A Hospital Based Study On Intracranial Atherosclerosis- Correlation With Extracranial Atherosclerosis And Risk Factors In North India

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Abstract: Background: The burden of intracranial atherosclerosis has been reported to be high in Asian population. Intracranial atherosclerosis besides being a common cause of stroke in many populations, it's not being studied well. Therefore we planned to conduct a study in stroke patients in our hospital to diagnose intracranial atherosclerotic disease using TCD and correlate with carotid artery disease and its risk factors. Materials & Methods: We enrolled all patients presenting with anterior circulation and lacunar stroke after talking informed consent. Institutional ethical clearance was taken for the same. Patients with posterior circulation stroke, hemorrhagic stroke, cardioembolic stroke and critically ill patients were excluded. Results: 55 patients were enrolled for the study, out of which 21 (38.2%) were female patients and 34 (61.8%) were male patients. Hypertension, diabetes, CAD, past stroke, substance abuse was found to be common risk factors. Intracranial atherosclerosis was found in 54.5 % patients, with involvement of ACA being in 21 (38.2%) patients and MCA in 16(29.1%). Conclusion: Intracranial atherosclerosis was found in more patients as compared to extracranial atherosclerosis. ACA was the most prevalent site of stenosis, followed by MCA which was found to be related with ICA stenosis. [Singla M Natl J Integr Res Med, 2020; 11(2):34-39]

Key Words: Intracranial atherosclerosis, Transcranial Doppler (TCD), stroke, risk factors

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Introduction: Worldwide stroke is one of the leading causes of morbidity and mortality resulting in approximately 4.4 million deaths each year[1].As per epidemiological studies conducted on stroke patients in India the cumulative incidence was found to be 105 to 152 per 100,000 persons per year and the prevalence rate ranged from 44.29 to 559/100,00 person per year[2].The crude annual incidence rate was found to be 140/100,000 persons per year in a task force for stroke registry conducted in Ludhiana city and age adjusted incidence rate was 181.67/100,000 persons per year[3].

According to TOAST classification, stroke can be large vessel (which can be atherosclerotic or embolic), cardio-embolic, small vessel, stroke of other determined etiology and stroke of undetermined etiology[4]. Besides cardio-embolic stroke, the pathophysiology of ischemic stroke usually revolves around atherosclerotic plaque formation over a number of years in the arteries of the Circle of Willis or other large arteries before the final cerebrovascular event. This event is presumably caused by a rupture of that plaque or progressive hemodynamic stenosis leading to decompensated low flow state with failure of the collaterals.[5,6] Out of these causes, large vessel intracranial atherosclerotic disease (ICAD) is reported to be in higher frequency among the South Asians.[7] According to one studyICAD is found to be responsible for at least 30–50% strokes amongst the Asian population.[7] Intracranial atherosclerosis has been shownto correlate well with atherosclerosis at other sites like carotidarteries and the aorta.[8] Carotid stenosis is another established risk factor of ischemic stroke. Intracranial Atherosclerotic Disease is an important cause of stroke in addition to extra-cranial internal carotid artery atherosclerosis and non-valvular atrial fibrillation. As per literature, intracranial atherosclerosis is found to be the most common cause of stroke in patients from Asia.[9, 10] It's also commonly seen in Hispanic and black population.[11] In studies done in Iran, the prevalence of intracranial stenosis was found to be 25.4% using TCD, performed in 169 patientswhich was comparable to other middle eastern population.[12] In a study done in India in West Bengal it was found that in patients without carotid artery disease, anterior cerebral artery was more affected.[13] Middle cerebral artery was more affected in patients with carotid artery disease, with it also being the most commonly affected artery. In a ten year data review of Hyderabad Stroke Registry, intracranial atherosclerosis was found to be the most common stroke subtype, with 78.3 % patients having large artery atherosclerosis and 21.7% had extracranial atherosclerosis.[14]

The major risk factors identified in a recent North Indian study were hypertension (a diastolic blood pressure >95 mmHg), hyperglycemia, tobacco

use, and low hemoglobin levels (<10 g%).[15] Another community-based study on biochemical risk factors from North India among urban, rural, and semi-urban people has documented elevated levels of fasting blood glucose, cholesterol, triglycerides, and low HDL with urbanization.[16]

Conventional cerebral angiographyis the gold standard to detect large artery intracranial stenosis [17]but as it's costly, not widely available and increases the risk of stroke.[18, 19, 20, 21]All these factors make it impractical for screening purposes. Similarly magnetic resonance angiography (MRA)due to its high cost and availability issues is not considered a viable option in all stroke patients.[22] There is the need of a screening tool that's not only widely available but effective and available at an affordable cost to make it relevant to low income countries where intracranial atherosclerosis is more prevalent. Transcranial Doppler (TCD) is considered a potentially valuable screening tool due to its wider availability and lesser cost.[23]Transcranial Doppler, a noninvasive ultrasound technique which is in use since 1982[24] uses a low frequency transducer 2 MHz to insonate the relevant cerebral arteries. The insonation is done through the thin temporal bone and thus measures the blood flow velocity and its alterations. Advantages offered by TCD are that it's inexpensive, repeatable, and portable. Even continuous monitoring of the cerebral blood flow (by patient's bedside) is also possible with TCD. It provides a relatively inexpensive, real-time measurement of cerebrovascular hemodynamics and blood flow characteristics within the basal arteries of the brain. Previous studies looking at TCD as diagnostic modality have shown encouraging results by reporting negative predictive values and sensitivities comparable to that of the MRA.[25]

However, the majority of these studies have been performed on the Western Population. Overall, studies on TCD are lacking in North India region, hence we planned to conduct this study to detect intracranial atherosclerotic diseasein our population and hence why this study was necessary.

