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Digital Subtraction Angiographic Pattern of Extracranial and Intracranial Atherosclerotic Arterial Stenosis among Ischemic Stroke Patients

HOSSAIN MA[1], RAHMAN HZ[2], SHAHIDULLAH M[3], ISLAM MR[4], HANNAN MA[5], RIZVI AN[6], SHEIKH AK[7], DEY SK[8], HABIB MA[9], AHMED A[10], RAKANUZZAMAN M[11], RAHMAN DM[12], AHTESAM MS[13], ISLAM MM[14]

Abstract:

***Background**: Stroke is the second leading cause of death in adult population throughout the world and is the most common cause of severe adult physical disability. Atherosclerotic stenosis is one of the predominant cause of ischemic stroke. The aim of this study was to evaluate the type, number and severity of intracranial and extracranial atherosclerotic stenosis and its association with different risk factors. **Methods:** This prospective observational study was conducted in the Department of Neurology, BSMMU, Dhaka, from July 2017 to August 2018. Only patients having significant (≥50%) symptomatic stenosis were included in this study. **Results**: In total 42 cases, 25 patients had extracranial stenosis, 13 patients had intracranial stenosis and 4 patients had both intracranial and extracranial stenosis. Overall 17 (40.47%) patients have intracranial involvement and 29 (69.04%) patients had extracranial involvement. The most commonly involved intracranial stenotic segment was MCA, present in 8 (32%) out of 25 intracranial segments followed by ICA 7 (28%) and intracranial vertebral artery 4(16%). Most commonly involved extracranial stenotic segment was ICA, present in 37 (77.08%) out of 48 extracranial segments. Diabetes was found to be the most common risk factor of intracranial stenosis (p value 0.022) while hypercholesterolemia was the major risk factor for severe (≥70%) stenosis. **Conclusion**: Extracranial arterial stenosis is more common than intracranial arterial stenosis. Anterior circulation stenosis is more common than posterior circulation stenosis. Intracranial stenosis is more prevalent in diabetic patients. Hypercholesterolemiaismore commonly seen in severe (e"70%) stenosis.*

***Key Words**: Atherosclerotic Stenosis, Digital Subtraction Angiography, Stroke etc.*

Introduction:

The World Health Organization definition of stroke is "Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than that of vascular origin"[1]. Stroke is the second leading cause of death in adult population throughout the world and is the most common cause of severe adult physical disability. It is also ranked as the sixth leading cause of disability-adjusted life years

1. Md. Alamgir Hossain,Resident, phase-B,MD (Neurology), BSMMU, Dhaka, Bangladesh.
2. Prof. (Dr.) Hasan Zahidur Rahman, Professor, Department of Neurology ,BSMMU, Dhaka, Bangladesh.
3. Md. Shahidullah, Associate Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
4. Prof. (Dr.) Md. Rafiqul Islam, Professor & Chairman, Department of Neurology, Dhaka, Bangladesh.
5. Prof. (Dr.) M.A Hannan, Professor & Ex Chairman,Department of Neurology, BSMMU, Dhaka, Bangladesh.
6. Prof. (Dr.) Abu Nasir Rizvi, Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
7. Dr. Abdul Kader Sheikh, Associate Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
8. Dr. Suvash Kanti Dey, Associate Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
9. Dr. Md. Ahsan Habib, Associate Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
10. Dr. Anis Ahmed, Assistant Professor, Department of Neurology, BSMMU, Dhaka, Bangladesh.
11. Dr. Md. Rakanuzzaman, Resident, Phase-B, MD (Neurology), BSMMU, Dhaka, Bangladesh.
12. Dr. Dewan Mushfiqur Rahman, Resident, Phase-B,MD (Neurology), BSMMU, Dhaka, Bangladesh.
13. Dr. Md. Saifullah Ahtesam, Resident, Phase-B, MD (Neurology), BSMMU, Dhaka, Bangladesh.
14. Dr. Md. Monirul Islam, Resident, Phase-B, MD (Neurology), BSMMU, Dhaka, Bangladesh.

