Clinical Features and Outcomes of Ischemic Stroke among Young Filipino Adults

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ABSTRACT

Background and Objective. The incidence of ischemic stroke typically increases with age; however, recent studies have shown a concerning trend of stroke cases among adults under the age of 45. This neurologic condition is called "Stroke in the Young" (SITY). SITY poses public health concerns due to its long-term consequences on individuals and their families. Despite significant impact, published literature on SITY among Filipinos is scarce. Given the potential differences in genetic background and lifestyle, the clinical characteristics and outcomes of SITY Filipinos may vary considerably from other populations. Therefore, the aim of this study is to describe the clinical features and outcomes of ischemic SITY Filipinos.

Methods. The study was a two-center, five-year retrospective cohort design involving 19- to 45-year-old patients admitted between January 1, 2017, and December 31, 2022, diagnosed clinically and radiologically with ischemic stroke for the first time. Medical records were reviewed, including demographic data, stroke symptoms, cardiovascular or non-cardiovascular risk factors, and laboratory results. Ischemic stroke subtypes were categorized into cardioembolic, small artery occlusion, stroke of other determined causes, and stroke of undetermined cause through the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification. Functional outcomes on hospital discharge were assessed by the Modified Rankin Scale (mRS). All data were analyzed using descriptive statistics in the Statistical Package for the Social Sciences (SPSS software, version 29).

Results. A total of 205 cases of ischemic SITY were chart reviewed. The mean age was 37.30, with a female predominance of 68.3%. The most reported cardiovascular risk factors were obesity (56.6%), hypertension (51.2%), heavy alcohol consumption (36.5%), and diabetes mellitus type 2 (19.5%). Concurrently, the non-cardiovascular risk factors identified were pregnancy, particularly in the postpartum period (4.8%), use of estrogen-containing pills (4.8%), and migraine without aura (4.4%). Based on TOAST classification, small vessel occlusion (42.1%) and large artery atherosclerosis (30.2%) were the most frequent ischemic stroke subtypes of SITY Filipino females.

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Mostly showed no symptoms of disability (35.1%) on hospital discharge.

Conclusion. This study highlights the difference in the clinical profile of young Filipino adults with ischemic stroke. Contrary to previous studies, ischemic stroke was more predominant among young females. Aside from hypertension, obesity has emerged as the leading cardiovascular risk factor for ischemic SITY. Moreover, non-cardiovascular risk factors, specific to females (pregnancy, use of estrogen-containing pills, and migraine), were also identified in the study. With regards to stroke subtypes, small vessel occlusion and large artery atherosclerosis were frequently seen in young female patients. These findings suggest a need for gender-specific approaches in the evaluation, management, and prevention of ischemic SITY.

Keywords: ischemic stroke, stroke in the young, cardiovascular, non-cardiovascular risk factors, Filipinos

INTRODUCTION

In 1970, the World Health Organization (WHO) defined stroke as rapidly developing clinical signs of focal or global cerebral dysfunction lasting 24 hours or longer, with no apparent cause other than vascular in origin.[1] The pathologic background of stroke may be ischemic or hemorrhagic disturbances of cerebral circulation. To date, almost 12 million new strokes and 7 million deaths from stroke are annually recorded worldwide.[2] According to the Global Burden of Disease (GBD) Study 2021, stroke is the second most common cause of mortality and the third leading cause of morbidity among non-communicable diseases. More specifically, ischemic stroke accounts for 65.3% of stroke cases, with high incidence in individuals aged more than 65.[3,4] While advanced age is a well-known risk factor for ischemic stroke, approximately 5.5% occur in individuals aged less than 45 years.[5] When this condition occurs, it is called ischemic stroke in the young (SITY). The age cut-offs for ischemic SITY vary across studies. Admittedly, there is no specific definition of term and unified age limit for SITY.[6] Some studies from Greece and Pakistan define SITY within 15 to 45 years of age, while studies from India and Philippines consider SITY at ages 19 to 45.[7-10]

SITY has been a public health concern due to its increasing trend and long-term consequences for patients and their families.[11,12] In 2021, the global incidence and prevalence of stroke cases among young adults is 44.63 per 100,000 and 514.58 per 100,000, respectively. Both incidence and prevalence of stroke in this age population increased significantly by 36% and 41% from years 1990 to 2021. Regional data showed that the highest incidence and prevalence rates are in Central Asia and Southeast Asia, with hypertension as the known primary risk factor.[13]

The long-term consequences of ischemic SITY, which placed substantial burden on patients and their families, included worsening disability, post-stroke fatigue and depression, caregiver burden, disruption of relationships with spouse, other family members, and friends, and not returning to work.[5,14-16] Despite this significant impact, published literature on SITY remains scarce in our locality.[10]

