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Review Article,

An Observational Study of Risk Factors and Their Association with Carotid Intima- Media Thickness in Cases of Ischemic Stroke

Dr. Arun Tyagi[1], Dr. A.K. Shrivastava[2], Dr. Marcia Waran[2], Dr. A. B. Khare[3]
Prof & HOD[1],
Prof [2], Assoc Prof,
Department of Medicine, DVVPF's Medical College, Ahmednagar (Maharashtra) India

Abstract:

Introduction Currently, ischemic heart diseases and stroke are the leading causes of morbidity and mortality worldwide and more than 80% of deaths occurring in the low and the middle-income countries. There are a number of risk factors associated with ischemic stroke; the important ones being hypertension, diabetes mellitus, tobacco use and hyperlipidemia. All the risk factors also contribute towards atherogenesis. Change in the carotid artery intima–media thickness (CIMT) is an indicator of generalized atherosclerosis. This study was conducted to find out correlation between risk factors and CIMT in the stroke patients of western Maharashtra.

Aims and objectives this observational study was conducted in department of medicine from February 2013 to June 2014 to study the risk factors and their association with CIMT if any, in patients of stroke. Fifty stroke patients admitted in the medical ICU were studied.

Results Thirty-five patients out of 50 studied had ischemic stroke. Tobacco use (82%) and hypertension (80%) were the commonest risk factors for stroke followed by, dyslipidemia, obesity, metabolic syndrome and diabetes mellitus. Twenty-four (68.5%) out of 35 ischemic stroke patients had CIMT value more than 1.00 mm. Out of 35 ischemic stroke patients 15 had carotid stenosis; four severe (>70%), five moderate (50% - 70%) and six patients had mild (<50%) stenosis. Out of the patients with carotid stenosis, 13 patients had hypertension, 12 were tobacco user, 8 dyslipidemia and 6 had diabetes mellitus.
Conclusion Increased CIMT is a marker of generalized atherosclerosis and it correlates directly with other risk factors like age, tobacco use, hypertension, diabetes and dyslipidemia.

Key words: stroke, ischemic, risk factors, carotid stenosis, cimt

Introduction:

Ischemic heart disease and stroke are the leading causes of morbidity and mortality worldwide and more than 80% of deaths occurring in the low and the middle-income countries.[1] Ischemic stroke is the most common type of stroke with a prevalence rate of 85%. The ischemic stroke can be embolic or atherothrombotic. There are a number of risk factors associated with ischemic stroke. The Indian Council of Medical Research (ICMR), WHO and several other studies have found that hypertension, diabetes mellitus, tobacco use, anemia, hyperlipidemia and carotid artery stenosis are the most important risk factors for ischemic stroke.[2,3,4,] Approximately 15% of ischemic strokes are caused by large vessel atherosclerosis. Risk factors for large vessel disease also differ from other stroke subtypes.[5,6] Large vessel atherosclerotic cerebrovascular disease is an important cause of stroke. It produces a higher risk of early recurrent ischemia than any other stroke subtype.[7] Extracranial ICA atherosclerosis is the most important cause of large vessel stroke. The prevalence of carotid plaques in general population is about 5.7%, though carotid stenosis is seen in only about 1.1% of general population. Most of the individuals with carotid

stenosis are silent with no sign or symptoms.[5, 8] A carotid bruit is an unreliable finding with a broad sensitivity of about (24-84%). It is present in about 5% of patients aged 45 to 80 years without clinically significant internal carotid disease.[9,10] Although the presence of a carotid bruit definitely warrants further evaluation, its absence does not exclude carotid vascular disease.[11] The severity of carotid stenosis is the main risk factor predicting occurrence of neurologic and other vascular events.[12] Though, in ACAS no association was found between the stroke rate and the severity of stenosis,[13] several studies have shown a strong and graded association between severity of carotid stenosis and stroke. Practically all the conventional cardiovascular and cerebrovascular risk factors like hypertension, diabetes mellitus, and dyslipidemia are associated with increased CIMT and increased incidence of stroke.[14,15,16,17] CIMT assessment is a well-established modality to investigate the development of atherosclerosis and may provide clue to cardiovascular and cerebrovascular disease risk in specific populations. CIMT can be reliably measured using ultrasonography. Ultrasound CIMT is a commonly accessible, safe, and reproducible modality if performed by trained sonographers with standardized equipment. CIMT can be measured using magnetic resonance imaging (MRI) also, though, given the additional complexity and cost of MRI when compared with ultrasound, CIMT measurement should not largely be performed with MRI in most patients. Crouse JR et al and Belcaro G et al reported that the high-resolution B-mode carotid ultrasonography provides a noninvasive method of measuring arterial wall thickness and the progression of atherosclerosis.[18,19] This study was therefore conducted to find the correlation if any, between modifiable risk factors and Carotid Intima media Thickness (CIMT).

