

Association of Metabolic Syndrome with Acute Stroke

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ABSTRACT

Objective : Stroke is the most common neurological emergency and causes significant mortality and morbidity in adults. Both diabetes and metabolic syndrome are recognized to increase the risk of ischemic stroke in men and women. The aim of this study is to find out association between metabolic syndrome and acute stroke in our population.

Methods : In this hospital based case-control study, 100 cases of acute stroke were studied from November 2011 to October 2013. Metabolic syndrome was defined by NCEPATP III criteria.

Results : 37% of acute stroke cases had metabolic syndrome as compared to 24% in controls. The study estimated that metabolic syndrome was more common among cases of acute ischemic stroke but not in cases of acute hemorrhagic stroke. Low HDL level, high blood pressure and increased fasting plasma glucose were significantly associated with acute stroke. Morbidity, at the end of one month post stroke, was more in acute stroke cases with metabolic syndrome.

Conclusion : Metabolic syndrome is strongly and positively associated with acute stroke.

Key Words : Metabolic Syndrome, Stroke

Introduction -

Stroke is the most common neurological emergency and the second leading cause of death and acquired disability in adults.^{1,2} A recent study revealed that the risk of stroke has increased by 100% in low and middle income countries over the last decade and the developing world suffers 85% of all stroke-related deaths worldwide.³ In South East Asia alone, where India comprises 81% of the population, 6.36 million DALYs are estimated to be lost due to stroke. The metabolic syndrome is a constellation of risk factors, including atherogenic dyslipidemia, hypertension, insulin resistance, and obesity, that cluster together and promote the development of atherosclerotic vascular disease. Both diabetes and metabolic syndrome are recognized to increase the risk of ischemic stroke in men and women.⁴

However, there have been very few studies in India to study the relationship between metabolic syndrome and stroke. Given its strong link to obesity, the prevalence of the metabolic syndrome is expected to substantially increase in the future alongside the growing obesity epidemic,⁵ a rise that will likely be associated with an even heavier burden of stroke on the society. Hence, this study was undertaken to determine the association of metabolic syndrome with acute stroke.

Aims and Objectives -

1. To determine the association of metabolic syndrome with acute stroke (both ischemic and hemorrhagic). To assess the relationship of and to compare the strength of association of metabolic syndrome and its various components with acute stroke versus controls.
2. To assess and compare the clinical outcomes (mortality and morbidity assessment by Modified Rankin Scale Score) at the end of one month in cases with and without metabolic syndrome.

Material and Methods -

This hospital based case-control study was carried out in patients admitted with acute stroke under Medicine Department at IGGMC, Nagpur from November 2011 to October 2013. 100 cases of

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consecutive, consenting, CT/MRI proven acute stroke with first episode of acute stroke were enrolled in this study. Acute stroke patients who were unable to communicate or had previous history of stroke or coronary syndrome were excluded. Controls were selected from healthy visitors or relatives of non-stroke patients. Persons having previous diagnosis of stroke or positive family history of stroke were excluded from controls. Data was collected by taking detailed history, clinical examination including anthropometry and obtaining various lab parameters according to predesigned proforma. Outcomes at the end of one month (death or disability) using Modified Rankin Scale was recorded. Metabolic syndrome was defined according to the Revised NCEP/ATP III criteria.⁶ The study was approved by the Institutional Ethics Committee.

Statistical Analysis -

The mean levels of continuous variables were compared using the student's 't'-test. The categorical variables, various components of metabolic syndrome were compared using the 'chi-square' test. Odd's ratios (OR) and 95% confidence intervals were computed wherever applicable. A p-value of <0.05 was considered statistically significant. Data was entered and analyzed using the SPSS software.

Results -

Out of 100 cases, 76 cases (76%) had ischemic stroke and 24 cases (24%) had hemorrhagic stroke. The metabolic syndrome was present in a significantly higher percentage of cases of acute stroke (37%) as compared to controls (24%). (Table 1)

Table 1 : Comparison of frequency of Metabolic Syndrome in acute stroke cases and controls

Metabolic Syndrome	Cases (n=100)	Controls (n=100)
Yes	37 (37%)	24 (24%)
No	63 (63%)	76 (76%)
2-value	3.98	
p-value	<0.05, S	

However, upon comparison of individual components of metabolic syndrome, it was found that significantly higher percentage of cases with acute stroke had low serum HDL ($p < 0.02$, OR 2.44, 95% CI=1.36-4.38), High blood pressure ($p < 0.01$, OR 14.08 95% CI 6.53-30.32) and high fasting plasma glucose ($p < 0.05$, OR 1.89, 95% CI=1.04-3.45) as compared to controls. There was no statistically significant difference in elevated serum triglyceride and increased waist circumference among cases and controls. (Table 2)

