

## Evaluation of Burden of Carotid Artery Disease In Ischemic Stroke Patients With And Without Hypertension

Hamad Khan, Khurram Haq Nawaz\*\*, Asif Hashmat\*, Hamid Mukhtar\*\*\*, Fawad Ahmad\*, Muhammad Anjum\*

Department of Medicine, Pak Emirates Military Hospital / National University of Medical Sciences (NUMS) Rawalpindi Pakistan, \*Department of Neurology, Pak Emirates Military Hospital / National University of Medical Sciences (NUMS) Rawalpindi Pakistan, \*\*Department of Neurology, Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan, \*\*\*Department of Neurology, Sims Services Hospital, Lahore Pakistan

### ABSTRACT

**Objective:** To evaluate the burden of carotid artery stenosis in ischemic stroke patients and its association with socio-demographic aspects of Hypertension.

**Place and Duration of Study:** Tertiary Care Hospital, Rawalpindi Pakistan, from Jan to Jun 2020.

**Study Design:** Cross-sectional study

**Methodology:** A total of 226 acute ischemic stroke patients, confirmed on CT/MRI brain, were subjected to ultrasound Doppler to look for significant carotid artery stenosis. The association of Hypertension was evaluated with the presence of carotid artery stenosis in such patients.

**Results:** Hypertension was recorded in 133(58.8 %) patients and clinically significant carotid artery stenosis was seen in 96(42.5%) patients. The presence of Hypertension and increasing age were significantly associated with carotid artery stenosis (*p*-value respectively).

**Conclusion:** The frequency of clinically significant carotid artery stenosis in hypertensive stroke patients remains higher in Pakistan. Prolonged Hypertension in advanced age may be a contributory factor in developing stroke.

**Keywords:** carotid artery disease, Hypertension, Ischemic stroke, Smoking.

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### INTRODUCTION

Stroke and its sequelae account for a hefty chunk of human morbidity and mortality across the world.<sup>1</sup> In a country like Pakistan, where health resources are always encumbered, stroke patients constitute a major portion of inpatient care admissions.<sup>2,3</sup> The concordance of stroke, metabolic and non-metabolic diseases has been widely discussed and explored.<sup>4</sup> These include Hypertension, DM vasculopathy, etc. Carotid artery stenosis has also been linked to many metabolic, endocrine, autoimmune and age-related deteriorating pathologies that affect the health of its lumen as well as walls.<sup>5</sup> The association of carotid artery stenosis with detrimental cardiovascular accidents is well established.<sup>6</sup> Atherosclerosis remains an important and well-determined cause of carotid artery stenosis and, hence, stroke. Various studies have notified the development of ischemic stroke in patients where carotid artery stenosis was recorded. Even more demonstrated the increased incidence of cerebrovascular accidents in a cohort of Hypertension,

DM and carotid artery stenosis.<sup>7</sup>

Hypertension brings about carotid artery stenosis and, hence, cerebrovascular accidents via a host of interlinked underlying mechanisms. The role of reactive oxygen species in vessel walls is amongst the most extensively implicated mechanisms.<sup>8</sup> The atherosclerotic plaque formed within the vessel wall either leads to vascular occlusion or the formation of microemboli when the plaque fissures, causing stroke/ischemia.<sup>9</sup>

A variety of risk factors thought to be linked with carotid artery stenosis in hypertensive stroke patients include duration and poor control of Hypertension, age, gender, BMI dyslipidemias, etc.<sup>10</sup> The co-presence of DM and ischemic heart disease is also considered to be adversely linked to carotid artery stenosis and stroke. Our research aims to report the burden of carotid artery stenosis in ischemic stroke and assess its affiliation with socio-demographic aspects of Hypertension.

