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CLINICAL PROFILE AND MORTALITY PREDICTIVE FACTORS POST-STROKE AMONG HOSPITALISED STROKE PATIENTS

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ABSTRACT

Correct identification and consistent preventative measures are critical steps in lowering mortality rate among stroke patients. In this study, we aimed to describe clinical profiles and predictive factors that influence post-stroke mortality among hospitalised patients. A retrospective analysis was carried out on 185 stroke patients who were admitted to Hospital Seberang Jaya. Data on demographic information, physical examination results, comorbidities, laboratory tests, medications taken, NIH stroke severity score (NIHSS) and Modified Rankin Score (mRS) were collected. Using mortality post-stroke as the outcome, a sequential series of logistic regression models were developed. Patients who survived post-stroke had a median NIHSS score of 3.0 (inter quartile rage [IQR]: 6.00) and a mean mRS score of 1.9 (SD: ±1.63). Based on categories, the highest percentage of mortality were ≤ 61 years, male, Chinese ethnicity, experienced ischemic stroke, with ≥ 3 comorbidities, with the uptake of ≥ 11 medications and duration of hospitalisation of ≥ 4 days. The best mortality prediction model for post-stroke patients included hemorrhagic stroke, recurrent stroke and comorbidities heart disease, chronic kidney disease, pneumonia and acute kidney injury (Hosmer and Lemeshow Test = 0.574). Model performance is good (R^2 = 0.718) with correctly predicts 72.0% (sensitivity) and with specificity of 98.1% for all mortality attributing to stroke. A mortality prediction model for hospitalised post-stroke patients was developed that will enable rapid identification of patients who are more susceptible for mortality post-stroke utilising the commonly available information in healthcare settings.

***Keywords*:** Post-stroke, Mortality, Clinical Profile, Hospitalised, Routine data

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INTRODUCTION

A stroke is a clinical syndrome that appears suddenly, causes signs of brain dysfunction, lasts longer than 24 hours, or results in death and has no other apparent cause other than vascular origin (Sacco *et al.* 2013).

Stroke is a disease with a significant disease burden as it is the second leading cause of death worldwide, accounting for 11 million deaths annually (World Health Orginization [WHO] 2021). In Malaysia, it ranks as the third most common cause of death, and in 2019, 47,928 stroke-related deaths, 443,995 prevalent cases and 512,726 stroke-related disability-adjusted life years (DALYs) were reported (Tan and Venketasubramanian 2022).

Stroke can be categorised into ischemic stroke and hemorrhagic stroke. Ischemic stroke occurs due to blockage in the artery transporting blood to the brain, accounts for 11 million cases and hemorrhagic strokes, which occur due to rupture of a weakened blood vessel, causing compression of the surrounding brain tissue, accounts for 5.3 million cases worldwide with 63% and 80% respectively occurring in low-income and middle-income countries (Bennett *et al.* 2014, Krishnamurthi *et al.* 2014). Data from Malaysia indicates that ischemic strokes account for 79.4% of the total stroke cases, while hemorrhagic strokes account for 18.2% of cases (Aziz *et al.* 2015).

Hospital Seberang Jaya (HSJ) is a tertiary healthcare institution that leads a cluster of three other tertiary healthcare institutions, namely Hospital Bukit Mertajam, Hospital Sungai Bakap and Hospital Kepala Batas in the state of Pulau Pinang, Malaysia (Danial *et al.* 2023). HSJ also serves as the state's main stroke centre (Chelladurai *et al.* 2021). In 2010, the HSJ stroke team launched the Perai Regional Integrated Stroke Intervention System, which featured a local hospital-based stroke database representative of the Pulau Pinang population as well as a protocol for managing the rapid thrombolysis system (Loh *et al.* 2021). This study is aimed to report on the clinical profiles and to identify the mortality predictive factors of patients admitted for stroke at HSJ using routinely available healthcare data. This study is important as identifying mortality predictive factors allows for the rapid recognition of patients at higher risk of post-stroke mortality. Conducted at HSJ, the state's leading stroke center, it is expected to offer the most accurate representation of Pulau Pinang's stroke population.

METHODS

Study Setting

This study was conducted at HSJ, a government healthcare facility that functions as the main stroke centre for all tertiary healthcare facilities in Pulau Pinang, Malaysia. There are some techniques in this manuscript that are similar to those in our previously published articles (Danial *et al.* 2023, Danial *et al.* 2019).

