

Original Research Article

Extracranial carotid artery wall abnormalities in patients with acute ischemic stroke

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ABSTRACT

Background: Stroke is the second most common cause of mortality worldwide. Large artery extracranial atherosclerosis is one of the major causes of ischemic stroke. The present study laid emphasis on causal relationship between the carotid wall abnormalities and occurrence of ischemic stroke. The aim and objectives of the study were to estimate the prevalence of carotid artery wall abnormalities in acute ischemic stroke patients and assessment of association between carotid wall abnormalities and vascular risk factors.

Methods: A cross-sectional observational study was conducted in department of neurology for a period of two years. Cases with acute ischemic stroke were included in the study. Carotid Intima media thickness (CIMT) was measured using carotid duplex ultrasound scanning at the level of carotid bifurcation.

Results: CIMT findings were abnormal in 87% of cases where the thickness was ≥ 0.8 mm. 38% of patients with Ischemic stroke had CIMT ≥ 1.2 mm. Mean CIMT was highest in patients with sedentary life style (CIMT-1.18 mm) and the differences were significant when compared to non-sedentary life style group. CIMT values were higher in patients with age 61-80 years (CIMT: 2.1 mm); with multiple vascular risks like diabetes and hypertension (CIMT: 1.16 mm); with diabetes mellitus alone (CIMT: 1.14 mm) and hypertension alone (CIMT-1.13 mm) respectively.

Conclusions: Highest mean CIMT value were observed in older adults with age range of 61 to 80 years. Individuals with sedentary life style habits and multiple vascular risk factors had higher mean CIMT value. Early identification of abnormal CIMT value combined with appropriate treatment can prevent stroke in future.

Keywords: Carotid artery, Stroke, Intima

INTRODUCTION

Carotid intima-media thickness (CIMT) is a marker of atherosclerosis and is also a predictor for ischemic stroke. Large artery atherosclerosis is the major cause for Ischemic stroke. Among the large arteries that supply blood to brain, carotid arteries are the major blood vessels present on either side of the neck which carry blood to brain. Involvement of carotid artery especially internal carotid artery (ICA) either by local atherosclerosis, dissection, carotid stenosis, embolus from heart, aorta-artery embolus all can lead to decrease blood supply to brain. The major blood vessels that originate from ICA

are middle cerebral artery (MCA), anterior cerebral artery (ACA) and anterior choroidal artery (AChA) that supply major vital regions of brain such as language area, vision region, auditory region, olfaction and gustatory region. Carotid Stenosis is usually observed at the bifurcation of common carotid arteries into internal and external artery. We measured intima media thickness at the level of common carotid artery bifurcation.

Literature review shows a causal relationship between ischemic stroke and carotid wall abnormalities but the exact pathophysiology is not known.^{1,2} CIMT ≥ 1.2 mm risk for stroke has been reported. Higher age has been

associated with CIMT.³ Most of the study looked into CIMT in patients with CAD.⁴ In the present study CIMT of the common carotid artery was measured with patient diagnosed with acute ischemic stroke.

METHODS

The study was conducted over a period of two year in the department of neurology at Princess Esra hospital, deccan college of medical sciences. The study period was from December 2018 to December 2020. The 100 patients were included in the study. Patients with acute ischemic stroke confirmed by either computed tomography (CT) or magnetic resonance imaging (MRI) brain who underwent CIMT measurement included in study consecutively.

Study design

It was cross-sectional observational study design. In this study design subjects enrolled according to inclusion and exclusion criteria. Patients selected consecutively. We estimated the prevalence of carotid wall abnormalities in acute ischemic stroke patients. Carotid artery Doppler study used to assess any abnormality in carotid arteries of patients with stroke and CIMT was measured.