In the Philippines, the reported incidence and prevalence of stroke in the general population are at 5.61% and 6%, respectively.[17] The prevalence of SITY among Filipinos has not been recorded due to the paucity of local data. SITY among Filipinos tends to occur younger than 10 years ago (mean age 37.9 versus 41.8).[18] Local studies have shown that there is a higher frequency of SITY in males compared to females.[18-20] The common risk factors include hypertension, smoking, and heavy alcohol consumption. Notably, ischemic stroke is the most common type of stroke, accounting for 69% of the cases, with underlying etiologies of small vessel occlusion and large artery atherosclerosis.[18] Identifying the risk factors and etiologies of ischemic SITY is essential in the management and future prevention of the disease. The Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification is the most widely used valuable tool for recognizing risk factors and pathogenesis of ischemic stroke among young adults.[9,21-24] By incorporating clinical features and diagnostic findings from neuroimaging, echocardiography, neurosonography, and cerebral angiography, the TOAST classification categorizes ischemic stroke into five subtypes: large artery atherosclerosis, cardioembolic, small artery occlusion, stroke of other determined causes, and stroke of undetermined cause.

The large artery atherosclerosis subtype is characterized by clinical and neuroimaging findings of significant (>50%) stenosis or occlusion of a major brain artery or its branches. Clinical findings may include cortical impairment, brainstem, or cerebellar dysfunction. The neuroimaging results may show cortical, brainstem, or cerebellar infarcts of greater than 1.5 cm in diameter on a computed tomography (CT) scan or magnetic resonance imaging (MRI). Large artery atherosclerosis can be supported by evidence of >50% intracranial and extracranial stenosis on arteriography or duplex scan. In this stroke subtype, potential source of cardioembolism must be excluded. For cardioembolic subtype of ischemic stroke, the definition involves at least one cardiac source of embolus, including cardiac dysrhythmia, myocardial infarction, cardiomyopathy, valvular heart disease, patent foramen ovale, and infective or nonbacterial thrombotic endocarditis. Clinical and brain imaging findings are similar to large artery atherosclerosis. The small-artery occlusion subtype may involve patients with lacunar syndromes, with normal neuroimaging results or less than 1.5 cm diameter of subcortical and brainstem lesions on CT and MRI. Patients within this subtype may either have a history of diabetes mellitus or hypertension. Stroke of other determined etiology has a rare cause of ischemic stroke, including nonatherosclerotic vasculopathy, hypercoagulable

states, and hematologic disorders. Patients in this category have clinical and brain imaging findings of ischemic stroke, regardless of size and location. Lastly, a stroke of undetermined cause, otherwise known as the cryptogenic subtype, refers to a stroke with no etiology despite extensive work-up, no identifiable cause due to incomplete evaluation, and two or more potential causes of stroke.[25] There are variations in ischemic stroke subtypes across regions. In the United States of America (USA), the cryptogenic subtype is the most common etiology of ischemic stroke.[26] While cardioembolic subtypes of stroke are more prevalent among young adults in Europe.[27] Large artery atherosclerosis and small vessel occlusion subtypes are common among Asians.[20,28,29]

Regarding outcome evaluation, the Modified Rankin Scale (mRS) and Barthel Index (BI) are considered the most prevalent and reliable measures of functional recovery after a stroke.[30] mRS consists of a 6-point grading scale (0 to 6) that describes the patient's independence in global activities. At higher grades (mRS ≥3), mRS emphasizes the need for help or caregiver assistance.[31] Most studies of SITY used the mRS to assess functional outcomes at hospital discharge. In general, the functional outcome of SITY patients at discharge is favorable, with mRS scores ranging from 0 (no symptoms) to 2 (slight disability).[19,24,32,33] Additionally, between 1.1% and 3.9% have mRS score of 6 (mortality).[5,19] BI is a 10-item scale that measures a patient's performance of activities in daily living (ADLs), including self-care and mobility. BI scores range from 0 (total dependence of ADLs) to 100 (full independence of ADLs). Patients with BI scores of <60 are likely associated with poor outcomes.[31] BI is a widely used longitudinal follow-up instrument for post-stroke patients.[34] A study from Italy reported that after completion of stroke rehabilitation, about 50% of SITY patients were independent (BI ≥95), 38.9% were partially dependent (BI 60-86), and 11.1% were fully dependent (BI <60).[32] Moreover, in Western and Eastern European centers, the functional disability of SITY after three months ranges between 2% and 21% (BI 0–14).[35] To our knowledge, no studies has compared the use of the mRS and BI for functional outcome assessment in young patients with ischemic stroke. However, a prospective study conducted in Germany involving 1530 ischemic stroke patients (mean age: 69) reported that mRS was more effective in assessing functioning and disability after a minor stroke. This is likely due to the ceiling effects of BI, which limits the sensitivity of evaluating minor deficits among patients with high levels of functioning.[36] Nevertheless, BI remains valuable in clinical practice, particularly for planning rehabilitation strategies and monitoring patients' progress over time. In contrast, mRS provides a rapid summary of functional disability, which is helpful for clinicians and patients in early clinical decisions and intervention.[37]

