

ORIGINAL ARTICLES

Duplex Study of Carotid Artery in Patients with Ischemic Stroke

NASREEN SULTANA¹, AKM FAZLUL BARI¹, TOUHIDUL KARIM MAJUMDER², MD.RAFIQU L ISLAM³, FERDOUS ARA HOSSAIN⁴, FARIDULALAM⁴

Abstract

Objective: To determine the frequency and characteristics of carotid artery stenosis in acute ischemic stroke patients and to assess the significance of common risk factors for carotid stenosis in these patients. **Method:** It was cross-sectional observational study which was carried out in neurology department of Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of January 2010 to December 2011 and one hundred patients admitted with acute ischemic stroke were included in the study. Doppler ultrasound was performed during hospitalization to find out carotid artery stenosis. Statistics analysis was done with SPSS - 14. **Results:** Out of one hundred (100) patients, eighty (80%) were males and twenty were (20%) were females. The patients were dividing into two groups with and without carotid stenosis. Less than 50% carotid artery stenosis (insignificant stenosis) was seen in 40 % (n=40) cases and significant stenosis was seen in 60% (n=60) patients. Overall 86% (n= 46) out of 60 patients were found to have carotid artery stenosis on the ipsilateral side corresponding to the ischemic lesion and 19% (n=11) had stenosis on the contralateral side. Out of significant stenosis, mild (50% stenosis) in 12% (n=7) patients, moderate (51-69%) stenosis in 50% (n= 30) patients and severe (>70%) stenosis in twenty (n=33%) patients . Near total occlusion was seen in three (5%) patients. The presence of stenosis was significantly correlated with older age and the presence of multiple risk factors. **Conclusion:** Carotid artery stenosis is strongly associated with ischemic stroke. Doppler studies are recommended for the high risk patients for the primary as well as secondary prevention of ischemic stroke.

Key word: Duplex study, Carotid artery, Ischemic stroke

Abbreviations: CAS (carotid artery stenosis) , ICA (internal carotid artery)

Introduction:

Stroke is the most common life-threatening neurological disorder and the most important single cause of disability. According to World Health Organization estimates for the year 2020, stroke will stay as the second leading cause of death along with Ischaemic heart disease, both in developing as well as developed countries¹. During the last three decades there is a decline in the incidence of the disease in the Western population while the burden of the disease in South Asian countries (India,

Pakistan, Bangladesh and Sri Lanka) has inclined and is expected to rise further². In Pakistan estimated stroke incidence is close to 250 per 100,000 populations, which means that there are 350,000 new stroke patients every year in the country³.

Clinically stroke is the result of a disturbance of cerebral circulation, either due to occlusion of main blood vessel due to thrombo-embolism or rupture of a blood vessel. About 85% of all strokes are of ischaemic origin; caused by thrombotic or embolic blockage of a cerebral artery⁴.

1. Associate Professor, Institute of Nuclear Medicine & Ultrasound. Dhaka

2. Assistant Professor, Dhaka Medical college Hospital, Dhaka.

3. Professor, Deptt. Of Neurology. Bangabandhu Sheikh Mujib Medical University.Dhaka

4. Professor, Institute of Nuclear Medicine & Ultrasound .Dhaka

Multiple risk factors are associated with Stroke. The Non-modifiable risk factors are age, sex, family history, race and ethnicity and the modifiable risk factors include hypertension, cardiac disease, diabetes mellitus hyperlipidaemia, cigarette smoking, alcohol abuse, physical inactivity, carotid stenosis, and transient ischaemic attack⁵. Carotid artery stenosis (CAS) is a major risk factor for stroke and for the symptomatic cerebrovascular disease. Approximately 20-30% of all ischemic strokes are caused by carotid occlusive disease⁶.

Current techniques for the assessment of carotid artery disease includes color Doppler Ultrasound, Digital Subtraction Angiography, Magnetic Resonance angiography and computed resonance angiography. Duplex ultrasonography is currently the principal and undoubtedly the most accurate non-invasive diagnostic modality available for evaluation of carotid artery stenosis. It provides information about the degree of carotid stenosis, the velocity and character of blood flow and plaque morphology⁷. Grading of carotid artery stenosis was done according to radiological society of consensus 2008⁸. Screening of carotid by duplex ultrasound is recommended for the high risk patient to find out the presence of carotid stenosis in order to plan out medical and surgical intervention for primary as well as secondary prevention of cardiovascular events.

