

Comparison among demographics, risk factors, clinical manifestations, and outcomes of stroke subtypes: Findings from a Malaysian stroke-ready hospital

¹Hong Chuan Loh *BPharm (Hons)*, ¹Kurubaran Ganasegeran *MBBS MScHR*, ¹Yi Fang Lim *MD*,
^{1,2}Irene Looi *MBBS FRCP*

¹Clinical Research Centre, ²Medical Department, Hospital Seberang Jaya, Ministry of Health, Penang, Malaysia

Abstract

Background and Objective: Distinguishing attributes of stroke subtypes is crucial to establish appropriate planning for patient care and preventive measures. This study aims to compare the associations among demographic characteristics, risk factors, clinical manifestations, and outcomes of different stroke subtypes in a Malaysian stroke-ready hospital. **Methods:** The study utilized data that were collected from the local hospital-based stroke database, which is part of the Perai Regional Integrated Stroke Intervention System. The database is representative of the population in mainland Penang. All confirmed local ischaemic stroke (IS) and haemorrhagic stroke (HS) cases aged 18 years and above admitted to Hospital Seberang Jaya from 1st January 2010 to 31st December 2019 were included. Descriptive and inferential statistics were employed. **Results:** There was a total of 1,805 patients with 1,572 (87.1%) IS patients and 233 (12.9%) HS patients. The mean (SD) age for IS patients was 62.75 (12.08) and 60.51 (13.65) for HS patients. Generally, there were more male than female patients: 957 (60.9%) male IS patients and 137 (58.8%) male HS patients. A significantly higher proportion of IS patients were aged ≥60 years old (59.9%, p=0.021), of Indian origin (15.5%, p=0.034), had diabetes (51.2%, p<0.001), hyperlipidaemia (17.8%, p<0.001), ischaemic heart disease (10.9%, p=0.011) and were smokers (54.2%, p=0.028) as compared to HS patients. The proportion of IS patients who exhibited hemiparesis (76.0%, p=0.012) and speech disturbances (54.8%, p=0.015) was higher than HS patients. Most IS patients ranged from no disability to moderate disability (65.3%, p<0.001) with a length of stay in the hospital of ≤ 7 days (77.6%, p<0.001).

Conclusion: Significant differences were observed on risk factors between IS and HS. IS was linked mainly with hemiparesis and speech disturbances, whereas HS patients mainly exhibited headaches, nausea and vomiting, altered sensorium, and seizures, in addition to more severe stroke and poor outcomes.

Keywords: Stroke, ischaemic, haemorrhagic, risk factors, clinical manifestations, outcomes

INTRODUCTION

Based on the Global Burden of Disease study in 2010, there were over 11 million ischaemic stroke (IS) and 5.3 million haemorrhagic stroke (HS) cases worldwide with 63% and 80% respectively occurring in low- and middle-income countries.^{1,2} According to the Acute Stroke Registry Malaysia 2010-2014, IS is the most common type of stroke and accounted for 79.4% of all stroke cases, followed by HS (18.2%).³ The unequal distribution of IS and HS makes comparisons between the two types of stroke difficult in terms of prognostic factors.

Identification of risk factors (RFs) is complex as stroke has different aetiologies and varieties. The INTERSTROKE study reported RFs such as waist-to-hip ratio, diabetes mellitus and a high apolipoprotein B/apolipoprotein A1 ratio were significantly associated with IS, whereas hypertension, cigarette smoking and physical activity levels showed higher significance in HS.⁴ Another study from Croatia concluded that atherosclerotic diseases and atrial fibrillation are more prevalent in IS patients than in HS patients.⁵ Clinical factors such as carotid atheroma, low high-density lipoprotein (HDL), and kidney

Address correspondence to: Dr. Kurubaran Ganasegeran, Clinical Research Centre, Hospital Seberang Jaya, Ministry of Health Malaysia, Jalan Tun Hussein Onn, Seberang Jaya, Penang, 13700, Malaysia. Tel: +604-3827333, email: medkuru@yahoo.com

Date of Submission: 17 August 2021; Date of Acceptance: 25 September 2021

<https://doi.org/10.54029/2022kdt>

disease were seen more commonly in IS than in HS.⁶ A systematic review that involved 4,387 stroke patients concluded that diabetes mellitus and acquired immunodeficiency syndrome conferred equal risk for both stroke subtypes and that hypertension was more prevalent in HS patients.⁷

While the computed tomography scan remains the most frequent technique used for distinguishing between IS and HS, it may not be available at all hospitals. Therefore, clinical manifestations may be the most important determinant for type of stroke, which is important in acute stroke care since early identification is critical to avoid complications and lasting disabilities.⁸ Many studies have documented numerous clinical manifestations, including neurological signs and symptoms. Some of them have proposed formulae that aid in differentiating the type of stroke through clinical evaluation. For instance, a study showed that in HS patients, dilated pupils, agitation, abrupt onset headache, seizure, etc., were all significantly more common than in IS patients who were more likely to experience a progressive headache.⁹

The type of stroke, the degree and length of blockage or bleeding, and the amount of brain tissue loss all influence the prognosis of stroke patients. Generally, HS has a worse prognosis than IS. As compared to IS, HS was usually associated with a greater risk of mortality, required a longer stay in both acute and rehabilitative hospitals, and had a more substantial initial clinical deficit with a higher number of neurological disorders as well as a poorer functional outcome upon admission.^{5,10}

Even though there have been epidemiological stroke studies globally, sometimes with mixed findings, there has been no research conducted locally in Malaysia to compare IS and HS patients. Such information is critical for planning and executing effective stroke management in health settings. The current study aims to compare the associations among demographic characteristics, RFs, clinical manifestations, and outcomes of different stroke subtypes in a Malaysian stroke-ready hospital.

