Subtypes, Risk Factors and Site of Stenosis of Ischaemic Stroke in a University Hospital in Bangladesh

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ABSTRACT

Stoke is the second most common cause of death and the most common cause of adult disability. To plan an efficient evaluation and treatment of an individual patient with ischaemic stroke, the clinician should be familiar with the subtyping of ischaemic stroke patients and the risk factors analysis of different aetiology. Eight hundred seventy-seven (877) patients have been selected for this cross-sectional study conducted in a university hospital of Bangladesh from 2014 to 2018, to whom brain imaging [Computed Tomography (CT)/ Magnetic Resonance Imaging (MRI)], vascular imaging [Magnetic Resonance Angiogram (MRA), Digital Subtraction Angiogram (DSA)], ECG and echocardiography have been done. We did subtyping according to TOAST criteria. The mean age of patients was 60.5 ± 11 years. Most patients (29.33%) belonged to the age group 51 – 60, where 70.47% of subjects were male and 29.53% were female. In this study, 43.87% of patients were in the large artery atherosclerosis group, 23.83.% in the small vessel occlusion group, 8.46% in the cardiac embolism group, 19.30% in the undetermined aetiology group and 4.54% in other determined aetiology. Among risk factors hypertension, diabetes mellitus, dyslipidaemia was present in 58.15%, 38.42%, and 38.88% of patients, respectively. In ischaemic stroke patients, large artery atherosclerosis was the most common subtype and hypertension was significant in this group. Extracranial stenosis was more common in ischaemic stroke.

INTRODUCTION

Worldwide stroke is the second most common cause of death (Katan & Luft, 2018) and the most known cause of severe disability (Adamson et al., 2004). Worldwide 5.7 million people died in 2005 and projected to rise to 7.8 million in the year 2030. According to Global burden of disease (GBD) 2016, death due to stroke in South Asia has increased from 15% to 21% and the mean global lifetime risk of stroke has increased from 22.8% to 24.9%. Strokes can be classified into ischaemic and haemorrhagic types (Donkor, 2018). Worldwide about 69% of stroke, 71% of stroke-related death and 78% of DALYs (disability-adjusted life years) lost occurred in low-income and middle-income countries. Over the last forty years, the stroke incidence in low- and middle-income countries has become more than doubled. During this time, stroke incidence has declined by 42% in high-income countries. Globally there was a 25% increase in the incidence of people ranging from 20 – 64 years of age, a 23% increase in prevalence in high-income countries, increase in mortality rate in South Asia from 1990 to 2010 (Feigin et al., 2010).

Stroke is the third leading cause of death in Bangladesh after heart disease and infectious disease. The mortality rate of stroke was 6% in 2006 and 8.57% in 2011. The prevalence rate of stroke in Bangladesh is around 0.3% until the year 2010 (Islam et al., 2013).

Ischaemic stroke is a heterogeneous disorder and there are multiple mechanisms for it (Ay et al., 2007). Pathophysiologically ischaemic stroke may occur due to thrombosis of large or small vessels, emboli from the heart or artery, hypoperfusion in the watershed area or border zone (Deb et al.,2010). In the western population, cardioembolic stroke is the dominant cause; in India, large artery atherosclerosis and Pakistan, lacunar stroke is the most common cause of ischaemic stroke (Assad et al., 2018). The important risk factors are uncontrolled hypertension, dyslipidaemia, diabetes mellitus, coronary artery disease, atrial fibrillation, smoking and those vary with stroke subtypes (Beg et al., 2015). Various aetiologies often result in variation in outcome, treatment, and likelihood of recurrence in ischaemic stroke. Large infarct resulting from occlusion of the internal carotid artery or proximal middle cerebral artery has the worst prognosis. Mortality is higher among patients with large-artery atherosclerotic lesions than lacunar stroke. Recurrent strokes are more common in patients with cardioembolic stroke. Anticoagulants may be prescribed to prevent recurrent cardio-embolic stroke. Carotid stenting and carotid endarterectomy are useful in preventing recurrent stroke with large artery atherosclerosis. Thus, determining the cause of stroke does influence the outcome and choice of treatment.

