STUDY OF CAROTID INTIMA MEDIA THICKNESS IN PATIENTS WITH ACUTE ISCHEMIC STROKE AND ITS CORRELATION WITH RISK FACTORS OF ISCHEMIC STROKE - A CASE CONTROL STUDY

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ABSTRACT: Stroke is the leading cause of mortality worldwide. Carotid Intima Media Thickness (CIMT) is a marker of atherosclerosis and is also a marker for ischemic stroke. AIMS: 1) To assess the value of carotid intima media thickness at which patients with risk factors can develop acute ischemic stroke. 2) To correlate carotid intima media thickness with risk factors of acute ischemic stroke. MATERIAL & METHODS: This study was done at KIMS Hospital, Bangalore between December 2010 to September 2012. This is a case control observational study which has a sample size of 50 cases and 50 controls. Method of collection of data was by patient evaluation which was done by taking detailed history, clinical examination and laboratory investigations through a proforma specially designed for this study. Cases were subjects who had ischemic stoke and Infarct proven by CT/MRI of brain, Controls were subjects without stroke matched to cases by age, gender and risk factors like diabetes, hypertension, smoking and dyslipidemia. Subjects in both groups underwent carotid Doppler investigation with 7.5 Mhz linear superficial array probe to determine CIMT and presence of plaques. **RESULTS:** Out of 50 cases, 46 had CIMT between 0.06-0.20 cm [92%] and out of 50 controls, 45 had CIMT between 0.06-0.20 cm[90%]. Most of our cases had CIMT above 0.06 cm, so we can hypothesize that people with risk factors having CIMT above 0.06 cm are more prone for ischemic cerebro vascular accidents. Mean CIMT in cases with risk factors is significantly increased when compared to controls with risk factors. **CONCLUSION:** People with risk factors [age > 50 years, DM, HTN, Smoking and Dyslipidemia] having CIMT above 0.06 cm are more prone for ischemic CVA, so people with risk factors should undergo screening for CIMT measurement by Carotid Doppler which is non invasive and cost effective and if their CIMT is above 0.06 cm they should undergo early medical intervention to take care of risk factors and lifestyle modifications, so that they can be prevented from ischemic CVA in future.

KEYWORDS: Atherosclerosis, stroke, diabetes mellitus, hypertension, age, smoking, dyslipidemia, carotid intima media thickness.

INTRODUCTION:

- Stroke, both ischemic and hemorrhagic is a common and devastating disorder. Currently stroke is the leading cause of mortality worldwide and more than 80% of deaths occurring in low and middle income countries. The incidence of stroke increases with increasing age and with elderly population worldwide.
- In most of ischemic strokes, the underlying pathophysiology is atherosclerosis. The risk factors for stroke are modifiable and non-modifiable. The modifiable risk factors are mostly related to atherosclerotic burden and include diabetes, hypertension, smoking and

hyperlipidemia. Several risk prediction scoring systems have been evolved to identify individuals with high risk.

• However, most of these scoring systems have some limitations. The carotid intima media thickness has emerged as a reliable independent marker of atherosclerosis and cerebrovascular disease. However well-defined population cut off value for CIMT is not there.

So in this study we are trying to see at what value of CIMT the individual with risk factors will be prone for stroke in our study population. An increased CIMT may help select patients at high risk for brain infarction and change in their lifestyle and prophylactic treatment with statins may prevent this devastating event.

METHODOLOGY: This study was done at Kempegowda Institute of Medical Sciences, Bangalore, between December 2010 to September 2012. This is a case control observational study which had a sample size of 50 cases and 50 controls.

SOURCE OF DATA: Cases were patients with ischemic stroke admitted to KIMS Hospital who fulfilled inclusion criteria and Controls were selected from inpatient and outpatient department of KIMS Hospital.

METHOD OF COLLECTION OF DATA: Method of collection of data was by patient evaluation which was done by taking detailed history, clinical examination and laboratory investigations through a proforma specially designed for this study.