Aims and objectives: To study the correlation between the risk factors and Carotid Intima- Media Thickness (CIMT) in ischemic stroke among stroke patients admitted in a tertiary care teaching hospital in Western Maharashtra.

Material and methods: This observational study was conducted in department of medicine from February 2013 to June 2014. Fifty stroke patients admitted in the medical ICU were studied. These patients were evaluated according to a preset format.

Inclusion Criteria: All patients above 18 years of age of either sex who were clinically diagnosed as stroke and consented to be included in the study.

Exclusion Criteria: Patients in whom CT Scan or MRI brain revealed pathology other than stroke like, tuberculosis, tumor, epidural or subdural hematoma and multiple sclerosis and also patients with neurological deficit secondary to trauma.

The diagnosis of different stroke subtypes was made, based on clinical examination and ancillary investigations. Ischemic stroke was diagnosed when a focal deficit was present and infarct was found on CT scan. Also, a normal CT scan without bleeding was considered to be an ischemic stroke. A detail history was taken regarding the onset and progression of neurological deficit with special emphasis on risk factors of cerebral infarction like hypertension, diabetes mellitus, ischemic heart disease, previous strokes or tias, valvular heart disease, alcohol use, smoking and obesity. In female patients detailed obstetrical, menstrual history and history of contraceptive pills was taken. Previous records were scrutinized when available. All patients underwent routine investigations including complete blood count, urinalysis, coagulation parameters, renal and liver function tests, blood sugar, electrolytes, lipid profile, skiagram chest and Electrocardiogram (ECG), echocardiography and Carotid Doppler study. Other relevant investigations were carried out on case to case basis.

Carotid Doppler examination:

Color Doppler scanning of carotid arteries was performed by a single trained sonographer using a (Siemens, Germany) with 7 MHz linear –array transducers. Ultrasound scans of the right and left last distal centimeter of the common carotid arteries (CCA), the carotid bulbs (CB) and the first proximal centimetre of the internal carotid arteries (ICA) in two different projections (anterior and posterior) were performed. All subjects had an intima- media thickness (IMT) measurement at the posterior wall of distal segments of the both ccas using the instrument`s electronic caliper. In addition, the carotid arteries were also studied for the presence and the site of plaques and quantify the degree of stenosis. Based on the morphological and hemodynamic criteria, the sonographic findings were classified into four groups:

1. No plaque;
2. One or more small plaques, narrowing of lumen diameter <50%.
3. Moderate stenosis with a reduction in lumen diameter >50% to <70%;
4. Significant stenosis with >70% reduction in lumen diameter.

Table 1- prevalence of different risk factors in stroke

Risk factor	Type of stroke				
	Hemorrhagic (total 10)	Ischemic (total 35)	Sah (total 2)	Cvst (total 3)	Total
Diabetes	3 (33.3%)	10 (28.6%)	0	2	15 (30%)
Hypertension	9 (90%)	28 (80%)	2	1	40 (80%)
Dyslipidemia	6 (60%)	16 (45.7%)	1	1	24 (48%)
Mets	4 (40%)	13 (37.1%)	1	--	18 (36%)
Raised whr	2 (20%)	20 (57.1%)	--	1	23 (46%)
Tobacco use	8 (80%)	29 (82.8%)	2	2	41 (82.8%)
Alcohol	--	11 (31.4%)	1	--	12 (24%)

Observations and results:

