

Research Article

**Assessment of metabolic syndrome and its relation with gender
in acute ischemic non-embolic stroke cases**

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ABSTRACT

Objective: To assess the metabolic syndrome and its relation with gender in acute ischemic non-embolic stroke cases.

Material and Methods: This study was conducted in Rural Health Centre Mochiwala from February 2017 to August 2017. Total 288 patients of stroke with infarction on CT scan (hypodense area on CT scan) and meeting the inclusion and exclusion criteria were included in the study. Demographic data (age and gender), history of presenting illness and previous known risk factors were obtained. Physical examination was done including blood pressure and waist circumference measurement. Venous sample for HDL cholesterol, triglycerides and fasting plasma glucose were taken after 8 hour of overnight fast. CT scan/MRI was done to confirm infarction. Source of embolus ruled out by ECG, echocardiography and carotid doppler angiography. All the relevant information were noted on a proforma.

Results: In this study population, 57.3% were male and 42.7% were female with mean age of 56 ± 7 years in men and 54 ± 7 years in females. Frequency of metabolic syndrome was 43.63% in men and 65.04% in women.

Conclusion: This study clearly shows that metabolic syndrome is an important risk factor for acute ischemic non-embolic stroke. It supports the potential for preventive efforts in persons with high risk of ischemic stroke.

Keyword: Metabolic syndrome, Acute ischemic non-embolic stroke, Blood pressure, Obesity

INTRODUCTION:

Stroke is one of the top four leading causes of morbidity and mortality throughout the world¹. It is an acute neurologic injury of vascular origin. A uniform definition of stroke is vital for epidemiological studies. According to World Health Organization (WHO), stroke is defined as 'rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hrs or longer, or leading to death, with no apparent cause other than that of vascular origin². This definition includes stroke

due to both cerebral infarction and hemorrhage. By applying this definition transient ischemic attacks (TIA), which is defined to last less than 24 hours, and patients with stroke symptoms caused by subdural hemorrhage, tumors, poisoning and trauma, are excluded. The term cerebrovascular disease includes all disorders in which an area of the brain is temporarily or permanently affected by ischemia or hemorrhage with one or more of the cerebral blood vessels affected by disease. Stroke is a generic term referring to a group of

disorders that include cerebral infarction, cerebral hemorrhage and subarachnoid hemorrhage³.

There are two types of stroke, ischemic and hemorrhagic. Ischemic stroke accounts for up to 85 percent of strokes and happens when blood supply to certain part of brain is blocked. Fifteen percent strokes are due to brain hemorrhage, which happen when blood vessel bursts and cause bleeding in the brain parenchyma. Approximately 45% of ischemic strokes are caused by small or large artery thrombus, 20% are embolic in origin and others have an unknown cause⁴. Thrombosis can form in the extracranial and intracranial arteries when the intima is roughened and plaque forms along the injured vessel. The endothelial injury (roughening) permits platelets to adhere and aggregate, then coagulation is activated and thrombus develops at the site of plaque. Blood flow through the extracranial and intracranial systems decreases and the collateral circulation maintains function. When the compensatory mechanisms of collateral circulation fail, perfusion is compromised, leading to decreased perfusion and cell death.

During an embolic stroke, a clot travels from a distant source and lodges in cerebral vessels. Microemboli can break away from a sclerosed plaque in carotid artery or from a cardiac source such as atrial fibrillation or a hypokinetic left ventricle⁴. Less common causes of ischemic stroke include carotid dissection and the presence of coagulopathies, such as those resulting from antiphospholipid antibodies. Other causes include arteritis, infection and drug abuse i.e. use of cocaine^{5, 6}.

