

Vascular Imaging Based Subtyping of Ischemic Stroke in BSMMU

SHAHIDULLAH M¹, DEY SK², AHMED A³, DAS P⁴, SULTANA N⁵

Abstract:

Background: Most strokes and stroke related death & disability happened in low and middle income countries. The clinician should be familiar with the sub typing of ischemic stroke patients and the risk factors analysis. Vascular imaging is necessary for classifying the patient. The main objective of this study was to evaluate the subtype of ischemic stroke patients and risk factor analysis of different etiology. **Method:** This is a hospital based prospective study in Bangladesh. Within the time frame of 2014 March to 2017 November; we analyzed 1978 patients of ischemic stroke within 10 days of symptom onset. Among them 877 patients have been selected for this study to whom brain imaging (CT/MRI), vascular imaging (MRA, DSA), ECG and echocardiography have been done. We did subtyping according to TOAST criteria. **Results:** The mean age of patients was 60.5±11 years with 70.47% subjects male and 29.53% female. Within the classification of TOAST, we have found 43.87% of patients were in large artery atherosclerosis group, 23.83.% in small vessel occlusion group, 8.46% in cardiac embolism group, 19.30% in undetermined etiology group and 4.54% in other determined etiology. Among risk factors hypertension in 58.15%, DM was found in 38.42%, hypercholesterolemia in 38.88% of patients. Hypertension was significantly high in large artery atherosclerosis group. **Conclusion:** In ischemic stroke patients, large artery atherosclerosis was the most common subtype and hypertension was significant in this group.

Keywords: Ischemic stroke, Subtype, TOAST criteria, Risk factor, HTN

Introduction:

Worldwide stroke is the second most common cause of death¹ and the most known cause of severe disability². Strokes can be classified into ischemic and hemorrhagic types³. Worldwide about 69% of stroke, 71% of stroke death and 78% of DALYs lost occurred in low-income and middle-income countries. Globally there was 25% increase in incidence of people ranging from 20-64 years of age, 23% increase in prevalence in high income countries, increase mortality rate in south Asia within 1990 to 2010⁴. Prevalence rate of stroke in Bangladesh is around 0.3%⁵. Ischemic stroke is a heterogeneous disorder and there are multiple mechanisms for it⁶. Pathophysiologically ischemic stroke may occur due to thrombosis of large or

small vessels, emboli from heart or artery, hypoperfusion in watershed area or border zone⁷. In western population cardioembolic stroke is the dominant cause, in India large artery atherosclerosis and in Pakistan lacunar stroke is the most common cause of ischemic stroke⁸. Among the important risk factors are uncontrolled hypertension, dyslipidaemia, diabetes mellitus, coronary artery disease, atrial fibrillation, smoking and those vary with stroke subtypes^{9,10}.

The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification was introduced in 1993 to classify ischemic stroke according to mechanism of ischemia. It is divided into 5 groups: large artery atherosclerosis (LAA), cardioembolism (CE), small vessel occlusion (SVO), stroke of other

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1. Dr. Md. Shahidullah, Associate Professor, Department Of Neurology, BSMMU
 2. Dr. Subash Kanti Dey, Associate Professor, Department Of Neurology, BSMMU
 3. Dr. Anis Ahmed, Assistant Professor, Department Of Neurology, BSMMU
 4. Dr. Panchanan Das, Associate Professor, Department Of Neurology, Cumilla Medical College
 5. Prof. Dr. Nahid Sultana, Professor, Department Of Community Medicine, Dhaka National Medical College

determined etiology (SODE), stroke of undetermined etiology (SUDE)¹¹. In retrospective study TOAST classification had been proven as valid and reliable¹². Many studies had been done to identify the risk factors in each sub types in different community. There is a little data regarding ischemic stroke subtypes and their risk factors in Bangladeshi people. We wanted to know the common etiology, subtypes and risk factors of each subtypes in ischemic stroke.