(DALY; one DALY is one lost year of healthy life) in 1990 and is projected to become the fourth leading cause by the year 2020[2].

Strokes are broadly categorized as ischemic or hemorrhagic. Ischemia causes about 80% of stroke cases and 20% are caused by hemorrhage. Ischemic stroke is due to occlusion of a cerebral blood vessel and causes cerebral infarction. The resultant neurologic syndrome corresponds to a portion of the brain that is supplied by one or more cerebral vessels[2].The principle cause of cerebral infarction is atherosclerosis and its sequelae. Atherosclerotic plaques are eccentric focal fibro-fatty intimal thickening and affect large, medium and small arteries[2].

A growing body of data suggest that there are important differences in the distribution of occlusive vascular disease among different ethnic origins [3]. Data from Northern Manhattan Stroke study have shown that intracranial stenosis to be the cause of ischemic stroke in 1% of Caucasian, 6% of African Americans and 11% of Hispanics [3]. In Europeans, intracranial stenosis appears to be the cause of ischemic stroke in 2-7% of the cases in Germany [4,5],10% in Greece and 12% in Spain [6].

For decades, it is well described that patients of Asian, African & Hispanic ancestry were at higher risk of intracranial atherosclerosis [7]. Different studies showed that intracranial stenosis is the most common vascular lesion among ischemic stroke patients from India, Thailand, Singapore, Korea, Japan, China.

For patients with major stroke, the mortality rate in a subsequent stroke is 40%. Prospective Study of Symptomatic Atherothrombotic Intracranial Stenosis (The GESICA Study) found that despite medical treatment, the 2 years recurrence risk rate of ischemic event in the territory of the stenotic artery was 38.2%. Patients with 70% to 99% intracranial stenosis have a > 2-fold risk of stroke in the territory of the stenotic artery than do patients with <70% stenosis [8]. Moreover, most recurrent strokes occurred in same arterial territory, were non lacunar, and nearly half of them were disabling. On the other hand, the stroke recurrence rate is 7% to 13% in patients with symptomatic extracranial stenosis who are treated with appropriate medication[9]. Hence stroke prevention is an important concept. Ability to accurately assess the site of stenosis has become important to identify the patient who would benefit from surgical/ radiological intervention.

Objectives of the study were to evaluate the pattern and distribution of stenosis by Digital Subtraction Angiography though it is invasive, relatively costly and its association with risk factors among ischemic stroke patients in the Bangladeshi population and in other countries for comparison.

Material and Method:

A cross-sectional study was conducted in Dept. of Neurology, BSMMU, Dhaka. An ethical approval was obtained from the Institutional Review Board(IRB). Purposive sampling was performed for 42 known cases of all age groups having the clinical diagnosis of stroke and ischemic stroke on imaging and presence of significant symptomatic stenosis in DSA. Written consent was obtained from all the participants. Patients with stroke of cardioembolic origin and stroke from non-atherosclerotic vasculopathy were excluded from the study. Proper history was taken, physical and neurological examination keeping in mind of the demographic and clinical variables, was done and all relevant investigations were completed. Fitness of the patient for DSA was assessed. DSA was done in the Paediatric Catheter Laboratory of Bangabandhu Sheikh Mujib Medical University (BSMMU). From DSA, information regarding location and degree of atherosclerotic stenosis, number of stenotic segments were obtained according to the specified objectives. Total 145 patients underwent DSA during the study period, among them 82 patients were ischemic stroke. Patients with normal DSA findings, stenosis due to non-atherosclerotic vasculopathy and significant stenosis in asymptomatic side were excluded from the study. Only patients with significant symptomatic stenosis (42 in number) were considered as cases.

