

THE ASSOCIATION OF CAROTID INTIMA MEDIA THICKNESS AND THE RISK OF ISCHEMIC STROKE

Fatima Imran^a, Rakhshanda Jabbar^b, Zonia Zaman^c

^a Associate Professor and HOD of Department of Radiology, Aziz Fatimah Medical College and Hospital, Faisalabad

^b Consultant Radiologist, Department of Radiology, DHQ Hospital, Faisalabad

^c Professor and HOD of Department of Obstetrics and Gynecology, Abwa Hospital, Faisalabad

ABSTRACT:

OBJECTIVES: The aim of the study was to find the association of carotid intima media thickness and the risk of ischemic stroke.

DURATION AND SETTING: This study was conducted from 15 October 2017 to 15 August 2018 in Outdoor patients Department of Radiology, Aziz Fatimah Hospital Faisalabad.

SUBJECTS AND METHODS: In this Case control study, a total of 130 participants including 65 cases of stroke and 65 non-stroke controls were included. A cross sectional B-mode ultrasonography with high resolution were used to measure the intima media thickness of carotid arteries in all patients. The measurement was based upon one longitudinal image taken by high resolution ultrasound. The relationship of intima media thickness with stroke was assessed on the basis of mean value of intima media thickness in stroke patients and non-stroke controls.

RESULTS: The mean age of stroke patients was 54.25 ± 8.65 years and mean age of control group was 50.45 ± 10.46 years. There were 41(63.08%) males in stroke patients and 34 (52.31%) male participants in control group. The comparison of carotid intima-media thickness significantly (P-value < 0.001) increased in patients of stroke (0.794 ± 0.121 vs. 0.613 ± 0.099 mm) as compared to controls. The stroke patients who were also smokers had a significantly (P-value < 0.001) higher CIMT (0.86 ± 0.19) as compared to ($0.61 \pm .068$) smokers in control group. The CIMT in diabetic stroke patients was noted significantly higher (0.83 ± 0.19 vs. 0.61 ± 0.07) in comparison to diabetic controls. The CIMT was found significantly (P-value < 0.001) higher among both hypertensive stroke patients (0.87 ± 0.24) and normotensive stroke patients (0.758 ± 0.18) as compared to hypertensive controls (0.60 ± 0.11) and normotensive controls (0.58 ± 0.10).

CONCLUSION: There is a significant association of CIMT with stroke, with a significantly higher value of CIMT among stroke patients. The risk factors like smoking, diabetes mellitus and hypertension are strong risk markers for high CIMT.

KEY WORDS: Carotid Intima media thickness, Stroke, risk factor

INTRODUCTION:

Stroke has a rising trend in the world and has become a major cause of morbidity and mortality globally both in developing and developed world. There has been a constant effort on the part of medical researchers to analyze this problem and search for factors that aid in its prevention^[1]. There are some malleable factors which contributes significantly in incidence of stroke. These modifiable factors include hypertension, diabetes mellitus, hyperlipidemia and smoking, which cause pathological changes in blood

vessels. Cerebrovascular and cardiovascular diseases are usually initiated due to reduction in diameter of vessels caused by hypertrophy or entropic inner modeling^[2].

Stroke is a condition in which blood supply to the brain shrinks or reduces. Stroke has severe

Corresponding Author:

Fatima Imran, Associate Professor

& HOD Of Department Of Radiology, Aziz Fatimah Medical College And Hospital, Faisalabad

Email: dr.fatimaimran@gmail.com

outcomes like a huge number of patients do not survive after stroke attack and the patients who survive many of them have to live with disabilities. The incidence of stroke is quite high throughout the world and about 30 million people experiences an acute stroke globally. Stroke has a high rate of mortality and it is considered as third most common cause of death. Similarly, stroke has adverse outcomes like most commonly long-term disability to even death in many cases. It is increasing both in industrialized and developing countries but most alarming situation is its sharp increase in low and middle-income countries where a large number of deaths are being caused by stroke.^[3,4]

Preclinical that is asymptomatic atherosclerotic changes can be determined by measuring carotid intima media thickness which has emerged on a noninvasive method. The measurement of CIMT can predict preclinical atherosclerosis. The atherosclerosis is a strong predictor of cerebrovascular and cardiovascular morbidity. The anatomic extent of atherosclerosis can be measured through measuring CIMT, which can also help in identification of progression of atherosclerosis. So measurement of CIMT can be used to ascertain high risk patients and prevention strategies can be employed^[5]. The carotid intima media thickness is measured through Doppler ultrasound and B-mode combination and is used as marker of sub clinical atherosclerosis. The use of CIMT is a simple and non-invasive method to stratify the risk of coronary artery disease and has proved its significance in many large population based studies^[6].