Carotid artery intima measurement

CIMT evaluated by B mode high resolution ultrasound Doppler imaging technique by radiologist. Measurement was done for bilateral common carotid artery at level of carotid bifurcation and mean CIMT was recorded for each patient. Normal intima-media thickness of common carotid artery is taken as 0.74±0.14 mm. CIMT value<0.8 mm is associated with normal healthy individual and in present study anything above 0.8 mm is considered abnormal.⁵ Value of CIMT ≥1 mm is associated with atherosclerosis as obtained from previous studies.^{5,6} After estimating prevalence of carotid wall abnormality in stroke cases, subgroup analysis was done for risk factors for stroke and their associations with CIMT. In order to avoid potential source of bias in selection of cases strict inclusion and exclusion criteria were followed. Data was collected using a uniform proforma for all cases and experienced radiologists were involved in measurement of CIMT. Sample size was estimated using expected prevalence of 93% of CIMT abnormality in stroke patients based on previous research studies and at 95% confidence interval and absolute precision of 5%. Data were collected using a proforma which consisted demography profile, vascular risk factors biochemical parameters and radiological profile (CT scan brain, MRI brain, carotid Doppler scanning).

Statistical analysis

Quantitative variables were expressed as percentage, continuous variables were expressed as mean, median and T value was calculated. P<0.05 was considered significant. Confidence interval (CI) was set at 95%.

Subgroup analysis of CIMT based on age, sex and vascular versus non-vascular risk factors were compared. Multivariate analysis done for vascular risk factors. Data obtained in study analyzed using SPSS version 18 (IBM).

Ethics statement

The study was approved by Institutional review board.

Inclusion criteria

Patients with age ≥18 years who gave consent for the study were included in the study. Duration of onset of acute Ischemic stroke included were less than 4 weeks. All the patients included in the study had undergone CT/MRI brain for the diagnosis of stroke. All the cases included in the study underwent Doppler neck vessel study for the measurement of CIMT.

Exclusion criteria

Patients who suffered acute ischemic stroke of more than 4 weeks, patients with hemorrhagic stroke or head injury were excluded from the study. Children and pregnant lady were excluded from the study. Patients with incomplete work up for stroke were also excluded.

RESULTS

Participants

Out of 135 cases, a total of 100 patients with acute ischemic stroke, were included in the cross-sectional study (Figure 1). Among the total subjects, 70% (n=70) were males and the rest were females the ratio was of 7:3, only those acute ischemic stroke subjects participated whose duration was 4 weeks and CT/MRI scans showed Infarct in the brain. The mean age of subjects were 56±10.10 years. Table 1 shows the demographic and baseline characteristics of the study group.

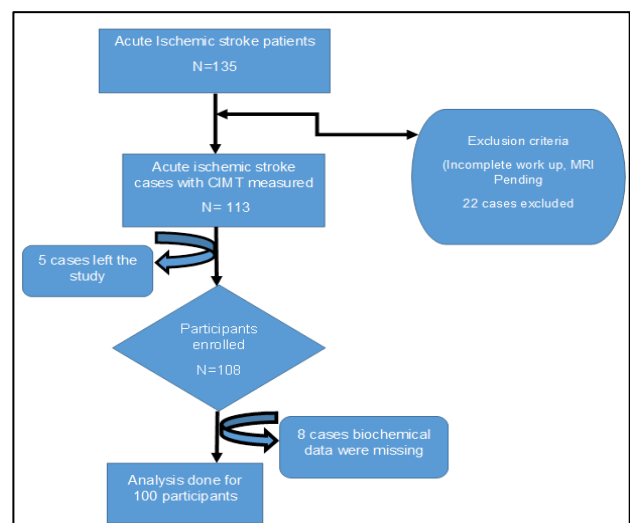


Figure 1: Flow diagram of study participants.

Table 1: Baseline characteristics of study samples.

Variables	Value, (N=100)
Mean age (years)	56.61±10.10
Males	70
Diabetes mellitus	56
Hypertension	73
Hypothyroidism	4
Smoking	33
Alcohol	8
Mean systolic BP (mmHg)	144±24.53
Mean diastolic BP (mmHg)	86.2±10.61

Biochemical parameters are shown in Table 2. The mean blood sugar levels among the study subjects were 136.32±50.13 mg/dl (Table 2). The values of high-density lipoprotein (HDL) infraction mean were abnormal as compared to rest of the lipid fractions and the mean value was 37.79±6.52.

