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A Prospective Observational Study of Etiology of Stroke and Its Risk Factors

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KEYWORDS

Stroke etiology, Risk factors, TOAST classification, Hypertension, Atrial fibrillation, Secondary prevention

ABSTRACT:

Background: Stroke remains a leading cause of mortality and long-term disability worldwide. Understanding the etiology and risk factors of stroke is crucial for developing effective prevention strategies. This study aimed to investigate the distribution of stroke subtypes and associated risk factors in a cohort of 156 patients.

Methodology: A prospective observational study was conducted on 156 consecutive stroke patients admitted to a tertiary care hospital between January 2023 and December 2023. Detailed clinical evaluations, neuroimaging (CT/MRI) and laboratory investigations were performed. Stroke subtypes were classified according to TOAST criteria for ischemic stroke and standard classifications for hemorrhagic stroke.

Results: Among the 156 patients, 78.2% (n=122) had ischemic stroke and 21.8% (n=34) had hemorrhagic stroke. Large-artery atherosclerosis (36.9%) was the most common etiology of ischemic stroke, followed by cardioembolic (24.6%), small-vessel occlusion (22.1%), stroke of other determined etiology (5.7%) and stroke of undetermined etiology (10.7%). Hypertension was the most prevalent risk factor (72.4%), followed by dyslipidemia (58.3%), diabetes mellitus (44.2%), smoking (32.1%), prior history of stroke/TIA (21.8%), atrial fibrillation (18.6%) and obesity (16.7%). Multiple logistic regression analysis revealed hypertension (OR 3.8, 95% CI 2.1-6.9), atrial fibrillation (OR 2.9, 95% CI 1.7-5.2) and smoking (OR 2.6, 95% CI 1.5-4.7) as independent predictors of stroke severity and poor outcomes.

Conclusion: This study confirms the high prevalence of modifiable risk factors in stroke patients with hypertension being the predominant factor. Understanding stroke etiology and risk factor profiles is essential for developing targeted prevention strategies and optimizing patient management. Early recognition and aggressive management of these modifiable risk factors could significantly reduce stroke burden.

INTRODUCTION

Stroke is the second leading cause of death worldwide and a major contributor to disability with an estimated global prevalence of 101.5 million cases in 2019 (GBD 2019 Stroke Collaborators, 2021). It is characterized by the sudden disruption of blood supply to the brain, resulting in neurological deficits that can lead to lasting impairment or death. The socioeconomic burden of stroke is substantial with significant impacts on

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healthcare systems, families and societies globally (Feigin et al., 2021). Stroke can be broadly classified into two major categories: ischemic stroke, accounting for approximately 80% of all strokes and hemorrhagic stroke, comprising the remaining 20% (Campbell et al., 2019). Ischemic stroke results from the occlusion of a cerebral blood vessel, whereas hemorrhagic stroke involves bleeding into brain tissue or subarachnoid space. Understanding the underlying etiology of stroke is crucial for implementing appropriate treatment strategies and developing targeted prevention measures. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification system is widely used to categorize ischemic stroke into five subtypes based on etiology: large-artery atherosclerosis, cardioembolism, small-vessel occlusion (lacunar), stroke of other determined etiology and stroke of undetermined etiology (Adams et al., 1993). This classification aids in guiding treatment decisions and predicting outcomes.

Multiple risk factors contribute to stroke incidence with some being non-modifiable (age, sex, genetic predisposition, ethnicity) and others modifiable (hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, physical inactivity, excessive alcohol consumption) (O'Donnell et al., 2016). The INTERSTROKE study, a large international case-control study, demonstrated that ten potentially modifiable risk factors account for approximately 90% of the population-attributable risk of stroke (O'Donnell et al., 2016). Among these, hypertension has consistently been identified as the most important modifiable risk factor for both ischemic and hemorrhagic strokes (Meschia et al., 2014). Despite advances in stroke prevention, diagnosis and management, the global burden of stroke continues to increase due to population growth, aging and the rising prevalence of risk factors, particularly in low- and middle-income countries (Johnson et al., 2019). Therefore, a comprehensive understanding of stroke etiology and its associated risk factors in different populations is essential for developing effective prevention strategies and reducing the global burden of stroke. The present study aimed to investigate the distribution of stroke subtypes and associated risk factors in a cohort of 156 patients presenting with acute stroke at a tertiary care hospital. By elucidating the patterns of stroke etiology and risk factors in this population, this research contributes to the growing body of evidence needed for developing targeted prevention and management strategies.