METHODS

Study setting and recruitment

The Hospital Seberang Jaya (HSJ) is a cluster-lead tertiary healthcare institution situated in the Perai region of mainland Penang, Peninsular Malaysia. HSJ developed the Perai Regional Integrated Stroke Intervention System which

includes a protocol for rapid thrombolysis system management as well as a local hospital-based stroke database that is representative of the population for mainland Penang. That local stroke database at HSJ was developed by collecting relevant clinical and epidemiological information on hospitalized stroke patients from medical records. Starting in January 2010, all information entered into the database was verified by a stroke neurologist prior to entry.

All confirmed IS and HS cases of patients aged 18 years and above that were admitted to HSJ from 1st January 2010 to 31st December 2019 were included in the study. Cases of other stroke subtypes such as transient ischaemic attack, cerebral venous thrombosis, and unclassified stroke, as defined in the World Health Organization classification system, were excluded. Diagnosis of IS and HS was based on clinical assessments by a neurologist and confirmed by computed tomography or magnetic resonance imaging of the brain.

Ethics statement

This study was registered at the National Medical Research Register and approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR-20-1476-55732) and the Committee waived the need for patient consent.

Variables selection

Demographic characteristics of cases (sex, age, ethnicity, education level, marital status), selected RFs (hypertension, diabetes, hyperlipidaemia, ischaemic heart disease (IHD), atrial fibrillation, family history of stroke, smoking status, alcohol consumption, physical activity), clinical manifestations (headache, nausea and vomiting, vertigo or dizziness, altered sensorium, visual alteration, speech disturbances, hemiparesis, tetraparesis, monoparesis, seizure) and stroke outcomes (disability, stroke severity, length of hospital stay) were selected based on their relative importance in accordance with practice guidelines¹¹ and on the presence of adequate data for analyses. Hypertension was defined as a mean systolic blood pressure of ≥ 140 mmHg or a mean diastolic blood pressure of ≥ 90 mmHg in repeated measures, or use of antihypertensive medications, as documented in medical records.^{12,13} Diabetes was defined as a fasting plasma glucose level of 7 mmol/L (126 mg/dL) or above or being prescribed with oral hypoglycaemic agents or an insulin regimen, as documented in medical

records.^{12,14} Hyperlipidaemia was defined as total cholesterol greater than 5.2 mmol/L with high plasma triglyceride concentration (>1.7 mmol/L), low HDL cholesterol concentration (<1 mmol/L for male, <1.2 mmol/L for female), and increased concentration of low-density-lipoprotein cholesterol (>2.6 mmol/L with cardiac RFs) or currently on statins, as documented in medical records.^{12,15} IHD was defined as a self-reported physician diagnosis for angina pectoris or myocardial infarction, or with a history of angioplasty, stenting procedures or coronary artery bypass graft surgery.¹² Atrial fibrillation is defined as a self-reported physician diagnosis with abnormal electrocardiogram findings, history of anti-arrhythmic drugs or with anti-coagulant therapy, as documented in medical records.¹⁶ Smoking status was defined as a current smoker who smoked at least one cigarette in the past month.¹² Disability was measured upon discharge using the modified Rankin Scale (mRS) and categorized as no disability to moderate disability (score 0-3) and severe disability ultimately to death (score 4-6).¹⁷ The severity of stroke was measured upon admission using the National Institutes of Health Stroke Scale (NIHSS) and

categorized as no stroke to mild stroke (score 0-4), moderate stroke (score 5-15), moderate to severe stroke (score 16-20) and severe stroke (score 21-42).¹⁸ Length of hospital stay was dichotomized as ≤ 7 days or > 7 days based on cut-points used in previous literature.¹⁹

Statistical analyses

Analyses were performed using the Statistical Package of Social Sciences software, version 20. Descriptive statistics were employed for all variables in the study. Pearson chi-square (χ^2) was used to compare associations between categorical variables. P-values less than 0.05 ($P<0.05$) was considered statistically significant.

RESULTS

There was a total of 1,805 patients with 1,572 (87.1%) IS patients and 233 (12.9%) HS patients. The mean (SD) age for IS patients was 62.75 (12.08) years and 60.51 (13.65) years for HS patients. Generally, there were more male than female patients with 957 (60.9%) for IS patients and 137 (58.8%) for HS patients.