Methods:

This was a prospective, cross-sectional study conducted in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka which is a tertiary care hospital and post graduate institute. We took medical data of hospitalized patients in neurology department from March 2014 to November 2018. We defined stroke according to WHO criteria as features of focal and global cerebral dysfunction that lasting for more than 24 hours with no other than vascular cause. Any ischemic 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 hemorrhagic stroke patients were excluded for enrollment. After clinical examination brain imaging (CT/ MRI), ECG, echocardiography and vascular imaging (MRA/ CTA, cerebral DSA) had been advised in all patients. As financial matters have to be paid by patient himself so all patients were not able to do all investigations necessary for the sub typing of ischemic stroke. They did duplex study of neck vessels as vascular imaging but they were not included in this study. Total 1978 ischemic stroke patients were enrolled but only 677 had been selected for this study. Sub typing of ischemic stroke into 5 categories were done according to the TOAST criteria¹¹: 1. Large-artery atherosclerosis – LAA, diagnosed by clinical features of cortical dysfunction and criteria of vascular imaging that is > 50% stenosis or occlusion of major artery or cortical artery; 2. Cardioembolism- 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, moya-moya found in vascular imaging; 5. Stroke of undetermined etiology- SUDE, diagnosed by when two or more causes were identified. Sub typing was done after all documents were available to the patient. Statistical analysis was performed using software SPSS for windows. Numerical data is presented as mean ± standard deviation (SD) and risk factors and sub typing are presented as percentages. Chi-square & Fisher's exact test was done to compare between qualitative data. Analysis was defined significant when p- value is <0.05.

Results:

We enrolled 1978 patients of ischemic stroke within 10 days of symptom onset. Among them 877 patients had been selected for this study to whom brain imaging (CT/ MRI), vascular imaging (MRA, DSA), ECG and echocardiography had been done. Of all 877 patients, 542 (61.78 %) were male and 335 (36.22 %) were female. The mean age of patients was 60.5 ± 11 years.

Table-I
Distribution of respondents by age and gender

Distribution of respondents by age and gender		
Age Group	Number	Percentage
<30	41	4.67%
30-40	76	8.67%
41-50	170	19.33%
51-60	257	29.33%
61-70	207	23.67%
>70	126	14.33%
Total	877	100%
By gender		
Male	618	70.47%
Female	259	29.53%
Total	877	100%

Table-II
The subtype of Ischemic Stroke

Category	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%

Table-III
Risk factors of different etiology

Category	Previous H/O stroke	DM	HTN	DL
LAA n= 385	53 (13.77%)	178 (46.23%)	318 (82.59%)	189 (49.09%)
CEn=74	6 (8.1%)	3 (4.05%)	10 (13.51%)	9 (12.16%)
SVO n= 209	12 (5.74%)	90 (43.06%)	87 (41.62%)	77 (36.84%)
SODEn= 40	3 (7.5%)	5 (12.5%)	4 (10%)	7 (17.5%)
SUDEn= 169	17 (10.09%)	61 (36.09%)	91 (53.84%)	59 (34.92%)
Total (n=877)	94 (10.37%)	337 (38.42%)	510 (58.15%)	341 (38.88%)
p value	.962	.201	.005*	.201

Most patients (29.23%) belonged to the age group 51-60, followed by 23.67% from 61-70 age groups. A total 67.33% was above the age of 50. The most common stroke subtypes was large artery atherosclerosis LAA (n=385, 43.87%), followed by small vessel occlusion SVO (n=209, 23.83%), Stroke of undetermined etiology SUDE (n=169, 19.30%), Cardio-embolism CE (n= 74, 8.46%), Stroke of other determined etiology SODE (n=40, 4.54%).

About risk factors, hypertension was found in (n=510, 58.15%) patients followed by dyslipidaemia (n=341, 38.88%) and diabetic mellitus (n=337, 38.42%). Among the risk factors, hypertension was significantly high (n=318, 82.59% of 385) in large artery atherosclerosis group which was significant, followed by stroke of undetermined etiology (n=91, 53.84% of 169). Diabetes mellitus was also high in large artery atherosclerosis group (n=178, 46.23% of 385), followed by small vessel occlusion (n= 90, 43.06% of 209).