Table 2: Biochemical risk markers in study sample.

Biochemical parameters	Mean±SD
Random blood sugar	136.32±50.13
Total cholesterol	181.07±40.28
Triglyceride (TG)	144.21±68
High density lipoprotein (HDL)	37.79±6.52
Low density lipoprotein (LDL)	114.15±35.36
Very low-density lipoprotein	29.17±13.53

CIMT

CIMT diagnosis was performed for all the 100 acute ischemic stroke subjects. The age range of study subjects was 37 to 82 years. Percentage of participants from different age groups was as follows; 62% from 41 to 60 years age group, 28% from 61 to 80 years age group, 9% from 20 to 40 years age group and 1% from 81 to 100 years age group. Age wise association of CIMT is shown in Figure 2. CIMT values were higher in age group 61 to 80 years (Mean CIMT: 1.21±0.39).

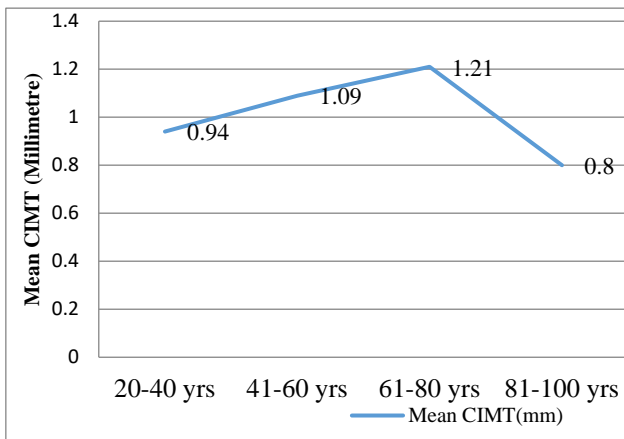


Figure 2: Age wise association of CIMT.

Atherosclerotic plaque and stenosis

Of the 100 patients, 14 patients (14%) showed significant stenosis (>70%) while 23 patients (23%) had carotid stenosis of ≥50%.

Atherosclerotic plaques were seen in 55 patients (55%).

Age and gender comparison with CIMT

Mean CIMT values in our study subjects were 1.11±0.38. Also, from gender perspective, men show more abnormal CIMT values as compared to females especially, in age group 61 to 80 years and this difference were significant when compared to females of same age group (p=0.04) (Table 3). While from Age perspective CIMT values were more abnormal in

Table 3: Age and sex distribution of CIMT.

Age group (years)	Number	CIMT (mean±SD)
20-40	9 (M-4, F-5)	0.94±0.31
41-60	62 (M-46, F-16)	1.09±0.38
61-80	28 (M-20, F-8)	1.21±0.39
81-100	1 (M-0, F-1)	0.8

Table 4: Sex distribution of CIMT compared to age group.

Age group (years)	CIMT(Mean±SD) (mm)		95%, CI	P
	Males	Females		
20-40	0.73±0.18	1.11±0.30	-0.025 to 0.785	0.06
41-60	1.09±0.35	1.09±0.45	-0.219 to 0.219	1
61-80	1.30±0.40	0.98±0.28	-0.639 to -0.0005	0.04
≥ 81	0	0.8		

Subjects with age ≥50 (1.16±0.38 mm) years as compared to other age subjects (p=0.009) (Table 3).

Vascular risk factors parameters and CIMT

The 87% (n=87) of study patients showed abnormal CIMT values i.e., values ≥0.8 mm and 38% showed CIMT values ≥1.2 mm. Mean CIMT values were higher in subjects with sedentary lifestyle as compared to those subjects who have a moderately active lifestyle.

This difference was statistically significant (p=0.04).

Subjects with systemic diseases such as hypertension and diabetes mellitus showed higher mean CIMT values while mean CIMT in smokers was same (Table 5).

Table 5: CIMT and related parameters.