It is difficult to include all stroke subtypes within a single classification system. The TOAST classification of subtypes was introduced to produce uniformity. The TOAST classification was the first classification system based on stroke mechanisms, vascular risk factors, early and long-term recurrence and survival were found to be different among the ischaemic stroke subtypes classified by TOAST. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification was introduced in 1993. It is divided into 5 groups: Large Artery Atherosclerosis (LAA), Cardio-embolism (CE), Small Vessel Occlusion (SVO), Stroke of Other Determined Etiology (SODE), Stroke of Undetermined Etiology (SUDE) (Adams et al., 1993). In a retrospective study, TOAST classification had been proven as valid and reliable (Fure et al., 2005).

Several studies had been done to identify the risk factors in each subtype in a different community. Data is scarce regarding ischaemic stroke subtypes and their risk factors in Bangladeshi people. We wanted to know the common aetiology, subtypes, and risk factors of each subtype in ischaemic stroke.

MATERIALS AND METHODS

This was a cross-sectional study conducted in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka which is a tertiary care hospital and postgraduate institute. Here patients get admitted through outdoor patient department service and no emergency admission was available. In this institute, interventional neurology works that include cerebral DSA, carotid stenting, vertebral stenting, endovascular coiling, and embolization are done by a neurologist.

This study was done in the Neurology Department of BSMMU from March 2014 to November 2018. After the approval from Institutional Review Board (NO. BSMMU/2014/3938), informed written consent was taken from all patients. Stroke was defined according to WHO criteria as features of focal and global cerebral dysfunction that lasts for more than 24 hours with no other than vascular cause. Any ischaemic stroke patients of more than 18 years of age and within 10 days of symptom onset, willing to be included were enrolled in this study. Any TIA, venous stroke or haemorrhagic stroke patients were excluded from enrollment.

A purposive non-random sampling method had been used in this study. The patients were diagnosed with ischaemic stroke by history, clinical examinations, and brain imaging. A total of 1,978 ischaemic stroke patients were enrolled in this study. Among them, 877 patients had been selected for subtyping of ischaemic stroke, to whom vascular imaging (MRA, CTA, DSA), ECG, echocardiography and other relevant biochemical tests had been done. All patients could not do the necessary investigations for subtyping due to financial constraints.

Demographic data and information about risk factors (hypertension, diabetes, dyslipidaemia, history of the previous stroke, and cardiac disease) were documented.

Subtyping of the ischaemic stroke into 5 categories was done according to the TOAST criteria (Adams et al., 1993). It is a commonly used classification system that uses the clinical feature, brain imaging findings, and vascular imaging along with some ancillary test.

1. Large Artery Atherosclerosis (LAA) diagnosed by clinical features of cortical dysfunction and criteria of vascular imaging that is > 50% stenosis or occlusion of the major artery or cortical artery.
2. Cardio-embolism (CE) diagnosed by major risk factors for embolism at least one and no apparent evidence of other subtypes.
3. Small Vessel Occlusion (SVO) diagnosed by clinical features of lacunar syndrome with no cortical features and lesion in brain imaging should be <1.5 cm.
4. Stroke of Other Determined Etiology (SODE) diagnosed by other evidence of stroke risk factors as hypercoagulability, evidence of vasculitis, dissection, and Moyamoya found in vascular imaging.
5. Stroke of Undetermined Etiology (SUDE) diagnosed by when two or more causes were identified. Subtyping was done after all documents were available to the patient.

Statistical analysis was performed using software SPSS 20 for windows. Numerical data are presented as mean ± standard deviation (SD) and risk factors and subtyping are presented as percentages.

RESULTS

Of all 877 patients, 606 (69.10%) were male and 271 (30.90%) were female (Table 1).

Table 1 Distribution of gender among the subtypes (*n* = 877)

Subtype	Male	Female	Total
Large Artery Atherosclerosis (LAA)	273	112	385
Cardio-embolism (CE)	22	52	74
Small Vessel Occlusion (SVO)	153	56	209
Stroke of Other determined Etiology (SODE)	24	16	40
Stroke of Undetermined Etiology (SUDE)	134	35	169
Total	606 (69.10%)	271 (30.90%)	877 (100%)

The mean age of patients was 60.5 ± 11 years. Most patients (32.27%) belonged to the age group 51 – 60 years, followed by 26.11% from 61 – 70 years age groups. A total of 67.5% was above the age of 50 years (Table 2).