Table 1 shows sample characteristics of stroke

Table 1: Sample characteristics (n=1,805)

Characteristics	Total patients (n=1,805)	IS (n=1,572)	HS (n=233)	χ^2 p-value
Sex				0.544
Male, n (%)	1,094 (60.6)	957 (60.9)	137 (58.8)	
Female, n (%)	711 (39.4)	615 (39.1)	96 (41.2)	
Age (years)				0.021
Less than 60, n (%)	742 (41.1)	630 (40.1)	112 (48.1)	
60 or more, n (%)	1,063 (58.9)	942 (59.9)	121 (51.9)	
Ethnicity				0.034
Malay, n (%)	957 (53.0)	826 (52.5)	131 (56.2)	
Chinese, n (%)	584 (32.4)	503 (32.0)	81 (34.8)	
Indian, n (%)	264 (14.6)	243 (15.5)	21 (9.0)	
Education level				0.240
(n=485)				
None, n (%)	50 (10.3)	45 (10.6)	5 (8.5)	
Primary, n (%)	179 (36.9)	162 (38.0)	17 (28.8)	
Secondary, n (%)	234 (48.2)	202 (47.4)	32 (54.2)	
Tertiary, n (%)	22 (4.5)	17 (4.0)	5 (8.5)	
Marital status				0.759
(n=1,219)				
Married, n (%)	978 (80.2)	849 (80.1)	129 (81.1)	
Single, n (%)	241 (19.8)	211 (19.9)	30 (18.9)	

subtypes. A higher proportion of patients aged 60 years or more were afflicted with IS (n=942, 59.9%) as compared to the proportion of patients aged 60 years or more who were diagnosed with HS (n=121, 51.9%). The proportion of Malay and Chinese patients with IS was lower (n=826, 52.5%; n=503, 32.0%) as compared to the proportion of Malay and Chinese patients with HS (n=131, 56.2%; n=81, 34.8%). However, there were more Indian patients with IS than HS (n=243, 15.5%; n=21, 9.0%).

A significantly higher proportion of IS patients were smokers (54.2% vs 41.3%), had diabetes (51.2% vs 33.8%), hyperlipidaemia (17.8% vs 8.5%) and IHD (10.9% vs 5.4%) in comparison to HS patients, and these differences were statistically significant (Table 2).

Table 2: Risk factors of stroke subtypes (n=1,805)

Risk factors	Total patients (n=1,805)	IS (n=1,572)	HS (n=233)	χ^2 p-value
Hypertension (n=1,784)				0.263
Yes, n (%)	1,299 (72.8)	1,123 (72.4)	176 (75.9)	
No, n (%)	485 (27.2)	429 (27.6)	56 (24.1)	
Diabetes (n=1,750)				< 0.001
Yes, n (%)	857 (49.0)	781 (51.2)	76 (33.8)	
No, n (%)	893 (51.0)	744 (48.8)	149 (66.2)	
Hyperlipidaemia (n=1,731)				< 0.001
Yes, n (%)	287 (16.6)	268 (17.8)	19 (8.5)	
No, n (%)	1,444 (83.4)	1,239 (82.2)	205 (91.5)	
IHD (n=1,725)				0.011
Yes, n (%)	175 (10.1)	163 (10.9)	12 (5.4)	
No, n (%)	1,550 (89.9)	1,338 (89.1)	212 (94.6)	
Atrial fibrillation (n=1,720)				0.377
Yes, n (%)	46 (2.7)	42 (2.8)	4 (1.8)	
No, n (%)	1,674 (97.3)	1,454 (97.2)	220 (98.2)	
Family history of stroke (n=1,719)				0.920
Yes, n (%)	40 (2.3)	35 (2.3)	5 (2.2)	
No, n (%)	1,679 (97.7)	1,460 (97.7)	219 (97.8)	
Smoking status (n=781)				0.028
Yes, n (%)	413 (52.9)	380 (54.2)	33 (41.3)	
No, n (%)	368 (47.1)	321 (45.8)	47 (58.7)	
Alcohol consumption (n=1,721)				0.186
Yes, n (%)	46 (2.7)	37 (2.5)	9 (4.0)	
No, n (%)	1,675 (97.3)	1,459 (97.5)	216 (96.0)	
Physical activity (n=1,719)				0.161
Yes, n (%)	26 (1.5)	25 (1.7)	1 (0.4)	
No, n (%)	1,693 (98.5)	1,470 (98.3)	223 (99.6)	

Table 3 shows the differences between clinical manifestations of stroke subtypes. A significantly lower proportion of IS patients had headaches (13.5% vs 34.3%), nausea and vomiting (11.1% vs 30.2%), altered sensorium (13.1% vs 21.0%) and seizures (1.5% vs 5.5%) as compared to HS patients. A higher proportion of IS patients had speech disturbances (54.8% vs 46.1%) and hemiparesis (76.0% vs 68.1%) in comparison to HS patients, and these differences were statistically significant.