Cardiovascular Risk Factors

The American Heart Association (AHA) identifies several cardiovascular risk factors that contribute to the likelihood of developing a stroke. These include high blood pressure, diabetes mellitus, high cholesterol, ischemic heart disease, smoking, heavy alcohol consumption, low physical activity, and obesity.[38] Moreover, the presence of valvular heart disease, mainly due to Rheumatic Heart Disease (RHD) and congenital heart disease, is noted to be associated with increased risk for ischemic stroke and recurrence.[39,40] While atrial fibrillation poses a risk for thrombus formation in the left atrium, it can lead to thromboembolic events such as stroke.[41]

Non-cardiovascular Risk Factors

Hypercoagulability is a commonly reported but underrecognized cause of ischemic stroke in young adults in the United States. The predominant underlying mechanisms for a hypercoagulable state include Factor V Leiden mutation, protein C and S deficiency, antithrombin III deficiency, antiphospholipid syndrome, systemic lupus erythematosus, and abnormalities of hematocrit level or platelet count.[42]

The Factor V Leiden mutation is an inherited form of venous thrombophilia. The incidence is common in Northern European and Middle Eastern descent but rare in Asian populations.[43] Protein C and protein S are essential inactivating clotting proteins. Both deficiencies lead to recurrent thrombotic disease. Antithrombin III deficiency primarily leads to venous blood clots, with an estimated incidence rate of 5% to 8% in SITY.[44] Moreover, autoimmune diseases such as antiphospholipid syndrome and systemic lupus erythematosus in young women are associated with a high burden of cerebral small vessel disease, which likely increases the risk of stroke.[45] Abnormalities in the complete blood count (CBC), such as high hematocrit levels, thrombocytosis, and thrombocytopenia, are found to be contributors to ischemic SITY.[46]

Other non-cardiovascular risk factors for ischemic stroke include excess homocysteine level secondary to an autosomal recessive mutation in the *MTHFR* gene causing thrombosis and cerebrovascular lesions in 50% of SITY.[47]

Stroke also affects 30 per 100,000 pregnancies that may occur during antepartum, peripartum, and postpartum periods.[48]

Epidemiologic studies show a higher risk of ischemic stroke among users of long-term pills containing high-dose estrogen compared to low-dose oral contraceptive pills.[49-51]

Migraines, in general, increase the risk of ischemic stroke by 1.2-fold.[52] The underlying mechanism of stroke in migraine involves Cortical Spreading Depression (CSD), which causes extreme vasoconstriction and alteration in cerebral blood flow, leading to cerebral ischemia or infarction.[53]

Furthermore, Moyamoya disease is commonly seen in young adults and children with ischemic stroke, characterized by progressive occlusion of the arteries of the circle of Willis and development of collateral vessels.[54]

In COVID-related ischemic stroke, clinical outcomes are worse than patients who do not have COVID.[55,56] There is

a 7-fold increase in the rate of large vessel stroke in young people with COVID-19.[57] The mechanism is attributed to the hypercoagulable state from systemic inflammation, cytokine storm, and postinfectious immune-mediated responses.[58,59]

Substance abuse, specifically amphetamines, cannabis, and cocaine, is also associated with the onset of ischemic SITY. The possible underlying cause of stroke in this case includes vasospasm, cerebral vasculitis, and hypertensive crisis.[60]

OBJECTIVES

The study aimed to describe the clinical features and outcomes of young Filipino adults who were newly diagnosed with ischemic stroke at two tertiary hospitals in Cebu: Chong Hua Hospital Fuente (CHH-Fuente) and Chong Hua Hospital Mandaue (CHH-Mandaue).

Specifically, this study aimed to (1) describe the baseline demographics and stroke symptoms of ischemic stroke in the young patients, (2) identify the cardiovascular and non-cardiovascular risk factors associated with ischemic stroke in the young, (3) report the diagnostic findings of ischemic stroke in the young, (4) identify the ischemic stroke etiology based on TOAST classification, and (5) describe the functional outcomes of ischemic stroke in the young using mRS.