Material and Methods: A cross-sectional descriptive study was conducted at our center during a period betweenJanuary 2017 and June 2018. The institutional ethics committee approved study protocol prior to the commencement of the study.203 Patients of ischemic stroke were admitted during this time period. Out of these, 38 patients were of posterior circulation stroke, 45 patients were found to have cardioembolic stroke. 33 patients had large stroke and critically ill. 19 patients refused to take part in the study because of financial constraints and they were not willing to take part in the study. Therefore 68 patients admitted with occurrence of ischemic stroke in the anterior circulation and lacunar stroke in the departments of Medicine, Neurology and Emergency wereincluded in the study.

Informed consent was taken from all the participants. Patients with posterior circulation stroke, hemorrhagic stroke, critically ill patientsand those who were unwilling to participate in study wereexcluded.Each patient with acute stroke was examined by a Medicine Resident and thefindings confirmed by a qualified stroke neurologist. Information was collected concerning details of demographics, risk factors, past history, general andneurological examination on each patient. The participants underwent clinical examination at the time ofadmission. Initial blood investigationsincluded complete blood count, blood glucose, renal and liverfunction tests, lipid profile and electrolytes. Atrial fibrillation was defined as documentation of thesame in at least one electrocardiograph recording at any pointof time.

Each patient underwent magnetic resonance imaging (MRI)of brain at 3 Tesla Machine. The MRI protocol included T1, T2, T2-FLAIR and DWIsequences. At the same time, time-of-flight magnetic resonanceangiogram (TOF MRA) was obtained in willing patients. Echocardiography and Carotid doppler was performed in each patient. Transcranialdopplerwas performed in all the patients on the samemachineDigi-Lite of RIMED Company. The patients were examined in the supine or sitting position. The two MHz probe was used and a constant angle of insonation was maintained. Temporal window of the patient was used to do the TCD. All tests were performed by one neurologist. The trans-temporal window was found between the angle of the eye and the pinna above the zygomatic ridge and is the major route for insonating the anterior and middle cerebral arteries. The MCA was identified through the transtemporal window, with the flow direction normally towards the probe, about 30–

60 mm from the skull surface. The ACA was insonated between depths of 65–80 mm with the probe directed antero-superiorly through the trans-temporal window. At the end velocities were recorded on the right and the left side. The results obtained were compared with the already published literature.If the mean blood velocity was greater than 120 cm/sec, an intracranial artery was considered to be stenotic. Intracranial arterial occlusion was diagnosed if mean velocity was reduced greater than 21% reduction compared with that of the contralateral vesselor if all basal arteries except the artery in question were detectable.14Before labeling a case as that of intracranial disease, it was mandatory to exclude cardio-embolic source of stroke. Carotid artery stenosis contributes significantly to the total burden. Therefore, the correlation of carotid stenosis with intracranial atherosclerosis becomes a pertinent topic of investigation. Also, coexistent stenosis of intracranial vessels along with extracranial vessels is expected to alter the pathophysiology of stroke.

Statistical Analysis: Data was described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square ($\chi 2$) test was performed and exact test was used when the expected frequency was less than 5. The sensitivity and specificity was calculated. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations was done using SPSS (Statistical Package for the Social Science) 17 version statistical program for Microsoft Windows.

Results: A In our prospective observational study, we recruited 68 patients. In 13 patients insonation was found difficult and window couldn't be made because of age and thickness of the bone. So 55 patients were included for final analysis.Out of these 55 patients, 21 (38.2%) were female patients and 34 (61.8%) were male patients with the mean age of 62.64 ± 9.78.The most common presenting complaint in this study was hemiparesis, which was seen in 35 patients (63.6%), of which 19 had left hemiparesis, while 15 had right sided weakness and 1 patient had weakness of both sides. 29 patients(52.7%) presented with dysarthria while facial deviation was presenting complaint in 13 patients (23.6%). Most common risk factors which were observed were hypertension, diabetes mellitus type 2, substance abuse, past stroke and coronary artery disease.Hypertension was the most common risk factor accounting for 43 patients (78.2%) followed by diabetes in 20 patients (36.4%). Substance abuse was seen in 19 patients (34.54%), alcohol use was most common amongst 9 patients (16.4%), drug abuse was seen in 6 patients (10.9%) and smoking was seen in 4 patients (7.3%). Past history of stroke was seen in 8 patients (14.5%). Coronary artery disease was seen in 3 patients (5.5%) (Table 1).