CASES : INCLUSION CRITERIA

Age 40-70 years Both the sexes Clinical symptoms/signs suggestive of ischemic stroke Infarct proven by CT/MRI of brain

EXCLUSION CRITERIA

Patients with valvular heart diseases Pregnancy and postpartum stroke Patients with past history of connective tissue disorders/vasculitis Recurrent strokes Patients on statin therapy for more than 1 year for any indication

CONTROLS: 50 controls from inpatient and outpatient department of KIMS HOSPITAL matched by age, gender and risk factors like diabetes, hypertension, smoking and dyslipidemia.

All patients were subjected to the following lab investigations complete hemogram, Blood urea, Serum Creatinine, RBS/FBS/PPBS, Fasting Lipid Profile, ECG, 2DECHO,CT or MRI BRAIN. Carotid atery Doppler by U/S.

CAROTID ARTERY DOPPLER - Ultrasonographic scanning of carotid arteries was performed using higher resolution B mode colour doppler imaging and an electrical linear transducer of 7.5Mhz was used.

CIMT is anechoic zone between two echogenic lines, first echo is lumen-intima surface, second echo is caused by media-adventitia interface.

CIMT is measured at 3 levels in both the carotids and in areas free of plaques-

- Common carotid artery
- Bifurcation of Common carotid artery
- Internal carotid artery
- Highest value in each carotid is taken and average of 2 measures is taken as CIMT.

After all the necessary tests , we have done the analysis of CIMT in Cases and Controls and Risk factors of Ischaemic stroke.

STATISTICAL METHODS: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean \pm SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent, student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven's test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square /Fisher exact test has been used to find the homogeneity of samples on categorical scale. ROC curve analysis to predict the CIMT as marker.

ETHICAL CLEARANCE: This study was approved by ethical committee of KIMS Bangalore.

RESULTS: Our study is a Comparative study of 50 cases and 50 controls in which we have studied the CIMT values and its correlation to the risk factors of Cerebrovascular Accident.

In age group of 40-50 years, there are 10 cases and 11 controls. In age group 51-60 years, there are 13 cases and 12 controls. In age group 61-70 years, there are 27 cases and 27 controls which corresponds to 54%. In age group 40-50 years CIMT in cases is 0.08 ± 0.03 , in controls, it is 0.07 ± 0.01 , In age group 51-60 years CIMT in cases is 0.11 ± 0.04 , in controls, it is 0.074 ± 0.01 , In age group 61-70 years, CIMT in cases is 0.13 ± 0.021 , in controls, it is 0.07 ± 0.02 , Mean CIMT(0.13 ± 0.021) is more in age group 61-70 years, as age increases CIMT also increased in cases in our study.

In cases, 74% (n=37) are males and 26% (n=13) are females. In controls, 74% (n=37) are males and 26% (n=13) are females. In cases, Mean CIMT in males is 0.097 ± 0.04 and in females 0.17 ± 0.030 . In controls, Mean CIMT in males is 0.07 ± 0.02 and in females 0.07 ± 0.024 . In cases, females had increased CIMT than males in our study, but females cases are less in number in our study.

Comparison of Average CIMT in Cases and Control, In 4 cases and 5 controls CIMT is between 0.01-0.05 cm, In 28 cases and 42 controls CIMT is between 0.06-0.10 cm, In 14 cases and 3 controls CIMT is between 0.11-0.15 cm, In 4 cases CIMT is between 0.16-0.20 cm, So in Out of 50 cases, 46 patients had CIMT between 0.06 - 0.20 cm (92%) and in controls, 45 had CIMT between 0.06 - 0.20 cm (90%). Mean CIMT in cases is 0.121 ± 0.015 cm and in controls, it is 0.07 ± 0.02 cm.

Comparison of Plaque in cases and control, Out of 50 cases 12 had plaques. Out of 50 controls, only 7 had plaques. Out of 50 cases, 12 had plaques and had increased CIMT 0.19cm, when compared to controls CIMT 0.08 cm.

Comparison of CIMT in DM as the only risk factor in cases and controls, In cases, there are 2 patients with only DM as risk factor, in them Mean CIMT is 0.08 cm. In controls, there are 2 patients with only DM as risk factor, in them Mean CIMT is 0.07 cm.

