

## ORIGINAL ARTICLE

# Carotid Artery Stenosis in Diabetic Patients Presenting With Acute Ischemic Stroke

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### ABSTRACT

**Background:** Stroke is the commonest life-threatening neurological disorder. The Abnormal narrowing or stenosis of the Carotid Artery is a major determinant of ischemic stroke in diabetic patients. The main objective of study was to estimate the frequency of carotid artery stenosis in diabetic patients presenting with acute ischemic stroke.

**Methods:** This was a Cross-Sectional study conducted at Medicine wards Jinnah Post-Graduate Medical Centre, Karachi from 5th December 2014 to 5th June 2015. Total 101 patients were included. During the hospitalization, patients were subjected to carotid Doppler ultrasonography to assess carotid artery stenosis. Patients were provided routine medical care during the hospitalization. Data was analyzed using SPSS v23.0. Chi-Square was used to analyze the differences between the categories. The p-value of <0.05 was considered as significance.

**Results:** Total 101 patients were included in the study. There were 71.8% males and 28.2% females. The mean age was 53.7±10.2 years. On analysis of risk factors, it was observed that 59% patients had hypertension, 34.2% patients were obese, 34.2% patients had dyslipidemia, 51.3% patients had history of smoking. On analysis of carotid artery stenosis among the diabetics, it was observed that 20.8% diabetics had carotid artery stenosis.

**Conclusion:** Stenosis of Carotid artery was common in patients suffering from acute ischemic stroke and diabetes mellitus. Among modifiable risk factor in patients with stroke having carotid artery stenosis, Hypertension was most common whereas fasting blood sugar FBS level greater than 100 g/dl lead to increased chances of having carotid artery stenosis.

**Keywords:** Diabetes Mellitus; Carotid Artery Stenosis; Ischemic Stroke; Dyslipidemia.

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### INTRODUCTION

Diabetes Mellitus (DM) a noteworthy hazard factor for cardio-vascular bleakness and mortality<sup>1</sup>. The hazard of emerging coronary, cerebrovascular and fringe blood vessel infection is raised four-fold among cases of DM<sup>2</sup>. When compared to Non-diabetics, the Diabetics have a speedy disease progression<sup>3</sup>. Hence, diabetes mellitus is a key risk factor of stroke<sup>4</sup>.

Stroke is a main source of mortality and normal

reason for physical inability in developing nations<sup>5</sup>. Stroke is one of the main causes of continuous inability and mortality worldwide, with the frequency logically expanding with age. The general hazard of intermittent stroke, deadly or non-fatal, is about 20% after five years<sup>6</sup>. As per WHO gauges for 2020 year, stroke would remain as the second driving reason for mortality alongside ischaemic coronary disease, in developed and developing countries as well<sup>7</sup>.

An ongoing study recommended an expected

21.8% occurrence of stroke or potentially Transient Ischemic Attack (TIA) in an urban slum of Karachi. In addition, stroke related casualty accounted for 7-20% in various studies from Pakistan<sup>8</sup>. Carotid supply route stenosis a significant hazard for stroke and symptomatic cerebrovascular disease<sup>9</sup>. Around 20-30% of ischemic stroke cases are due to carotid occlusion. A hospital-based study revealed that moderate to severe Coronary Artery Stenosis is common in general non-diabetic population of Karachi. Risk factors for Coronary Artery Stenosis development can be either modifiable or non-modifiable<sup>10</sup>. Non-modifiable risk factors are include family history, age, gender, race and ethnic background where as the modifiable risk factors comprise of hypertension, diabetes mellitus, dyslipidaemia, cigarette smoking, alcohol abuse, cardiac disease, and physical inactivity.

While one study conducted to determine Coronary Artery Stenosis prevalence in general population with stroke patients' reports that prevalence of Coronary Artery Stenosis in diabetic subgroup is 7%. Coronary Artery Stenosis can be evaluated through different diagnostic modalities<sup>11</sup>. Angiography was the principal demonstrative imaging methodology produced for assessment of vessel. The presentation of ultra-sound in 1960, figured tomography in 1970, X-ray in 1980 and with their consequent improvement, Color Doppler Imaging, Computed Tomography and Magnetic Resonance angiography ended up accessible for the non-intrusive assessment of vascular framework. Duplex ultrasonography currently is the most accurate non-invasive primary diagnostic modality available for assessment of the stenosis of carotid artery. Ultra-sound is setting up its role in screening and determination of carotid pathology because of patient comfort, less hazards, minimal effort and precision in distinguishing carotid atherosclerosis and is routinely done<sup>12</sup>.