Discussion:

Our goal was to know the sub typing of ischemic stroke and risk factor of each subtype according to TOAST criteria. It is commonly used classification system that uses clinical feature, brain imaging findings, and vascular imaging plus some ancillary test. It is the largest single center study about sub typing of ischemic stroke in Bangladesh. 877 patients had been selected for the study among 1978 patients as rest of the patients did not get the opportunity to do basic investigations for enrollment. This study finds male predominance than female in ischemic stroke and almost two thirds of patients are above the age of 50. Renjen PN and his associates¹⁰ found male is greater than female in India. Bhowmik NB et al.¹³ found (67.7%) in Bangladesh, Shakya D and associates¹⁴ found (51.1%) in Nepal. The finding is also similar in developed countries. A study of 1136 patients done by Caso V et al.¹⁵ found female was lesser than (46%) male. Marija B et al.¹⁶ found female

dominance (52%) in their study, but they took both ischemic and hemorrhagic 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 Renjen PN and associates¹⁰. A study of 2450 patients done by Bouzidi and associates¹⁷ found mean age was 63.2, and another of 679 patients done by Bhowmik NB et al.¹³ found 60.4 years. In Nepal mean age was 63.2 years done by Shakya D and associates¹⁴. However in Europe Caso V et al.¹⁵ found mean age as 72.68(±13.27).

This study finds large artery atherosclerosis (LAA) is the most common sub type as 43.67% (n=385). Kaul S et al.¹⁸ found 37.6% as LAA in India of total 2072 patients similar to our findings. Again a study conducted in Singapore by Dev Silva et al. within South Asian population found 41% as LAA¹⁹. Wong LK found 47% in Thailand, Harris S et al.²⁰ found 59.6% in Indonesia, as LAA. Also in Chinese population the result was similar as 37.4% done by Tan YF²¹. In India study done by Shubhakaran KP²² and Raghuvanshi S²³ showed also similar result. In contrary, Kolominsky-Raba PL et al.²⁴ Kang DW et al.²⁵ Aquil N et al.²⁶ found 15.3%, 16.28%, 31% ischemic stroke patients as LAA respectively. This variation could be due to ethnic origin. More cerebral DSA in our study population can be one explanation for finding more LAA as there are facility to do cerebral DSA in our department and MRA or CTA is more expensive than DSA.

In our analyses small vessel occlusion (SVO) were 23.83% which was the second most common sub type. Most of the studies done in this sub continent and south Asia found comparable result like this study. Kaul S et al¹⁸ and Raghuvanshi S²³ in India, Zafar et al.⁸ in Pakistan, Harris S et al.²⁰ in Indonesia found 19.9%, 17.24%, 27.7% respectively. Murthy Raju ISSVP²⁷ Kaul S²⁸ also found similar result in their study like 23.4% and 18% respectively. In developed countries the percentage of SVO is somewhat higher than in this study. Biswas M²⁹ in USA, Ihle-Hansen H et al.³⁰ in Norway, Wu CY³¹ in Taiwan, De silva DA¹⁹ in Singapore found 45.2%, 31.4%, 39.4%, 35% respectively. Aquil N²⁶ in Pakistan got 43% in their study that is higher than this study.

We found 8.46% of total ischemic stroke patients as cardio embolism (CE) similar to other study done in this sub continent like Aquil N et al.²⁶ and Syed NA et al.³² in Pakistan as 8% and 6% respectively, Kaul S et al¹⁸ & Shubhakaran KP²² in India as 10% both . Contrary, Kolominsky-Raba PL et al.²⁴ found CE as 27%, Kang DW et al.²⁵ as 40.59%, Ihle-Hansen H et al.³⁰ as 31.4%. This may be due to different population origin and the increased rate of cardiac disease, more extensive work like ECG, Echocardiography, Holter monitoring, Trans-esophageal echocardiography and less cerebral angiography for evaluation of ischemic 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 Zafar F et al.⁸, Sharif F et al.³³, Taj F et al.³⁴ and in India Pathak A. et al.³⁵ found hypertension 62.7%, 71%, 78% and 65% respectively. This finding is also consistent with study in middle East, Korea as Rukn SA. et al.³⁶ and Kim et al.³⁷ found hypertension as 66% and 61.1% respectively. Zafar F. et al.⁸ also found DM as 36.6% which was also comparable to this study. In this study hypertension was significantly associated in large artery atherosclerosis which is also comparable with Zafar F. et al.⁸.

Conclusion:

The most common subtype of ischemic stroke in our study was large artery atherosclerosis. Hypertension was significantly high in large artery atherosclerosis group. Among male patients hypertension, diabetes, dyslipidaemia were significantly high.

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