Acute ischemic stroke had significant association with metabolic syndrome. ($p < 0.05$, OR 1.97, 95% CI=1.08-3.60). When cases of Acute ischemic stroke were compared with controls for various components of metabolic syndrome, we observed that low serum HDL, High blood pressure, high fasting plasma glucose and increased waist circumference were significantly higher in cases. (Table 2)

6 (25%) out of 24 cases of acute hemorrhagic stroke had metabolic syndrome as compared to 4 (16.66%) out of 24 controls. ($p > 0.05$, NS). However low serum HDL ($p < 0.01$, OR 3.83, 95% CI=1.99-7.38) and high blood pressure ($p < 0.01$, OR 28.17, 95% CI=9.64-82.55) was present in a significantly higher percentage of cases of acute hemorrhagic stroke as compared to controls. Other components like high serum triglyceride, high fasting blood glucose and increased waist circumference were similar in both groups.

Metabolic Syndrome was significantly higher in women with acute stroke as compared to men with acute stroke. ($p < 0.05$, OR 2.368)

MRS score at the time of hospitalization was significantly more in cases with Metabolic syndrome (Table 3)

It was found that the cases of acute stroke with metabolic syndrome had a significantly higher percentage of severe disability (MRS 4-5) at the end of one month post stroke (32.43%) as compared to the cases of acute stroke without metabolic syndrome who had a significantly higher percentage of mild to moderate disability (MRS 0-3) (74.60%). (Table 4)

Table 2 : Comparison of frequency of metabolic syndrome and its various components in cases of acute ischemic stroke and controls

Metabolic Syndrome and its components	Ischemic Stroke (n=76)	Controls (n=76)	OR	2-value	p-value
Metabolic Syndrome	31 (40.79%)	20 (26.34%)	1.97 (1.08-3.60)	5.05	p<0.05, S
High Sr. Triglyceride (≥150 mg %)	16 (21.05%)	19 (25%)	0.79 (0.41-1.54)	0.45	p>0.05, NS
Low Sr. HDL (<40mg% in males; <50mg% in females)	39 (51.31%)	24 (31.57%)	2.31 (1.30-4.12)	8.26	p<0.05, S
High Blood Pressure (≥130 systolic and/or ≥85 mm of Hg diastolic)	67 (88.15%)	28 (36.84%)	12.49 (6.03-25.84)	55.49	p<0.05, S
High Fasting plasma sugar (≥100mg %)	33(43.42%)	20(26.31%)	2.23 (1.23-4.06)	7.12	p<0.05, S
Increased Waist circumference (>80cm in females; >90cm in males)	24(31.57%)	14(18.42%)	2.14 (1.10-4.15)	5.22	p<0.05, S

Table 3 : Comparison of severity of disability in cases of acute stroke with metabolic syndrome and those without metabolic syndrome at the time of admission

	Patients with Metabolic Syndrome (n=37)	Patients without Metabolic Syndrome (n=63)	OR	2-value	p-value
Mild to moderate disability (MRS 1 to 3)	15 (40.54%)	47 (74.60%)	0.23 (0.12-0.42)	23.58	p<0.01 S
Severe disability (MRS 4 to 5)	22 (59.45%)	16 (25.39%)			

Table 4 : Comparison of severity of disability at the end of one month in cases of acute stroke with metabolic syndrome and those without metabolic syndrome

Modified Rankin Scale Score	Patients with Metabolic Syndrome (n=37)	Patients without Metabolic Syndrome (n=63)	OR	2-value	p-value
Mild to moderate disability (MRS 0 to 3) n (%)	19 (51.35%)	47 (74.60%)	0.36 (0.20-0.66)	11.29	<0.01 S
Severe disability (MRS 4 to 5) n (%)	12 (32.43%)	5 (7.93%)	5.41 (2.34-12.49)	18.0	<0.01 S
Death (MRS 6), n (%)	6 (16.21%)	11 (17.46%)	0.86 (0.41-1.81)	0.14	0.70 NS

Discussion -

This hospital based case-control study showed that metabolic syndrome was strongly and positively associated with acute ischemic stroke. We found that a significantly higher percentage of cases with acute stroke had low serum HDL, high blood pressure, and a high fasting plasma sugar as compared to controls. These findings were consistent with the Framingham Offspring study (22%)⁷, Md. Javed Iqbal et al⁸ study (54%) from Bangladesh and the Bernadette Boden-Albala et al⁹ study (also known as the NOMAS study).

