

## Original Article

### **Frequency, characteristics and risk factors of Carotid Artery Stenosis in ischaemic stroke patients at Civil Hospital Karachi**

Niaz Ahmed Shaikh, Shaheen Bhatti, Muhammad Irfan, Gunpat Khatri, Aneel Sham Vaswani, Nasrullah Jakhrani  
Civil Hospital, Karachi, Pakistan.

#### **Abstract**

**Objective:** To determine the frequency and characteristics of carotid artery stenosis in acute ischaemic stroke patients and to assess the significance of common risk factors for carotid stenosis in these patients.

**Method:** One hundred consecutive patients admitted with acute ischaemic stroke were included in the study. The relevant history, physical examination and laboratory investigations were done as per the Performa. Doppler ultrasound was performed during the hospitalization to find out carotid artery stenosis. Statistics analysis was done with SPSS v 14.

**Results:** Out of one hundred (100) patients, sixty one (61%) were males and thirty nine (39%) were females. Thirty nine patients (39%) were found to have carotid artery stenosis, all of them on the ipsilateral side corresponding to the ischaemic lesion. Eleven (11) of these patients had stenosis on the contra lateral side as well. The presence of stenosis was significantly correlated with older age and the presence of multiple risk factors. Majority (52%) of the lesions were severe to critical as determined by Doppler peak systolic velocity. Fifty nine (59%) were non calcified.

**Conclusion:** Carotid artery stenosis is strongly associated with ischaemic stroke. Doppler studies are recommended for the high risk patients for the primary as well as secondary prevention of ischaemic stroke (JPMA 60:8; 2010).

## 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 countries.<sup>1</sup> 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 further.<sup>2</sup> In Pakistan estimated stroke incidence is close to 250 per 100,000 population, which means that there are 350,000 new stroke patients every year in the country.<sup>3</sup>

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 artery.<sup>4</sup>

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 attack.<sup>5</sup> Carotid artery stenosis (CAS) is a major risk factor for stroke and for the symptomatic cerebrovascular disease. Approximately 20-30% of all ischaemic strokes are caused by carotid occlusive disease.<sup>6</sup>

Current techniques for the assessment of carotid artery disease include colour 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 morphology.<sup>7</sup>

Very few studies have so far been conducted to determine the frequency of carotid artery stenosis in patients with acute ischaemic stroke in Pakistan.

A hospital based review revealed the rate of moderate to severe carotid stenosis as 13.4% in the Karachi population, although this study was limited by sample size.<sup>8</sup>

The need to conduct this study was to detect an established and preventable cause of stroke with the help of Doppler Ultrasonography, which may subsequently help to plan out future treatment modality (medical and/or surgical) for prevention of further cerebrovascular events.

## Patients and Methods

This cross sectional non interventional study was carried out on one hundred (100) consecutive patients with acute ischaemic stroke admitted in the Department of Medicine, Civil Hospital Karachi. The patients included were of both sexes and age above 18 years.

Patients having history of head injury, evidence of intracranial haemorrhage 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 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 Ischaemic heart disease.

Acute ischaemic 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 haemorrhage.

Hypertension was conveniently defined for the study purpose as a systolic blood pressure (SBP) of  $\geq 180$  mmHg or a diastolic blood pressure (DBP)  $\geq 100$  mmHg on admission or a SBP of  $\geq 140$  mm Hg and or DBP  $\geq 90$  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  $\geq 200$ mg 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, were 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  $\geq 200$ mg, 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>0.05 was considered level of significance.

## Results

Out of one hundred (100) patients with acute ischaemic stroke, sixty one (61%) were males and thirty nine (39%) were females. The patients were divided in two groups, with and without carotid artery stenosis. The gender difference in two groups of patients was not statistically significant ( $p < 0.35$ ). The age group difference in patients with and without stenosis

**Table 1: Comparison of risk factors in patients with and without Carotid Artery Stenosis.**

Risk Factor	Without carotid stenosis n=61/100	With carotid stenosis n=39/100	P-value
Age Groups			0.010
18 - 40	05 (8.2%)	00 (00%)	
41 - 60	28 (45.9%)	11 (28.2%)	
61 - 80	28 (45.9%)	25 (64.1%)	
>80	00 (0%)	03 (7.7%)	
Gender			0.35
Male	35 (57.4%)	26 (66.66%)	
Female	26 (42.6%)	13 (33.3%)	
Hypertension	37 (60.65%)	30 (76.92%)	0.092
Smoking	24 (39.35%)	17 (43.59%)	0.674
Ischaemic heart disease	6 (9.8%)	17 (43.59%)	0.0001
Diabetes mellitus	20 (32.78%)	11 (28.20%)	0.629
Hyperlipidaemia	12 (19.65%)	10 (25.65)	0.482