Comparison of CIMT in HTN as the only risk factor in cases and control, In cases, there are 2 patients with only HTN as risk factor, in them Mean CIMT is 0.07 cm. In controls, there are 2 patients with only HTN as risk factor, in them Mean CIMT is 0.06 cm.

Comparison of CIMT in only Smokers in cases and controls, In cases, there are 5 patients with only smoking as risk factor, in them Mean CIMT is 0.07 cm. In controls, there are 7 patients with only smoking as risk factor, in them Mean CIMT is 0.06 cm.

Comparison of CIMT in Dyslipidemia as the only risk factor in cases and controls, In cases, there are 5 patients with only dyslipidemia as risk factor, in them Mean CIMT is 0.29 ± 0.049 . In controls, there are 5 patients with only dyslipidemia as risk factor, in them Mean CIMT is 0.045 ± 0.007 .

Comparison of CIMT in DM+HTN in cases and controls, In cases, there are 3 patients with DM+HTN as risk factors, in them Mean CIMT is 0.14 cm. In controls, there are 3 patients with DM+HTN as risk factors, in them Mean CIMT is 0.06±0.08 cm.

Comparison of CIMT in HTN+ Smokers in cases and controls, In cases, there are 4 patients with HTN +Smoking as risk factors, in them Mean CIMT is 0.13±0.06 cm. In controls, there are 4 patients with HTN + Smoking as risk factors, in them Mean CIMT is 0.06 cm.

Comparison of CIMT in DM + Dyslipidemia in cases and controls,In cases, there are 7 patients with DM+ Dyslipidemia as risk factors, in them Mean CIMT is 0.082±0.01 cm. In controls, there are 7 patients with DM+ Dyslipidemia as risk factors, in them Mean CIMT is 0.067 cm.

Comparison of CIMT in HTN + Dyslipidemia in cases and controls, In cases, there are 9 patients with HTN+ Dyslipidemia as risk factors, in them Mean CIMT is 0.11 ± 0.02 cm. In controls, there are 8 patients with HTN+ Dyslipidemia as risk factors, in them Mean CIMT is 0.10 ± 0.03 cm.

Comparison of CIMT in Smokers + Dyslipidemia in cases and controls, In cases, there are 5 patients with Smoking+ Dyslipidemia as risk factors, in them Mean CIMT is 0.07 ± 0.02 cm. In controls, there are 5 patients with Smoking+ Dyslipidemia as risk factors, in them Mean CIMT is 0.05 ± 0.02 cm.

Comparison of CIMT in DM +HTN+ Smokers in cases and controls, In cases, there are 4 patients with DM + HTN +Smoking as risk factors, in them Mean CIMT is 0.075 cm. In controls, there are 4 patients with DM + HTN +Smoking as risk factors, in them Mean CIMT is 0.06 cm.

Comparison of CIMT in DM +HTN+ Dyslipidemia in cases and controls, In cases, there are 11 patients with DM + HTN +Dyslipidemia as risk factors, in them Mean CIMT is 0.09 ± 0.04 cm. In controls, there are 10 patients with DM + HTN +Dyslipidemia as risk factors, in them Mean CIMT is 0.082 ± 0.006 cm.

Comparison of CIMT in HTN+ Dyslipidemia +Smokers in cases and controls, In cases, there are 4 patients with HTN +Dyslipidemia+ Smoking as risk factors, in them Mean CIMT is

0.12±0.03cm. In controls, there are 3 patients with HTN +Dyslipidemia+ Smoking as risk factor, in them Mean CIMT is 0.095 cm.

Comparison of CIMT in DM+ HTN+ Dyslipidemia +Smokers in cases and controls, In cases, there are 5 patients with DM +HTN + Dyslipidemia+ Smoking as risk factors, in them Mean CIMT is 0.12±0.03cm. In controls, there are 5 patients with DM +HTN + Dyslipidemia+ Smoking as risk factors, in them Mean CIMT is 0.08 cm.