Study Design and Data Collection

In HSJ, a hospital-based stroke database will be routinely updated based on stroke admissions (Loh *et al.* 2021). We used the hospital-based stroke database to identify the hospitalised stroke patients who fulfils our inclusion and exclusion criteria. After the initial

identification, subsequently, information such as demographic characteristics, results of physical examination, presence of comorbidities, results of laboratory testing, stroke severity score during admission (using National Institutes of Health Stroke Scale [NIHSS]) (Ortiz and Sacco 2019), prescribed medication during hospitalisation and disability upon discharge (using the modified Rankin Scale [mRS]) (Banks and Marotta 2007) was captured from the patients' medical records using a data collection form. Patients admitted for stroke and warded for more than 24 hours were included, but patients under the age of 18 years old and admissions for reasons other than stroke were excluded.

Sample Size Estimation

Sample size were estimated using the formula for sample size (n) without finite population correction (Chow *et al.* 2017). The estimated prevalence of stroke patients in Malaysia is at 0.3% (Amal *et al.* 2011). Fixing a Type I error probability at 0.05 and a precision of 0.01, a minimum of 115 stroke patient samples was required for the study. To compensate for missing data for the minimum samples collected, an additional 60% of samples were collected, totaling 185 subjects included in this study.

Statistical Analysis

Using Pearson's chi-square test for categorical variables and, depending on the degree of data skewness, either the t-test or the Mann-Whitney test for continuous variables, the baseline characteristics of stroke patients were examined (Danial *et al.* 2019).

Model Development and Performance

Mortality post-stroke was fixed as the model outcome. Only variables that had less than 10% of missing data were considered to be included for the model development process. For compensating the missing data, multiple imputation using the iterative technique was used to generates replacement values. From the initial univariate analysis, variables that had significance value of $p > 0.05$, were excluded from the subsequent multiple logistic regression. Collinearity diagnostics were performed to eliminate predictors that might highly intercorrelate. Only variables that had the variance inflation factor (VIF) value of < 10 and tolerance value of > 0.1, was included for model development. Mortality post-stroke risk models were sequentially developed by continuous addition of stroke category, stroke episode and comorbidities. Variables age category, sex and ethnicity were used to adjust the final model. Predictors of the final mortality risk post-stroke modes were presented as odds ratio (OR) with 95% confidence interval (CI). For the sequentially developed mortality risk post-stroke models, Hosmer and Lemeshow goodness of fit test, Nagelkerke R^2 value and p-value were reported. The steps of model development and performance were carried out in accordance with the method described by Danial *et al.* (2019).

The SPSS statistical package (version 22; SPSS Inc., Chicago, IL) was used for all analysis. p-values < 0.05 were considered statistically significant (two-sided).

RESULTS

Univariate Analysis

This study included 185 medical records, out of which 160 patients survived after a stroke and 25 patients did not survive after a stroke. The mortality incidence is estimated at 13.5% ([25/185] ×100) from this study.

Univariate analysis was performed between patients who survived and patients who did not survive post-stroke (see Table 1). Significant differences in survival were observed from variables such as gender (p = 0.041); currently or previously smoking (p = 0.043); stroke category (p < 0.001), stroke episode (p < 0.001); physical examination parameters, comorbidities such as chronic kidney disease (p = 0.002), pneumonia (p < 0.001), acute kidney injury (p = 0.001); laboratory data, number of total comorbidities (p = 0.005), the total medication prescribed (p = 0.008), duration of hospitalisation (p = < 0.001) and previous hospitalisation (p = < 0.001). The median NIHSS score that evaluates the stroke severity during admission for those who survived post-stroke was 3.0 (inter quartile rage [IQR] = 6.00). On the other hand, for patients who did not survive post-stroke, there was no documented NIHSS score. This may be due to the possibility that these patients had severe strokes upon admission and immediate treatment might have been initiated. Disability upon discharge was evaluated using the mRS score revealed that patients who survived had lower score (mean = 1.9 [SD = ± 1.63]) compared with those who did not survive (mean = 6.0 [SD = ± 0]).

Table 1: Demographic characterisation of patients based on survivability who were admitted for stroke at General Hospital Seberang Jaya, Malaysia.