Our study aimed to find the prevalence of carotid artery pathology in diabetics. At the international level, a significant body of research has been done on this issue but the situation is very different in Pakistan, where there is no such significant research that has been conducted on this subject. The present study was an endeavor in this direction, generating data, which could be utilized in early identification and developing treatment services for patients with carotid artery disease in diabetic. Main objective of study is to find out the frequency of carotid artery stenosis in diabetic patients presenting with acute ischemic stroke.

## METHODS

This was a cross-sectional study and was conducted at Medicine wards Jinnah Post-Graduate Medical Centre, Karachi from 5th December 2014 to 5th

June 2015 after the Institutional Review Board (IRB) approval. Total 101 patients were included. The inclusion criteria were aged above 18-70 years, ischemic stroke and diabetes. The exclusion criteria was hemorrhage/space occupying lesion on brain scan, transient ischemic attack, Patients demonstrating meningeal irritation evident by neck stiffness and positive kerning test, having other serious co morbidity such as heart failure and Chronic obstructive pulmonary disease (COPD) or malignancy.

Carotid artery stenosis was defined as obstruction of >70% by Doppler ultrasound<sup>13</sup>. Acute ischemic stroke was considered as a focal neurological deficit (weakness of right or left side of body) of acute onset lasting for >24 hours with hypodensity on CT scan of brain<sup>14</sup>. Diabetes mellitus was considered when FBS >126mg/dl<sup>15</sup>. Hypertension was considered when systolic BP exceeding 140mmHg and diastolic blood pressure BP exceeding 90 mm Hg). Obesity was considered when BMI is >30 since, smoking was considered as one pack/day in more than one year. Dyslipidemia was considered as total cholesterol >240mg/dl.

A point-by-point history and exhaustive physical examinations of patients were done on a proforma. Each patient experienced underwent examinations like Total Cholesterol, ECG, X-ray and CT filter cerebrum. During the hospitalization, patients were subjected to carotid Doppler ultrasonography to assess carotid artery stenosis. Patients were provided routine medical care during the hospitalization.

Data was analyzed using SPSS v23.0. Mean±S.D were calculated for the continuous variable like age and FBS level. Results on categorical variables like gender, HTN, smoking, obesity, dyslipidemia and patient outcome variable were expressed in frequencies and percentages. Age, gender, HTN, smoking, obesity and dyslipidemia were stratified to see the effect modifiers. A p-value was considered as significant when of <0.05, Chi-Square test was applied to assess the difference among categories. The study was conducted in compliance with the declaration of Helsinki.

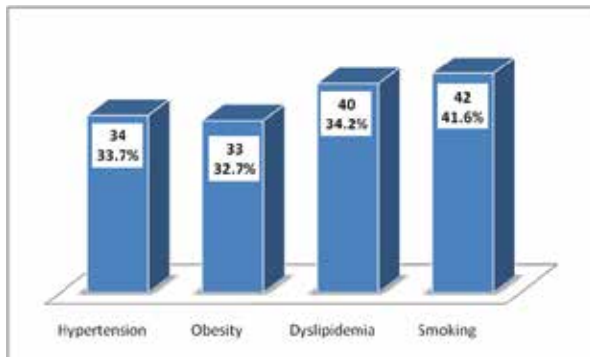
## RESULTS

Among 101 patients, male subjects were 60(59.4%) and females subjects were 41(40.6%) while mean age of our study population was 53.7±10.2 years. The age was stratified into two groups and frequency of patients belonged to each group was also calculated. The detailed results are presented in Table 1.

**Table 1: Descriptive statistics of study population.**

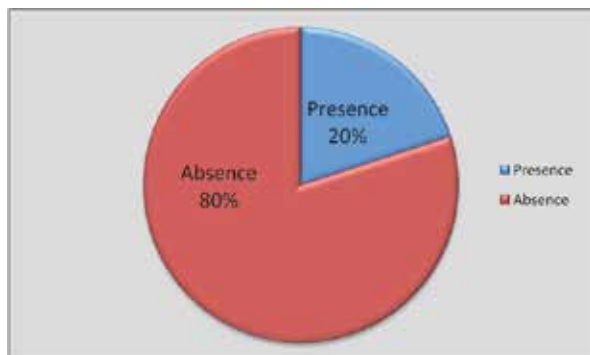
Age (years) Mean±SD		53.7±10.2
		n (%)
Gender	Male	60(59.4)
	Female	41(40.6)
Age Groups	<50 years	31(30.7%)
	≥50 years	70(69.3%)

Among the risk factors, total 34(33.7%) patients had hypertension, total 33(32.7%) patients were obese, total 40(34.2%) patients had dyslipidemia, whereas total 42(41.6%) patients had history of smoking as presented in Figure 1.