When an ischemic stroke occurs, the blood supply to the brain is interrupted and brain cells are deprived of glucose and oxygen they need to function. As thrombosis or emboli cause a decrease in blood supply to brain tissue, events occur at cellular level, referred to as ischemic cascade. Common risk factors for stroke are divided into two groups, modifiable and non-modifiable. Modifiable risk factors include smoking, alcoholism, diabetes mellitus, hypertension, dyslipidemia, physical inactivity,

obesity and cocaine abuse. Non-modifiable risk factors include gender, increasing age, race and prior stroke. Among relative risk factors of stroke, metabolic syndrome is gaining concern. According to National Cholesterol Education Program (NCEP)/Adult Treatment Panel (ATP) III and International Diabetes Federation (IDF), major features of metabolic syndrome include obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension⁷. Data on known modifiable risk factors for stroke shows an alarmingly high prevalence within population of Pakistan. Hypertension is the single most preventable cause of stroke, which affects one in three adults aged greater than 45 and 19% of the population aged 15 and above⁸. The National Health Survey of Pakistan showed that diabetes mellitus is present in 35% of population more than 45 years of age. The overall prevalence of obesity is 28% in women and 22% in men⁹. The prevalence of tobacco use is 40% in men and 12% in women¹⁰. With high prevalence of all these metabolic risk factors, the prevalence of metabolic syndrome in Pakistan is reported to be from 18% to 46%¹¹.

The metabolic syndrome should be considered as a prime target for preventive medicine. The primary management goals for metabolic syndrome are to reduce the risk of cerebrovascular and cardiovascular diseases by lifestyle modification and treatment.

Pakistan is the sixth most populated country in the world, with estimated population of 167 million¹². Non-communicable diseases including stroke now accounts for 41% of total disease burden of Pakistan¹³. In a population dense country like Pakistan, an estimated 4.8% may be suffering from stroke¹⁴; this translated to 7.2 million individuals, compared to 700,000 annually in the United States.

The incidence and mortality of stroke vary greatly among different populations and has declined in several foreign studies. An estimated 94% of deaths from stroke in South Asia occur in people younger than 70 years in contrast to only 6% in countries with established economies owing to

greater loss in the disability adjusted life years (DALYs) ¹⁵. The stroke epidemic of the developing countries like Pakistan disables individuals in their prime of life, which puts economical and social burdens on the family and society. Measures should be taken to prevent the cerebrovascular disease as not only ‘‘prevention is better than cure’’ but cost effective as well.

MATERIAL AND METHODS:

This study was conducted in Rural Health Centre Mochiwala from February 2017 to August 2017. Total 288 patients of stroke with infarction on CT scan (hypodense area on CT scan) and meeting the inclusion and exclusion criteria were included in the study. Inclusion criteria was: Patients of any gender and more than 14 years of age having acute neurological deficit with hypodense area on CT scan brain without any source of emboli on echocardiography (valvular heart disease, intra-cardiac thrombus and vegetations) and carotid doppler (narrowing of carotids).

Patients having no established infarction on CT scan brain, Patients having definite source of emboli like atrial fibrillation, valvular heart disease, infective endocarditis etc, Patients having acute myocardial infarction, Patients having recurrent TIAs and Patients having chronic ailment like CRF, CCF, and CLD were excluded from the study.

Demographic data (age and gender), history of presenting illness and previous known risk factors were obtained. Physical examination was done including blood pressure. Waist circumference was measured at midpoint between the lower margin of last palpable rib and the top of iliac crest, using a stretch resistant tape, at the end of normal expiration after overnight fast. Venous sample for HDL cholesterol, triglycerides and fasting plasma glucose were taken after 8 hour of overnight fast. CT scan was done to confirm infarction. Source of embolus ruled out by ECG, echocardiography and carotid doppler angiography. All the relevant information were noted on a proforma (attached).

All data was entered into SPSS version 10 and analyzed. Mean and SD was calculated for numerical variables and frequencies & percentages were calculated for categorical variables. Chi square test was applied to see the association between different variables. P-value was considered significant if less than 0.05.