Patients and Methods:

This cross sectional observational study which was carried out on one hundred (100) consecutive patients with acute ischemic stroke admitted in the Department of Neurology, BSMMU, Dhaka .The patients included were of both sexes and age above 18 years.

Patients having history of head injury, evidence of intracranial hemorrhage or space occupying lesion on computed tomographic scan of brain, patients who recovered from neurological deficit within 24 hours, patients having signs and symptoms of posterior circulation infarct and patients having signs of meningeal irritation were excluded from the study. Doppler ultrasound was performed during the hospitalization in all those patients with Siemens Acuson Antares 10MHz linear transducer, who

fulfilled the inclusion criteria. The risk factors were evaluated by history, physical examination, electrocardiogram and laboratory investigations during hospitalization. These included age, sex, hypertension, diabetes mellitus, hyperlipidaemia smoking and Ischemic heart disease. Acute ischemic stroke was defined as focal neurological deficit of sudden onset lasting for >24 hours with evidence of cerebral infarction or a normal CT scan of brain without evidence of hemorrhage. Hypertension was conveniently defined for the study purpose as a systolic blood pressure (SBP) of > 180 mmHg or a diastolic blood pressure (DBP) > 100 mmHg on admission or a SBP of > 140 mm Hg and or DBP > 90 mm Hg, seventy two hours after admission. Patients previously known to be hypertensive by history or those who were on anti hypertensive medication were also included. Diabetes mellitus was considered when subjects gave history of diabetes mellitus and/or were on oral hypoglycemic drugs or insulin treatment or had random blood sugar > 200mg on two occasions during the hospital stay. Coronary artery disease (CHD) was considered if the patient had a recent or past history of myocardial infarction, was on anti angina drugs, or had typical ECG findings of recent / previous ischaemic events. The patients having non specific ST segment and/or T wave changes were not included in this analysis.

A smoker was conveniently defined as a person who smoked at least one cigarette per day for the preceding three months or more or was using tobacco in any form.

Hyperlipidaemia was conveniently defined when a patient had a previous diagnosis of it and/or was on lipid lowering agents or had fasting serum cholesterol of > 200mg, seventy two hours after admission in the hospital.

Statistical package for social sciences (SPSS-14) was used to analyze data. Qualitative variables were analyzed by finding their frequencies and percentages. Chi-square test was used to check proportion difference between patients with and without carotid artery stenosis, for gender, age groups and risk factors. P value 0.05 was considered level of significance.

Results:

Out of one hundred (100) patients, eighty (80%) were males and twenty (20%) were females (Table-I). The patients were divided into two groups with and without carotid stenosis. Less than 50% carotid artery stenosis (insignificant stenosis) was seen in 40 % (n=40) cases and significant stenosis was seen in 60% (n=60) patients(Table-I).. Overall 86% (n= 46) out of 60 patients were found to have carotid artery stenosis on the ipsilateral side corresponding to the ischemic lesion. Another 19% (n=11) had stenosis on the contralateral side (Table-I). Distribution of degree of stenosis was mild (50% stenosis) in 12% (n=7) of patients, moderate (51-69%) stenosis in 50%(n= 30) of patients and severe (>70%) stenosis in twenty (n=33%) of

patients and near total occlusion were seen in three (5%) patients(Table-II). The presence of stenosis was significantly correlated with older age and the presence of multiple risk factors. Risk factors associated with carotid artery stenosis either alone or in combination, its relation with degree of stenosis and comparison with patients without stenosis was shown in Table III. Degree of carotid artery stenosis was mild in nine lesions (18%), moderate in fifteen lesions (30%), severe in twenty one lesions (42%) and critical in five lesions (10%) .On ipsilateral side, homogenous plaque was found in twenty three patients (59%), heterogeneous in fourteen (35.9%), and thrombosed in two patients (5.1%) only table-IV. Images of various types of carotid plaques are shown in Fig. 1-4.

Table-I*Summation of study result*

Total No of patients: 100	Significant carotid artery stenosis : 60% (n=60)
	Insignificant carotid artery stenosis : 40% (n=40)
Male: 80(80%)	
Female: 20(20%)	Ipsilateral stenosis 81% (n= 49)
	Contra lateral stenosis 19% (n= 11)

Table-II*Distribution of different significant carotid artery stenosis : 60% (n=60)*

PSV of ICA/CCA ratio	Number with %
2 (50% stenosis in ICA)	N=7 (12%)
2-4(51-69% stenosis in ICA)	N=30(50%)
>4 (>70% stenosis in ICA)	N= 20(33%)
Near total occlusion	N= 03(05%)