Table 2 Distribution of age among the subtypes (*n* = 877)

Subtype	<30 yrs	31 – 40 yrs	41 – 50 yrs	51 – 60 yrs	61 – 70 yrs	>70 yrs	Total
Large Artery Atherosclerosis (LAA)	4	9	64	165	106	37	385
Cardio-embolism (CE)	11	11	34	7	6	5	74
Small Vessel Occlusion (SVO)	0	10	66	57	60	16	209
Stroke of Other determined Etiology (SODE)	10	17	3	7	3	0	40
Stroke of Undetermined Etiology (SUDE)	7	14	25	47	54	22	169
Total	32	61	192	283	229	80	877
Percentage	3.65	6.95	21.90	32.27	26.11	9.12	100

The most common stroke subtypes were Large Artery Atherosclerosis LAA (43.87%), followed by Small Vessel Occlusion SVO (23.83%), Stroke of Undetermined Etiology SUDE (19.30%), Cardio-embolism CE (8.46%), and Stroke of Other Determined Etiology SODE (4.54%) (Table 3).

Table 3 Distribution of the subtypes of ischaemic stroke among the participants (*n* = 877)

| Subtype	Number of patients	Percentage
Large Artery Atherosclerosis (LAA)	385	43.87
Cardio-embolism (CE)	74	8.46
Small Vessel Occlusion (SVO)	209	23.83
Stroke of Other Determined Etiology (SODE)	40	4.54
Stroke of Undetermined Etiology (SUDE)	169	19.30
Total	877	100

Regarding risk factors, hypertension was found in 58.15% of patients followed by dyslipidaemia and diabetes mellitus at 38.88% and 38.42% respectively. Among the risk factors, hypertension was significantly high (82.59% of 385) in the large artery atherosclerosis group which was statistically significant. Diabetes mellitus was also high in the large artery atherosclerosis group (46.23% of 385), followed by small vessel occlusion (43.06% of 209) (Table 4).

Table 4 Distribution of risk factors of different etiology (*n* = 877)

Category	Previous H/O stroke	DM	HTN	DL
Large Artery Atherosclerosis (LAA)	53 (13.77%)	178 (46.23%)	318 (82.59%)	189 (49.09%)
Cardio-embolism (CE)	6 (8.1%	3 (4.05%)	10 (13.51%)	9 (12.16%)
Small Vessel Occlusion (SVO)	12 (5.74%)	90 (43.06%)	87 (41.62%)	77 (36.84%)
Stroke of Other Determined Etiology (SODE)	3 (7.5%)	5 (12.5%)	4 (10%)	7 (17.5%)
Stroke of Undetermined Etiology (SUDE)	17 (10.09%)	61 (36.09%)	91 (53.84%)	59 (34.92%)
Total	94 (10.37%)	337 (38.42%)	510 (58.15%)	341 (38.88%)
p-**value**	0.962	0.201	0.005*	0.201

HTN: Hypertension, DM: Diabetes Mellitus, DL: Dyslipidaemia

Among the large artery atherosclerosis group, 189 patients (49.09%) had 70 – 99% stenosis followed by 116 (30.12%) patients who had complete occlusion (Table 5). Also, 75.56% of stenosis was extracranial and 24.44% was intracranial (Figure 1).
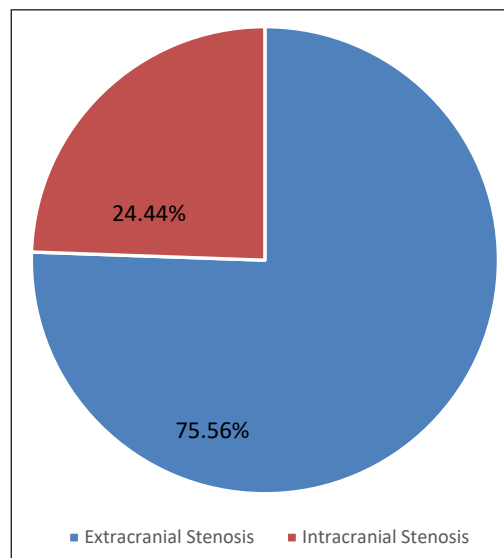
Figure 1 Distribution of site of significant (>50% stenosis) vascular pathology