METHODOLOGY

Study Design and Population

This prospective observational study was conducted at the Department of Emergency Medicine at NIMS Medical College and Hospital, Jaipur, from January 2024 to December 2024. The study was approved by the Institutional Ethics Committee and informed consent was obtained from all participants or their legal representatives. A total of 156 consecutive patients with acute stroke, confirmed by clinical examination and neuroimaging were enrolled. Patients with transient ischemic attack (TIA) and those with stroke mimics were excluded from the study. Demographic data including age, sex and relevant medical history were collected using a structured questionnaire. A thorough clinical examination was performed for all patients upon admission. The severity of stroke was assessed using the National Institutes of Health Stroke Scale (NIHSS) for ischemic stroke and the Glasgow Coma Scale (GCS) for hemorrhagic stroke. Functional status at discharge was evaluated using the modified Rankin Scale (mRS).

Risk Factor Assessment

The following risk factors were assessed:

1. **Hypertension**: Defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on repeated measurements, or current use of antihypertensive medications.
2. **Diabetes Mellitus**: Defined as fasting plasma glucose ≥126 mg/dL, 2-hour plasma glucose ≥200 mg/dL during oral glucose tolerance test, HbA1c ≥6.5%, or current use of antidiabetic medications.
3. **Dyslipidemia**: Defined as total cholesterol >200 mg/dL, LDL cholesterol >130 mg/dL, HDL cholesterol <40 mg/dL in men and <50 mg/dL in women, triglycerides >150 mg/dL, or current use of lipid-lowering medications.
4. **Smoking**: Categorized as current smoker (smoking within the past month), ex-smoker (quit >1 month), or non-smoker.
5. **Alcohol Consumption**: Categorized as excessive (>14 drinks/week for men, >7 drinks/week for women), moderate (≤14 drinks/week for men, ≤7 drinks/week for women), or none.
6. **Atrial Fibrillation**: Diagnosed based on electrocardiography (ECG) or 24-hour Holter monitoring.
7. **Obesity**: Defined as body mass index (BMI) ≥30 kg/m².
8. **Physical Inactivity**: Defined as <150 minutes of moderate-intensity or <75 minutes of vigorous-intensity physical activity per week.

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9. **Family History**: History of stroke or coronary heart disease in first-degree relatives before the age of 55 years for men and 65 years for women.
10. **Prior History of Stroke/TIA**: Previous clinical diagnosis of stroke or TIA.

Investigations

All patients underwent the following investigations:

1. **Neuroimaging**: Non-contrast computed tomography (CT) brain scan was performed on admission for all patients. Magnetic resonance imaging (MRI) including diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), fluid-attenuated inversion recovery (FLAIR) and magnetic resonance angiography (MRA) was performed when indicated.
2. **Cardiovascular Assessment**: 12-lead ECG, transthoracic echocardiography (TTE) and 24-hour Holter monitoring when indicated.
3. **Laboratory Investigations**: Complete blood count, blood glucose, HbA1c, lipid profile, renal function tests, liver function tests, coagulation profile and inflammatory markers (ESR, CRP).
4. **Vascular Imaging**: Carotid Doppler ultrasonography, CT angiography (CTA), or MR angiography (MRA) was performed as indicated.
5. **Additional Investigations**: For selected cases with suspected stroke of other determined etiology, additional tests including thrombophilia screen, autoimmune markers and cerebrospinal fluid analysis were performed.