MATERIALS AND METHODS

Study Design and Population

The study was a two-center, five-year retrospective cohort design involving 19 to 45-year-old patients admitted between January 1, 2017, and December 31, 2022, diagnosed clinically and radiologically with ischemic stroke for the first time. The selected age range for defining SITY was based on previous studies in India and Philippines.[9,10] Patients with incomplete work-ups for hypercoagulability, echocardiography, and neurosonography were still included in the study. However, patients were excluded for history of ischemic or hemorrhagic strokes, brain tumors, transient ischemic attacks, onset of ischemic stroke during hospitalization, and lack of cranial CT scan or MRI confirming an ischemic stroke.

Following the hospital's Institutional Review Board approval, the list of ischemic stroke diagnoses was obtained from the hospital's International Classification of Disease (ICD) database. Data collection involved a thorough chart review of patients' demographics, admission dates, comorbidities, stroke symptoms, vital signs, pertinent laboratory tests specific to various risk factors, and functional outcomes on discharge. Ischemic stroke subtypes were determined according to TOAST classification. The functional outcomes of patients were assessed using mRS at time of hospital discharge. However, mRS scores were not recorded for all patients. To ensure uniformity in outcome reporting, we estimated and calculated the missing mRS scores by chart review of the attending physicians' progress note.

Study Size

Our study included all young adults aged 19 to 45 with clinical and radiologic findings of ischemic stroke at CHH-Fuente and CHH-Mandaue admitted from January 1, 2017, to December 31, 2022.

Demographic Profile

The baseline demographic profile included age, biological sex, and pre-existing co-morbidities.

Cardiovascular Risk Factors

The cardiovascular risk factors included in the study were hypertension, diabetes mellitus type 2, dyslipidemia, heavy alcohol consumption (>5 standard alcoholic beverages per day), current or previous smoker (one who smoked at the time of stroke or had quit smoking within one year), ischemic heart disease, valvular heart disease, family history of stroke, atrial fibrillation, congenital heart disease, and obesity (body mass index of ≥25 based on the WHO Asian classification of obesity).

Non-cardiovascular Risk Factors

For the non-cardiovascular risk factors, the study included the following: the use of estrogen-containing contraceptive pills, pregnancy (antepartum, peripartum, postpartum), migraine with or without aura, antiphospholipid antibody syndrome, systemic lupus erythematosus, abnormalities in hematocrit level and platelet count, antithrombin III deficiency, protein C and S deficiency, hyperhomocysteinemia, factor V Leiden mutation, prothrombin gene mutation, Moyamoya disease, and COVID-19 infection.

Clinical and Laboratory Characteristics on Admission

The basic blood tests taken during admission included fasting blood sugar (FBS), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), hematocrit, and platelet levels. For COVID-19 confirmation, either reverse transcription polymerase chain reaction (RT-PCR) or antigen test was used. The cardiovascular studies were noted, which included electrocardiogram (ECG), transthoracic/transesophageal echocardiography (TTE/TEE), 24-hour Holter monitoring, and carotid duplex scan. Furthermore, the neuroimaging studies involved were cranial magnetic resonance imaging with angiography and venography (MRI with MRA and MRV), cranial computed tomography (CT) scan, and transcranial Doppler (TCD) ultrasound. The test for hypercoagulability included prothrombin gene mutation, factor V Leiden mutation, antinuclear antibody ratio, anti-dsDNA, anticardiolipin antibodies, antithrombin III, homocysteine levels, protein C and S, and complement 3 or 4.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS software, version 29) was used to calculate the descriptive

statistics for the study population. The results were reported in frequencies, percentages, means, and standard deviations of patients' demographics, cardiovascular, non-cardiovascular risk factors, stroke symptoms, laboratory results, stroke subtypes, and functional outcomes on discharge.

Ethics Approval

This retrospective chart review study involving human participants followed the ethical standards of the institutional and national research committees, as well as the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical standards. The Institutional Review Board (IRB) of Chong Hua Hospital approved this study (IRB code 9022-09).

Table 1. Baseline Demographic Characteristics

Profile	Mean	SD
Age (years)	37.30	5.55
	No. of Patients	**%**
Biological sex		
Male	65	31.7
Female	140	68.3
Body Mass Index (Asian classification by WHO)		
Underweight (<18.5)	7	3.4
Normal (18.5 to 22.9)	49	23.9
Overweight (23 to 24.9)	33	16.1
Obese (≥25)	116	56.6

SD – standard deviation, WHO – World Health Organization

RESULTS

From January 1, 2017, to December 31, 2022, a total of 1,838 medical records with ischemic stroke diagnoses were identified through ICD database searches from both CHH-Fuente and CHH-Mandaue. Of the 1,838 ischemic stroke patients, 230 were between 19 and 45 years of age. Among the 230 patients, 25 were excluded due to history of brain tumors (4), hemorrhagic strokes (5), ischemic strokes (8), and onset of stroke during hospitalization (6). Two patients were excluded from the study due to the absence of CT scan or MRI procedures. In total, 205 medical records of SITY patients were included in this study (Figure 1).