The atherosclerosis is a process of vascular wall damage and carotid intima media thickness is indicator of this process. CIMT is a cost effective, reliable and safe method which can be used as marker of vascular disease like stroke. It has recently been seen as a strong predictor of future vascular events such as myocardial infarction and stroke^[7]. The measurement of carotid intima media thickness can be used to determine cardiovascular morbidity and also to assess the success of drug intervention to lower the abnormal lipid profile^[8].

The thickness of tunica and intima media of carotid artery is measured by high-resolution

carotid ultrasonography. Many studies in different developing and developed countries have shown significant correlation between common-carotid-artery intima media thickness and the prevalence of cardiovascular and cerebrovascular disease. This correlation has been observed cross sectionally and prospectively^[9,10]. Not much work has been done on this topic in Asian populations especially in our country the available data is very limited. So, this study was planned to investigate the association of carotid-artery intima-media thickness with the incidence of stroke in our study population.

METHODOLOGY:

This cross sectional case control study was conducted in the outpatient department of Radiology, Aziz Fatimah Hospital, Faisalabad. The study was started by taking ethical approval from Hospital ethics committee. All the patients were briefly described about the study purpose and process of research and informed written consent was taken prior to include in the study. In this study a total of 130 participants were enrolled consisting of 65 cases of stroke and 65 controls. The sample size was calculated with the help of WHO sample size calculator taking level of significance= 5%, power of test= 80%, population standard deviation of 0.50, test value of population mean (mean value of CIMT in cases group) = 0.849, anticipated population proportion (mean value of CIMT in control group) = 0.602,^[11]

All patients of more than 40 years of age & both sexes presenting with ischemic stroke were enrolled in the cases group and participants who do not have stroke were selected for control group. The participants both from cases and controls who had congestive cardiac failure, renal disease, thyroid disease, hepatic disease, ketosis, HIV infection, any other infections, known coagulation disorders and known vitamin deficiencies were excluded from the study to minimize the confounding and biasedness.

From all the patients' basic demographic information like age, gender, diabetes and smoking status and hypertension status was taken and recorded on a predesigned performa. Along with all this information, a patient was

diagnosed as hypertensive if he had a blood pressure of > 140 mmHg and diastolic blood pressure of > 90 mmHg. A cross sectional B-mode ultrasonography with high resolution were used to measure the intima media thickness of carotid arteries in all patients. The measurement was based upon one longitudinal image taken by high resolution ultrasound. The relationship of intima media thickness with stroke was assessed on the basis of mean value of intima media thickness in stroke patients and non-stroke controls. The measurement of intima media thickness is defined as the difference between maximal intima media thickness of near and far wall. The CIMT is measure on both side.

All the collected data was entered and analyzed by Statistical Software for Social Science (SPSS v 23). Mean and standard deviation was calculated for quantitative variables and

frequencies along with percentages were presented for qualitative variables. Independent sample t-test was applied to compare the CIMT between stroke cases and non-stroke controls. P-value < 0.05 was taken as significant.