### METHODOLOGY

The cross-sectional study was conducted at the Department of Neurology in a Tertiary Care Hospital in Rawalpindi, Pakistan from January to June 2020

**Correspondence:** Dr Hamad Khan, Department of Medicine, Pak Emirates Military Hospital Rawalpindi Pakistan  
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after approval from the Ethical Committee (A/28/EC/221/2020). The sample size was calculated using the WHO calculator, using a population proportion of 50-70% carotid artery occlusion and 14.4% carotid artery occlusion.<sup>11</sup>

**Inclusion Criteria:** Patients of either gender with acute ischemic stroke, confirmed on CT/MRI brain, were included.

**Exclusion Criteria:** Patients below 40 or above 80 years of age, those with a history of myocardial infarction, diabetes mellitus, valvular heart disease, and history of brain damage secondary to other medical, neurological or autoimmune illness, cancer, irradiation and hemorrhagic stroke were excluded.

Non-probability purposive sampling techniques were employed. CT/MRI brain imaging was used to define/diagnose ischemic stroke in all the patients as advised by Neuro-physician and reported by consultant Radiologists. Detection of significant carotid artery stenosis via ultrasound Doppler by a consultant radiologist was performed. Carotid artery disease was defined as occlusion of 50-70% or above considered clinically significant stenosis, albeit various global studies report considerable variations. The clinically insignificant occlusion was regarded to be less than 50 %.<sup>12</sup>

All the patients, or their next of kin in case of the critically ill, gave their written informed consent to participate in the study.

We recorded the demographics, drug history, presence and duration of Hypertension, dyslipidemias, tobacco smoking and any other comorbid conditions. Apart from history, new ACC/AHA Hypertension guidelines for adults were employed in the study to label hypertension.<sup>13</sup> Dyslipidemias were assessed by checking for serum low-density lipoprotein, total cholesterol and triglycerides levels.<sup>14</sup>

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance

## RESULTS

We observed 226 stroke cases in this study. The mean age was 60.25±7.62 years, ranging from 38 to 80 years. The sample had 166(73.5%) patients above 55

years and 60(26.5%) below 55 years of age. Males accounted for 116(51.3%) of cases, while females accounted for 110(48.7%).

Hypertension was recorded in 133(58.8 %), patients and clinically significant carotid artery stenosis was seen in 96(42.5 %) patients. Various characteristics of the study population are shown in Table-I.

The presence and longer duration of Hypertension (*p*-value: 0.037) and advanced age (*p*-value <0.001), had a statistically significant association with carotid artery stenosis in stroke patients (Table-II).

**Table-I: Characteristics of Study Participants (n=226)**

Parameters	n(%)
<b>Age (years)</b>	
Mean±SD	60.25±7.62
Range (min-max)	38 years-80 years
<b>Gender</b>	
Male	116(51.3%)
Female	110(48.7%)
<b>Carotid artery stenosis</b>	
<50%	130(57.5%)
50-70%	96(42.5%)
Mean duration of Hypertension	6.13±2.233 years
<b>Hypertension</b>	
Present	133(58.8%)
Absent	93(41.2%)

## DISCUSSION

Our study underlines the importance of Hypertension and associated vascular stenosis as a notable contributory factor leading to calamitous cardiovascular events. Physical and microvascular disturbances in long-standing Hypertension may result in rapid atherosclerosis, which may cause narrowing of carotid arteries, paving the way for ischemic stroke to set in.

The clinically significant carotid artery stenosis seen in 42.5 % of our sample was quite higher than the other internationally conducted studies.<sup>5,14</sup> This might implicate that the local population has a higher tendency to develop clinically significant carotid artery stenosis and hence stroke.

Hypertension carries a higher risk of various adverse physical and metabolic sequelae. With these sequelae acting as important confounding variables, assessing the association of stroke and carotid artery stenosis with Hypertension becomes difficult.<sup>15</sup> Prolonged and inadequately controlled Hypertension, female gender and older age are the elements that may expedite the development of carotid artery stenosis.<sup>16</sup>

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**Table-II: Association of Various Factors with presence of Carotid Artery Stenosis (n=226)**