Most patients presented with hemiparesis, headache, and slurred speech (Figure 2). The study population's median age was 37.30 years, and was predominantly female (68.3%) and obese (56.6%), as shown in Table 1. The cardiovascular risk factors of ischemic SITY included obesity (56.6%),

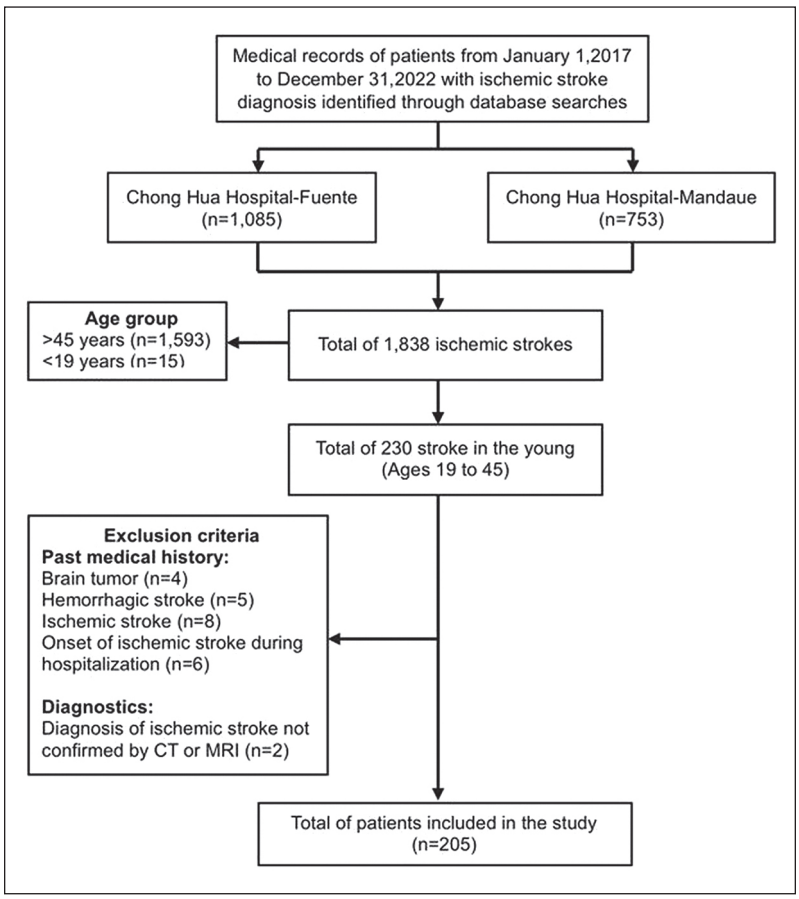

Figure 1. Flow diagram of study population.

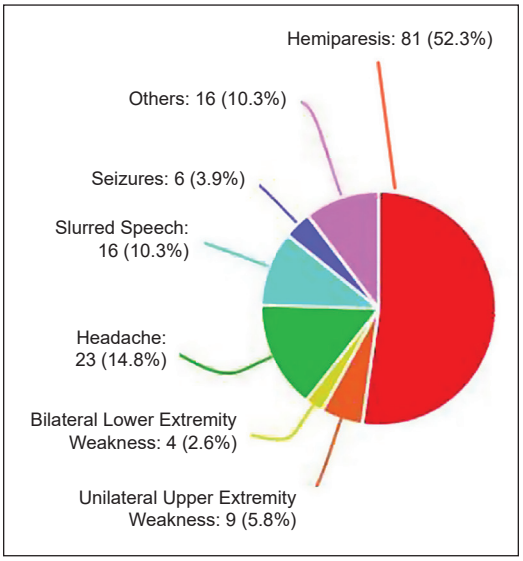

Figure 2. Common presenting symptoms of SITY.

hypertension (51.2%), heavy alcohol consumption (36.5%), and diabetes mellitus type 2 (19.5%). Concurrently, the non-cardiovascular risk factors were estrogen-containing contraceptive pill use (4.8%), pregnancy, in particular the postpartum period (4.8%), and migraine without aura (4.4%), as reported in Table 2.