Table 4 shows the differences between patient outcomes and stroke subtypes. A higher proportion of IS patients had no to moderate disability (65.3% vs 37.1%), mild severity (56.3% vs 30.6%), and a length of hospital stay of ≤ 7 days (77.6% vs

Table 3: Clinical manifestations of stroke subtypes (n=1,805)

Clinical manifestations	Total patients (n=1,805)	IS (n=1,572)	HS (n=233)	χ^2 p-value
Headache (n=1,716)				< 0.001
Yes, n (%)	275 (16.0)	203 (13.5)	72 (34.3)	
No, n (%)	1,441 (84.0)	1,303 (86.5)	138 (65.7)	
Nausea and vomiting (n=1,727)				< 0.001
Yes, n (%)	232 (13.4)	168 (11.1)	64 (30.2)	
No, n (%)	1,495 (86.6)	1,347 (88.9)	148 (69.8)	
Vertigo or dizziness (n=1,715)				0.060
Yes, n (%)	417 (24.3)	355 (23.6)	62 (29.5)	
No, n (%)	1,298 (75.7)	1,150 (76.4)	148 (70.5)	
Altered sensorium (n=1,703)				0.002
Yes, n (%)	239 (14.0)	195 (13.1)	44 (21.0)	
No, n (%)	1,464 (86.0)	1,298 (86.9)	166 (79.0)	
Visual alteration (n=1,702)				0.444
Yes, n (%)	112 (6.6)	101 (6.8)	11 (5.3)	
No, n (%)	1,590 (93.4)	1,395 (93.2)	195 (94.7)	
Speech disturbances (n=1,743)				0.015
Yes, n (%)	937 (53.8)	837 (54.8)	100 (46.1)	
No, n (%)	806 (46.2)	689 (45.2)	117 (53.9)	
Hemiparesis (n=1,742)				0.012
Yes, n (%)	1,307 (75.0)	1,162 (76.0)	145 (68.1)	
No, n (%)	435 (25.0)	367 (24.0)	68 (31.9)	
Tetraparesis (n=1,646)				0.551
Yes, n (%)	32 (1.9)	27 (1.9)	5 (2.5)	
No, n (%)	1,614 (98.1)	1,418 (98.1)	196 (97.5)	
Monoparesis (n=1,637)				0.283
Yes, n (%)	33 (2.0)	31 (2.2)	2 (1.0)	
No, n (%)	1,604 (98.0)	1,408 (97.8)	196 (99.0)	
Seizure (n=1,352)				0.001
Yes, n (%)	27 (2.0)	18 (1.5)	9 (5.5)	
No, n (%)	1,325 (98.0)	1,171 (98.5)	154 (94.5)	

59.7%) in comparison to HS patients. These differences were statistically significant.

DISCUSSION

Overall, there were more male than female patients in both IS and HS cases. When comparing IS patients to HS patients, more IS patients were older (aged ≥ 60), of Indian origin, had diabetes, hyperlipidaemia, IHD and were smokers. There were also more IS patients with hemiparesis, speech disturbances, and milder disabilities with

a shorter length of stay in the hospital than HS patients.

In this study, we found that there were more IS (87.1%) cases than HS (12.9%) cases, consistent with a local study and the Acute Stroke Registry Malaysia 2010-2014.^{3,18} Stroke afflicted predominantly males (60.6%), however, there were no disparities of stroke subtypes between sexes. Based on the estimated major disease burden (1990-2016), the global lifetime risk of stroke for both males and females was similar.²⁰

Table 4: Outcomes of stroke subtypes (n=1,805)

Clinical manifestations	Total patients (n=1,805)	IS (n=1,572)	HS (n=233)	χ^2 p-value
Disability (n=1,625)				<0.001
No to moderate disability, n (%)	1,006 (61.9)	934 (65.3)	72 (37.1)	
Severe disability to death, n (%)	619 (38.1)	497 (34.7)	122 (62.9)	
Stroke severity (n=1,573)				<0.001
None to mild stroke, n (%)	848 (53.9)	803 (56.3)	45 (30.6)	
Moderate stroke, n (%)	543 (34.5)	480 (33.7)	63 (42.9)	
Moderate to severe stroke, n (%)	84 (5.3)	66 (4.6)	18 (12.2)	
Severe stroke, n (%)	98 (6.2)	77 (5.4)	21 (14.3)	
Length of hospital stay				<0.001
≤ 7 days, n (%)	1,359 (75.3)	1,220 (77.6)	139 (59.7)	
> 7 days, n (%)	446 (24.7)	352 (22.4)	94 (40.3)	

There was a significantly higher proportion of IS patients aged above 60 years old than patients with HS. This finding was in line with a study that showed advanced age to be significantly associated with IS patients.⁶ Due to the long-term effects of advancing age on cardiovascular and cerebrovascular systems, as well as the gradual existence of stroke RFs over time, the risk of IS increases significantly over time. Therefore, it is paramount to pay extra attention to geriatric patients. We found that Malays and Chinese had a greater susceptibility to HS, while Indians were more likely to suffer from IS. Similar ethnic distribution of stroke subtypes was demonstrated in a study conducted in Singapore.²¹ While the findings can be due to disparities in the metabolic, lifestyle, or socioeconomic status of different ethnic groups, differences in stroke outcomes among different ethnic groups have also been reported in other studies.^{22,23} Previous study indicated that a higher level of education was linked to a lower risk of total and IS incidents, but not HS incidents.²⁴ Nevertheless, our study showed no disparities between IS and HS in terms of educational levels. We also found that marital status was not associated with IS and HS and the finding aligned with a study conducted at Northeast Ethiopia.²⁵

Our study indicated that IS patients had a higher prevalence of vascular RFs such as diabetes, hyperlipidaemia, and IHD as opposed to HS patients. In the general population, hypertension is one of the most significant RF for stroke, and the risk of stroke rises linearly as blood pressure rises above 115/75 mmHg.²⁶ The proportion of patients with IS (72.4%) and HS (75.9%) with hypertension was about the same in our

study. Proper management of blood pressure is crucial as population attributable risk (PAR) for hypertension was 29.9%.²⁷ Since a blood pressure target level in the event of an acute IS remains debatable²⁸, future studies are recommended to determine what level of blood pressure will result in the best possible clinical outcomes.