ROC curve analysis for predicting the CIMT as Marker, Receiver Operator Characteristics Curve(ROC). The diagnostic performance of a test, or the accuracy of a test to discriminate diseased cases from normal cases is evaluated using Receiver Operating Characteristic (ROC) curve analysis (Metz, 1978; Zweig & Campbell, 1993). According to this The sensitivity and specificity of CIMT as marker in our study is 74% and 70%.

DISCUSSION: In our study, we had both cases and controls in age groups of 40 - 50, 51-60 and 61-70 years, mean age being 60 years and more no of patients are in age group 61-70 years [27 cases]. As the age increases, Mean CIMT in cases has increased drastically compared to controls that is Mean CIMT in cases in age group 41-50 is 0.08 cm, 51-60 is 0.11 cm and 61-70 years is 0.13 cm. In cases, mean CIMT is 0.121 cm (range 0.04 – 0.019 cm) and in controls, mean CIMT is 0.07 cm (range 0.04 – 0.15 cm). In study done by RATNAKAR SAHOO, when the differences in mean CIMT were compared among different age groups in the cases, there was significance with P <0.05.

In our study there are 37 males and 13 females in both cases and control groups, In cases, Mean CIMT in males is 0.097 ± 0.04 cm and in females is 0.17 ± 0.03 cm. In controls, Mean CIMT is 0.07 ± 0.02 cm in both males and females. Mean CIMT is more in female cases than males as female cases are less in number in our study. Mean CIMT is significantly more in male cases when compared to male controls with P<0.0001. In Study done by RATNAKAR SAHOO, differences in mean CIMT between males and females in cases were not significant; however the difference was significant in both the genders when compared to controls with P < 0.001.

In our study Mean CIMT in cases with risk factors is significantly increased when compared to controls with risk factors.

In our study, Carotid plaques are present in 12 cases and 7 controls. Mean CIMT in cases with plaques is 0.19±0.031 cm and in cases without plaques is 0.09±0.03 cm. Mean CIMT in controls with plaques is 0.08±0.02 cm and in controls without plaques is 0.068±0.02 cm. So Mean CIMT is high in cases and controls with plaques when compared to cases and controls without plaques. In study done by RATNAKAR SAHOO, Carotid plaques were present in 18 patients when compared to 7 in controls and CIMT was higher in patients with plaques (0.095) when compared to patients without Plaques (0.07 cm).

In cases, mean CIMT is 0.121 cm (range 0.04 - 0.019 cm) and in controls, mean CIMT is 0.07 cm (range 0.04 - 0.15 cm). Mean CIMT is significantly more in cases when compared to controls with P-0.03. In study done by RATNAKAR SAHOO, mean CIMT in cases was 0.0782 cm(range 0.05 - 0.15 cm) and in controls it was 0.059cm (range 0.04 - 0.09 cm) with P<0.0001.

In our study, the sensitivity of CIMT as marker in our study is 74% and specificity is 70%.

In a study done by RATNAKAR SAHOO, sensitivity was 48% and specificity was 96%.

In our study, out of 50 cases, 46 had CIMT between 0.06-0.20 cm [92%] and out of 50 controls, 45 had CIMT between 0.06-0.20 cm[90%]. Most of our cases had CIMT above 0.06 cm so we

can hypothesize that people with risk factors having CIMT above 0.06 cm are more prone for Ischemic cerebrovascular accidents so early intervention with anti platelets , statins, tight B.P control and diabetes control and lifestyle changes is essential in these people to avert future ischemic CVA.

CONCLUSION: People with risk factors [like age > 50 years, DM , HTN , Smoking and Dyslipidemia] having CIMT above 0.06 cm are more prone for Ischemic Cerebro Vascular Accident, so people with risk factors should undergo screening for CIMT measurement by Carotid Doppler which is non invasive and cost effective and if their CIMT is above 0.06 cm they should undergo early medical intervention to take care of risk factors and lifestyle modifications, so that they can be prevented from ischemic CVA in future.