The minimum, maximum, and standard deviation (SD) values of the clinical and basic laboratory parameters of SITY are shown in Table 3. Furthermore, the number of patients who underwent the diagnostic procedures and the proportion of those with abnormal findings are presented in Table 4. Cranial MRI with MRA and MRV was performed in 63.41% of SITY patients (130 of 205); pertinent findings included infarction, aneurysm, venous and arterial thrombosis. Eighty-four percent (173 of 205) had cranial CT scans, of which 40.46% (70) showed normal findings, while 59.53% (103) reported infarctions. A CBC of 203 patients revealed 6.89% (14) had thrombocytosis and hemoconcentration, while 93.1% (189) had normal results. FBS was tested in 165 patients, showing elevated levels in 53.93% (89). Among the 175 patients with lipid profiles, 32.57% (57) had dyslipidemia. The electrocardiogram (ECG) of 202 patients revealed 15.3% (31) abnormalities, including ischemic changes (13), atrial fibrillation (9), and infarction (9). Additionally, transthoracic echocardiography (TTE) of 182 patients showed that 52.74% (96) had abnormal findings of cardiomyopathy (49), valvular heart disease (42), congenital heart disease (3), and prosthetic valve replacement (2). Transesophageal echocardiography (TEE) was performed in two patients, with normal results. 24-hour Holter monitoring was done in 30 patients, of which two had recordings of cardiac dysrhythmias. Of the 163 who underwent carotid Doppler scan, 22.08% (36) showed abnormalities of stenosis and occlusion. One hundred twenty-three patients had transcranial Doppler (TCD), of which 31.7% (39) had stenosis and occlusion of the intracranial vessels. Non-cardiovascular tests results included: positive antinuclear antibody ratio (ANA) in 17.8% (13 of 73), positive anti-dsDNA in 25% (2 of 8), low C3 in 15.38% (2 of 13), low C4 in 14.28% (2 of 14), low protein S in 16.12%(5 of 31), low protein C in 6.25% (2 of 32), positive anti-cardiolipin antibody in 8.88% (4 of 45), positive factor V Leiden mutation in 7.69% (2 of 26), positive prothrombin mutation in 50% (1 of 2), and low anti-thrombin III in 3.7% (1 of 27). Thirty-two patients tested for homocysteine levels had normal results. COVID-19 reverse transcription polymerase chain reaction (RT-PCR) and antigen testing showed a positive result of 1.83% (2 of 109).

Based on the TOAST classification, small vessel occlusion (42.1%) and large artery atherosclerosis (30.2%) were the most frequent ischemic stroke subtypes in the study population. Both subtypes were more prevalent in females than males (Table 5).

Majority of functional outcomes of SITY patients at discharge showed no symptoms of disability (35.1%), slight disability (22%), no significant disability (20.5%), moderate disability (14.1%), severe disability (5.4%), and death (2.92%), as reported in Table 6.

Table 2. History of Cardiovascular and Non-cardiovascular Risk Factors of Patients with SITY (Multiple Response)

Factors	No. of Responses (n= 205)	%
Cardiovascular risks		
Obesity (Asian classification by WHO)	116	56.6
Hypertension	105	51.2
Heavy Alcohol Consumption	75	36.5
Diabetes Mellitus Type 2	40	19.5
Current or Previous Smoker	38	0.19
Ischemic Heart Disease	13	6.34
Dyslipidemia	12	5.8
Valvular Heart Disease	4	1.9
Family History of Stroke	7	3.4
Infective Endocarditis	2	0.98
Non-cardiovascular risks		
Oral Contraceptive Containing Estrogen	10	4.8
Pregnancy (Postpartum)	10	4.8
Migraine without Aura	9	4.4
Antiphospholipid Antibody Syndrome	5	2.3
COVID-19	2	0.98
Protein S Deficiency	2	0.98
Migraine with Aura	1	0.5
Protein C Deficiency	1	0.5

SITY – stroke in the young, WHO – World Health Organization

Table 3. Clinical and Basic Laboratory Characteristics of SITY

Parameters	Minimum	Maximum	SD
Systolic blood pressure	80.0	260.0	141.26 ± 33.51
Diastolic blood pressure	50.0	160.0	88.40 ± 18.88
Fasting blood sugar	53.0	410.0	117.65 ± 51.09
Total cholesterol level	75.0	278.5	196.20 ± 205.46
High-density lipoprotein	21.0	303.98	111.81 ± 43.02
Low-density lipoprotein	11.3	124.0	43.10 ± 12.90
Serum viscosity			
Hematocrit	21.0	65.30	41.25 ± 7.13
Platelet	11.5	861.0	292.32 ± 103.67