The detail history regarding potential risk factors associated with atherosclerotic ischemic stroke

was obtained from each patient and from the medical records. Patients were labeled as hypertensive if their blood pressure surpassed 140 (systolic) and/or 90 (diastolic) mmHg on repeated measurements during hospitalization or when taking anti-hypertensive medications. A diagnosis of diabetes mellitus was based on the American Diabetic Association criteria for diagnosing DM. A person who uses to smoke tobacco in any form (cigarette, tamak, jorda, gul etc) for at least 1 year, he/she was considered as positive for cigarette smoking. Hypercholesterolemia is defined as patients receiving cholesterol-reducing agents or overnight fasting cholesterol level ≥200 mg/dL, or low- density lipoprotein ≥130 mg/dL.

Locations of significant stenosis were categorized as intracranial or extracranial and further in the anterior or posterior circulation. A stenotic lesion which is at or above the petrous part of ICA for carotid system and distal to the point where the vertebral artery pierced the dura at the level of foramen magnum for vertebra-basilar system, is considered as intracranial stenosis Lesions were described as single or multiple based on the number. The degree of stenosis was measured according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET). Data were entered into a database (Microsoft Office Excel 2010). Statistical analyses were performed using statistical software SPSS 24, SPSS Inc., Chicago,USA. The results were analyzed by descriptive statistics and chi-square test.

Results:

Out of 42 cases, there were 31 males and 9 females. The mean age (SD) were 61.55 ± 8.85 years. There was no association between stenosis and age (p>0.05). Out of 42 patients, 25(59.5%) had extracranial stenosis, 13(31%) patients had intracranial stenosis and 4(9.5%) patients had both extracranial and intracranial stenosis. Overall 17(40.47%) patients had intracranial involvement and 29 (69.04%) had extracranial involvement. Out of 73 stenotic segment, 54(73%) stenosis located in anterior circulation and 19(27%) in posterior circulation. 21(50%) patients had single stenosis and 21(50%) had multiple stenosis. Out of 42 patients, 17(40.5%) patients had severe stenosis, 14(33.3%) patients had total occlusion and 11 (26.2%) patients had moderate stenosis.

Total 48 extracranial stenotic segments were present, among which the most commonly involved segment was the internal carotid artery (ICA) in its proximal part after bifurcation 37 (77.08%) followed by the extra cranial segments of the vertebral artery 10(20.83%), common carotid artery (CCA) 1(2.08%). Total 25 intracranial stenotic segments were present in 17 patients (isolated and combined). The most commonly involved segment was the middle cerebral artery (MCA) 8(32%) in its stem. It was followed by the internal carotid artery (ICA) 7 (28%); intracranial segments of the vertebral artery (VA), posterior cerebral artery (PCA), anterior cerebral artery (ACA), basilar artery (BA), and superior cerebellar artery, with the following number of stenotic segments: 4 (16%), 2 (8%), 2 (8%), 1 (4%), 1(4%) respectively. Out of 13 patients with intracranial stenosis 10 (76.9%) had single lesion, 3 (23.1%) had multiple lesions. Out of 25 patients with extracranial stenosis, 11

Table-I

Association between number and type of stenosis

Number VS Type of Stenosis					
Number of stenosis	Type of Stenosis			Total	P-Value
	Intra Cranial Stenosis	Extra Cranial Stenosis	Both Intra and Extra Cranial Stenosis		
	N (%)	N (%)	N (%)	N (%)	
Single	10 (76.9)	11 (44)	0 (0)	21 (50)	0.017*s
Multiple	3 (23.1)	14 (56)	4 (100)	21 (50)	
Total	13 (100)	25 (100)	4 (100)	42 (100)	

Table-II

Association of risk factors with type of stenosis

Risk Factor VS Type of Stenosis Risk Factors	Type of Stenosis			Total	P-Value
	Intracranial Stenosis N (Column%)	Extracranial Stenosis N (Column%)	Both Intra and Extracranial Stenosis N (Column%)	N (Column%)	
Hypertension	12 (92.3)	21 (84)	4 (100)	37 (88.1)	0.560 ns
DM	10 (76.9)	7 (28)	2 (50)	19 (45.2)	0.016*s
Smoking	5 (38.5)	13 (52)	1 (25)	19 (45.2)	0.506 ns
Alcoholism	0 (0)	1 (4)	0 (0)	1 (2.4)	0.706 ns
Hypercholesterolemia	6 (46.2)	12 (48)	2 (50)	20 (47.6)	0.989 ns
Previous Vascular Event	5 (38.5)	11 (44)	3 (75)	19 (45.2)	0.430 ns