Parameters	Value
Mean CIMT, (mm) (n=100)	1.11±0.38
Median CIMT, (mm) (n=100)	1
Abnormal CIMT, (≥0.8 mm)	87%
CIMT ≥1 mm	57%
CIMT ≥1.2 mm	38%
Mean CIMT in diabetes, (n=51)	1.14±0.42
Mean CIMT in diabetes with hypertension, (39/51)	1.16±0.39
Mean CIMT in hypertensives, (n=73)	1.13±0.37
Mean CIMT in hypertensive with diabetes, (39/73)	1.16±0.39
Mean CIMT in smokers, (n=33)	1.16±0.44
Mean CIMT in alcoholics, (n=8)	0.89±0.32
Mean CIMT in patients with sedentary habits, (n=50)	

Normal intima media thickness of common carotid artery is taken as 0.74±0.14 mm. Some studies say less than 0.8 mm is associated with normal healthy individual and above 1 mm associated with increase CVD risk. Here we are taking ≥0.8 mm as cut off for abnormal CIMT. CIMT ≥1.2 mm risk for stroke.

Table 6: Relationship between mean CIMT and various risk factors for ischemic stroke in study samples.

Variables	Mean CIMT, risk factor (mean±SD*) (mm)		P
	Present	Absent	
Male gender	1.13±0.38	1.06±0.38	0.4
Age ≥50 (years)	1.16±0.38	0.93±0.32	0.009
Hypertension	1.13±0.37	1.04±0.40	0.29
Diabetes mellitus	1.14±0.42	1.07±0.34	0.37
Smoker	1.16±0.44	1.09±0.37	0.40
Alcoholic	0.89±0.32	1.12±0.40	0.11
Sedentary habits	1.18±0.39	1.03±0.36	0.04
Systolic BP >140 mmHg	1.12±0.36	1.08±0.41	0.61
Diastolic BP >90 mmHg	1.11±0.38	1.10±0.39	0.89
RBS >200 mg/dl	1.12±0.51	1.10±0.36	0.86
TC ≥200 mg/dl	1.10±0.41	1.11±0.37	0.9
LDL ≥130 mg/dl	1.15±0.40	1.08±0.39	0.39
HDL ≤40 mg/dl	1.12±0.38	1.11±0.38	0.9
TG ≥150 mg/dl	1.16±0.38	1.00±0.37	0.04

*SD: Standard deviation, TC: Total cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglyceride.

On comparison of vascular risk factors with those without risk factors, CIMT value were markedly higher in patients having single and multiple risk factors. Patients with triglyceride (TG) ≥150 mg/dl had higher CIMT (1.16±0.38 mm) when compared to patients with low TG (p=0.04). Significant differences were observed among sedentary and non-sedentary sub groups, age ≥50 year's vs age less than 50 years and those cases with hypertriglyceridemia (Table 6).

DISCUSSION

Ischemic strokes are considered as an important cause of morbidity and mortality worldwide. The mortality rate of ischemic strokes is 28% at 30 days. To combat this neurological debilitating condition, it is paramount to understand the pathophysiology behind. Earlier studies have observed prevalence of abnormalities in the carotid wall of patients suffering from ischemic stroke. It is important to discover the major relationship between carotid wall abnormalities and occurrence of ischemic stroke. In the above study, CIMT was used as a diagnostic tool to identify morphological differences in carotid arteries of ischemic patients. The observations showed that 87% (n=87) of subjects showed abnormal CIMT values (≥0.8 mm) while 38% (n=38) showed ≥1.2 mm value which is earlier reported as high risk for stroke. Hence abnormality in the thickness of the inner layers of the carotid artery due to the presence of plaque makes 38% of our patients susceptible to ischemic stroke.

About 30–60% of strokes are caused by atherosclerotic disease.⁶ Present study showed 14 of the study cases had significant carotid stenosis, 23 were at the initial stage of stenosis and 55 had plaques on the walls.

We found that hypertension was still the major risk factor for stroke. The mean CIMT values for patients suffering with this co-morbidity was 1.13±0.37 which was also abnormal. Hypertension was found to be the most potent risk factor of stroke as 73% (n=73) subjects were suffering from the co-morbidity.