SD – standard deviation, SITY – stroke in the young

DISCUSSION

Based on this study, we were able to determine the clinical profile of young Filipino patients with ischemic stroke and identify both cardiovascular and non-cardiovascular risk factors contributing to the occurrence of the disease. Hypertension, heavy alcohol consumption, and diabetes mellitus type 2 were the common risk factors for ischemic SITY Filipinos.[19] While our study supported this report, we observed differences in the distribution of risk factors. In particular, obesity was the most prevalent risk factor found in

our study, affecting 56% of patients, followed by hypertension at 51.2%. Furthermore, our study revealed a higher incidence of SITY among females (68.3%) compared to males (31.7%), which contrasts with earlier studies, reporting male predominance and hypertension as the leading risk factors.[19-21] This increase in the number of stroke cases among females may, in part, be attributed to the female-specific, non-cardiovascular risk factors, such as pregnancy in the postpartum period (4.8%), use of estrogen-containing pills (4.8%), and migraine without aura (4.4%). Although rare, these factors may contribute to SITY and should be considered during stroke risk assessment among females.[61]

Table 4. Summary of Diagnostic Procedures and Findings of SITY

Diagnostic procedures (N=205)	Abnormal findings, n (%)		Normal findings, n (%)	Patients with procedure, n (%)	Patients without procedure, n (%)
Magnetic resonance imaging (with MRA and MRV)		130 (100)	-	130 (63.41)	75 (36.58)
	Infarction	130			
	Arterial thrombosis	26			
	Venous thrombosis	5			
	Aneurysm	1			
Computed tomography scan	Infarction	103 (59.53)	70 (40.46)	173 (84.39)	32 (15.60)
Complete blood count	Thrombocytosis, hemoconcentration	14 (6.89)	189 (93.1)	203 (99.02)	2 (0.97)
Fasting blood sugar	High	89 (53.93)	76 (46.06)	165 (80.48)	40 (19.51)
Lipid profile	Dyslipidemia	57 (32.57)	118 (67.42)	175 (85.36)	33 (16.09)
Electrocardiogram		31 (15.3)	171 (84.65)	202 (98.53)	3 (1.46)
	Ischemic changes	13			
	Atrial fibrillation	9			
	Infarction	9			
Transthoracic echocardiography		96 (52.74)	86 (47.25)	182 (88.78)	23 (11.21)
	Cardiomyopathy	49			
	VHD	42			
	CHD (PFO, ASD, VSD)	3			
	Prosthetic valve replacement	2			
Transesophageal echocardiography	-	-	2 (100)	2 (0.97)	203 (99.02)
24-hour Holter monitor	Atrial flutter, atrial fibrillation	2 (6.66)	28 (93.33)	30 (14.63)	175 (85.36)
Carotid doppler		36 (22.08)	127 (77.91)	163 (79.51)	42 (20.48)
	Stenosis	28			
	Occlusion	8			
Transcranial doppler		39 (31.7)	84 (68.29)	123 (60)	82 (40)
	Stenosis	24			
	Occlusion	15			
Antinuclear antibody ratio	Positive	13 (17.8)	60 (82.19)	73 (35.60)	132 (64.39)
Anti-dsDNA	Positive	2 (25)	6 (75)	8 (3.90)	197 (96.09)
C3	Low	2 (15.38)	11 (84.61)	13 (6.34)	192 (93.65)
C4	Low	2 (14.28)	12 (85.71)	14 (6.82)	191 (93.17)
Protein S	Low	5 (16.12)	26 (83.87)	31 (15.12)	174 (84.87)
Protein C	Low	2 (6.25)	30 (93.75)	32 (15.60)	173 (84.39)
Anti-cardiolipin antibody	Positive	4 (8.88)	41 (91.11)	45 (21.95)	160 (78.04)
Factor V Leiden mutation	Positive	2 (7.69)	24 (92.30)	26 (12.68)	179 (87.31)
Prothrombin	Positive	1 (50)	1 (50)	2 (0.97)	203 (99.02)
Anti-thrombin	Low	1 (3.70)	26 (96.29)	27 (13.17)	178 (86.82)
Homocysteine	High	-	32 (100)	32 (15.60)	173 (84.39)
COVID-19	Positive	2 (1.83)	107 (98.1)	109 (53.17)	96 (46.82)

MRA – magnetic resonance angiography, MRV – magnetic resonance venography, VHD – valvular heart disease, CHD – congenital heart disease, PFO – patent foramen ovale, ASD – atrial septal defect, VSD – ventricular septal defect

Table 5. Subtypes of Ischemic Stroke Based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification

