

ORIGINAL ARTICLES

Association of Carotid Atherosclerosis with Metabolic Syndrome in Patients with Ischemic Stroke

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Abstract:

Background: Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities that increase the risk for stroke and cardiovascular disease. This study evaluated the association of carotid atherosclerosis with MetS and also assessed the association between intracranial and extracranial carotid atherosclerosis with metabolic syndrome among first-ever ischemic stroke patients. **Methods:** This cross-sectional observational study was conducted at the Stroke and Neuro intervention clinic, the indoor and outdoor Department of Neurology, BSMMU, from November 2021 to September 2022, following ethical approval. A total of 60 patients with first-ever ischemic stroke (≥ 40 years of age) were included in this study. After obtaining informed written consent, a detailed history, physical examination and necessary investigations were performed. Revised NCEP ATP III criteria for the Asia-Pacific region defined MetS. Duplex study of Neck vessels and CT Angiogram of Brain and Neck vessels were done to diagnose carotid atherosclerosis. Stenosis was labeled in cases showing $\geq 50\%$ of luminal narrowing. The association between carotid atherosclerosis and metabolic syndrome was then investigated. **Results:** The mean age of the study patients was 62.38 ± 12.38 (SD) years with male predominance (55%). Approximately half of the study patients had diabetes mellitus (51.7%) and hypertension (46.7%). Overall, metabolic syndrome was found in 65% of cases. About 41.7% of patients had carotid atherosclerosis, whereas 58.3% had intracranial atherosclerosis. MetS patients had a significantly higher frequency of carotid atherosclerosis than those without MetS (53.85% vs 19.04%, $p=0.009$). Carotid atherosclerosis patients had a significantly higher frequency of having raised FPG (56% vs 28.6%, $p=0.033$), triglyceride (80% vs 45.7%, $p=0.008$), blood pressure $>130/85$ mmHg (80% vs 40%, $p=0.002$) and reduced HDL-C (72% vs 42.9%, $p=0.025$) than patients without any carotid atherosclerosis. MetS containing 5 components, raised FPG, raised TG and HTN were independent predictors of carotid atherosclerosis. No association was found between intracranial and extracranial carotid atherosclerosis with MetS. **Conclusion:** MetS, especially raised FPG, blood pressure and triglyceride were significantly associated with carotid atherosclerosis among first-ever ischemic stroke patients.

Key words: Metabolic Syndrome, Carotid Atherosclerosis, Ischemic stroke.

Introduction

Metabolic syndrome (MetS) is a cluster of health problems including abdominal obesity, hypertension, hyperglycemia, atherogenic hypertriglyceridemia and low HDL cholesterol.¹ MetS is associated with an increased risk for cardiovascular

disease and with a 2-fold increase in cardiovascular outcome and a 1.5-fold increase in all causes of mortality.² It is a common metabolic disorder that results from the increasing prevalence of obesity and the disorder has been defined by various diagnostic criteria.² Metabolic syndrome has been defined by NCEP ATP III criteria by the presence of three or

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more of the following five criteria: fasting plasma glucose ≥ 100 mg/dl (5.5mmol/l) or antidiabetic treatment, TG ≥ 150 mg/dl, HDL-C <40 mg/dl (Male), <50 mg/dl (Female), BP $\geq 130/85$ mmHg or taking antihypertensive drugs, waist circumference ≥ 90 cm for men and ≥ 80 cm for women.³ Among the metabolic syndrome components, those with high BP, Hyperglycemia and abdominal obesity showed a significantly higher proportion of intracranial artery stenosis.⁴

The principal cause of cerebral infarction is atherosclerosis and its sequelae. Atherosclerosis affecting extra-cranial and intracranial blood vessels is an important and well-recognized cause of cerebral infarction. Atherosclerotic stenosis of the internal carotid artery causes 10-15% of all ischemic strokes.⁵ Yet to our knowledge, very few studies have been done to evaluate the association of carotid atherosclerosis with metabolic syndrome among first-ever ischemic stroke patients. Therefore, this study was designed to find out the association of carotid atherosclerosis with metabolic syndrome and also see the association between intracranial and extracranial carotid atherosclerosis with metabolic syndrome among first-ever ischemic stroke patients.

