and 34% occur in people under 70 years old. The death due to stroke occur in 51% of men and 49% of women [12, 13].

Developments in neuroscience and technology in the field of stroke acute care and intervention had led to an increasing trend of long-term complications such as post-stroke epilepsy. The trend towards a younger stroke population also has a major impact on post-stroke recovery. Neural plasticity and regeneration after stroke often encounter problems such as seizures that are difficult to control, neurological deficits, anxiety, and worsening the quality of life. Precise prediction of the risk of post-stroke epilepsy, drug selection, and seizure control are very important in the prognosis of stroke patients [14, 15].

We found no significant correlation between age of onset in the occurrence of post-stroke epilepsy. Some studies showed younger age had a correlation and the higher incidence of post-stroke epilepsy in age < 65 years than in age > 85 years, although the correlation was still not be clear [16–18]. In this study, age of onset stroke had homogenous data in both groups that might cause no significant correlations.

A significant correlation was found in men that had been to be a risk factor to develop post-stroke epilepsy and had 3.325 times more likely than women. In a few studies, gender was not an independent risk factor related to post-stroke epilepsy. Conrad and colleagues showed a higher percentage of men (53.8%) than women (46.2%) in post-stroke epilepsy patients [19]. Dziadkowiak et al. also

showed a higher number of 86 men than 78 women in their study [20]. So did both studies by Bladin et al. and Lamy et al. also showed a higher percentage of men than women in post-stroke epilepsy patients [21, 22].

Sex difference in epilepsy is still an interesting topic and relevant to public health and clinical studies. Few studies in epilepsy showed a higher prevalence of epilepsy in men than women which might be caused by different inherent cerebral development normally [23]. Specific incidence of epilepsy based on gender showed the vulnerability of the brain to develop epilepsy. Although epilepsy commonly happened in men, more complex epilepsy syndrome and poorly controlled seizures can happen in women. Some studies showed there was hormonal change affects seizure patterns in women, especially during the menstrual cycle, and also menopause phase significantly influences seizure patterns and treatment [24]. Few studies related epidemiology of epilepsy based on gender had inconsistent results [25–29].

The data showed dominant ischemic stroke in both groups, and so did also subcortical location of the stroke. There were no significant correlations between type and location of the stroke in post-stroke epilepsy. Many studies showed hemorrhagic stroke as a significant predictor of post-stroke epilepsy compared to ischemic stroke, although the mechanisms were not known clearly [8]. In this study, we had imbalanced composition between hemorrhagic and ischemic stroke that might cause no significant correlations.

Cortical location showed as a significant risk factor for early post-stroke seizures. Some studies also showed cortical infarction had been an independent risk factor to develop late-onset seizure. Post-stroke seizures also developed more often in wider brain lesions involving some lobes and in some locations such as the frontal lobe, parieto-temporal lobe, supramarginal gyrus, also temporal superior gyrus [3, 30]. But other studies showed no significant correlation between ischemic location in seizure development either in cortical or subcortical [18, 19]. In the last decade, there were shifted mindsets about the origin of seizure onset in epilepsy. Many studies showed more complex interaction of neuronal networks in subcortical and cortical areas in which epileptogenesis happened. So then comes the thought that any brain injury location can induce epileptic seizure as long as the functional neuronal connection was intact [31, 32].

The severity of stroke as measured by NIHSS showed a significant correlation and higher NIHSS had 5.094 more times more likely to develop post-stroke epilepsy. Post-stroke epilepsy correlated with the severity of stroke in which many studies showed higher NIHSS significantly had more risk to develop epilepsy [19]. Others with an indicator of Glasgow Coma Scale, urinary incontinence, dysarthria, and Barthel index showed that the severity of stroke correlated with the occurrence of post-stroke epilepsy [3, 16]. Stroke with more severe clinical symptoms is considered to have extensive cortical involvement. Extensive brain injury might be the predisposition to the epileptogenesis process through various complex biochemical pathways [7, 8].