Characteristics	No. (%) of participants			
	Composition	**Alive (n = 160)**	**Dead (n = 25)**	***p*-value**
Demographics				
Age (years), mean (SD)	61 (13.7)	60 (13.2)	64 (16.4)	0.155
Gender				0.041
Male	129 (69.7)	112 (60.5)	17 (9.2)	
Female	56 (30.3)	48 (26.0)	8 (4.3)	
Ethnicity				
Malay	87 (47.0)	78 (42.1)	9 (4.9)	0.296
Chinese	64 (34.6)	54 (29.2)	10 (5.4)	
Indian	25 (13.5)	22 (11.9)	3 (1.6)	
Others	9 (4.9)	6 (3.3)	3 (1.6)	
Currently or previously smoking	48 (26.0)	46 (24.9)	2 (1.1)	0.043
Stroke category				< 0.001
Ischemic stroke	171 (92.4)	157 (84.8)	14 (7.6)	
Hemorrhagic stroke	14 (7.6)	3 (1.6)	11 (6.0)	
Stroke episode				< 0.001
First	137 (74.1)	128 (69.2)	9 (4.9)	
Recurrent	48 (25.9)	32 (17.3)	16 (8.6)	

(*continued on next page*)

Table 1: (*Continued*)

Characteristics	No. (%) of participants			
	Composition	**Alive (*n* = 160)**	**Dead (*n* = 25)**	***p*-value**
NIHSS score, median (IQR)	3.0 (6.00)	3.0 (6.00)	NA	0.248
mRS score, mean (SD)	2.5 (2.00)	1.9 (1.63)	6.0 (0)	0.981
Physical examinations				
Systolic (mm Hg), median (IQR)	164.9 (44.00)	162.0 (44.00)	140.0 (43.00)	0.010
Diastolic (mm Hg), mean (SD)	91.6 (18.23)	93.5 (17.99)	79.4 (15.42)	0.001
Pulse (bpm), mean (SD)	81.5 (16.92)	80.5 (15.86)	87.7 (21.91)	0.049
Comorbid conditions				
Hypertension	137 (74.1)	116 (62.7)	21 (11.4)	0.230
Diabetes	87 (47.0)	74 (40.0)	13 (7.0)	0.593
[a]Heart disease	44 (23.8)	39 (21.1)	5 (2.7)	0.633
Dyslipidemia	43 (23.2)	40 (21.6)	3 (1.6)	0.164
Chronic kidney disease	10 (5.4)	5 (2.7)	5 (2.7)	0.002
Pneumonia	9 (4.9)	2 (1.1)	7 (3.8)	< 0.001
Acute kidney injury	7 (3.8)	2 (1.1)	5 (2.7)	0.001
Laboratory data				
Hemoglobin (g/dl), median (IQR)	14.1 (2.50)	14.1 (2.40)	12.0 (5.20)	0.002
Hematocrit test (L/L), median (IQR)	42.1 (8.50)	42.3 (7.90)	33.6 (13.30)	0.008
Albumin (g/L), median (IQR)	36.0 (4.00)	37.0 (3.00)	33.0 (14.00)	0.004
APTT (sec), median (IQR)	36.0 (7.70)	35.6 (6.85)	42.8 (19.15)	0.050
Total comorbidities, mean (SD)	2.2 (1.43)	2.1 (1.41)	3.0 (1.37)	0.005
Total medication used, median (IQR)	10.0 (7.00–13.00)	9.0 (7.00–13.00)	13.0 (7.00–13.00)	0.008
Duration of hospitalisation (days), median (IQR)	3.0 (1.00–4.00)	2.0 (1.00–3.00)	5.9 (2.00–9.00)	< 0.001
Previous hospitalisation (number), median (IQR)	1.0 (1.00–2.00)	1.0 (1.00–2.00)	1.0 (1.00–2.00)	0.020

Note: NIHSS = NIH Stroke Scale; mRS = Modified Rankin Score; APTT = Activated partial thromboplastin time.
Data are presented as number (no.) and percentages (%) unless otherwise stated.
[a]Heart Disease is defined as presence of vascular or/and heart failure aetiology

Logistic Regression

Categories of patients admitted for stroke who were at a higher risk of mortality were patients aged ≤ 61 years (52.0%); male (68.0%); Chinese ethnicity (40.0%); non-smoker (92.0%); experienced ischemic stroke (56.0%); with recurrent stroke episodes (64.0%); with 3 or more comorbidities (60.0%); with the uptake of 11 or more medications (60.0%) and with 4 days or more duration of hospitalisation (60.0%).