RESULTS:

In this case control study a total of 130 participants including 65 cases and 65 controls were enrolled. The mean age of stroke patients was 54.25 ± 8.65 years and mean age of control group was 50.45 ± 10.46 years. There were 41(63.08%) males in stroke patients and 34 (52.31%) male participants in control group. The ratio of smokers was considerably higher in stroke patients in which 28 (43.08%) cases were smokers as compared with control group in which 21 (32.31%) participants were

Table 1: Distribution of Demographic characteristics of cases and controls

Characteristics	Stroke Cases (n=65)		Controls (n=65)	
	Frequency	Percentage	Frequency	Percentage
Age of the participants				
Mean \pm SD	54.25 \pm 8.65		50.45 \pm 10.46	
Gender of the participants				
Male	41	63.08%	34	52.31%
Female	24	36.92%	31	47.69%
Smoking status of the participants				
Yes	28	43.08%	21	32.31%
No	37	56.92%	44	67.69%
Type-2 Diabetes mellitus				
Yes	29	44.62%	22	33.85%
No	36	55.38%	43	66.15%
Hypertension status of the participants				
Yes	49	75.38%	38	58.46%
No	16	24.62%	27	41.54%
Dyslipidemia status of the participants				
Yes	18	27.69%	13	20.00%
No	47	72.31%	52	80.00%

Table 2: Association of Carotid intima-media thickness with Stroke, smoking, diabetes mellitus and hypertension

Characteristics	Stroke Cases (n=65)		Controls (n=65)		P-value
	n	Mean \pm SD	n	Mean \pm SD	
Overall IMT	65	0.794 \pm 0.121	65	0.613 \pm 0.099	< 0.001
Smokers	28	0.86 \pm 0.19	21	0.61 \pm .068	< 0.001
Nonsmokers	37	0.73 \pm 0.12	44	0.58 \pm 0.09	< 0.001
Diabetics	29	0.83 \pm 0.19	22	0.61 \pm 0.07	< 0.001
Non-diabetics	36	0.78 \pm 0.18	43	0.56 \pm 0.09	< 0.001
Hypertensive	49	0.87 \pm 0.24	38	0.60 \pm 0.11	< 0.001
Normotensive	16	0.758 \pm 0.18	27	0.58 \pm 0.10	<0.001

smokers. The incidence of comorbidity of type-2 Diabetes Mellitus was found to be higher in case group having 29 (44.62%) cases who also had diabetes mellitus in contrast to 22 (33.85%) participants among controls who had Diabetes Mellitus. The hyper tension status also revealed a considerably higher rate of hypertension (75.38% vs. 58.46%) among stroke patients as compared to controls. The incidence of dyslipidemia was greater in stroke patients 18 (27.69%) as compared to controls in which 13 (20.00%) participants diagnosed to have dyslipidemia as elaborated in table 1.

The comparison of carotid intima-media thickness between stroke cases and control showed that it was significantly (P-value< 0.001) increased in patients of stroke with a measurement of 0.794 \pm 0.121 mm as compared to controls without stroke having a measurement of 0.613 \pm 0.099 mm. The stroke patients who were also smokers had a significantly (P-value< 0.001) higher CIMT (0.86 \pm 0.19) as compared to (0.61 \pm .068) smokers in control group. The IMT in diabetic stroke patients was noted significantly higher (0.83 \pm 0.19 vs. 0.61 \pm 0.07) in comparison to Diabetic Controls. The IMT was found significantly (P-value< 0.001) higher among both hypertensive stroke patients (0.87 \pm 0.24) and normotensive stroke patients (0.758 \pm 0.18) as compared to hypertensive controls (0.60 \pm 0.11) and normotensive controls (0.58 \pm 0.10) as elaborated in detail in table 2.

DISCUSSION:

Many studies have proved carotid intima media thickness as a significant indicator for risk of occurrence of stroke. The increased intima media thickness is strongly associated with incidence of stroke and the increase in CIMT considerably increases the chance of stroke. There is variation in predicting the hemorrhagic or ischemic stroke on the basis of CIMT, in case of hemorrhagic stroke no significant association has been found between increased intima media thickness of carotid artery and hemorrhagic stroke. This type of stroke has been found more significantly associated with arterial hypertension whose occurrence in the patient can increase the risk for this event up to 3.34 fold^[12]. Another study by Ariesen et al. have also shown that the risk of hemorrhagic stroke increases 3.68 times in presence of arterial hypertension. In case of ischemic stroke the results are quite different; the chances of development of ischemic stroke are significantly amplified in patients of increased carotid intima media thickness along with presence of other risk factors of atherosclerotic disease. A person with increased carotid intima media thickness has almost 80.8% increased chances of getting ischemic stroke^[13].