Mean CIMT values were 1.14±0.28 in patients suffering with diabetes mellitus (n=56) hinting towards more carotid wall abnormalities in these subjects. A study conducted back in 2004 observed that two-third of all ischemic stroke types on admission had Diabetes mellitus.⁷ The mean CIMT values observed in 33% of subjects who had a history of smoking was 1.16±0.44 which was higher than standard values. There is a causal relationship between smoking and risk of stroke. It was observed in an earlier study that 22% of stroke was attributable to smoking.⁸ Subjects with a history of alcohol (n=8) did not have much abnormal CIMT values (0.89±0.32), making alcohol the least influencing risk factor.

Majority of study cases belonged to age group 41 to 60 years (n=62) followed by 60 to 80 years (n=28),

indicating people ≥ 50 years are more susceptible to carotid wall abnormalities. In a prior study, it was observed that occurrence of stroke increases after 60 years of age.^{3,9} An earlier study on carotid arteries in stroke patients also indicated the highest number of stroke patients were in age group 60-69 years which was calculated to be 32%, followed by age group 70-79 years which was 26%.^{10,11} There was significant difference ($p=0.009$) in CIMT among adults ≥ 50 years when compared to younger age. In our study, 70% of subjects were males ($n=70$) and they showed more abnormal CIMT values as compared to females. From a lifestyle point of view, subjects living sedentary life style showed more abnormal results as compared to subjects with moderately active life style.

Thus, while determining the susceptibility of carotid wall abnormality to various vascular risk factors, we observed that CIMT value was higher for stroke cases with sedentary life style, older age adults, men in age group of 61 to 80 years and patients with hypertriglyceridemia. These differences were statistically significant.

We observed a higher mean CIMT value when compared to previous studies reported from India. A case control study by Sahoo et al from India showed, 0.798 mm CIMT value in the acute Ischemic stroke patient and 0.6 mm in the control group.¹ In a Chinese study it was found that patient with hypertension without history of stroke had elevated CIMT and this was independent predictor of stroke. Hence, they suggested more attention to be paid for evaluation of CIMT in patients with elevated blood pressure.¹² In present study there was no significant difference in mean CIMT among hypertensive and non-hypertensive adults with acute ischemic stroke.

Among all risk factors mean CIMT was highest in patients with sedentary life style. CIMT was higher in patients with multiple risk factors having hypertension and diabetes. The present study shows the presence of carotid wall abnormalities ($\text{CIMT} > 0.8$ mm) in majority of the cases with more than half of patient showing evidence of vascular atherosclerosis ($\text{CIMT} \geq 1$ mm) in patients with acute ischemic stroke, but further large-scale studies are necessary to prove carotid wall abnormalities as the major cause behind ischemic strokes. Also, hypertension was found to be the most prominent risk factor for Ischemic stroke. Carotid wall abnormalities (Abnormal CIMT) were higher in older age (61-80 years), patients with sedentary life style, and individual with multiple risk factors like diabetes mellitus and hypertension. Among lipid fractions, patient with higher triglyceride levels had higher CIMT value. Mean CIMT value was higher in females with age group 20-40 years compared to males of same age group.

Limitations

There are several limitations of the study. First of all, the study being a cross sectional observational study with

limited number of cases. Secondly, we try to measure CIMT of the common carotid's artery only, whether the value changes with another artery is unknown. Here we did not compare with controls of age and sex matched. Aetiological subtypes of strokes were not studied. Advantage of the study, its one among few studies conducted in stroke patients. Causal relationship has been studied. However, large scale-controlled studies would help in future directions.

CONCLUSION

CIMT was abnormal in majority of patients with ischemic stroke. Highest mean CIMT was observed in individuals with age range of 61 to 80 years followed by individuals who followed sedentary life style. Mean CIMT increased in patients with multiple vascular risk factors. Early identification of abnormal CIMT in subjects with early medical intervention can prevent stroke in future.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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