Materials and Methods

This cross-sectional observation study was executed in the Department of Neurology, BSMMU from November 2021 to September 2022. After the approval from the Institutional Review Board, patients with first-ever ischemic stroke (≥ 40 years of age) were approached for this study. Patients who

had posterior circulation stroke, cardio-embolic stroke, non-atherosclerotic carotid stenosis (vasculitis, Moyamoya disease, Fibromuscular dysplasia, Aortic dissection) were excluded from the study. After describing the aim, purpose and procedure of the study, a total of 60 patients were finally enrolled who met the inclusion and exclusion criteria. Informed written consent was taken from the patient or the patient's attendant. A detailed history of the patient and a thorough clinical examination was done. Abdominal waist circumference (at the level of umbilicus), fasting lipid profile, fasting plasma glucose, and resting blood pressure were measured in each patient. The patients with metabolic syndrome and without metabolic syndrome were selected by using NCEP ATP III criteria for the Asia-Pacific region. Vascular imaging (Duplex study of neck vessels and CT angiogram of the brain and neck) was done to measure carotid stenosis and to see the presence of carotid atherosclerosis. Cases showing $\geq 50\%$ of luminal narrowing were labeled as stenosis. Data were done SPSS 24, Windows 10 version.

Result

The mean age of all respondents was 62.38 ± 12.38 years (42-92 year) with the majority belonging to 60-69 years of age (36.7%). In this study, 55% (33) of the respondents were male and the rest were female (27). We found, 51.7% of the respondents had diabetes mellitus, 46.7% had hypertension, 18.3% had dyslipidemia, 11.7% had ischemic heart disease (IHD) and 10% had a family history of stroke (Table I).

Table-I
Demographic and clinical distribution of study participants (n=60)

Variable	Patients with MetS n=39(%)	Patients without MetS n=21(%)	Total n=60(%)	p-value
Age group (years)				
<50	4(10.3)	3(14.3)	7(11.7)	
50-59	11(28.2)	3(14.3)	14(23.3)	
60-69	16(41)	6(28.6)	22(36.7)	0.174*
70-79	6(15.4)	3(14.3)	9(15)	
80-89	1(2.6)	4(19)	5(8.3)	
>90	1(2.6)	2(9.5)	3(5)	
Mean($\pm$ SD)	60.05 $\pm$ 10.22	66.71 $\pm$ 14.98	62.38 $\pm$ 12.38	0.046**
Abdominal Waist circumference (cm)	89.05 $\pm$ 12.05	80.38 $\pm$ 9.69		0.004**
Gender	Male		33(55)	
	Female		27(45)	
	Diabetes mellitus		31(51.7)	
	Hypertension		28(46.7)	
Co-morbidities	Dyslipidemia		11(18.3)	
	IHD		7(11.7)	
	Family history of stroke		6(10)	

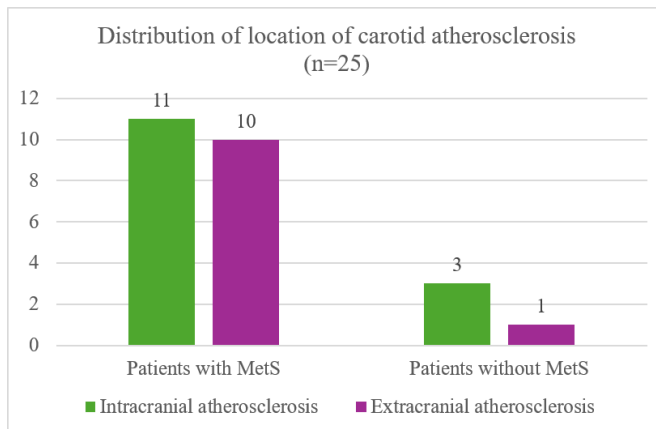
Values are expressed as Mean $\pm$ SD and within parenthesis percentage (%) over column in total and * Chi-squared Test (χ^2) and ** Student t-test were performed to determine the p-value.

Table-II
Association between carotid atherosclerosis and metabolic syndrome (n=60)

	Patients with MetS n=39(%)	Patients without MetS n=21(%)	Total n=60(%)	p-value
Carotid atherosclerosis	21(53.84)	4(19.04)	25(41.7)	0.009*
No Carotid atherosclerosis	18(46.2)	17(80.95)	35(58.3)	

Values are expressed as Mean±SD and within parenthesis percentage (%) over column in total and * Chi-squared Test (χ^2) was performed to determine the p value.

In our study, 39 (65%) patients had metabolic syndrome, and 21 (35%) had no metabolic syndrome. On the other hand, 35 (58.30%) had carotid atherosclerosis, and the rest [25 (41.70%)] had no carotid atherosclerosis. We found a statistically significant (P-value=0.009) association between MetS and carotid atherosclerosis [Table II].



Among patients with carotid atherosclerosis, 14(56%) of the respondents had intracranial atherosclerosis and 11(44%) had extracranial atherosclerosis. With further analysis

In analyzing the association between carotid atherosclerosis and components of metabolic syndrome (MetS), we found a significant correlation with elevated fasting plasma glucose (FPG) (P-value=0.033), elevated triglycerides (TG) (P-value=0.008), and elevated blood pressure (P-value=0.002) [Table III]. In regression analysis, these associations remained significant: metabolic syndrome [OR 4.958; 95%CI p-0.013;(1.409-17.446)], elevated fasting plasma glucose [OR 3.182, p=0.009; 95%CI (1.677-35.385)], elevated triglycerides [OR 4.750; 95%CI (1.453-15.525)], and elevated blood pressure [OR 6.0, p=0.003; 95%CI (1.824-19.734)] [Table IV].