Table-III*Risk factors and degree of stenosis in ICA (total patients with stenosis n=60)*

	PSV ratio of ICA/CCA =2 (50% stenosis)	PSV ratio of ICA/CCA =2-4 (51-69% stenosis)	PSV ratio of ICA/CCA =>4 (>70% stenosis)	Total N=60
Single risk factor	02	04	01	7(12%)
Two risk factors		15	05	20(33%)
Three or more risk factor		25	08	33(55%)

Table-IV
Plaque morphology

Plaque morphology (sonographically)	Number and %
Homogenous plaque	Number of patients =35 (58%)
Heterogeneous plaque	Number of patients =12 (20%)
Calcified plaque	Number of patients = 10(17%)
Ulcerated plaque	Number of patients = 03(05%)



Fig.-1 : *Hypochoic plaque in color Doppler*

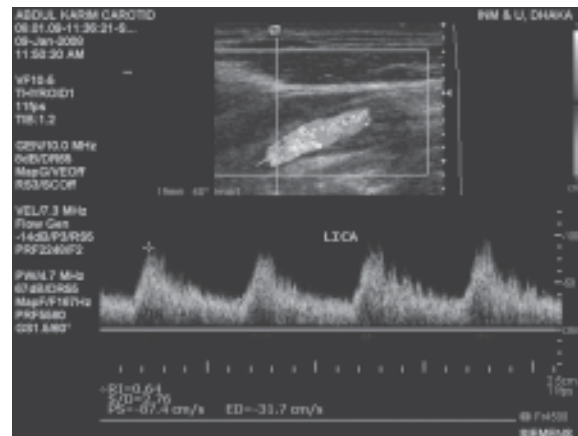


Fig.-2: *Doppler spectrum in LICA*

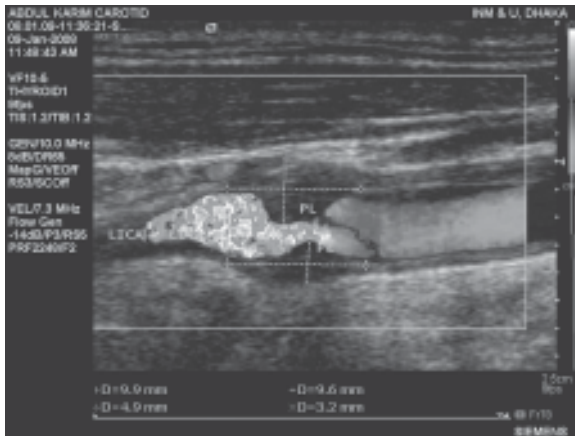


Fig.-3: *Heterogeneous plaque in bulb of LICA*



Fig.-4: *Heterogeneous plaque in bulb of LICA*

Discussion:

Large multicenter prospective studies such as North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Symptomatic Trial (EST) have shown the etiological significance of carotid lesions in ischemic stroke patients⁹. The risk of ischemic stroke increases with the degree of carotid stenosis¹⁰. Because

patients with symptomatic occlusion of the internal carotid artery (ICA) and compromised cerebral blood flow are at risk for future ischemic infarcts therefore early identification and accurate determination of the degree of carotid artery stenosis is useful in risk-factor management, with appropriate medical or surgical intervention¹¹.

The frequency of Carotid Artery Stenosis (CAS) was 39% in this study, as compared to 44% by Laeeq Ahmed¹² and 48.5% by Mozzam Ali¹³. However another local study conducted by Khan et al found CAS in only 18.18% of patients¹⁴ but this study included only those patients who had stenosis of greater than 70%. The lower figures (8%) were also noted by Tan¹⁵ from Taiwan and by Alexandrore et al¹⁶ who reported stenosis of equal or greater than 70% in 17% of 348 patients.

We also evaluated the presence of well known common risk factors in our patient population and compared these risk factors in patients with and without carotid artery stenosis. Advanced age, male gender, hypertension smoking, Ischaemic heart disease and hyperlipidaemia significantly contributed to the presence of atherosclerotic plaque, but in majority of cases more than one risk factor was involved in both in the frequency as well as the severity of carotid artery stenosis.