In present study, fifty patients were included in the study. Out of these 50, 35 patients (21 males, 14 females) had ischemic stroke, 10 haemorrhagic, three patients had cortical venous sinus thrombosis (CTVS) and two patients suffered from subarachnoid hemorrhage (SAH). Out of 35 patients of ischemic stroke, 16 were from 61 to 70 years age-group. Among cases of ischemic stroke, tobacco use (82.8%) was the commonest risk factor in our study, closely followed by Hypertension (80%). Raised WHR (57.1%), Dyslipidemia (48%), Metabolic Syndrome (37.1%) and alcohol (31.4%) were other modifiable risk factors in the list. (Table 1) In present study, out of 35 patients with ischemic stroke, severe carotid stenosis was present in 4 (11.42%) patients, moderate in 5 (14.2%) and mild carotid stenosis was found in six (17.1%). Overall, 16 (42.8%) patients had carotid stenosis. All the patients with stenosis greater than 70% had carotid bruit; one with stenosis in between 50% to 70% had carotid bruit. No one with stenosis <50% had bruit. (Table 2) In this study, mean CIMT was highest in carotid bulb followed by internal carotid artery as was brought out Samia Khan et al.[20] Out of 35 patients of ischemic stroke, 24 (68.6%) patients had CIMT more than one mm. All the patients of increased CIMT were above 50 years of age with maximum number (16) from age group of 61-70 years. (Table 3) There was male preponderance; 16 (66.7%) males and 8 (33.3%) females had more than 01 mm CIMT. Out of 24 patients with increased CIMT, there were 23 tobacco users, 20 hypertensives, 13 dyslipidemics, 9 diabetics and 6 alcohol users. On calculating CIMT among different risk groups, out of 35 patients of ischemic stroke, 65.6% tobacco users, 57.14% hypertensives, 37.14% patients of dyslipidemia, 25.7% diabetics and 17.1% alcohol users were found to have CIMT value of more than 1 mm (Table 4). Age, hypertension, diabetes mellitus, dyslipidemia and tobacco use were significantly associated with increased CIMT values (Table

Table no 2: carotid artery stenosis and carotid bruit

Degree of stenosis	No. Of patients	Patients with Carotid Bruit
No stenosis	20	0
<50%	6	0
50%-70%	5	1
>70%	4	4

Discussion:

As per the World Health Organization (WHO), stroke is the third largest killer in India after coronary artery disease and all types of cancers.[21] Current treatment for patients with established stroke is relatively ineffective and role of neuroprotective medication is not well established. About 70% of stroke survivors remain vocationally impaired and more than 30% requires assistance with activities for daily living. Risk factors

identification and effective intervention offers a real hope of reducing stroke morbidity and mortality. Certain risk factors have been consistently identified as significant predictor of stroke, while some are less consistent. Seventy present of patients in this study were of ischemic stroke and 20% had haemorrhagic one. Similar results were found in other studies as well.[22] Mean age of patients in our study was 59.5 +/ - 14.21 years with females being older than males. Tobacco use is one of most potent modifiable risk factors for atherosclerosis and stroke. Out of 35 patients of ischemic stroke 29 (82.8%) were tobacco user. This was statistically significant. All these patients had other coexisting risk factors like hypertension [28 (80%)], obesity [20 (57.1%)], dyslipidemia [16 (45.7%)], Mets [13 (37.1%)] and diabetes mellitus [10 (28.6%)]. Fifteen patients had carotid artery stenosis out of whom only four patients had severe stenosis (5).[23]

Table no 3: change in cimt according to age & sex

Risk Factors		Normal CIMT		CIMT > 01 mm		Ischemic Stroke	
		Total Numbers 11		Total Numbers 24		Total Numbers 35	
		No.	%	Nos.	%	Nos.	%
Age in years	<40	3	27.3%	---	----	3	8.6%
	41-50	3	27.3%	3	12.5%	6	17.1%
	51-60	1	9.1%	2	8.3%	3	8.6%
	61-70	2	18.1%	14	58.3%	16	45.7%
	71-80	1	9.1%	5	20.9%	6	17.1%
	>80	1	9.1%	--	--	1	2.9%
Sex	M	5	45.5%	16	66.7%	21	60%
	F	6	54.5%	8	33.3%	14	40%

Carotid Artery Disease:

In our study, out of 35 ischemic patients, only five patients had carotid bruit. Carotid bruit is considered a clinical sign of low sensitivity but moderate specificity.[24] Out of these five patients with carotid bruit, four had severe stenosis (>70%) and one had moderate (>50% to <70%) stenosis on ultrasonography. Carotid artery stenosis is an established risk factor for ischemic stroke and TIA.[5] in current study, severe carotid stenosis (>70%) was present in four patients, moderate (50-70%) in five and mild (<50%) in six patients out of 35 cases of ischemic stroke. Out of these 15 patients with carotid artery stenosis, 13 patients had coexisting hypertension, 12 had were tobacco user, eight had dyslipidemia and six patients were diabetic.