Vascular risk factors such as hypertension and diabetes mellitus in this study were not significantly correlated with post-stroke epilepsy. From many studies showed that general lifestyles, vascular risk factors, and metabolic such as hypertension, and diabetes mellitus were not correlated with the occurrence of post-stroke epilepsy in accordance with this study [4, 16, 22].

In this study, we found that ischemic stroke was correlated with seizure onset at the peak of onset in 1–2 years after stroke. But as mentioned before that there was an imbalance composition of hemorrhagic and ischemic stroke samples in this study. Many studies showed the onset peak of late seizure post-stroke in 6–12 months with linear correlation risk of post-stroke epilepsy year after year [21, 22, 33]. We also found 31 patients (50%) had focal-to-bilateral seizures, 26 patients had generalized seizures and 5 patients had focal seizures that in accordance with previous studies. From Conrad and colleagues showed a dominant generalized seizure pattern (56%) compared with focal onset (44%) in post-stroke epilepsy [19]. Other studies also showed a dominant generalized seizure pattern in Ischemic stroke (65%) compared to focal impaired awareness (25%) followed by focal aware (10%). But in hemorrhagic stroke were found dominant focal impaired awareness (40%), generalized tonic–clonic (35%), and focal aware (25%) [19, 20]. Many studies also showed that post-stroke epilepsy correlated with the poor functional outcome in accordance with our study that 95.16% of patients had mRS > 2 [34–36]. There is no previous study yet examining the risk factors which correlated with seizure onset, seizure pattern, also the functional outcome in patients with post-stroke epilepsy.

Interestingly, we found a significant correlation between gender with EEG pattern in our study, that women had more often abnormal EEG recording results compared with men that often had normal EEG. EEG studies to differ interictal wave patterns in women and men in epilepsy case were not clear yet. The study in define characteristics of the brain structurally and functionality based on gender still be an interesting topic and being researched. Structurally there were some differences in brains between men and women [37]. With EEG and brain mapping showed different waves between men and women. Interhemispheric correlation and coherences, hemispheric specialization, cortical functional unit specialization, and task

activation dominant might be correlated with different wave patterns in women and men recorded by EEG and brain mapping [38].

Our study has a few limitations. We reviewed the medical history of patients retrospectively. This small sample may have limited the derivation of adjusted Odd Ratios with multiple predictor variables. We did not include patients with acute symptomatic seizure during acute onset of stroke that may be a risk of further epilepsy, also did not evaluate functional outcome of epilepsy because of some limitation data. Further studies are needed with a prospective, larger sample, and multicentred study to determine more comprehensive epidemiological data, risk factors, EEG patterns, clinical epilepsy concerning seizure pattern, seizure control, anti-seizure medications, and also functional outcomes of post-stroke epilepsy patients. We also recommend further studies with distinguished samples between ischemic and hemorrhagic stroke to determine the characteristics in own type of stroke.

Conclusion

Our study confirmed that most patients had focal-to-bilateral seizure patterns that occurred 1–2 years after stroke, and had poor functional outcomes. Men had 3.325 times more likely to develop post-stroke epilepsy than women. Also, NIHSS score ≥ 15 correlated and 5.094 times more likely to develop post-stroke epilepsy. Ischemic stroke had a peak of epilepsy onset at 1–2 years after stroke and women had significant abnormalities showing on EEG recording than men.

Abbreviations

EEG	Electroencephalography
ILAE	International League Against Epilepsy
mRS	Modified Rankin Scale
NIHSS	National Institute of Health Stroke Scale
WHO	World Health Organization

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Author contributions

AKW designed the study, collected and analyzed the patient data, and arranged the manuscript. MH designed the study, analyzed the patient data, evaluated and substantively revised the manuscript. RD and NS analyzed the patient data, evaluated and substantively revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The dataset generated and/or analyzed during this current study is available in the figshare repository (https://doi.org/10.6084/m9.figshare.21342048.v2).

Declarations

Ethics approval and consent to participate

This study protocol has been reviewed and got ethical approval from the Health Research Ethic Commission of Dr. Saiful Anwar General Hospital Malang Indonesia with No. 400/128/K.3/102.7/2022. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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