Older age is an important and well known risk factor for the development of Carotid artery atherosclerosis. In our study the majority (56%) of patients with stroke were older than 60 years and when we compared this age subgroup having carotid stenosis (28/39) to the patients having no stenosis (28/61), the difference was statistically significant ($P < 0.010$). All three patients of more than 80 years had carotid stenosis. These findings were consistent with certain international studies. An Indian study by Sethi et al¹⁷ found that mean age of patients with carotid lesion was 60.03 years as compared to 48.83 years in patients without any carotid lesion. Kerényi¹⁸ also noted that mean age of the patient with CAS was 66.9 ± 12.8 years. The majority of our patients with carotid artery stenosis were male but this gender difference was found to be not significant ($P < 0.442$). Hypertension was the most common risk factor present in 76.92% of cases either as a single risk factor or associated with other risk factors. Elevated systolic blood pressure accelerates the progression of intima medial thickness (IMT) in the carotid artery, however isolated hypertension occurs in only less than 20% of patients with stroke and is usually associated with other risk factors that is why antihypertensive treatment alone may fail to prevent

stroke^{19,20}. Smoking is widely accepted as one of the important risk factor for ischaemic stroke in western countries, and is associated with the progression of carotid plaques¹⁸. Smoking is associated with raised fibrinogen levels, increased packed cell volume, and decreased macrophage activity changes in lipid biochemistry. Smoking increases arterial wall stiffness and alters the pattern of arterial blood flow¹⁹⁻²¹. In our study smoking was present in 43.59% cases. However an independent association of smoking with carotid artery stenosis could not be confirmed as nearly all the smokers had at least one other risk factor, mainly hypertension. Atherosclerosis is presumed to be accelerated in diabetes for a number of reasons. First, diabetes is associated with an increased risk of traditional coronary heart disease (CHD) risk factors, including hypertension, dyslipidaemia, obesity, and hyperinsulinaemia, other metabolic disturbances unique to diabetes, such as increased levels of circulating glucose, advanced glycation end products, and oxidation of lipoproteins might also increase the risk and rate of atherosclerosis²². Interestingly Diabetes was found to be less common as compared to patients without stenosis in our study.

Higher LDL cholesterol levels are associated with higher incidence of carotid atherosclerotic disease while high levels of HDL cholesterol have protective role¹⁹. In the present study hyperlipidaemia in ischaemic stroke patients having carotid artery stenosis was 25.64%.

In our study very significant number (43%) of patients with CAS had Ischaemic heart disease ($P < 0.0001$). A local study conducted by Khan et al²³ showed that 25% of patients with coronary artery disease had carotid artery stenosis of more than 50% while overall about 94% of patients had some evidence of plaque. In Japanese patients who underwent coronary artery bypass grafting (CABG) because of severe coronary artery disease, a high incidence of carotid stenosis was noted²³.

The role of calcification in atherosclerotic disease with regard to clinical symptoms has been studied in pathologic and sonographic studies. Calcium is postulated to give stability by stiffening the plaque resulting in protection against biomechanical stress

and subsequent disruption thus preventing cerebrovascular events. Most studies favour that plaque having high contents of calcium and fibrous tissues are less symptomatic than non-calcified lipid rich plaque or thrombosed plaque. Nandalur et al²² found that calcified plaques were 21 times less likely to be symptomatic than noncalcified plaques. In our study similar trends were found and majority (59%) of our stroke patients having carotid artery stenosis had non calcified plaques (shown in Fig. 1-4).

Limitations:

The present study has some limitations. As this study was a single hospital-based study conducted on patients having a different clinical and risk factor profile, these results cannot be applied to the general population.

Conclusions and Recommendations:

The Carotid Artery Stenosis is a well known risk factor for the development of the ischaemic stroke and a significant number of patients in our study were found to have stenosis. The present study shows that the combined presence of multiple risk factors like age, hypertension, smoking and ischaemic heart disease is strongly associated with carotid artery stenosis. High risk patients should be screened by Doppler ultrasonography for the presence of carotid stenosis in order to plan out medical and surgical intervention for the primary as well as secondary prevention of cerebrovascular events.

References:

1. Alam I, Haider I, Wahab F, Khan W, Taqweem MA, Nowsherwan. Risk factors stratification in 100 patients of acute stroke. *J Postgrad Med Inst* 2004; 18: 583-91.
2. Saleheen D, Bukhari S, Haider SR, Nazir A, Khanum S, Shafqat S et al. Association of Phosphodiesterase 4D gene with ischaemic stroke in a Pakistani population. *Stroke* 2005; 36:2275-277.
3. Khealani BA, Javed ZF, Syed NA, Shafqat S, Wasay M. Cost of Acute Stroke Care at a tertiary care hospital in Karachi, Pakistan. *J Pak Med Assoc* 2003; 53:552-55.