The outcomes of the multiple logistic regression showed that the age group of ≤ 61 years and males have higher rates of mortality post-stroke compared to other age categories and females. In terms of ethnicity, the others category had 7.48 (95% confidence interval (CI) 0.59–95.57) higher mortality rates compared to Malay, Chinese and Indian ethnicity. Comparison based on stroke category indicates that patients that experienced hemorrhagic stroke had mortality rate of odds ratio (OR) = 38.69 (95% CI 7.76–192.91) compared with those that experienced ischemic stroke. Moreover, higher rate of mortality with associated with patients with recurrent stroke (OR = 9.22; 95% CI 2.52–33.72) compared with stroke patients whom had first episode of stroke. Similarly, higher mortality rates were observed among patients with 3 or more comorbidities (OR = 1.37; 95% CI 0.39–4.83); with the uptake of 11 or more medications (OR = 1.12; 95% CI 0.32–3.92) and with duration of hospitalisation of 4 or more days (OR = 4.86; 95% CI 1.49–15.82) compared to their counterparts (see Table 2).

Overall, types of stroke category ($p < 0.001$), stroke episode ($p < 0.001$), and duration of hospitalisation ($p = 0.009$) were significant factors that influenced the mortality post-stroke.

Model Performance

The OR variables for Hosmer and Lemeshow Test and Nagelkerke R square for successive models are shown in Table 3. In Model 1, only the stroke category of hemorrhagic stroke was included and it performed poorly (Hosmer and Lemeshow Test = 0.799; Nagelkerke $R^2 = 0.336$ and $p < 0.001$). As for model 2, the Hosmer and Lemeshow and Nagelkerke R^2 improved with the addition of recurrent stroke episode (Hosmer and Lemeshow Test = 0.860; Nagelkerke $R^2 = 0.267$ and $p < 0.001$). Subsequently, with the inclusion of comorbidities heart disease, chronic kidney disease, pneumonia, and acute kidney injury it further improved the prediction model (Hosmer and Lemeshow Test = 0.574; Nagelkerke $R^2 = 0.718$ and $p < 0.001$). Therefore, the best model was determined to be Model 3.

Table 2: Factors associated with survivability of patients who were admitted for stroke at General Hospital Seberang Jaya, Malaysia using simple and multiple logistic regression.

Variables		Survived, *n*(%)	Died, *n*(%)	Crude OR	(95% CI)	*p*-value[a]	Adj. OR	(95% CI)	*p*-value[b]
Age category	≤ 61 years	82 (51.2%)	13 (52.0%)	1.00(ref.)		0.970	1.00(ref.)		0.850
	≥ 62 years	78 (48.8%)	12 (48.0%)	0.97	(0.42, 2.26)		0.89	(0.26, 2.97)	
Gender	Male	112 (70.0%)	17 (68.0%)	1.00(ref.)		0.644	1.00(ref.)		0.920
	Female	48 (30.0%)	8 (32.0%)	0.91	(0.37,2.25)		0.94	(0.27,3.30)	
Ethnicity	Malay	78 (48.8%)	9 (36.0%)	1.00(ref.)		0.296	1.00(ref.)		0.448
	Chinese	54 (33.8%)	10 (40.0%)	1.61	(0.39,2.86)	0.337	1.79	(0.51,6.27)	
	Indian	22 (13.8%)	3 (12.0%)	1.18	(0.59,4.93)	0.814	1.35	(0.22,8.47)	
	Others	6 (3.8%)	3 (12.0%)	4.33	(0.59,4.93)	0.063	7.48	(0.59,95.57)	
Smoking status	No	114 (71.3%)	23 (92.0%)	1.00(ref.)		0.043*	1.00(ref.)		0.098
	Yes	46 (28.7%)	2 (8.0%)	0.22	(0.05,0.95)		0.18	(0.03,1.37)	
Stroke category	Ischemic	157 (98.1%)	14 (56.0%)	1.00(ref.)		< 0.001*	1.00(ref.)		<0.001*
	Hemorrhagic	3 (1.9%)	11 (44.0%)	41.12	(10.26,164.88)		38.69	(7.76,192.91)	
Stroke episode	First	128 (80.0%)	9 (36.0%)	1.00(ref.)		< 0.001*	1.00(ref.)		<0.001*
	Recurrent	32 (20.0%)	16 (64.0%)	7.11	(2.88,17.56)		9.22	(2.52,33.72)	
No. of comorbidities	≤ 2	97 (60.6%)	10 (40.0%)	1.00(ref.)		0.057	1.00(ref.)		0.625
	≥ 3	63 (39.4%)	15 (60.0%)	2.31	(0.98,5.46)		1.37	(0.39,4.83)	
No. of medications	≤ 10	93 (58.1%)	10 (40.0%)	1.00(ref.)		0.094	1.00(ref.)		0.864
	≥ 11	67 (41.9%)	15 (60.0%)	2.08	(0.88,4.92)		1.12	(0.32,3.92)	
Duration of hospitalisation	≤ 3days	127 (79.4%)	10 (40.0%)	1.00(ref.)		< 0.001*	1.00(ref.)		0.009*
	≥ 4days	33 (20.6%)	15 (60.0%)	5.77	(2.38,14.02)		4.86	(1.49,15.82)	