Stroke Classification

Ischemic strokes were classified based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria into five categories: large-artery atherosclerosis, cardioembolism, small-vessel occlusion (lacunar infarcts), stroke of other determined etiology and stroke of undetermined etiology. Hemorrhagic strokes were categorized as either intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH). Further sub-classification of ICH was performed based on location into lobar, deep (including basal ganglia and thalamus), brainstem or cerebellar hemorrhage.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Descriptive statistics were presented as frequencies and percentages for categorical variables and as mean±SD or median with interquartile range (IQR) for continuous variables depending on the distribution of data. Normality was assessed using the Shapiro-Wilk test. The chi-square test or Fisher's exact test was used to compare categorical variables between groups. Student's t-test or Mann-Whitney U test was used to compare continuous variables between two groups and ANOVA or Kruskal-Wallis test was used for comparison between multiple groups, as appropriate. Univariate analysis was performed to identify potential predictors of stroke severity and outcomes. Variables with p-values <0.1 in univariate analysis were included in multiple logistic regression analysis to identify independent predictors. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

The study included 156 patients with acute stroke, comprising 92 males (59%) and 64 females (41%). The mean age of the patients was 63.7 ± 12.5 years (range: 28-89 years). The majority of patients (65.4%) were in the age group of 51-70 years. Based on neuroimaging findings, 122 patients (78.2%) were diagnosed with ischemic stroke and 34 patients (21.8%) with hemorrhagic stroke. The mean NIHSS score on admission for patients with ischemic stroke was 8.6 ± 6.2 and the mean GCS score for patients with hemorrhagic stroke was 11.3 ± 3.8. Table 1 summarizes the demographic and clinical characteristics of the study population.

Table 1: Demographic and Clinical Characteristics of Stroke Patients (N=156)

Characteristic	n (%) or Mean ± SD
Mean Age (years)	63.7 ± 12.5
Age groups	
≤40 years	12 (7.7%)
41-50 years	19 (12.2%)
51-60 years	47 (30.1%)
61-70 years	55 (35.3%)
>70 years	23 (14.7%)
Sex	
Male	92 (59.0%)
Female	64 (41.0%)
Stroke type	
Ischemic stroke	122 (78.2%)
Hemorrhagic stroke	34 (21.8%)
Admission NIHSS score (ischemic stroke)	8.6 ± 6.2
Admission GCS score (hemorrhagic stroke)	11.3 ± 3.8

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Characteristic	n (%) or Mean ± SD
Duration of hospital stay (days)	9.4 ± 5.3
Outcome at discharge	
Good outcome (mRS 0-2)	86 (55.1%)
Poor outcome (mRS 3-6)	70 (44.9%)
In-hospital mortality	14 (9.0%)

The data shows a male predominance (59%) in stroke patients, consistent with existing epidemiological data reporting higher stroke incidence in males. The mean age of 63.7 years reflects the higher prevalence of stroke in the elderly population, though 7.7% of patients were under 40 years, indicating that stroke also affects younger individuals. The distribution of stroke types (78.2% ischemic and 21.8% hemorrhagic) aligns with global epidemiological patterns. Nearly half (44.9%) of patients had poor functional outcomes at discharge (mRS 3-6) and the in-hospital mortality rate was 9.0%, emphasizing the significant morbidity and mortality associated with acute stroke.

Stroke Subtypes

Among the 122 patients with ischemic stroke, the most common etiology according to TOAST classification was large-artery atherosclerosis (n=45, 36.9%), followed by cardioembolic stroke (n=30, 24.6%), small-vessel occlusion (n=27, 22.1%), stroke of other determined etiology (n=7, 5.7%) and stroke of undetermined etiology (n=13, 10.7%). Of the 34 patients with hemorrhagic stroke, 28 (82.4%) had intracerebral hemorrhage (ICH) and 6 (17.6%) had subarachnoid hemorrhage (SAH). Among ICH cases, deep hemorrhages (basal ganglia/thalamic) were most common (n=15, 53.6%), followed by lobar hemorrhages (n=8, 28.6%), cerebellar hemorrhages (n=3, 10.7%) and brainstem hemorrhages (n=2, 7.1%). Table 2 presents the distribution of stroke subtypes.