Discussion

MetS consists of metabolic abnormalities, such as obesity, high blood pressure (BP), hyperglycemia and dyslipidemia (high level of triglyceride TG, low level of high density lipoprotein cholesterol), which increases the risk for atherosclerosis and cardiovascular disease.⁶ The clinical outcomes of coronary heart disease, stroke are largely attributable to the process of atherosclerosis.⁷ The main goal

Table-III
Association between carotid atherosclerosis and MetS Components (n=60)

MetS component	Carotid atherosclerosis n=25(%)	No carotid atherosclerosis n=35(%)	Total n=60(%)	p-value
Central obesity	16(64)	14(40)	30(50)	0.067*
Raised FPG (≥ 100 mg/dl)	14(56)	10(28.57)	20(33.3)	0.033*
Raised TG(≥ 150 mg/dl)	20(80)	16(45.7)	36(60)	0.008*
low HDL-C	18(72)	15(42.86)	33(55)	0.025*
Raised blood pressure ($\geq 130/85$ mg/dl)	20(80)	14(40)	34(56.7)	0.002*

Values are expressed within parenthesis percentage (%) over column in total and * Chi-squared Test (χ^2) was performed to determine the p-value

(Figure 01), 21 patients with MetS had carotid atherosclerosis among whom 11 had intracranial and 10 had extracranial atherosclerosis. Among patients without MetS, 04 had carotid atherosclerosis [03 had intracranial and 01 had extracranial atherosclerosis].

of this cross-sectional study was to evaluate the association of carotid atherosclerosis with metabolic syndrome.

In this study, the mean age of the respondents was 62.38±12.38 years (42-92 year) with majority of the

Table-IV

Correlation between metabolic syndrome and carotid atherosclerosis in multivariate analysis (n=60)

MetS components	OR	p-value	95%CI	
			Lower	Upper
MetS	4.958	0.013	1.409	17.446
Abdominal waist circumference	2.667	0.376	0.427	9.570
Raised FPG	3.182	0.009	1.677	35.385
Raised TG	4.750	0.010	1.453	15.525
low HDL-C	2.489	0.105	0.070	1.286
Hypertension	6.0	0.003	1.824	19.734

respondents being male (55%). According to this study, the majority of the respondents had diabetes mellitus (51.7%), hypertension (46.7%), dyslipidemia (18.3%), IHD (11.7%) and family history (10%). The prevalence of hypertension, DM, central obesity, current smoking was 20.4%, 14.1%, 35.8%, 34%, respectively found in a previous study.⁸

The majority of the respondents in this study had metabolic syndrome (65%), rest had no metabolic syndrome (35%). In a previous study, approximately 50% of the total 378 ischemic stroke patients had stenosis and the prevalence of MetS was significantly higher in the stenosis group (67.6%) than in the subjects without stenosis (39.5%).⁹ In a similar study conducted recently also showed the overall prevalence of MetS was 54.5% and multivariate analysis showed MetS was associated with a 20% higher risk of carotid plaque presence (95% confidence interval: 1.01, 1.42; P = 0.036).¹⁰

According to this study, among respondents with metabolic syndrome, about 21(58.3%) respondents had significant carotid atherosclerosis. Among them, 11(52.4%) had intracranial atherosclerosis and the rest 10(47.6%) had extracranial atherosclerosis. In a previous study, patients with intracranial atherosclerosis had higher levels of metabolic abnormality than extracranial atherosclerosis.¹¹

We found a significant association of raised FPG, triglyceride, HDL-C and blood pressure with carotid plaque (p<0.05). While in multivariate logistic regression, metabolic syndrome, raised FPG (p=0.035), raised TG (p=0.010) and HTN (p=0.003) were independent predictors for carotid atherosclerosis in this study. In a previous study, the ischemic stroke patients with carotid plaque had elevated TG (32.6% versus 19.5%, P=0.004), hypertension (70.5% versus 43.9%, P< 0.001), and impaired FBG (41.1% versus 18.5%, P< 0.001).¹²

Conclusion

Our study revealed that metabolic syndrome patients had a significantly higher frequency of carotid atherosclerosis. Also, raised fasting plasma glucose, raised triglycerides and hypertension were independent predictors for carotid atherosclerosis in ischemic stroke patients.

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Conflicts of Interest

The authors declare that they have no conflicts of interest related to this work.

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