The second most prevalent RF after hypertension was diabetes, consistent with a previous study.²⁹ Nearly half of our IS patients had diabetes (51.2%) as compared to one-third of HS patients. The proportion was generally higher than in other Asian countries but second highest to Kuwait (65.0%).³⁰ The Framingham study discovered that diabetes patients had a 2.5 to 3.5 times higher rate of IS than non-diabetic patients aged 45 to 74 years old,³¹ whereas diabetes was found to have a negative link with HS in the University of Iowa-Cooperative Aneurysm Study.³² Diabetes was not only linked to a higher incidence of IS, but also to a change in the clinical presentations and outcomes.³³ The cut-off value for IS patients with diabetes was 210.5 mg/dl, while the cut-off value for individuals with IS without diabetes was 113.5 mg/dl.³⁴ Diabetes was also associated with a higher incidence of IS especially among the younger aged patients and those with other co-morbid conditions, as opposed to those without diabetes³⁵ with a PAR of nearly 20%.²⁷ Nevertheless, a study showed that 5% to 28% of people have undetected diabetes or reduced glucose tolerance.³⁶

Hyperlipidaemia and IHD showed significant differences between stroke subtypes. The proportion of IS patients with hyperlipidaemia (17.8%) and IHD (10.9%) was low compared to those with hypertension and diabetes and the

same was true among populations in neighbouring countries like Japan (56.6%; 13.9%)³⁷, Singapore (98.1%; 23.3%)³⁸, and Taiwan (43.2%; 13.4%).³⁹ Due to the causative role of hyperlipidaemia in small-vessel disease, it increases the risk of IS substantially.⁴⁰ IS patients had higher hypercholesterolemia and lower HDL-cholesterol levels than HS patients.⁴¹ The Heart Protection Study showed that treatment with statins in patients with other vascular illnesses was linked to a lower incidence of IS.⁴² As a preventive measure, hyperlipidaemia screening and lipid-lowering medication are indicated for high-risk IS patients. However, there was a reverse epidemiological association between lipid levels and stroke outcomes, in which high lipid profiles at IS onset during admission were linked with better short-term functional outcome.⁴³ Future research on the temporal profile of this relationship is required.

It is established that IHD and IS shared many comparable RFs and aspects of pathophysiology, particularly with arteriosclerosis. Nevertheless, there is a discrepancy among them on the frequency and intensity of the RFs involved.⁴⁴ IHD is one of the leading causes of mortality after IS.⁴⁵ A longitudinal study showed that individuals with lower long interspersed nucleotide element-1 methylation in blood were at higher risk of IHD and stroke events, contributing to its overall mortality.⁴⁶ IHD does not cause signs and symptoms until an artery is severely narrowed or blocked completely. As many are only aware of the disorder when they arrive at a medical emergency, IHD screening and subsequent diagnosis during subclinical stages of the disease are crucial to ensure sufficient treatment (medical treatment or coronary revascularization) being provided to enhance the prognosis.⁴⁷

We also explored the differences between lifestyle RFs and stroke subtypes. A significantly higher proportion of IS patients were smokers (54.2% vs 41.3%), consistent with previous studies. The Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Disease demonstrated cigarette smokers have a 1.66 higher risk to suffer from IS.⁴⁸ Smoking was independently associated with silent brain infarcts in first-ever IS patients⁴⁹ with 8.1% being attributed to IS in the German population.⁵⁰ A Korean study observed a decrease of smoking PAR with age in both sexes with 45.1% and 5.9% in young males and females respectively, 37.4% and 7.7% in middle-aged males and females respectively, as well as 16.7% in elderly males.¹² Knowing that approximately five million

Malaysians aged 15 years and above (22.8%) are current smokers,⁵¹ it is not surprising that the IS diagnosis of more than half of our IS patients may be attributable to smoking. Nevertheless, the number of smokers was determined solely based on patient or caretaker interviews and might underestimate the number of smokers. There were no urine tests for nicotine or salivary tests for cotinine to detect cigarette smoking and tobacco use.