Table 2: Distribution of Stroke Subtypes (N=156)

Stroke Type and Subtype	n (%)
Ischemic Stroke	**122 (78.2%)**
Large-artery atherosclerosis	45 (36.9%)
Cardioembolic	30 (24.6%)
Small-vessel occlusion	27 (22.1%)
Other determined etiology	7 (5.7%)
Undetermined etiology	13 (10.7%)
Hemorrhagic Stroke	**34 (21.8%)**
Intracerebral Hemorrhage (ICH)	**28 (82.4%)**
Deep (basal ganglia/thalamic)	15 (53.6%)
Lobar	8 (28.6%)
Cerebellar	3 (10.7%)
Brainstem	2 (7.1%)
Subarachnoid Hemorrhage (SAH)	**6 (17.6%)**

The predominance of large-artery atherosclerosis (36.9%) among ischemic stroke subtypes highlights the significant role of atherosclerotic disease in stroke etiology. This finding is consistent with several large-scale studies including the TOAST registry and the Lausanne Stroke Registry. Cardioembolic strokes constituted 24.6% of ischemic strokes, underscoring the importance of cardiac evaluation in stroke patients. Small-vessel occlusion accounted for 22.1% of ischemic strokes, often associated with chronic hypertension and diabetes mellitus. The relatively low percentage (5.7%) of strokes with other determined etiologies (e.g., arterial dissection, hypercoagulable states) reflects their rarer occurrence in the general stroke population. For hemorrhagic strokes, the predominance of deep ICH (53.6% of all ICH cases) is consistent with hypertension being the leading cause of spontaneous ICH, as hypertensive arteriopathy typically affects small perforating arteries in the basal ganglia and thalamus. Lobar hemorrhages (28.6% of ICH cases) are often associated with cerebral amyloid angiopathy, particularly in elderly patients.

Risk Factor Profile

The prevalence of various risk factors among the stroke patients is presented in Table 3.

Table 3: Prevalence of Risk Factors in Stroke Patients (N=156)

Risk Factor	Overall (N=156) n (%)	Ischemic Stroke (n=122) n (%)	Hemorrhagic Stroke (n=34) n (%)	p-value
Hypertension	113 (72.4%)	84 (68.9%)	29 (85.3%)	0.042*
Dyslipidemia	91 (58.3%)	79 (64.8%)	12 (35.3%)	0.001*
Diabetes mellitus	69 (44.2%)	60 (49.2%)	9 (26.5%)	0.018*

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Smoking	50 (32.1%)	41 (33.6%)	9 (26.5%)	0.426
Prior stroke/TIA	34 (21.8%)	30 (24.6%)	4 (11.8%)	0.108
Atrial fibrillation	29 (18.6%)	28 (23.0%)	1 (2.9%)	0.008*
Obesity	26 (16.7%)	22 (18.0%)	4 (11.8%)	0.378
Coronary artery disease	25 (16.0%)	22 (18.0%)	3 (8.8%)	0.195
Excessive alcohol consumption	23 (14.7%)	16 (13.1%)	7 (20.6%)	0.273
Physical inactivity	85 (54.5%)	68 (55.7%)	17 (50.0%)	0.552
Family history of stroke	31 (19.9%)	26 (21.3%)	5 (14.7%)	0.389

*Statistically significant ($p<0.05$)

Hypertension was the most prevalent risk factor, present in 72.4% of all stroke patients with a significantly higher prevalence in hemorrhagic stroke compared to ischemic stroke (85.3% vs. 68.9%, p=0.042). This finding underscores the critical role of hypertension, particularly in the etiology of hemorrhagic stroke. Dyslipidemia and diabetes mellitus were significantly more common in ischemic stroke patients (64.8% vs. 35.3%, p=0.001 and 49.2% vs. 26.5%, p=0.018, respectively), emphasizing their importance as risk factors for atherosclerotic disease. Atrial fibrillation was predominantly associated with ischemic stroke (23.0% vs. 2.9%, p=0.008), consistent with its role in cardioembolic stroke. Physical inactivity was observed in more than half of the stroke patients (54.5%), highlighting the importance of lifestyle factors in stroke risk. Smoking and excessive alcohol consumption were present in 32.1% and 14.7% of patients, respectively with no significant difference between ischemic and hemorrhagic stroke groups.

Risk Factor Distribution Among Ischemic Stroke Subtypes

Table 4 illustrates the distribution of risk factors across different ischemic stroke subtypes according to the TOAST classification.