Table 5 Degree of stenosis among different aetiology (*n* = 877)

| Degree of stenosis	Large Artery Atherosclerosis (LAA)	Stroke of Other Determined Etiology (SODE)	Stroke of Undetermined Etiology (SUDE)
<50%	0	17 (42.50%)	74 (43.79%)
50 – 69%	80 (20.79%)	4 (10.00%)	39 (23.07%)
70 – 99%	189 (49.09%)	3 (7.50%)	43 (25.45%)
100%	116 (30.12%)	16 (40.00%)	13 (7.69%)
Total	385	40	169

DISCUSSION

The goal of this study was to analyze and evaluate the subtyping of ischaemic stroke and the risk factor of each subtype according to TOAST criteria. A total of 69.10% of respondents of this study was male, and it showed male predominance than female in ischaemic stroke and almost two-thirds of patients are above the age of 50. Beg et al. (2015) found in India that the number of males is greater than that of female, Bhowmik et al. (2016) found 67.7% in Bangladesh, Shakya et al. (2019) found 51.1% in Nepal. The finding is also similar in developed countries. A study of 1,136 patients done by Caso et al. (2010) found that the number of females was lower (46%) than that of the male. Bender et al. (2017) found female dominance (52%) in their study, but they took both ischaemic and haemorrhagic stroke including SAH in their study.

The mean age of this present study was 60.5 ± 11 years which was comparable to the study done by (Beg et al., 2015). A study done by Cotter et al. (2011) found that the mean age was 63.2, and another study of 679 patients done by Bhowmik et al. (2016) found the mean age to be 60.4 years. In Nepal, Shakya et al. (2019) conducted a study where the mean age was 63.2 years. However, in Europe, Caso et al. (2010) found the mean age as 72.68 (±13.27).

This study revealed that with 43.67% ($n = 385$), Large Artery Atherosclerosis (LAA) is the most common subtype. Kaul et al. (2018) found 37.6% as LAA in India of 2,072 total patients like our findings. Again, a study conducted in Singapore by De Silva et al. (2007) within the South Asian population found 41% as LAA. Harris et al. (2018) in Indonesia found 59.6%, as LAA. Also, in the Chinese population, the result was similar to 37.4% which was done by Tan et al. (2018). In India, a similar study was done by Kannan et al. (2017). In LAA, imaging finding of infarction should be more than 1.5 cm in the cortical, subcortical, cerebellar or brain stem region (Figures 2 and 3). Supporting evidence by angiography of stenosis of more than 50% in extracranial (Figure 4) or intracranial (Figure 5) was evident.
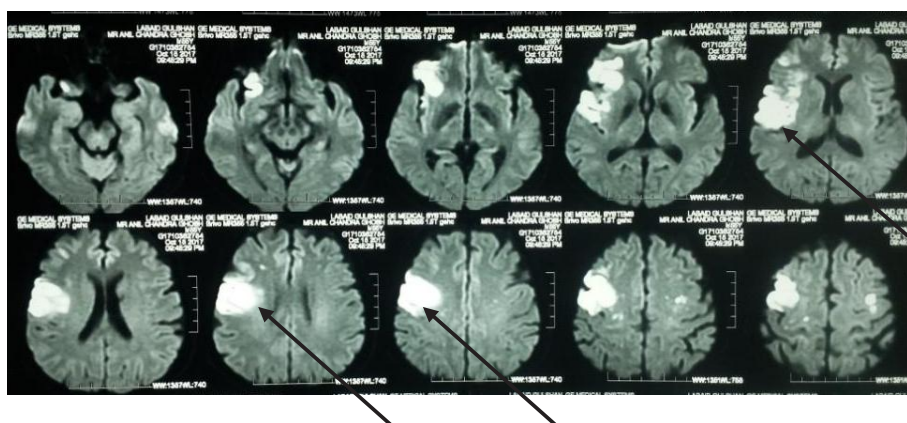
Figure 2 MRI of a patient of LAA (arrow showed infarction in both cortical and subcortical area which was >1.5 cm)
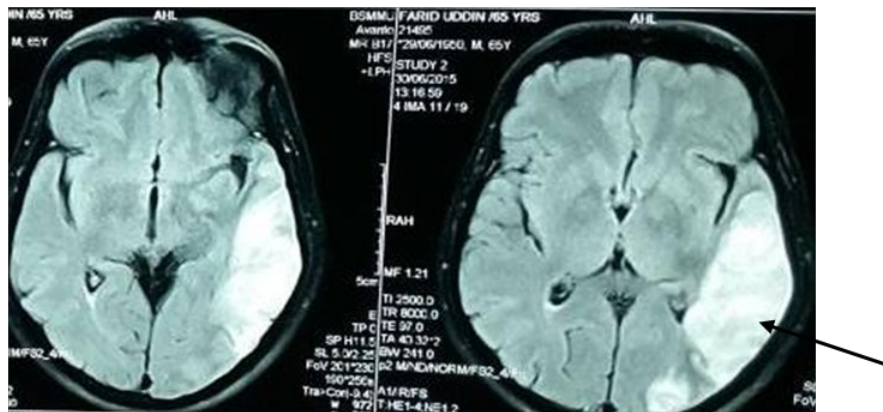
Figure 3 Large infarction in MCA territory (arrow showed infarction in left MCA territory, this is in favour of large artery atherosclerosis)