**Figure 1: Frequency distribution of risk factors.**

On analysis of carotid artery stenosis among the diabetics, it was observed that diabetics 21(20.8%) had carotid artery stenosis as presented in Figure 2.



**Figure 2: Presence (20%) and absence (80%) of carotid artery stenosis (CAS) in diabetic patients.**

Among 21 carotid artery stenosis (CAS) patients, 10 were male and 11 were females while there was Insignificant association of CAS with gender (p=0.162). 18.4% were from age group<50 years and 21.5% from age group>50 years while insignificant association was found for CAS with age group (p=0.520).32.4% were found with hypertension, 14.2% with smoking, and 20% with dyslipidemia while 33.3% were obese. Significant association of carotid artery stenosis was found with hypertension (p=0.040) and obesity (p=0.031) while there was insignificant association of smoking (p=0.133) and dyslipidemia (p=0.224) with CAS as presented in Table 2.

**Table 2: Stratification of CAS with respect to effect modifiers.**

Parameters	Carotid Artery Stenosis (CAS)		Total (n=101)	p-value
	Positive (n=21)			
Gender	Male	10(16.7)	60	0.162
	Female	11(26.8)	41	
Age Group	<50 years	6(18.4)	31	0.520
	≥50 years	15(21.5)	70	
Hypertension		11(32.4)	34	0.040*
Smoking		6(14.2)	42	0.133
Dyslipidemia		8(20)	40	0.224
Obesity		11(33.3)	33	0.031*

\* Significant at > 0.05 levels

**DISCUSSION**

Current study was carried out to find out the frequency of carotid artery stenosis in diabetic patients presenting with acute ischemic stroke. On analysis of carotid artery stenosis among the diabetics, it was observed that diabetics 20.8% patients had carotid artery stenosis. Among male and female patient, carotid artery stenosis was found among 16.7% and 26.8% respectively while among patients with age<50 years and ≥50 years, 18.4% and 21.5% were found with carotid artery stenosis.

Further, 32.4% were found with carotid artery stenosis among hypertensive patients while 14.2% of smokers were found with carotid artery stenosis. Carotid artery stenosis was found among 20% for dyslipidemia patients while 33.3% among obese patients. Cardiovascular disease (CVD) is a major cause of death and disability among people with diabetes. Adults with diabetes historically have a higher prevalence rate of CVD than adults without diabetes, and the risk of CVD increases continuously with rising fasting plasma glucose levels, even before reaching levels sufficient for a diabetes diagnosis<sup>13</sup>. Atherosclerosis is quickened in diabetes mellitus for various causes. Initially, diabetes mellitus is related with an expanded hazard of customary coronary disease hazard factors, like hypertension, dyslipidaemia, overweight, and hyper-insulinemia, furthermore metabolic aggravations extraordinary to diabetes mellitus, for example, expanded dimensions of coursing glucose, propelled glycation finished results and oxidation of lipo-proteins may likewise build the hazard and frequency of atherosclerosis<sup>16,17</sup>.

A study conducted in Karachi done by Khan et al.<sup>18</sup> demonstrated that 25% cases with coronary artery disease had coronary artery stenosis of over half while by and large about ninety four percent of patients demonstrated evidence of plaque. In addition, among Japanese patients undergoing

coronary artery bypass grafting in light of coronary artery disease, a raised rate of carotid artery stenosis was observed<sup>19</sup>.