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LIST OF ABBREVIATIONS USED [alphabetical order]

ARIC	Atherosclerosis Risk in Communities
BMI	Body Mass Index
Са	Calcium
CBF	Cerebral Blood Flow
CCA	Common Carotid Artery
СР	Cerebral Plaque
CHD	Coronary Heart Disease
CIMT	Carotid Intima Media Thickness
CVA	Cerebrovascular Disease
DM	Diabetes Mellitus
FBS	Fasting Blood Sugar
HTN	Hypertension
HDL	High Density Cholesterol
IC	Internal Capsule
ICA	Internal Carotid Artery
ICH	Intracranial Hemorrhage
IDL	Intermediate Density Lipoprotein
KIMS	Kempegowda Institute of Medical Sciences
LACS	Lacunar Syndrome
LDL	Low Density Lipoprotein
LI	Lacunar Infarcts

LMN	Lower Motor Neuron
LOC	Loss of Consciousness
Lp(a)	Lipoprotein a
MCA	Middle Cerebral Artery
MI	Myocardial Infarction
MRI	Magnetic Resonance Imaging
NCEP	National Cholesterol Education Program
PPBS	Postprandial Blood Sugar
RBS	Random Blood Sugar
VLDL	Very Low Density Lipoprotein
PCA	Posterior Cerebral Artery
PICA	Posterior Inferior Cerebellar Artery
RIND	Reversible Ischemic Neurological Disease
SCA	Superior Cerebellar Artery
TACS	Total Anterior Circulation Syndrome
ТС	Total Cholesterol
TIA	Transient Ischemic Attack
UMN	Upper Motor Neuron
WHO	World Health Organisation

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Ago in yoong	Cases		Controls	
Age in years	No	%	No	%
40-50	10	20.0	11	22.0
51-60	13	26.0	12	24.0
61-70	27	54.0	27	54.0
Total	50	100.0	50	100.0
Mean ± SD 60.62±8.66 60.42±8.35				
Table 1: Age distribution of patients studied				

Samples are age matched with P = 0.907

Age in years	Cases	Controls	P value		
40-50	0.08±0.03	0.07 ± 0.01	0.151		
51-60	0.11±0.04	0.074 ± 0.01	0.014*		
61-70	0.13 ± 0.021	0.07±0.02	0.105		
Table 2: Comparison of CIMT in two groups studied according to age in years					

Conder	Cases		Controls	
denuer	No	%	No	%
Male	37	74.0	37	74.0
Female	13	26.0	13	26.0
Total	50	100.0	50	100.0
Table 3: Gender distribution of patients studied				

Samples are gender matched with P = 1.000

Gender	Cases	Controls	P value	
Male	0.097 ± 0.04	0.070 ± 0.02	< 0.001**	
Female	0.17 ± 0.030	0.07 ± 0.024	0.217	
Table 4: Comparison of CIMT in two groups studied according to gender				

СІМТ	Cases		Controls		
CINT	No	%	No	%	
0.01-0.05	4	8.0	5	10.0	
0.06-0.10	28	56.0	42	84.0	
0.11-0.15	14	28.0	3	6.0	
0.16-0.20	4	8.0	0	0.0	
Total	50	100.0	50	100.0	
Mean ± SD	0.121±0.015 0.07±0.02				
Inforanco	Mean CIMT is significantly more in Cases				
interence	when compared to controls with P=0.035*				
Table 5: Comparison of Average					
CIMT in two groups studied					

Dlagua	Cases		Controls		
Plaque	No	%	No	%	
Absent	38	76.0	43	86.0	
Present	12	24.0	7	14.0	
Total	50	100.0	50	100.0	
Incidence	Incidence of Plaque are statistically more in cases (24.0%) when compared to Controls (14.0%) with P=0.202				
Table 6: Comparison of Plaque in two groups studied					

Plaque	Cases	Controls	P value	
Absent	0.098±0.03	0.068±0.02	< 0.001**	
Present	0.19±0.031	0.08±0.02	0.342	
Table 7: Comparison of CIMT in two groups				
studied according to absence/presence of plaque				



In above graph, if blue line is exactly meeting the dotted diagonal line then it indicates that the test cannot differentiate between two groups under study. Here the blue line is far away from dotted diagonal line and area covered under it is 0.743 which indicates that the test used will differentiate between two groups studied.

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