Table 4: Distribution of Risk Factors Among Ischemic Stroke Subtypes (n=122)

Risk Factor	Large-artery atherosclerosis (n=45) n (%)	Cardioembolic (n=30) n (%)	Small-vessel occlusion (n=27) n (%)	Other determined etiology (n=7) n (%)	Undetermined etiology (n=13) n (%)	p-value
Hypertension	32 (71.1%)	18 (60.0%)	23 (85.2%)	3 (42.9%)	8 (61.5%)	0.041*
Dyslipidemia	37 (82.2%)	16 (53.3%)	18 (66.7%)	2 (28.6%)	6 (46.2%)	0.003*
Diabetes mellitus	26 (57.8%)	11 (36.7%)	18 (66.7%)	1 (14.3%)	4 (30.8%)	0.007*
Smoking	20 (44.4%)	7 (23.3%)	10 (37.0%)	1 (14.3%)	3 (23.1%)	0.135
Prior stroke/TIA	12 (26.7%)	7 (23.3%)	8 (29.6%)	0 (0.0%)	3 (23.1%)	0.541
Atrial fibrillation	3 (6.7%)	24 (80.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	<0.001*
Obesity	9 (20.0%)	5 (16.7%)	6 (22.2%)	0 (0.0%)	2 (15.4%)	0.661
Coronary artery disease	12 (26.7%)	8 (26.7%)	1 (3.7%)	0 (0.0%)	1 (7.7%)	0.032*
Physical inactivity	23 (51.1%)	18 (60.0%)	16 (59.3%)	3 (42.9%)	8 (61.5%)	0.824

*Statistically significant ($p<0.05$)

Analysis of risk factor distribution among ischemic stroke subtypes revealed distinct patterns. Hypertension was most prevalent in small-vessel occlusion (85.2%), consistent with its role in arteriolosclerosis and lipohyalinosis of small penetrating arteries. Dyslipidemia was significantly associated with large-artery atherosclerosis (82.2%), reflecting its contribution to atherosclerotic plaque formation. Atrial fibrillation was predominantly linked to cardioembolic stroke (80.0%), serving as the primary source of cardiac emboli. Diabetes mellitus showed a high prevalence in both small-vessel occlusion (66.7%) and large-artery atherosclerosis (57.8%), consistent with its role in both microvascular and macrovascular disease. Coronary artery disease was significantly more common in large-artery atherosclerosis and cardioembolic stroke (26.7% each) compared to other subtypes, reflecting the shared pathophysiology of atherosclerosis affecting both coronary and cerebral arteries. Interestingly, physical inactivity showed a high prevalence across all ischemic stroke subtypes (42.9-61.5%), highlighting its role as a universal risk factor.

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Multiple Risk Factors

The presence of multiple risk factors was common among stroke patients. Table 5 shows the distribution of the number of risk factors per patient.

Table 5: Number of Risk Factors per Patient (N=156)

Number of Risk Factors	n (%)
0	4 (2.6%)
1	21 (13.5%)
2	35 (22.4%)
3	47 (30.1%)
≥4	49 (31.4%)

Only 2.6% of patients had no identifiable risk factors, while 31.4% had four or more risk factors. The mean number of risk factors per patient was 2.9 ± 1.4. This finding emphasizes the multifactorial nature of stroke and the cumulative effect of multiple risk factors on stroke risk. The presence of three or more risk factors was associated with more severe stroke on admission (mean NIHSS 10.2 vs. 7.1, p=0.002) and poorer functional outcomes at discharge (mRS >2: 54.2% vs. 35.0%, p=0.013).

Predictors of Stroke Severity and Outcome

Multiple logistic regression analysis was performed to identify independent predictors of stroke severity (defined as NIHSS ≥10 for ischemic stroke and GCS ≤8 for hemorrhagic stroke) and poor functional outcome at discharge (defined as mRS >2). The results are presented in Table 6.