The symptoms of a stroke vary depending on which part of the brain was impacted and the quantity of tissue that was damaged. In this study, IS patients had more hemiparesis (76.0%) and speech disturbances (54.8%). These two clinical manifestations were the most common presenting signs and symptoms of IS⁵² and they are also included among the stroke warning signs ("F.A.S.T." - Facial drooping, Arm weakness, Speech difficulties, and Time) that aid in detecting and improving responsiveness to the needs of stroke patients. Because "time is brain," the general public's ability to recognize stroke symptoms is critical and it is important to develop educational techniques in order to provide health education to the community. A study conducted in Malaysia during a blood pressure screening programme found that overall knowledge about stroke was good among the general public throughout the country.⁵³ On the other hand, HS patients in our study had more headaches (34.3%), nausea and vomiting (30.2%), altered sensorium (21.0%), and seizures (5.5%). Headaches, nausea and vomiting, as well as seizures, are the most prevalent symptoms of HS.^{54,55} Still, headache in HS is usually acute at onset, while a gradual, progressive headache is more common in IS.⁵⁶ In contrast to our finding, altered sensorium was predominantly observed in IS.⁵⁷⁻⁵⁹ For individuals with stroke, brain imaging is still the gold standard diagnostic approach. Clinical manifestations, alternatively, are useful for identifying stroke subtypes and assisting physicians to make primary diagnoses in small district hospitals and centres where imaging facilities are not available. These findings may be useful to improve patient care, treatment, and timely referral to a more comprehensive stroke centre.⁵⁶

When we looked at stroke outcomes based on mRS, NIHSS, and length of hospital stay, HS patients had more severe outcomes, being associated with higher fatalities as compared to IS patients. Previous studies showed similar results.^{60,61} Stroke is one of the primary causes

of morbidity and mortality in Malaysia, as it is in many other countries. With the growing proportion of elderly in the population and recent advancements in stroke prevention and treatment, the epidemiology of stroke is changing with time.⁶² Therefore, knowing the disproportions between stroke severity and outcomes between IS and HS is important. This is because predicting stroke morbidity and mortality risks can help physicians to make a prognosis objectively, prioritise care to patients at risk, counsel patients and families about end-of-life options, and determine whether stroke fatality numbers are similar to expectations based on different patients with stroke.⁶³

There were several limitations to this study. The accuracy and completeness of medical records documentation are critical to study data; nevertheless, data verification enhances data reliability. Stroke patients usually have more than one RF. In this study, we only presented the result by looking at each RF independently. We realise that in reality, there may be other confounding effects that can affect the results and hence, future studies are suggested to investigate such relationships. Post-discharge stroke information was not presented in this study as data were missing. For example, sometimes patients are discharged to other facilities. Thus, we are not able to provide more comprehensive data on the differences in stroke outcomes between IS and HS at different post-discharge time points. We did not include variables such as employment status and acquired immunodeficiency syndrome since they are either not common among our stroke population or information about those factors is not widely available in the medical records. However, if such information can be obtained for a future study, it might provide a better understanding of stroke management as a whole.

In conclusion, our findings suggest two non-modifiable RFs (age and ethnicity), three vascular RFs (diabetes, hyperlipidaemia, and IHD), and one lifestyle RF (smoking) were associated with significant differences between IS and HS. In addition, IS was linked mainly with hemiparesis and speech disturbances, while HS was associated with higher proportions of patients with headaches, nausea and vomiting, altered sensorium, and seizures, in addition to more severe stroke and poorer outcomes. Public health campaigns like prevention programs at the hospital and community levels that promote physical activity, healthy diet, and lifestyle changes can lead to a greater reduction in the burden of stroke. We propose a nationwide study to identify the

disparities of stroke clinical manifestations and outcomes between IS and HS in order to better understand the epidemiology of stroke and to improve current stroke management.

Financial support: None

Conflict of interest: None

REFERENCES

1. Bennett DA, Krishnamurthi RV, Barker-Collo S, et al. The global burden of ischemic stroke: findings of the GBD 2010 study. *Global Heart* 2014;9:107-12.
2. Krishnamurthi RV, Moran AE, Forouzanfar MH, et al. The global burden of hemorrhagic stroke: a summary of findings from the GBD 2010 study. *Global Heart* 2014;9:101-6.
3. Aziz ZA, Lee YY, Ngah BA, et al. Acute stroke registry Malaysia, 2010-2014: Results from the national neurology registry. *J Stroke Cerebrovasc Dis* 2015;24:2701-9.
4. O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet* 2016;388:761-75.
5. Bilić I, Dzamonja G, Lusić I, Matijaca M, Caljkusić K. Risk factors and outcome differences between ischemic and hemorrhagic stroke. *Acta Clinica Croatica* 2009;48:399-403.
6. Zhang J, Wang Y, Wang G-N, et al. Clinical factors in patients with ischemic versus hemorrhagic stroke in East China. *World J Emerg Med* 2011;2:18-23.
7. Namale G, Kamacooko O, Kinengyere A, et al. Risk Factors for hemorrhagic and ischemic stroke in Sub-Saharan Africa. *J Trop Med* 2018;2018:4650851.
8. Tintinalli JE, Stapeczynski JS, Ma OJ, Cline D, Meckler GD, Yealy DM. Tintinalli's emergency medicine: a comprehensive study guide: McGraw-Hill Education New York, 2016.
9. Ojaghaghighi S, Vahdati SS, Mikaeilpour A, Ramouz A. Comparison of neurological clinical manifestation in patients with hemorrhagic and ischemic stroke. *World J Emerg Med* 2017;8:34-8.
10. Salvadori E, Papi G, Insalata G, et al. Comparison between ischemic and hemorrhagic strokes in functional outcome at discharge from an intensive rehabilitation hospital. *Diagnostics* (Basel, Switzerland) 2020;11.
11. Ministry of Health Malaysia. Clinical practice guidelines. Management of ischaemic stroke. 2012.
12. Park TH, Ko Y, Lee SJ, et al. Identifying target risk factors using population attributable risks of ischemic stroke by age and sex. *J Stroke* 2015;17:302-11.
13. Ministry of Health Malaysia. Clinical practice guidelines. Management of hypertension. 2018.
14. Ministry of Health Malaysia. Clinical practice guidelines. Management of type 2 diabetes mellitus. 2015.
15. Ministry of Health Malaysia. Clinical practice guidelines. Management of dyslipidaemia. 2017.