Carotid Intima Media Thickness (CIMT):

In current study, 24 (68.5%) out of 35 ischemic stroke patients had CIMT value more than 1.00 mm. Sixteen males and eight females had raised CIMT value. Out of all the patients of ischemic stroke, 23 out of 29 tobacco users (79.3% of), 20 out of 28 (71.4%) hypertensives, 13 out of 16 (81.3%) patients of dyslipidemia, 9 of 10 (90.%) diabetics and 6 out of 11 (63.6%) alcohol users had CIMT value of more than 01 mm (Table 4). Zureik M et al and Nikic P have shown an increased carotid artery intima-media thickness (CIMT) as an early marker and a valid index of generalized atherosclerosis.[25, 26] In present study, age, hypertension, diabetes, dyslipidemia, tobacco use and alcohol consumption were the risk factors for stroke, positively associated with the increased CIMT. CIMT reflects exposure to cardiovascular risk factors and can be considered as an intermediate feature in causal pathway between risk factors and stroke. These findings are consistent with those of Tsivgoulis G ET al.[27] Hypertension is major risk factors in stroke. Hypertension induces blood vessel injury that leads to the vessels becoming rigid. The increase in intravascular pressure induces stress on the vessel wall and this in turn, alters the vessel wall thickness through vascular remodeling. Hypertension-induced atherosclerosis leads to smaller in size and stiff blood vessels. Type 2 diabetes also is associated with significant increase in cardiovascular risk factors. Atherogenesis in diabetes mellitus may be secondary to the glucose toxicity to the endothelium and glycosylation processes. Evidently, hypertension and other conventional risk factors are directly associated with CIMT.[14] Change in CIMT is as an indicator of generalized atherosclerosis and an independent risk factor of ischemic stroke.[28,29] Increased CIMT can also be used determine cardiovascular morbidity and may also help evaluate the efficacy of lipid lowering drugs [4] [5].[30,31]

Summary and conclusion:

In this study, strokes of vascular etiology were studied regarding risk factors and association with

CIMT. The different subtypes of stroke were- Ischemic 70%, Haemorrhagic 20%, subarachnoid hemorrhage 4%, cortical venous sinus thrombosis 6%. Highest number of patients belonged to 51-60 years are group with male predominance. A positive relationship between age, sex, hypertension, diabetes mellitus, tobacco use, obesity, metabolic syndrome (Mets) and stroke was observed and that was statistically significant. Tobacco use and hypertension were commonest risk factors for CVA. Other risk factors were dyslipidemia, obesity, metabolic syndrome and diabetes mellitus. Hypertensions was undetected in half of subjects and in remaining were on irregular treatment. Increased CIMT is a marker of generalized atherosclerosis and it correlates well with other risk factors like tobacco use, hypertension, diabetes and dyslipidemia. In every patient of stroke, routine evaluation of carotid artery intima-media thickness should be considered.

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Table 4: prevalence of increased cimt in different risk factors

Risk Factors	Normal CIMT		CIMT > 01 mm		Ischemic Stroke	
	Total Numbers 11		**Total Numbers 24**		**Total Numbers 35**	
	No.	**%**	**Nos.**	**%**	**Nos.**	**%**
Diabetes Mellitus	1	10.0%	9	90.0%	10	28.6%
Hypertension	8	28.6%	20	71.4%	28	80.0%
Dyslipidemia	3	18.7%%	13	81.3%	16	45.7%
Tobacco Use	6	20.7%	23	79.3%	29	82.85%
Alcohol Use	5	36.4%	6	63.6%	11	31.4%

Table no: 5 associations of risk factors with cca-imt

Pearson Chi-Square	Value	Degree of Freedom (df)	Significance Level (sig) (2-sided)	P value
Age	12.96	5	0.02376	<0.05
Sex	1.832	1	0.1761	>0.05
DIABETIS	11.576	1	0.001	<0.01
Hypertension	6.798	1	0.025	<0.05
Dyslipidemia	9.941	1	0.002	<0.01
Smoking	14.635	1	0.000	<0.001
Alcohol	15.020	1	0.000	<0.001