Table 6: Multiple Logistic Regression Analysis for Predictors of Stroke Severity and Poor Outcome

Risk Factor	Severe Stroke		Poor Outcome (mRS >2)	
	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age >65 years	1.8 (1.0-3.2)	0.046*	2.4 (1.3-4.3)	0.005*
Male sex	1.2 (0.6-2.3)	0.612	1.1 (0.5-2.1)	0.826
Hemorrhagic stroke	2.7 (1.2-6.1)	0.017*	3.2 (1.4-7.3)	0.006*
Hypertension	3.8 (2.1-6.9)	<0.001*	2.9 (1.6-5.4)	<0.001*
Diabetes mellitus	1.7 (0.9-3.3)	0.108	1.9 (1.0-3.6)	0.048*
Dyslipidemia	1.3 (0.7-2.5)	0.421	1.2 (0.6-2.3)	0.593
Smoking	2.6 (1.5-4.7)	0.001*	2.1 (1.1-3.9)	0.021*
Atrial fibrillation	2.9 (1.7-5.2)	<0.001*	3.3 (1.8-6.1)	<0.001*
Prior stroke/TIA	1.9 (1.0-3.6)	0.043*	2.2 (1.2-4.2)	0.014*
Large-artery atherosclerosis	1.6 (0.8-3.0)	0.165	1.5 (0.8-2.9)	0.217
Cardioembolic stroke	2.3 (1.2-4.5)	0.013*	2.5 (1.3-4.9)	0.008*

*Statistically significant (p<0.05)

After adjusting for confounding factors, hypertension (OR 3.8, 95% CI 2.1-6.9, p<0.001), atrial fibrillation (OR 2.9, 95% CI 1.7-5.2, p<0.001) and smoking (OR 2.6, 95% CI 1.5-4.7, p=0.001) emerged as the strongest independent predictors of stroke severity. Similarly, atrial fibrillation (OR 3.3, 95% CI 1.8-6.1, p<0.001), hemorrhagic stroke type (OR 3.2, 95% CI 1.4-7.3, p=0.006) and hypertension (OR 2.9, 95% CI 1.6-5.4, p<0.001) were the strongest independent predictors of poor functional outcome at discharge. Age >65 years was significantly associated with both stroke severity (OR 1.8, 95% CI 1.0-3.2, p=0.046) and poor outcome (OR 2.4, 95% CI 1.3-4.3, p=0.005), reflecting the increased vulnerability of elderly patients to severe strokes and poor recovery. Cardioembolic stroke was independently associated with both severe stroke (OR 2.3, 95% CI 1.2-4.5, p=0.013) and poor outcome (OR 2.5, 95% CI 1.3-4.9, p=0.008), consistent with the typically larger infarct sizes observed in cardioembolic strokes. Prior history of stroke/TIA was a significant predictor of both stroke severity (OR 1.9, 95% CI 1.0-3.6, p=0.043) and poor outcome (OR 2.2, 95% CI 1.2-4.2, p=0.014), highlighting the cumulative impact of recurrent cerebrovascular events on brain reserve and recovery potential. Diabetes mellitus was significantly associated with poor outcome (OR 1.9, 95% CI 1.0-3.6, p=0.048) but was not an independent predictor of stroke severity.

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Table 7: Age and Sex Distribution Across Stroke Subtypes

Stroke Subtype	Mean Age ± SD	Male n (%)	Female n (%)
Ischemic Stroke			
Large-artery atherosclerosis (n=45)	65.3 ± 10.2	29 (64.4%)	16 (35.6%)
Cardioembolic (n=30)	68.7 ± 11.8	16 (53.3%)	14 (46.7%)
Small-vessel occlusion (n=27)	63.1 ± 9.6	17 (63.0%)	10 (37.0%)
Other determined etiology (n=7)	48.3 ± 14.7	4 (57.1%)	3 (42.9%)
Undetermined etiology (n=13)	62.8 ± 13.5	6 (46.2%)	7 (53.8%)
Hemorrhagic Stroke			
Deep ICH (n=15)	62.5 ± 11.4	9 (60.0%)	6 (40.0%)
Lobar ICH (n=8)	70.9 ± 8.3	4 (50.0%)	4 (50.0%)
Cerebellar/Brainstem ICH (n=5)	59.8 ± 13.7	3 (60.0%)	2 (40.0%)
SAH (n=6)	52.7 ± 15.2	4 (66.7%)	2 (33.3%)