Table 1. Demographic Profile Of Patients And Their Risk Factors	
Age	62.64 ± 9.78
Sex	
Female	21(38.2%)
Male	34(61.8%)
Risk Factors	
HTN	43(78.2%)
DM	20 (36.4%)
CAD	3 (5.5%)
Past H/O Stroke	8 (14.5%)
Alcoholic	9 (16.4%)
Drug Abuse	6 (10.9%)
Smoker	4 (7.3%)

On looking for evidence of extracranial disease, carotid Doppler revealed significant carotid artery disease (>50% stenosis in symptomatic patients) was seen in 19 patients (34.6%). Of these, right sided disease was seen in 10 patients (18.2%), left sided disease in 5 patients (9.1%) and bilateral involvement was seen in 4 patients (7.3%) and showed prevalence of 34.5% significant carotid disease.

In our study, we observed that 16 (29.1%) patients have reduced flow in the MCA territory and 21 (38.2%) patients have reduced flow in the ACA territory and 7 patients (12.7%) had involvement of both the arteries. Therefore 54.5% were found to have intracranial atherosclerosis in total. ACA atherosclerosis was found more commonly as compared to MCA on TCD though MCA territory strokes were more common in our patients (Table 2).

On comparing both extracranial circulation (using Carotid Duplex) with intracranial circulation (using TCD), out of 16 patients having

abnormal MCA circulation, 11 patients had associated extracranial involvement as well. Out of 21 patients having ACA involvement, 5 patients had overlap with carotid involvement.

Table 2. Number Of Patients Having Intracranial And Extracranial Involvement

Carotid Duplex	No. Of Patients	Percentage
B/L Significant	4	7.3%
Left Significant	5	9.1%
Non Significant	36	65.5%
Right Significant	10	18.2%
Total	55	100.0%
MCA	No. Of Patients	Percentage
Normal	39	70.9%
Abnormal	16	29.1%
Total	55	100.0%
ACA	No. Of Patients	Percentage
Normal	34	61.8%
Abnormal	21	38.2%
Total	55	100.0%

On comparing risk factors in intracranial and extracranial atherosclerois, hypertension, diabetes mellitus were found in both the groups as most common risk factors. Patients with underlying Coronary artery disease had associated carotid artery disease more as compared to intracranial atherosclerosis. Patients with previous history of stroke had more intracranial involvement. People consuming alcohol and drugs had more intracranial atherosclerosis, with MCA artery involvement of more as compared to ACA (Table 3).

Table 3. Correlation Of Risk Factors With Extracranial And Intracranial Atherosclerosis

	Carotid Duplex		MCA		ACA	
DM	9	47.4 %	7	43.8 %	8	38.1 %
HTN	15	78.9 %	12	75.0 %	17	81.0 %
CAD	3	15.8 %	2	12.5 %	2	9.5%
Past H/O Stroke	2	10.5 %	5	31.3 %	7	33.3 %
Alcoholic	5	26.3 %	7	43.8 %	8	38.1 %
Drug Abuse	3	15.8 %	5	31.3 %	5	23.8 %
Smoker	2	10.5 %	2	12.5 %	3	14.3 %

Discussion: Our results showed that extracranial disease was found in 19 patients (34.6%) on carotid Doppler. Evidence of intracranial atherosclerosis was found in more patients i.e., in 54.5% as compared to extracranial disease. Another important aspect of our results was that ACA atherosclerosis was found more commonly as compared to MCA on TCD though MCA territory strokes were more common in our patients. The reason why ACA stenosis is manifesting less as a cause of strokeis not clear and requires further evaluation.

Hypertension, diabetes, smoking and dyslipidemia are major risk factors for intracranial atherosclerosis.26In our study also, most common risk factors observed were hypertension, diabetes mellitus type 2, substance abuse, past stroke and coronary artery disease. Risk factors for carotid artery stenosis and intracranial stenosisare largely similar, and include hypertension, diabetes mellitus, CAD. No risk factor preferentially caused atherosclerosis inmultiple territories. Concurrent atherosclerosis in extracranialand intracranial arteries was also studied. Hypertension emerged as the strongest risk factor for concurrent stenosis, followed by diabetes, CAD and smoking. Stenosis of the large branches of the Circle of Willis can lead to stroke by hypoperfusion or by artery to artery embolism.[27,28] Main limitations of our study are the small number ofpatients. We could not perform CT angiography/ MR angiography in all the patients because of financial reasons, therefore could not correlate with our TCD findings.

Conclusion: we would like to state that intracranial atherosclerosis a common cause of stroke in our population and TCD can be used as a good screening modality. ACA was the mostprevalent site of stenosis in patients without ICA stenosisand had the strongest association with risk factors likehypertension, diabetes and smoking, even though MCAterritory is the commonest affected by stroke. Additionally, presence of ICA stenosis was more commonly associated with MCA stenosis as compared to ACA stenosis, though reason for this kind of patternneeds to be studied in larger populations.

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