RESULTS:

Total 288 patients of acute ischemic stroke were included in this study. Mean age of the patients was 55.13 ± 7.6 . Metabolic syndrome was found in 52.7% patients. (Shown in figure). Out of 288 patients male patients were 165 (57.29%) and metabolic syndrome was found in 72 (43.64%) patients. Female patients were 123 (42.71%) and metabolic syndrome was found in 80 (65%) female patients. Strong association was found between gender and metabolic syndrome. P. Value 0.005. (See table No.1)

The mean waist circumference was 100.27 ± 11.799 centimeters (ranging from 80 to 128 centimeters). The mean systolic blood pressure was 137.92 ± 16.801 mm of Hg (ranging from 110 to 182 mm of Hg) while the mean diastolic blood pressure was 85.53 ± 16.801 mm of Hg (ranging from 64 to 102 mm of Hg). The mean triglycerides level was 150.26 ± 17.948 mg/dl (ranging from 112 to 188 mg/dl). The mean HDL level was 44.64 ± 5.832 mg/dl (ranging from 35 to 55 mg/dl). The mean fasting blood glucose level was 117.60 ± 38.271 mg/dl (ranging from 70 to 235 mg/dl). (see table No.2)

Results of the different components of the metabolic syndrome were also shown in table 2. The most prevalent components were hypertension and low HDL, these were positive in 167 patients (57.98%) followed by diabetes and raised triglycerides level in 135 patients (46.87%). On the other hand, the least prevalent component was waist circumference.

It was positive in 131 patients (45.48%). Only 04 patients were found to have the 5 components of the metabolic syndrome and only 07 patients were without any component of metabolic syndrome.

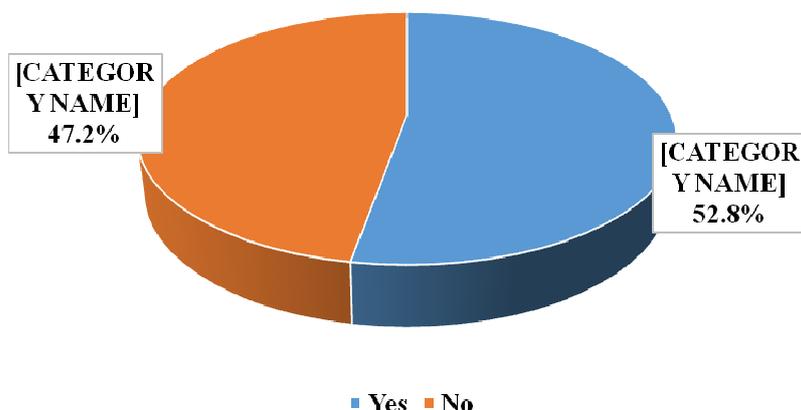


Table No.1 Gender distribution of the patients.

Gender	Metabolic Syndrome		Total	P. Value
	Yes(%)	No(%)		
Male	72(43.64)	93	165 (57.29%)	0.001
Female	80 (65%)	43 (35%)	123 (42.71%)	
Total	152 (52.8%)	136 (47.2%)	288	

Table No.2 Frequency of components of metabolic syndrome

Variables	Frequency (n=288)			Percentage
	Males	Females	Total	
Systolic blood pressure ≥ 130	103	72	175	60.76%
Diastolic blood pressure ≥ 85	100	71	171	59%
Hypertension (Blood Pressure $\geq 130/85$)	100	67	167	57.98%
Waist Circumference ≥ 102 cm in males and ≥ 88 cm in females	57	74	131	45.48%
HDL Level ≤ 40 mg/dl in males and ≤ 50 mg/dl in females	65	102	167	57.98%
Triglycerides Level ≥ 150 mg/dl	93	42	135	46.87%
Fasting blood glucose ≥ 100 mg/dl	79	58	137	47.56%
Diabetes Fasting blood glucose ≥ 126 mg/dl	64	51	115	39.93%

DISCUSSION:

Acute ischemic stroke is a common neurological disorder encountered worldwide. It is one of the top four causes of death throughout world. Ischemic stroke accounts for up to 85% of all strokes. Various risk factors for stroke include

diabetes mellitus, ischemic heart disease, hypertension, dyslipidemia and obesity. The incidence of cerebrovascular diseases increases with age.