4. Schillinger M, Ahmadi R, Minar E. Carotid artery stenting for the prevention of thromboembolic stroke. *Vasc Dis Prev* 2004; 1:109-16.
5. Basharat RA, Yousuf M, Iqbal J, Khan MM. Frequency of known risk factors for stroke in poor patients admitted to Lahore General Hospital in 2000. *Pak J Med Sci* 2002; 18: 280-83.
6. Strickman NE, Loyalka P. Carotid artery stenosis: an endovascular specialist's perspective. *Tex Heart Inst J* 2005; 32: 318-22.
7. Zaidi NR, Khan NA, Dodhy K, Mahmood K. Carotid duplex imaging is better modality than Angiography to diagnose carotid artery stenosis in patient for Endarterectomy. *Ann King Edward Med Coll* 2004; 10: 380-83.
8. Grant EG, Benson CB, Moneta GL et al. Carotid artery stenosis: Grayscale and Doppler ultrasound diagnosis—Society of Radiologist in Ultrasound consensus conference. Department of Radiology, University of Southern California (USA), Kech School of Medicine, USC University Hospital, Los Angeles, California Ca 90033, USA.
8. Syed NA, Zakaria A, Khealani BA, Wasay M, Baig SM, Sophie Z. Should carotid endarterectomy be performed for symptomatic carotid stenosis in Pakistan? *J Pak Med Assoc* 2003; 53: 589-93.
9. Tan TY, Chang KC, Liou CW, Reynolds PS, Tegeler CH. Lack of relationship between severity of stroke and severity of extracranial lesion in Taiwanese first-ever ischaemic stroke patients. *J Neuroimaging* 2001; 11: 381-84.
10. Lastas A, Graziene V, Barkauskas E, Salkus G, Rimkevicius A. Carotid artery atherosclerotic plaque: clinical and morphological immuno histochemical correlation. *Med Sci Monit* 2004; 10: 606-14.
11. Biller J, Thies WH. When to operate in carotid artery disease. *Am Fam Physician* 2000; 61: 400-6.

12. Ahmad L. Hyperlipidaemia and its correlation with carotid artery occlusion in patients with ischemic stroke (Dissertation) Karachi. College of Physicians and Surgeons Pakistan 2002.
13. Atif MA, Ali H, Mahmood T. Frequency of carotid atherosclerosis in cerebral infarction. *Pak J Med Sci* 2008; 24: 69-73.
14. Khan SN, Vohra EA. Risk factors for stroke: A hospital based study. *Pak J Med Sci* 2007; 23: 17-22.
15. Tan TY, Chang KC, Liou CW, Schminke U. Prevalence of carotid artery stenosis in Taiwanese patients with one ischaemic stroke. *J Clin Ultrasound*.2005; 33: 1-4.
16. Alexandrova NA, Gibson C, Maggisano P. Carotid artery disease and peripheral vascular disease. *Stroke* 1995; 26: 175.
17. Sethi SK, Solanki RS, Gupta H. Color and duplex doppler imaging evaluation of extracranial carotid artery in patients presenting with transient ischaemic attack and stroke : a clinical and radiological correlation. *Indian J Radiol Imaging* 2005; 5: 91-8.
18. Kerenyi L, Mihalka L, Csiba L, Bacso H, Bereczki D. Role of hyperlipidemia in atherosclerotic plaque formation in the internal carotid artery. *J Clin Ultrasound* 2006; 34: 283-88.
19. Katsumata T, Nishiyama Y, Yamaguchi H, Otori T, Nakamura H, Tanaka N et al. Extracranial carotid plaque is increasing in Japanese ischaemic stroke patients *Acta Neurol Scand* 2006; 116: 20-5.
20. Hadjiev DI, Mineva PP, Vukov MI. Multiple modifiable risk factors for first ischaemic stroke: a population-based epidemiological study. *Eur J Neurol* 2003; 10: 577-82.
21. Aldoori MI, Rahman SH. Smoking and stroke: a causative role Heavy smokers with hypertension benefit most from stopping. *BMJ* 1998; 317: 962-63.
22. Wagenknecht LE, Zaccaro D, Espeland MA, Karter AJ, O'Leary DH, Haffner SM. Diabetes and progression of carotid atherosclerosis: the insulin resistance atherosclerosis study. *Arterioscler Thromb Vasc Biol* 2003; 23: 1035-41.
23. Khan S, Ahmed SA, Nuri MMH, Khalid M, Rashid A, Mehmood A. Role of Carotid Doppler in coronary artery disease. *Pak Armed Forces Med J* 2006; 56: 257-63.