The metabolic syndrome is a risk factor for stroke that seemingly has an underlying metabolic causation. The most accepted and unifying hypothesis to describe the pathophysiology of metabolic syndrome is insulin resistance, which is caused by incompletely understood defect in insulin action.¹⁰ Central obesity is the centerpiece of the metabolic alterations. There is evidence that excess body weight is a predictor of stroke (total, ischemic, and hemorrhagic) in men. Increased waist circumference is an important component of the most recent and frequently applied diagnostic criteria for the metabolic syndrome. However measuring waist circumference does not reliably distinguish increases in subcutaneous adipose tissue versus visceral fat; this distinction requires CT/MRI. Relative increase in visceral versus subcutaneous adipose tissue with increasing waist circumference in Asian and Asian Indians may explain the greater prevalence of the syndrome in these population compared with African American men in whom subcutaneous fat predominates.¹⁰ Accordingly, increased abdominal adiposity contributes to dyslipidemia, hyperglycemia, and hypertension. Recent evidence suggests that increased obesity and insulin resistance state is associated with inflammation. Furthermore, The elevations of inflammatory markers are associated with metabolic risk factors and with accelerated atherosclerotic diseases.¹¹

Hypertension remains the most common modifiable risk factor for stroke in the general population. In our study, hypertension had the strongest and more

consistent relationship with acute stroke among all the metabolic syndrome components. Hypertension is multifactorial in origin. In insulin resistant state normal physiological vasodilatory property of insulin is lost but effect of sodium reabsorption in kidneys persist so also its stimulatory effect on sympathetic nervous system. Hypertension accelerates the atherosclerotic process in carotid and vertebral arteries¹² that usually starts in the larger extracerebral arteries, particularly in the carotid bifurcation. This process with time spreads distally to the smaller intracerebral arteries, leading to increased vascular resistance and hypertension during exercise and hence the increased risk of cardiovascular events. The presence of hypertension as part of the metabolic syndrome was associated with increased risk of acute ischemic as well as hemorrhagic stroke.

Dyslipidemia is a hallmark of the metabolic Syndrome. It is characterized by elevated TG and low HDL-C levels. Hypertriglyceridemia consequently reduces cholesteryl ester content of the lipoprotein core leading to reduction in HDL-C. With fasting TG>180mg/dl, there is always predominance of small dense LDL-C which increases atherogenic risk in patients with metabolic syndrome.¹⁰ There is a controversy regarding the association between serum TG levels and stroke.¹³ It has been shown that postprandial hypertriglyceridemia is associated with carotid artery atherosclerosis. Nonetheless, in the Copenhagen City Heart Study, a log-linear association between serum TG levels and nonhemorrhagic stroke was found, which was independent of age and sex.¹⁴ In general, in the majority of studies, an inverse association between HDL-C and stroke risk has been documented. In the Northern Manhattan Stroke Study, increased levels of HDL-C were associated with a reduced risk of ischemic stroke in the elderly and among different racial or ethnic groups.⁹ In our study we also found that decreased HDL-C level was significantly associated with acute stroke.

Because the Metabolic Syndrome represents a condition associated with substantially high risk, it

appears logical that targeted management should involve pharmacological treatment together with “therapeutic lifestyle changes” to reduce obesity, control hypertension and hyperglycemia, and improve dyslipidemia. Previous evidence shows that relatively modest lifestyle interventions can have favorable impact on components of the metabolic syndrome, at least in the relatively short term. It is known that good cardiorespiratory fitness and physical activity are related to decreased risk of stroke¹⁵. Because of additional evidence from our study showing an association between metabolic syndrome and stroke, the threat to public health will continue to increase as the metabolic syndrome becomes more common. Early identification, treatment, and ultimately prevention of the metabolic syndrome present a major challenge for health care professionals and public health policy-makers facing an epidemic of overweight and sedentary lifestyle.

Conclusions :

So we conclude

1. Metabolic syndrome was strongly and positively associated with acute ischemic stroke but not with acute hemorrhagic stroke.
2. The high blood pressure, low serum HDL and high fasting plasma glucose were the components of metabolic syndrome which were significantly associated with acute stroke.
3. Acute stroke cases with metabolic syndrome were associated with higher morbidity at the end of one month of follow up.

We recommend screening of patients with acute stroke for metabolic syndrome. Large population based cohort studies are required to confirm these findings.

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