16. Ministry of Health Malaysia. Clinical practice guidelines. Management of atrial fibrillation. 2012.
17. Hommel M, Cornu C, Boutitie F, Boissel JP. Thrombolytic therapy with streptokinase in acute ischemic stroke. *N Engl J Med* 1996;335:145-50.
18. Loh HC, Nazri N, Ganasegeran K, Aziz ZA, Looi I. Socio-demographics and clinical characteristics affecting pre-hospital delays in acute stroke patients: A 6-year registry study from a Malaysian stroke hospital. *Neurol Asia* 2020;25.
19. Zhu HF, Newcommon NN, Cooper ME, et al. Impact of a stroke unit on length of hospital stay and in-hospital case fatality. *Stroke* 2009;40:18-23.
20. Carcel C, Woodward M, Wang X, Bushnell C, Sandset EC. Sex matters in stroke: A review of recent evidence on the differences between women and men. *Front Neuroendocrinol* 2020;59:100870.
21. Sun Y, Lee SH, Heng BH, Chin VS. 5-year survival and rehospitalization due to stroke recurrence among patients with hemorrhagic or ischemic strokes in Singapore. *BMC Neurol* 2013;13:133.
22. Cushman M, Cantrell RA, McClure LA, et al. Estimated 10-year stroke risk by region and race in the United States. *Ann Neurol* 2008;64:507-13.
23. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke epidemiology in South, East, and South-East Asia: A Review. *J Stroke* 2017;19:286-94.
24. Wu XY, Wu Q, Xie MJ, Li WD, Liao LZ. Education and stroke: evidence from epidemiology and Mendelian randomization study. *Sci Rep* 2020;10:21208.
25. Abdu H, Tadese F, Seyoum G. Comparison of ischemic and hemorrhagic stroke in the medical ward of Dessie Referral Hospital, Northeast Ethiopia: A retrospective study. *Neurol Res Int* 2021;2021:9996958.
26. Lewington S. Prospective studies collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903-13.
27. Willey JZ, Moon YP, Kahn E, et al. Population attributable risks of hypertension and diabetes for cardiovascular disease and stroke in the northern Manhattan study. *J Am Heart Assoc* 2014;3:e001106-e001106.
28. Dubow J, Fink ME. Impact of hypertension on stroke. *Curr Atheroscler Rep* 2011;13:298-305.
29. Mortel KF, Meyer JS, Sims PA, McClintic K. Diabetes mellitus as a risk factor for stroke. *South Med J* 1990;83:904-11.
30. Al-Hashel JY, Al-Sabah AA, Ahmed SF, et al. Risk factors, subtypes, and outcome of ischemic stroke in Kuwait: A national study. *J Stroke Cerebrov Dis* 2016;25:2145-52.
31. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA* 1979;241:2035-8.
32. Adams HP, Jr., Putman SF, Kassell NF, Torner JC. Prevalence of diabetes mellitus among patients with subarachnoid hemorrhage. *Arch Neurol* 1984;41:1033-5.
33. Papatheodorou K, Banach M, Edmonds M, Papanas N, Papazoglou D. Complications of diabetes. *J Diabetes Res* 2015;2015:189525.
34. Snarska KK, Bachórzewska-Gajewska H, Kapica-Topczewska K, et al. Hyperglycemia and diabetes have different impacts on outcome of ischemic and hemorrhagic stroke. *Arch Med Sci* 2017;13:100-8.
35. Kissela BM, Khouri J, Kleindorfer D, et al. Epidemiology of ischemic stroke in patients with diabetes. *Diabetes Care* 2005;28:355.
36. Ntaios G, Egli M, Faouzi M, Michel P. J-shaped association between serum glucose and functional outcome in acute ischemic stroke. *Stroke* 2010;41:2366-70.
37. Matsuo R, Ago T, Kiyuna F, et al. Smoking status and functional outcomes after acute ischemic stroke. *Stroke* 2020;51:846-52.
38. Yeo SH, Toh M, Lee SH, Seet RCS, Wong LY, Yau WP. Impact of medication nonadherence on stroke recurrence and mortality in patients after first-ever ischemic stroke: Insights from registry data in Singapore. *Pharmacoepidemiol Drug Saf* 2020;29:538-49.
39. Tang SC, Yin JH, Liu CH, et al. Low pulse pressure after acute ischemic stroke is associated with unfavorable outcomes: The Taiwan Stroke Registry. *J Am Heart Assoc* 2017;6:e005113.
40. Kraft P, Schuhmann MK, Garz C, et al. Hypercholesterolemia induced cerebral small vessel disease. *PLoS One* 2017; 12(8): e0182822.
41. Khan MN, Khan HD, Ahmad M, Umar M. Serum total and HDL-cholesterol in ischemic and hemorrhagic stroke. *Ann Pak Inst Med Sci* 2014;10:22-6.
42. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.
43. Tuttolomondo A, Di Raimondo D, Di Sciacca R, et al. Effects of clinical and laboratory variables at admission and of in-hospital treatment with cardiovascular drugs on short term prognosis of ischemic stroke. The GIFA study. *Nutr Metab Cardiovasc Dis* 2013;23:642-9.
44. Soler EP, Ruiz VC. Epidemiology and risk factors of cerebral ischemia and ischemic heart diseases: similarities and differences. *Curr Cardiol Rev* 2010;6:138-49.
45. Hankey GJ. Long-term outcome after ischaemic stroke/transient ischaemic attack. *Cerebrovasc Dis* 2003;16 (Suppl 1):14-9.
46. Baccarelli A, Wright R, Bollati V, et al. Ischemic heart disease and stroke in relation to blood DNA methylation. *Epidemiology* 2010;21:819-28.
47. Greenland P, Gaziano JM. Clinical practice. Selecting asymptomatic patients for coronary computed tomography or electrocardiographic exercise testing. *N Engl J Med* 2003;349:465-73.
48. Mannami T, Iso H, Baba S, et al. Cigarette smoking and risk of stroke and its subtypes among middle-aged Japanese men and women: the JPHC Study Cohort I. *Stroke* 2004;35:1248-53.
49. Putala J, Kurkinen M, Tarvos V, Salonen O, Kaste M, Tatlisumak T. Silent brain infarcts and leukoaraiosis in young adults with first-ever ischemic stroke. *Neurology* 2009;72:1823-9.