**Table 2: Risk factors and degree of Stenosis.**

Risk Factors	Degree of Stenosis				Total
	Mild	Moderate	Severe	Critical	
Hypertension	02	08	15	05	30
Ischaemic heart disease	00	04	10	03	17
Smoking	00	04	10	03	17
Hyperlipidaemia	00	02	07	01	10
Diabetes	00	05	06	00	11
Single Risk Factor	02	04	01	00	07
Two Risk factors	00	02	07	03	12
Three or More Risk Factors	00	05	11	02	18
None	02	00	00	00	02

was compared and found to be significant ( $p < 0.01$ ). Fifty six (56%) of our patients were in the older age group ( $> 60$  years). Overall Thirty nine (39%) patients were found to have Carotid artery stenosis, all of them on the ipsilateral side of the stroke. Eleven (11) of these patients had also stenosis on the contralateral side as well, making it to a total of fifty (50) lesions. Twenty six patients (66.7%) were males and thirteen (33.3%) were females. Twenty eight (28) of those patients with stenosis (72%) were of more than 60 years age including three patients

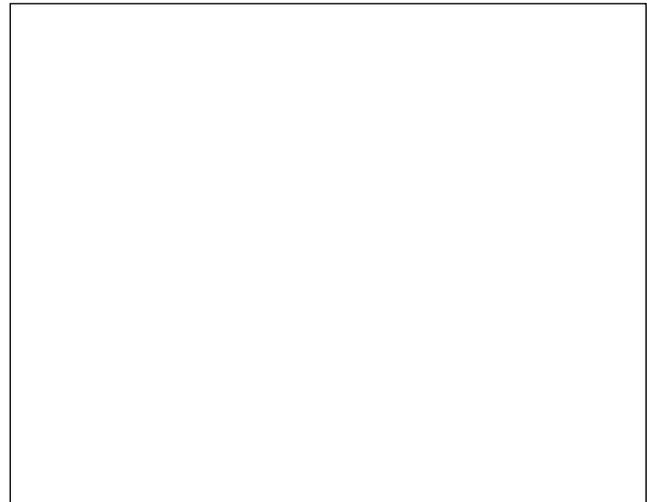


Figure-1: Degree of Stenosis.

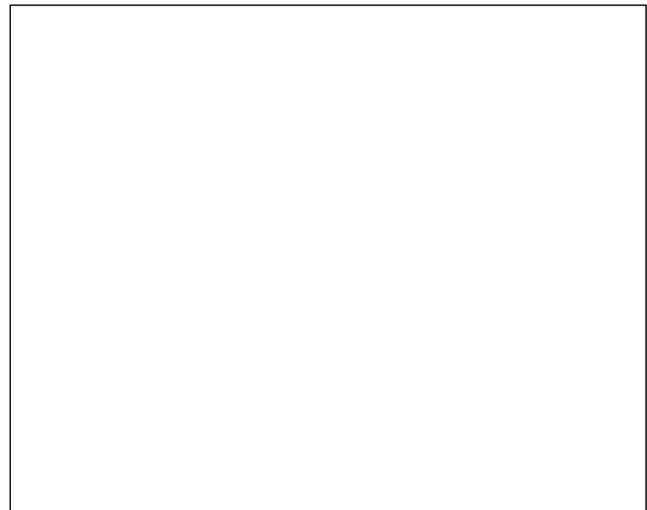


Figure-2: Characteristics of Carotid Artery Lesions.

of more than 80 years of age, all of whom had carotid stenosis (Table-1).

Risk factors associated with carotid artery stenosis either alone or in combination, its relation with degree of stenosis and comparison with patients without stenosis is shown in Table 1-2. 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%) (Figure-1-2). On ipsilateral side, non calcified plaque was found in twenty three patients (59%) Calcified in fourteen (35.9%), and thrombosed in two patients (5.1%) only (Figure-2).

## 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 ischaemic stroke patients.<sup>9</sup> The risk of ischaemic stroke increases with the degree of carotid stenosis.<sup>10</sup> Because patients with symptomatic occlusion of the internal carotid artery (ICA) and compromised cerebral blood flow are at risk for future ischaemic 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 intervention.<sup>11</sup>

The frequency of Carotid Artery Stenosis (CAS) was 39% in this study, as compared to 44% by Laeeq Ahmed<sup>12</sup> and 48.5% by Mozzam Ali.<sup>13</sup>

However another local study conducted by Khan et al found CAS in only 18.18% of patients<sup>14</sup> but this study included only those patients who had stenosis of greater than 70%. The lower figures (8%) were also noted by Tan<sup>15</sup> from Taiwan and by Alexandrore et al<sup>16</sup> who reported stenosis of equal or greater than 70% in 17% of 348 patients.

We also looked into 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 al<sup>17</sup> 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. Kerenyi<sup>18</sup> also noted that mean age of the patient with CAS was  $66.9 \pm 12.8$  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.<sup>19,20</sup>

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 plaques.<sup>18</sup> 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 flow.<sup>21</sup> 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 atherosclerosis.<sup>22</sup> 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 role.<sup>19</sup> 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 al<sup>23</sup> 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 noted.<sup>24</sup>

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 al<sup>25</sup> 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.

## Limitations:

The present study has some limitations. As this study was a single hospital-based study conducted on patients belonging to lower socioeconomic status having a different clinical and risk factor profile, these results cannot be applied to the general population. As Doppler sonography was performed by more than one sonographer so an observer bias in categorization of the carotid stenosis could not be ruled out.

## 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.

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