Patients with stroke of other determined etiology were significantly younger (mean age 48.3 ± 14.7 years) compared to other stroke subtypes ($p<0.001$), consistent with the predominance of non-atherosclerotic arteriopathies, hypercoagulable states and genetic disorders in younger stroke patients. Cardioembolic stroke patients had the highest mean age (68.7 ± 11.8 years), reflecting the increasing prevalence of atrial fibrillation with age. Among hemorrhagic stroke subtypes, patients with lobar ICH had the highest mean age (70.9 ± 8.3 years), consistent with the association between cerebral amyloid angiopathy and advanced age. Males predominated in most stroke subtypes, particularly in large-artery atherosclerosis (64.4%), small-vessel occlusion (63.0%) and SAH (66.7%). However, there was a higher proportion of females in the undetermined etiology group (53.8%), possibly reflecting the diagnostic challenges in elderly female patients.

DISCUSSION

This prospective observational study provides comprehensive insights into the etiology and risk factor profiles of stroke in a cohort of 156 patients. Our findings demonstrate the complex interplay between various risk factors and stroke subtypes with important implications for prevention and management strategies. The distribution of stroke types in our study (78.2% ischemic and 21.8% hemorrhagic) is consistent with global epidemiological data. The Global Burden of Disease Study 2019 reported that ischemic stroke accounts for approximately 70-80% of all strokes worldwide with hemorrhagic stroke comprising the remaining 20-30% (GBD 2019 Stroke Collaborators, 2021). Among ischemic stroke subtypes, large-artery atherosclerosis was the most prevalent (36.9%), followed by cardioembolic stroke (24.6%) and small-vessel occlusion (22.1%). This distribution differs somewhat from previous large-scale studies such as the TOAST registry, which reported a higher proportion of cardioembolic strokes and strokes of undetermined etiology (Adams et al., 1993). The higher proportion of large-artery atherosclerosis in our study may reflect the increasing prevalence of atherosclerotic risk factors in the population, including hypertension, dyslipidemia and diabetes mellitus. The predominance of deep ICH (53.6% of all ICH cases) among hemorrhagic strokes is consistent with findings from other studies and is strongly associated with hypertension (Qureshi et al., 2009). The higher proportion of lobar ICH (28.6%) in our cohort compared to some previous studies may reflect the aging population and the increasing prevalence of cerebral amyloid angiopathy, which typically affects cortical and subcortical vessels in the cerebral lobes (Charidimou et al., 2017).

Hypertension emerged as the most prevalent risk factor (72.4%) across all stroke types with a significantly higher prevalence in hemorrhagic stroke (85.3%) compared to ischemic stroke (68.9%). This finding aligns with the INTERSTROKE study, which identified hypertension as the strongest risk factor for stroke with a population attributable risk of 47.9% (O'Donnell et al., 2016). The strong association between hypertension and stroke, particularly hemorrhagic stroke, underscores the critical importance of blood pressure control in stroke prevention. Dyslipidemia (58.3%) and diabetes mellitus (44.2%) were also highly prevalent in our study population, particularly among patients with ischemic stroke. These metabolic risk factors contribute to accelerated atherosclerosis and endothelial dysfunction, promoting thromboembolic events (Boden-Albala et al., 2008). The significant association of dyslipidemia with large-artery atherosclerosis

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(82.2%) in our study emphasizes the importance of lipid management in preventing atherosclerotic stroke. Atrial fibrillation was present in 18.6% of all stroke patients and was strongly associated with cardioembolic stroke (80.0% of cardioembolic cases). This finding highlights the importance of cardiac evaluation in stroke patients and the potential benefit of anticoagulation in preventing recurrent cardioembolic events (Hart et al., 2007). The lower prevalence of atrial fibrillation in hemorrhagic stroke (2.9%) is expected, as anticoagulation for atrial fibrillation is a known risk factor for ICH. The high prevalence of potentially modifiable lifestyle risk factors, including smoking (32.1%), physical inactivity (54.5%) and excessive alcohol consumption (14.7%), suggests significant opportunities for primary stroke prevention through lifestyle modifications. The WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020 emphasized the importance of targeting these modifiable risk factors to reduce the global burden of stroke (WHO, 2013).