Classification	Biological sex	
	Male (n=65), n (%)	Female (n=140), n (%)
Small vessel occlusion	18 (27.7)	59 (42.1)
Large artery atherosclerosis	17 (26.2)	42 (30.2)
Stroke of determined etiology	13 (20.0)	14 (10.1)
Stroke of undetermined etiology	10 (15.3)	10 (5.9)
Cardioembolism	7 (10.8)	15 (10.8)

Table 6. Modified Rankin Scale (mRS) on Discharge

Classification	No. of patients (n=205)	%
0 No symptom	72	35.1
1 No significant disability	42	20.5
2 Slight disability	45	22.0
3 Moderate disability	29	14.1
4 Moderate severe disability	6	2.92
5 Severe disability	5	2.43
6 Death	6	2.92

The results of our study were similar to those of previous studies, identifying small vessel occlusion and large artery atherosclerosis as the predominant ischemic stroke subtypes in some Asian populations.[20,28,29] The high prevalence of small vessel occlusion in the region was likely associated with dietary habits and uncontrolled hypertension.[62] Likewise, the occurrence of large artery atherosclerosis stroke subtype may be attributable to the concurrent atherosclerosis of intracranial (31.7%) and extracranial vessels (22.08%), which were common among Asians.[63] Interestingly, in contrast to other studies, our study showed a higher frequency of small-vessel occlusion and large-artery atherosclerosis in females than in males, at 42.1% and 30.2%, respectively.[64,65] To date, this biological sex difference in ischemic stroke subtypes remains unclear, warranting further investigation.[66]

Our study demonstrated a relatively lower mortality rate of 2.92%, slightly lower than the previously reported 3.9% among young Filipinos with stroke.[9] Furthermore, most SITY patients had good functional outcomes, with 35.1% scoring zero in mRS. Nevertheless, the initial outcomes for SITY are favorable; this young population remains vulnerable to stroke recurrence when underlying risk factors are inadequately addressed and managed.

Limitations

The study only involved cases from two major tertiary hospitals in Cebu, Philippines. It sought to determine the prevalent subtypes of ischemic stroke and their functional outcomes upon discharge. However, given the retrospective nature of this study, no causal relationships could be established between the identified stroke risk factors and clinical outcomes. One potential source of bias in this study is selection bias. The limited setting of the two tertiary hospitals in Cebu may result in underrepresentation of young Filipinos with ischemic stroke. Work-up bias may also be present, as some patients failed to undergo comprehensive evaluation for ischemic stroke due to lack of financial resources and discretion of some physicians regarding the extent of further diagnostic work-up. This incomplete evaluation may lead to an underestimation of clinical findings. In this study, only 60% of the study population had undergone TCD, 79.51% had a carotid duplex scan, 88.78% had TTE, less than 1% had TEE, 14.63% had 24-hour Holter monitor, and <1% to 35.6% had work-up for hypercoagulable states. The possibility of inter-rater variability and reporting bias are also considered in this study, which may have resulted from estimating the missing mRS scores through chart review of progress notes.

Recommendations

We recommend future researches to include a broader and more diverse population involving multiple centers across different regions. To minimize work-up bias, standardized diagnostic protocols are suggested, although this poses a challenge because not all patients can comply with extensive diagnostic work-up. Additionally, prospective data collection, including consistent documentation of functional outcomes by mRS, is recommended to reduce reporting bias.

Generalizability

Our study has potential for generalizability, as it utilizes validated tools such as the TOAST classification for stroke subtyping and the modified Rankin Scale (mRS) for assessing functional outcomes. However, the accuracy of the TOAST classification depends on the complete clinical and diagnostic data. Accurate classification of stroke etiology in young adults requires access to a comprehensive investigation, which is often limited by resource constraints. Incomplete workups may result in misclassification or underrepresentation of specific stroke subtypes. This limitation remains a challenge when applying TOAST classification. Furthermore, implementing a standardized protocol that includes routine and consistent documentation of mRS in patient charts is essential to ensure uniform assessment of functional outcomes.

CONCLUSION

This study highlights the difference in the clinical profile of young Filipino adults with ischemic stroke. Contrary to previous studies, predominance of ischemic stroke among young females was observed. Instead of hypertension, obesity has emerged as the leading cardiovascular risk factor for ischemic SITY. Moreover, non-cardiovascular risk factors, specific to females (pregnancy, use of estrogen-containing pills, and migraine), were also identified in the study. With regards to stroke subtypes, small vessel occlusion and large

artery atherosclerosis were frequently seen in young female patients. These findings suggest a need for gender-specific approaches in the evaluation, management, and prevention of ischemic SITY.

Data Availability

Access to data within the hospital is secured with a password to ensure confidentiality and protection. Only authorized investigators on the approved list are granted access to this valuable information, promoting responsible use and safeguarding of patient privacy.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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