Table-III

Association of risk factors with severity of stenosis

Risk Factors VS Severity of stenosis Risk factors	Severity		Total	P-Value
	<70% N (Column%)	≥70% N (Column%)	N (Column%)	
Hypertension	10 (90.9)	27 (87.1)	37 (88.1)	0.737 ns
DM	6 (54.5)	13 (41.9)	19 (45.2)	0.470 ns
Smoking	3 (27.3)	16 (51.6)	19 (45.2)	0.163 ns
Alcoholism	0 (0)	1 (3.2)	1 (2.4)	0.547 ns
Hypercholesterolemia	2 (18.2)	18 (58.1)	20 (47.6)	0.023*s
Previous Vascular Event	3 (27.3)	16 (51.6)	19 (45.2)	0.163 ns

Table-IV

Frequency of extracranialstenotic segments in study population

Extracranial segments	Number of stenosis	%
ICA	37	77.08
VA(extracranial)	10	20.83
CCA	1	2.08
Total	48	100

Table-V

Frequency of intracranial stenotic segments in study population

Intracranial segments	Number of stenosis	%
MCA	8	32
ICA	7	28
VA(Intracranial)	4	16
PCA	2	8
ACA	2	8
BA	1	4
SCA	1	4
Total	25	100

(44%) had single lesion and 14 (56%) had multiple lesions. Single stenosis was found statistically significant for intracranial location (p value 0 .017). Diabetes mellitus was significantly associated with intracranial stenosis (pvalue 0.016) and Hypercholesterolemia was significantly associated with severe (≥70%) stenosis (p value 0.023).

Discussion:

This descriptive observational study was carried out with an aim to evaluate the Digital Subtraction Angiographic pattern of intracranial and extracranial atherosclerotic stenosis among ischemic stroke patients selected from Inpatient, Outpatient and Stroke & Neuro-Intervention clinic of BSMMU. Only the patients with single or multiple significant symptomatic stenosis (≥50% stenosis) were included in this study.In our study out of 42 patients, 25(59.5%) had extracranial stenosis, 13 (31%) patients had intracranial stenosis and 4 (9.5%) patients had both extracranial and intracranial stenosis. Overall 17 (40.47%) patients had intracranial involvement and 29 (69.04%) had extracranial involvement. Wong[10] found 33% to 50% intracranial stenosis in Chinese population with total 345 occlusive arterial segments. Suwanwela[11] found 47% intracranial stenosis in Thailand in 100 patients with significant stenosis, Chang [12]found 47.9% intracranial stenosis in Singapore with 200 cases in total. Shrivastava[2] in a CTA based study found 56% intracranial stenosis in Indian population although only 32 of their 60 cases had significant stenosis.

In contrary, extracranial stenosis is predominant type of lesion in Europe and North America. Sacco RL at al. (1995) found intracranial stenosis in 1%, 6% and 11% among US Whites, US Blacks and US Hispanics respectively. Analyzing the above mentioned study suggest that intracranial stenosis is much more common condition in Asian population than European and US Whites. In our study we found 40.47% intracranial stenosis which to close to the result found by Wong[10] in Chinese population. But a bit away from other studies conducted in our Asian counterpart like Thailand, Singapore, India. This discrepancy of results can be explained by different imaging tools used in other studies (DuplexUSG, TCD, CTA, MRA rather DSA we used), different cut off value for significant stenosis (30% in some study's 50% we used), larger sample size, different inclusion and exclusion criteria, ethnic and geographical difference.