Socio-Demographic Factors	Carotid Artery Stenosis		p-value
	No Significant Stenosis (<50% Narrowing)	Clinically Significant (50-70% Narrowing)	
<b>Hypertension (Mean Systolic 150mmHg)</b>			
Present	63(47.4%)	70(52.6%)	<0.001
Absent	67(72%)	26(28%)	
<b>Duration of Hypertension</b>			
< 10 years	32(58.2%)	23(41.8%)	0.036
10 years or more	31(39.7%)	47(60.3%)	
<b>Gender</b>			
Male	70(60.3%)	46(39.7%)	0.378
Female	60(54.5%)	50(45.5%)	
<b>Age</b>			
55 year or less	39(81.3%)	9(18.8%)	<0.001
>55	91(51.1%)	87(48.9%)	
<b>Education</b>			
< 10 years	73(58.4%)	52(41.6%)	0.766
10 years or more	57(54.4%)	44(43.6%)	
<b>Dyslipidemias</b>			
Yes	35(49.3%)	36(50.7%)	0.091
No	95(61.3%)	60(38.7%)	
<b>Smoking</b>			
Non Smoker	78(65.5%)	41(34.5%)	0.010
Smoker	52(48.5%)	55(51.4%)	

Stroke itself is a multifactorial entity with its risk factors and casualty. It can be caused by any anomaly in the interplay of its various genetic, neurophysiological and biochemical components.<sup>17</sup> Alteration in the biochemical profile of the body occurring as a result of poorly controlled DM, dyslipidemias, CRF, CLD20, etc., may lead to enhancement of the atherosclerotic phenomenon causing the blockade of major vessels, leading to various kinds of cerebrovascular accidents, including stroke.<sup>18,19</sup>

We could not find a significant association between hyperlipidemia and smoking in our cohort. Similar trends were reported a study, which found a positive association of advanced age with Hypertension (44% in 18-39 years vs. 82% in 60-79 years) in ischemic stroke patients.<sup>20</sup> The study, however, reported a considerably higher incidence of Hypertension (79%) in its sample in contrast to ours.

Our study does not report any association between smoking and hyperlipidemia with carotid artery stenosis. Similarly, a Japanese study by Wada *et*

*al.* reported dyslipidemia, diabetes and smoking among other risk factors to be positively associated with ischemic stroke and carotid artery disease.<sup>19</sup> A larger sample size with more sensitive parameters could define such associations in further studies.

Our study finds that a protracted course of Hypertension is firmly associated with clinically substantial carotid artery stenosis. Identical observations were reported by earlier studies, including an Indian study by Saxena *et al.*, *p*-value <0.0001 and OR 6.2 (2.4-16.6) for age >60 years) and a study by Kajitani *et al.* in 2017 (*p*-value <0.01 and Mean±SD 0.91±0.15 for age >65 years).<sup>17-21</sup> An effectively controlled hypertension, accompanied by necessary lifestyle modification to remove other risk factors, could act synergistically to minimize the risk of vasculopathy and stroke in the long term. Further studies could demonstrate this relation elaborately.

Focusing on prevention and early treatment strategies for Hypertension could cut back the risk of future stroke and its catastrophic sequelae. Sensitizing and strengthening the primary healthcare components to effectively prevent and control hypertension could not only ameliorate the burden of Hypertension and its sequelae, like cerebrovascular accidents but also reduce the workload of neurology and other tertiary healthcare domains.<sup>22</sup>

### LIMITATION OF STUDY

Doppler ultrasound, being an operator-dependent apparatus, always carries a likelihood of misreporting the actual findings. More studies employing a larger sample size, more sophisticated tools and longitudinal epidemiological data to demonstrate such a relationship are to be put forward.

### CONCLUSION

There is a higher frequency of carotid artery stenosis with systolic Hypertension and, hence, a higher chance of ischemic stroke in such patients. Prolonged systolic Hypertension in advanced age may be a contributory factor in developing stroke. Patients should, thus, be warned about the possible complications of ischemic events in prolonged and poorly controlled systolic Hypertension.

**Conflict of Interest:** None.

Following authors have made substantial contributions to the manuscript as under:

HK & KHN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AH & HM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

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FA & MA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity

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