Note: [a]Simple Logistic Regression; [b]Multiple Logistic Regression; Crude OR = Crude Odds Ratio; Adj. OR = Adjusted Odds Ratio; 95% CI = 95% confidence interval; **p*-value < 0.05.

Table 3: Odd Ratio and Goodness of Fit for Sequential Models of Mortality Predictions for patients who were admitted for stroke at General Hospital Seberang Jaya.

	Models		
Variable	**1**	**2**	**3**
	Stroke category	**Stroke category + Stroke episode**	**Stroke category + Stroke episode Comorbidities**
Hemorrhagic stroke	42.95 (10.19–180.99)	58.23 (11.10–305.58)	182.88 (16.34–2047.47)
Recurrent stroke		12.64 (3.59–44.50)	32.97 (3.92–277.34)
Heart disease			0.09 (0.01–0.95)
Chronic kidney disease			129.89 (7.79–2166.78)
Pneumonia			78.79 (6.85–906.27)
Acute kidney injury			30.86 (2.34–398.802)
Hosmer and Lemeshow Test	0.799	0.860	0.574
Nagelkerke R^2	0.336	0.267	0.718
p-value	< 0.001	< 0.001	< 0.001
Predictive ability	90.8	90.8	94.6
Specificity	98.1	98.1	98.1
Sensitivity	44.0	44.0	72.0

Note: Data are presented as odd ratios (95% confidence interval) unless otherwise stated.

DISCUSSION

The short-term mortality incidence reported from our study is 13.5%. This incidence rate is comparable to other studies that reported on the short-term mortality rate after a stroke in Malaysia, which ranged from 7.8% to 34% (Chen *et al.* 2019; Jaya *et al.* 2002; Ong and Raymond 2002). The reduction in stroke mortality rates has been observed to be consistent with the country's ongoing development of stroke care, according to statistics gathered by the Malaysian National Stroke Registry, which indicated that between 2009 and 2017, fewer stroke patients were discharged from hospitals with subpar clinical outcomes (Hwong *et al.* 2021; Chen *et al.* 2019).

The availability of acute thrombolysis management, as well as patients receiving treatment from a multidisciplinary stroke team in a stroke unit (Jeng *et al.* 2008), may have contributed to our site's moderate mortality rate. Recent studies, however, found no differences in survival between post-stroke patients treated in neurologists' and non-neurologists' centers. These studies suggested that the post-thrombolysis care and the overall thrombolysis service system were more crucial elements than the specialisations of the prescribers (Chew *et al.* 2021; Lee *et al.* 2015). Furthermore, thanks to the Angels Initiative's increased accessibility to thorough training in stroke assessment and thrombolysis, non-neurologists are now better prepared for urgent stroke interventions (Angels 2022).

Over the past two decades, the incidence and mortality rates of ischemic and hemorrhagic strokes have declined in high-income countries. In contrast, low- and middle-

income countries have experienced a 22% increase in hemorrhagic stroke incidence and a 6% rise in ischemic stroke incidence (Feigin *et al.* 2017). From this study, patients who had experienced hemorrhagic stroke had higher mortality rate of about 39% in contrast to patients with ischemic stroke. This figure is slightly higher than the previously reported mortality rates that ranged between 27.3%–36.8% (Basri and Ali 2003; Grover and Thiagarajah 2014). This could be a direct indicative on the rise of young hypertensive adults. Hypertension was the most prevalent comorbidity (> 70%) among our study subjects with a higher percentage of the patients belonged to the age category of ≤ 61 years.