Contrary, Kang et al. (2003); Kolominsky-Rabas et al. (2001); Tian and Fan (2018) found 15.3%, 16.28%, and 31% of ischaemic stroke patients as LAA respectively. This variation could be due to ethnic origin. The use of cerebral DSA was more in our study because our department has more facility for it and MRA or CTA is more expensive than DSA. This may be a cause for finding more LAA in this study.

Figure 4 Severe Stenosis of ICA Origin (Arrow showed severe stenosis at the origin of Internal Carotid Artery, it\s in favor of large artery atherosclerosis)

Figure 5 Left MCA severe stenosis (arrow showed severe stenosis of the left middle cerebral artery after the bifurcation of internal carotid artery)

In this research, Small Vessel Occlusion (SVO) was 23.83% which was the second most common subtype. Most of the studies done in this sub-continent and South Asia found the comparable result to this study. Kaul et al. (2018) and Kannan et al. (2017) in India, Assad et al. (2018) in Pakistan, Harris et al. (2018) in Indonesia found 19.9%, 17.24%, and 27.7% respectively. Kannan et al. (2017) and Kaul et al. (2018) also found a similar result in their study with 23.4% and 18% respectively. In developed countries, the percentage of SVO is somewhat higher compared to our study. Jacková (2017) in the Crez Republic, Lee et al. (2010) in Taiwan, De Silva et al. (2007) in Singapore found 45.2%, 31.4%, 39.4%, and 35% respectively.

We found 8.46% of total ischaemic stroke patients as Cardio-embolism (CE) like another study done like Tian et al. (2018) as 8% and, Kaul et al. (2018) in India as 10%. In contrast, Kolominsky-Rabas et al. (2001) found CE as 27%, Kang et al. (2003) as 40.59%. This may be due to different population origin and the increased rate of cardiac disease, more extensive work like ECG, Echocardiography, Holter monitoring, Transesophageal echocardiography, and less cerebral angiography for evaluation of ischaemic stroke patients.

In this study, hypertension was the most common risk factor (58.15%) followed by dyslipidaemia (38.88%) and diabetes (38.42%). This is consistent with the other study in this subcontinent. In Pakistan, Assad et al. (2018), Manosalva and Jeerakathil (2016), Taj et al. (2010) and in India, Pathak et al. (2018) found hypertension 62.7%, 71%, 78% and 65% respectively. This finding is also consistent with a study in the Middle East, Korea as Kim et al. (2003), Rukn et al. (2019) found hypertension as 66% and 61.1% respectively. Assad et al. (2018) also found diabetes mellitus as 36.6% which was also comparable to this study.

In this study, hypertension was significantly present in large artery atherosclerosis which is also comparable with Assad et al. (2018). In our study, 75.56% of stenosis was extracranial. This finding is also comparable to the findings of Flaherty et al. (2013) and Barnett et al. (2010) which was 78.63% and 78.4% respectively.

Some limitations exist in this study as it was a hospital-based study and cardiac evaluation was limited only to ECG and echocardiography.

CONCLUSION

The most common subtype of ischaemic stroke in this study was the large artery atherosclerosis group and extracranial stenosis was more common than intracranial stenosis. This finding will lead to a future study that can identify the pathophysiology of LAA in this ethnic group. There were differences in risk factors between the subtypes of ischaemic stroke. Hypertension was significantly high in the large artery atherosclerosis group.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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