The prevalence of carotid artery stenosis ranges from 4% to 11%, and it increases with age and varies by race<sup>17</sup>. In this study, occurrence of coronary artery stenosis was noted in 20.8% cases as compared to Razzaq, who noted frequency of Coronary artery stenosis as 31%<sup>10</sup>. In another study, conducted in Iran noted a minimal occurrence of coronary artery disease. Stenosis was noted in 1.8% cases, and critical stenosis was noted in 1.1% cases<sup>20</sup>. In this study, more prevalent carotid disease was observed maybe due to more severe Coronary artery disease in local sample and contrasting with Iranian sample. Tanimoto and his group<sup>19</sup> observed coronary artery stenosis among 19.6% cases with 29.1% as diabetics. However, in our study male to female ratio was 3:1 while Atif in his study noted a 1.6:1 ratio conducted in Karachi<sup>21-25</sup>. In another study done by Masood<sup>25</sup> in Iran, the ratio was as 1.1:1.6. Khan et al. in their study in Karachi reported a ratio of 1.05:1<sup>26</sup>.

The major risk factors in this study included smoking, dyslipidemia and hypertension. Other studies also established hypertension as a major risk factor<sup>27,28</sup>. One of the study reported hypertension and diabetes as most prevalent risk factors for cerebral ischemic stroke. In that study out of total 50 patients, 32 had hypertension (64%) and 22 had diabetes (44%). Kannel et al. analyzed the parts of circulatory strain as an indicator of consequent stroke. They evaluated various components of blood pressure as forecaster of ensuing stroke and found that the systolic pressure was the most predictable entity. Other factors such as the mean arterial pressure and the pulse pressure had a positive correlation with the subsequent events. Various other studies have demonstrated similar findings and systolic hypertension in the elderly is now a recognized cause of adverse events. There is an argument that the association of Hypertension and carotid artery stenosis are based upon a single recording and not replicate measurements and their study demonstrated the same<sup>29,30</sup>.

In diabetics, the incidence of hypertension is increased. In another study, Christlieb et al. found that in patients with non-insulin dependent diabetes isolated systolic hypertension is commonly seen. Although not identified, yet these factors are reflective of the changes in with the diabetes walls of arteries and are exclusively associated. Sethi et al. stated that medial calcification of arterial wall and their stiffening can be explained as a cause of hypertension<sup>30</sup>.

Although atherosclerosis is very common in this diabetes, yet it is to be noted that it is not always related to medial calcification of arteries. It is still being investigated whether a rise in the systolic pressure and the pulse pressure signifies only presence of atherosclerosis or is in fact a contributory factor in its development. Another school of thought strongly believes that the arterial wall prop-

erties are changed due to atherosclerosis leading to increased systolic pressure as the vascular compliance is decreased. Carotid artery stenosis is strongly linked with older age, which is an important and well-recognized contribution of atherosclerosis. Our study group comprised of a majority of patients who were more than 50 years of age (68%).

Sethi et al. in their study observed that patients presenting with a lesion in carotid artery were much older when compared to subjects who did not have a lesion in carotid artery<sup>30</sup>. Smoking is related with elevated levels of fibrinogen, expanded pressed cell volumes, and diminished macrophage movement changes in lipid natural chemistry. Smoking is also a well-recognized known cause of change in blood flow dynamics. The other notable known risk factors playing a key role in development and pathogenesis of generalized atherosclerosis are cigarette smoking and dyslipidemia. The interplay between these risk factors their effect on the flow and pressure in the carotid bulb is still being investigated, as it can be a contributing factor in development and successive progression of plaques in carotid artery<sup>31</sup>. In this study, there were 51.3% cases, who were smoker. Anyhow, an autonomous relationship of smoking with coronary artery stenosis could not be affirmed as about every one of the smokers had something like one other hazard factor, predominantly hypertension.

## CONCLUSION

Stenosis of Carotid artery was common in patients suffering from acute ischemic stroke and diabetes mellitus. Among modifiable risk factor in patients with stroke having carotid artery stenosis, Hypertension was most common whereas fasting blood sugar FBS level greater than 100 g/dl lead to increased chances of having carotid artery stenosis.

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## CONFLICT OF INTEREST

The authors declared that there was no conflict of interest.

## ETHICS APPROVAL

Ethical review was obtained from institutional review board.

## PATIENT CONSENT

Patient/attendant consent was obtained.

## AUTHORS' CONTRIBUTIONS

WS given the conception and design of the study, helped in the acquisition of data and manuscript

writing. LS did the data collection and interpretation of the data. RP also collected the data for study and assisted in the literature search. MS performed the data entry, statistical analysis. TS also assisted in the statistical analysis and manuscript writing. While AA carried out the critical analysis, manuscript review and proof reading.

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