A very high prevalence of increased CIMT has been found in patients with ischemic stroke, studies show that in patients with ischemic stroke, up to 71% patients have increased value of CIMT. In patients having high CIMT, also have

some other risk factors which are significantly related to CIMT. The risk factor consists of HDL, LDL, age, serum hsCRP and fibrinogen levels, but hsCRP, fibrinogen and age are the factors which are most significantly associated with CIMT. The risk of higher CIMT becomes more severe with elevation of fibrinogen^[14,15]. There are some other factors which are associated with increased carotid intima media thickness like hypertension, diabetes and smoking but some studies have found these factors as statistically insignificant,^[16] but the result of this present study showed significantly higher value of CIMT among smokers and diabetics as compared to non-smokers and non-diabetics both in cases group and control group. Numerous studies conducted previously have revealed a positive relationship of increased intima media thickness of carotid artery with stroke. The increase in thickness of intima media of carotid artery enhances the chance of stroke very considerably^[17].

This present study shows a strong association of the intima-media thickness and stroke ($P = 0.000$) in the Pakistani population. According to the results of this present study the comparison of carotid intima-media thickness between stroke cases and non-stroke control showed that it was significantly ($P\text{-value} < 0.001$) increased in patients of stroke with a mean value of 0.794 ± 0.121 mm as compared to controls without stroke having a measurement of 0.613 ± 0.099 mm. These results have agreement with previous studies, like the study of Sexena Y, et al 2017, who found that the cases (0.77 ± 0.36 mm) had higher mean value of CIMT than the age-matched controls (0.56 ± 0.13 mm), and the difference was highly significant ($p < 0.0001$)^[18]. But some studies have given different results higher than the result of this present study like study by Das SK et al who found the mean CIMT of 0.849mm in stroke patients^[11], and some other Indian studies like study by Mukherjee et al, found smaller value of mean CIMT as 0.66mm^[19].

There is direct relationship between intima media thickness and atherosclerosis. The pathogenesis of cardiovascular and cerebrovascular events including stroke is based upon this pathologic vascular phenomenon of intima media thickness and its association with stroke^[20]. Literature shows that

stroke is more common in males as compared to females as this present study has revealed that 63% of stroke patients were males. It is supported by many other studies like study by Sridharan et al^[21].

Many studies have revealed that hypertension, Diabetes Mellitus and smoking were the common risk factors of stroke^[22]. And in results of this present study it was observed that all these factors also significantly raise the intima media thickness in comparison to their counterparts.

Carotid intima-media thickness (IMT) is increasingly used as a surrogate and intermediate end point of early atherosclerosis. The carotid intima media thickness can be measured very easily with modern ultrasound scanners as a routine clinical procedure for use in clinical and epidemiological research. On the basis of numerous large population based studies it can be concluded that intima media thickness can be used as predictor for several clinical events such as stroke and other cardiovascular event like myocardial infarction. So it can be concluded that intima media thickness have more information for future cardiovascular events as it was considered classically.

CONCLUSION:

It can be concluded from this study that there is a significant association of CIMT with stroke, and a significantly higher value of CIMT was found in stroke patients. The risk factors like smoking, Diabetes Mellitus and hypertension are strong risk markers for high CIMT. It become necessary to screen out these risk factors. Similarly high risk patient for ischemic stroke can be identified using these risk factors as substitute marker for the ischemic stroke. On the other hand, in patients of ischemic stroke the presence of these factors make it necessary to take appropriate interventions for prevention of further severe cardiovascular event.

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Sl. No.	Author	Journal	Year
1	Dr. Fahim Usman fahim.usman@pau.edu.com	Brain Collection and Neurological Imaging	2018
2	Dr. Bishalendra Jaiswal Bishalendra.jaiswal@pau.edu.com	Electronic Survey and Manuscript Drafting	2018
3	Dr. Zameer Zameer zameer.zameer@pau.edu.com	Proof Reading and Manuscript Finalization	2018

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O son of Adam, when you see that your Lord, the Glorified, bestows His Favors on you while you disobey Him, you should fear Him (take warning that His Wrath may not turn those very blessings into misfortunes).

Hazrat Ali (Karmulha Wajhay)