According to Malaysia's National Health and Morbidity Survey (2006–2015), the prevalence of hypertension among those aged 60 and lower is higher (Ab Majid *et al.* 2018). While it was stated that awareness, treatment and control had improved over the previous 10 years in all age groups, it was evident that the improvements in those under 60 were relatively modest when compared with the older age group. (Hwong *et al.* 2021). Additionally, diabetes, hyperlipidemia and obesity were all on the rise in Malaysia. These risk factors have been linked to an increase in stroke incidence in people under the age of 65, with the largest increases of 53.3% and 50.4% in men and women (Tan and Venketasubramanian 2022), respectively, as reported in this study. The outcome of the risk factors in various ethnicities may be attributed to differences in metabolic, lifestyle or socioeconomic status (Demaerschalk *et al.* 2018; Bladin *et al.* 2020).

Hemorrhagic stroke type and recurrent stroke episodes were important predictive of mortality among post stroke patients from our study. It has been reported that patients who have had a hemorrhagic stroke have a poorer health outcome, which is often linked to mortality (Salvadori *et al.* 2020). Recurrent stroke episodes, on the other hand, have been identified as a strong independent factor that elevates mortality and functional dependency in stroke patients (Petty *et al.* 1998; Khanevski *et al.* 2019). Furthermore, Hwong *et al*. (2021) reported similar findings on the 3 days as the median time of hospitalisation post-stroke as reported in this study (Hwong *et al.* 2021). Cheah *et al*. (2016) reported that the mortality post-stroke occurred 8 days for ischemic stroke and 3.8 days for hemorrhagic stroke after admission (Cheah *et al.* 2016).

In this study, the most important predictors of post-stroke mortality were comorbidities heart disease, chronic kidney disease, pneumonia and acute kidney injury. Heart disease accounts for one-third of stroke patients and is the second most common cause of acute cerebrovascular events. Additionally, the most significant and changeable risk factors for cardioembolic stroke were atrial fibrillation and atrial flutter (Jørgensen *et al.* 1997). Also, cardiovascular disease has been identified as the leading cause of death in the chronic kidney disease (CKD) patient population, and decreased estimated glomerular filtration rate (eGFR) is linked to an increased risk of cardiovascular death (Wu *et al.* 2020). A potential cause for the high incidence of pneumonia among CKD patients could be due to their weakened immunity. Following a stroke, the risk of aspiration pneumonia may be elevated by physiological dependence and swallowing dysfunction. Pneumonia is a major stroke complication that can raise in-hospital mortality (Armstrong and Mosher 2011; Koennecke *et al.* 2011), especially in patients with severe disease and multiple comorbidities. From the developed mortality prediction model, the presence of heart disease, chronic kidney disease, pneumonia and acute kidney injury may further complicate the condition of stroke and contribute to the progression of the mortality. Model 3 demonstrates a precision of estimates with a specificity of 98.1% and a sensitivity of 72.0%.

This study was conducted at one center and may not represent the whole Malaysian population because hospital specialties and local population characteristics varies, but because it was conducted in a main stroke referral center for all tertiary healthcare institutions in Pulau Pinang thus this increases the generalisability of the study findings.

Also, longitudinal cohort studies are difficult to conduct because they are costly and time-consuming (Hwong *et al.* 2021).

CONCLUSION

In this study, mortality prediction model for stroke patients was developed using routinely available information in healthcare settings. The prediction model is hoped to help the rapid patient identification who are at a higher risk of mortality post-stroke. This allows for tailored treatment and enhances the chances of survival. This study is significant because it contributes to previously unreported data on risk factors that affect post-stroke mortality in the population of Pulau Pinang's mainland, Malaysian peninsula. We hope that by the early recognition of risk factors that affect mortality in patients with multiple comorbidities and polypharmacy, this study will assist healthcare professionals in cautions treatment of the stroke patients.

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DECLARATIONS

Ethics Approval and Consent to Participate

Ethical approval was obtained prior to the commencement of this study from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (MOH). Study approval number: NMRR-21-1851-61427. The need to obtain consent from study participants was waived as there is no direct interaction with the study participants in accordance with the MREC, MOH regulations. This study was performed in accordance with the Declaration of Helsinki and Malaysian Guideline for Good Clinical Practice.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and analysed during the current study are not publicly available due to data confidentiality policy as dictated in the study approval letter by the MREC, MOH but are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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