There are several explanation of intracranial atherosclerotic disease (ICAD) being more prevalent in Asians including Bangladesh than in Westerners. It is postulated that during human population evolution and diversification, those who settled in Europe had acquired a stroke-suppressor genotype increases their resistance against atherogenesis, but with protection confined to the intracranial large arteries. The contemporary affluent lifestyle accelerates the development of atherosclerosis. In the whites, it involved the whole arterial bed except the intracranial vessels. People living in non-Western countries used to have a healthier way of living. They did not develop significant atherosclerotic disease until recently when a westernized life style was adopted[13].Unlike the whites, their intracranial arteries are not spared. Predisposition of Asian populations toward hypoadiponectinemia may represent another explanation of increased ICAD[14].

In our study, out of 7 stenotic segments, 54 (73%) were located in anterior circulation and 19 (27%) were located in posterior circulation. study in Iran conducted by Borhani-Haghighi[15] found anterior circulation involvement in 301(88%) patients and posterior circulation involvement in 128(37.4%) patients in their total 342 patients underwent DSA.

There is statistically significant association found between single stenosis and intracranial location ($p < 0.05$). So single stenosis more likely to be located in intracranial site. In a study conducted by Dae[16] evaluated about pattern of atherosclerotic carotid stenosis in Korean patients with stroke, found prevalence of intracranial stenosis was significantly higher in the single-stenosis group than in the multiple stenosis group ($P < .05$).

We found that out of 48 extracranial stenotic segments, the most commonly involved segment was the internal carotid artery (ICA) in its proximal part after bifurcation: 37 (77.08%) followed by the extracranial segments of the vertebral artery-

10(20.83%). 25 intracranial stenotic segments were present in 17 patients (isolated and combined). The most commonly involved segment was the middle cerebral artery (MCA)-8(32%) in its stem. It was followed by the internal carotid artery (ICA) 7 (28%) and intracranial segments of the vertebral artery (VA) 4 (16%).

In a CTA based study conducted by Shrivastava[2] found MCA as the most commonly involved intracranial stenosis segment, present in 10 (41.6%) out of 24 intracranial segments and ICA as the most commonly involved extracranial stenosis segment, present in 14 (66.6%) out of 21 extracranial segments. These results were supported by Dae[16], Borhani-Haghighi[15]and Mazighi[17].

Only DM but not age, sex, hypertension, dyslipidemia, smoking, previous vascular event was significantly associated with intracranial stenosis. This result coincides with findings of a study conducted by Borhani-Haghighi[15] in Iran. In another study Sung [9] in Taiwanese patients found that DM was the most important determinant of IICS and an independent risk factor for both Isolated ICS and Combined EIS but not for isolated ECS. These results were also supported by Mendes [18] and Hossein[19].

In our study we found association of hypercholesterolemia with severity of stenosis. hypercholesterolemia is significantly associated with severe stenotic lesion (≥70% stenosis). In a study conducted by Turan[8] using data on patients enrolled in the Warfarin-Aspirin Symptomatic Intracranial Disease(WASID) trial found that history of a lipid disorder was the only independent predictor of severe intracranial stenosis (odds ratio1.62; 95% CI, 1.09 to 2.42; P 0.02).

A different interventional procedure can be planned on the basis of the results of our study. The effects of antiplatelet, anticoagulant, and lipid-lowering drugs can be evaluated in the treatment of extracranial and intracranial stenosis with the help of the present study. Limitation of the present study was that the sample size was small and it was a hospital rather than a community based study. Further studies can be conducted by performing a large multicentric study in a different regions of Bangladesh.

Conclusion:

Extracranial arterial stenosis is more common than intracranial arterial stenosis. Frequency of intracranial atherosclerotic stenosis is almost similar to other Aasian populations. Anterior circulation stenosis is more common than posterior circulation stenosis. Single stenosis is more commonly associated with intracranial location. Intracranial stenosis is more prevalent in diabetic patients. Hypercholesterolemia is more commonly seen in severe (≥70%) stenosis.

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