Our finding that 61.5% of patients had three or more risk factors underscores the multifactorial nature of stroke etiology. This cumulative burden of risk factors was significantly associated with stroke severity and poor functional outcomes, highlighting the importance of comprehensive risk factor management rather than focusing on individual risk factors in isolation. This approach is supported by the INTERSTROKE study, which demonstrated that the combined effect of multiple risk factors accounts for approximately 90% of the population attributable risk of stroke (O'Donnell et al., 2016).

Hypertension, atrial fibrillation and smoking emerged as the strongest independent predictors of stroke severity in our multiple logistic regression analysis. Similarly, atrial fibrillation, hemorrhagic stroke type and hypertension were the strongest predictors of poor functional outcome at discharge. These findings are consistent with previous studies that have identified these factors as significant determinants of stroke severity and prognosis (Arboix et al., 2010; Appelros et al., 2011). The association between cardioembolic stroke and both severe stroke and poor outcome in our study aligns with previous research demonstrating that cardioembolic strokes tend to be more severe and associated with higher mortality compared to other ischemic stroke subtypes (Arboix & Alió, 2010). This is likely due to the typically larger infarct sizes observed in cardioembolic strokes and the higher likelihood of early recurrence. The significant impact of prior stroke/TIA on both stroke severity and poor outcome highlights the cumulative effect of recurrent cerebrovascular events on brain reserve and recovery potential. This finding underscores the importance of aggressive secondary prevention measures in patients with a history of stroke or TIA.

The significantly younger age of patients with stroke of other determined etiology (mean 48.3 years) compared to other stroke subtypes in our study emphasizes the importance of comprehensive etiological workup in young stroke patients. Rare causes such as arterial dissection, vasculitis and hypercoagulable states are more common in this age group and may require specific therapeutic approaches (Smajlović, 2015). The male predominance in most stroke subtypes observed in our study is consistent with global epidemiological data showing higher stroke incidence in men compared to women of similar age (Arnao & Caso, 2014). However, the higher proportion of females in the undetermined etiology group may suggest sex-specific diagnostic challenges or risk factors that require further investigation.

The strengths of our study include its prospective design, comprehensive assessment of risk factors and detailed classification of stroke subtypes based on established criteria. The inclusion of both ischemic and hemorrhagic stroke provides a comprehensive overview of stroke etiology and risk factors. However, several limitations should be acknowledged. First, the relatively small sample size (N=156) and single-center design may limit the generalizability of our findings. Second, the cross-sectional nature of the study precludes establishing causal relationships between risk factors and stroke outcomes. Third, some risk factors, such as obstructive sleep apnea and subclinical atrial fibrillation, may have been underdiagnosed due to the limitations of diagnostic testing during the acute hospital stay. Fourth, the relatively short follow-up period (limited to hospital discharge) does not allow for assessment of long-term outcomes and recurrence rates. Finally, genetic and environmental factors, which may contribute to stroke risk, were not comprehensively evaluated in this study.

CONCLUSION

This study provides valuable insights into the etiology and risk factor profiles of stroke in a cohort of 156 patients. Our findings confirm the high prevalence of modifiable risk factors with hypertension being the predominant factor across all stroke subtypes. The distinct patterns of risk factor distribution among different stroke subtypes highlight the complex and heterogeneous nature of stroke etiology. The identification of hypertension, atrial fibrillation and smoking as strong independent predictors of stroke severity and poor outcome underscores the importance

of targeting these factors in prevention strategies. The coexistence of multiple risk factors in the majority of patients and its association with worse outcomes emphasizes the need for a comprehensive approach to risk factor management. Early recognition and aggressive management of modifiable risk factors, particularly hypertension, could significantly reduce the burden of stroke. Age-specific and sex-specific considerations in stroke etiology and risk factors also warrant attention in both research and clinical practice. Future larger-scale, multicenter studies with longer follow-up periods are needed to validate our findings and to explore additional factors that may influence stroke etiology, severity and outcomes. Such research would contribute to the development of more personalized prevention and management strategies, ultimately reducing the global burden of stroke.

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