50. Weikert C, Berger K, Heidemann C, *et al.* Joint effects of risk factors for stroke and transient ischemic attack in a German population: the EPIC Potsdam Study. *J Neurol* 2007;254:315-321.
51. Lim KH, Teh CH, Pan S, *et al.* Prevalence and factors associated with smoking among adults in Malaysia: Findings from the National Health and Morbidity Survey (NHMS) 2015. *Tob Induc Dis* 2018;16:01-01.
52. Nor AM, Davis J, Sen B, *et al.* The Recognition of Stroke in the Emergency Room (ROSIER) scale: development and validation of a stroke recognition instrument. *The Lancet Neurology* 2005;4:727-734.
53. Ching S, Chia YC, Chew BN, *et al.* Knowledge on the action to be taken and recognition of symptoms of stroke in a community: findings from the May Measurement Month 2017 blood pressure screening Programme in Malaysia. *BMC Public Health* 2019;19:1602.
54. Connolly ES, Jr., Rabinstein AA, Carhuapoma JR, *et al.* Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/american Stroke Association. *Stroke* 2012;43:1711-1737.
55. Moore SA, Rabinstein AA, Stewart MW, David Freeman W. Recognizing the signs and symptoms of aneurysmal subarachnoid hemorrhage. *Expert review of neurotherapeutics* 2014;14:757-768.
56. Ojaghaghaghī S, Vahdati SS, Mikaeilpour A, Ramouz A. Comparison of neurological clinical manifestation in patients with hemorrhagic and ischemic stroke. *World J Emerg Med* 2017;8:34-38.
57. Qari FA. Profile of stroke in a teaching university hospital in the western region. *Saudi medical journal* 2000;21:1030-1033.
58. Siddique MAN, Nur Z, Mahbub MS, Alam MB, Miah MT. Clinical presentation and epidemiology of stroke: a study of 100 cases. *Journal of Medicine* 2009;10:86-89.
59. Omkar Prasad B, Susmita C, Ksh Gomti D. Clinico-epidemiological study of acute ischemic stroke in a tertiary hospital of northeastern state of India. *Int J Biomed Adv Res* 2013;4:9.
60. Wei JW, Heeley EL, Wang J-G, *et al.* Comparison of Recovery Patterns and Prognostic Indicators for Ischemic and Hemorrhagic Stroke in China. *Stroke* 2010;41:1877-1883.
61. Huang WY, Chang CW, Chen CM, *et al.* Characteristics of ischemic stroke and intracranial hemorrhage in patients with nephrotic syndrome. *BMC nephrology* 2021;22:213.
62. Kadojić D, Dikanović M, Bitunjac M, Vuletić V, Čengić L, Rostohar Bijelić B. Epidemiology of stroke. *Periodicum biologorum* 2012;114:253-257.
63. Smith EE, Shobha N, Dai D, *et al.* A Risk Score for In- Hospital Death in Patients Admitted With Ischemic or Hemorrhagic Stroke. *J Am Heart Assoc* 2013;2:e005207.