Among the related risk factors, metabolic syndrome (MetS) is gaining concern. The term

“metabolic syndrome” consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular diseases and stroke. According to National Cholesterol Education Program (NCEP)/Adult Treatment Panel (ATP) III and International Diabetes Federation (IDF), major features of metabolic syndrome include obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension. Each of these factors can lead to ischemic stroke. Our study demonstrated that frequency of metabolic syndrome (according to NCEP/ATP III and IDF 2005) in acute ischemic non-embolic stroke patients was 52.8% (152 out of 288). Our observation was supported by Gorter et al who found metabolic syndrome in 40 to 50% of patients with various cerebrovascular diseases¹⁶. Metabolic syndrome was present in 56% of patients with ischemic stroke in a study conducted by Koren-Morag et al¹⁷. De Silva recorded metabolic syndrome in 61% of South Asian patients with ischemic stroke¹⁸. In Framingham offspring study, metabolic syndrome was found to be a more important risk factor for ischemic stroke as compared to diabetes mellitus¹⁹. The Atherosclerosis Risk in Communities (ARIC) study also noted that patients with metabolic syndrome have higher risk of incident stroke provided the metabolic syndrome contains either high blood pressure or elevated fasting blood sugar²⁰. These various studies conducted show a similar frequency of metabolic syndrome in ischemic stroke patients worldwide.

In our study, metabolic syndrome was found in 65.04% females as compared to 43.63% males. The Northern Manhattan study, which included Hispanic, African-American, and Caucasian subjects, reported an increased risk of stroke among women with metabolic syndrome compared to men²¹. Koren-Morag et al similarly reported that metabolic syndrome without diabetes mellitus was a significant risk factor for ischemic stroke in both sexes, but the effect was more pronounced in women¹⁷. So female sex is also a

risk factor for metabolic syndrome which can in turn lead to ischemic stroke.

Dyslipidemia, which is characterized by high triglycerides and low HDL, has always been considered as a hallmark of the metabolic syndrome. Our data has shown strong association between dyslipidemia and ischemic stroke as triglyceride levels ≥ 150 mg/dl was present in 136 (46.87%) cases and HDL levels ≤ 50 mg/dl was present in 167 patients (57.98%). According to Copenhagen City Heart Study, a 47% reduction in ischemic stroke was found for 1.0 mmol/l (39 mg/dl) rise in HDL²². Our study is also in consistence with Milionis et al, which stated that high TG levels and low HDL levels had a relationship with ischemic stroke²³. The British regional heart study, a prospective study consisting 7735 men followed up for 16.8 years, also revealed a significant association between HDL levels and ischemic stroke²⁴.

Increased waist circumference which represents abdominal obesity, has a strong association with stroke in our study as a waist circumference greater than 102 cm in men and 88 cm in female was present in 131 patients. A study by Isomma et al noticed obesity in 76% patients with normal glucose tolerance and 92% of diabetic patients with ischemic stroke²⁵.

High blood pressure has emerged as an important component of metabolic syndrome in our patients as 167 patients (57.98%) had blood pressure $\geq 130/85$ mm of Hg. In one study conducted by Wang Y et al, it was concluded that frequency of hypertension was 70% among patients of ischemic stroke²⁶. McNeill et al found high blood pressure as an important component of metabolic syndrome, which increased the risk of ischemic stroke by 1.5-2 times²⁷.

Impaired fasting glucose and diabetes has a strong association with stroke in our study, as fasting blood sugar greater than 100 mg/dl was present in 137 (47.56%) patients. These results were supported by study conducted by Basharat et al, which concluded that the most frequent risk factor of stroke was hypertension 86.8% followed by

diabetes mellitus 59.8%, dyslipidemia 59.1%, and smoking 18.1%. They also concluded that low HDL is an emerging risk factor of ischemic stroke²⁸.

So, our study proved that metabolic syndrome has a similar risk of ischemic stroke worldwide. It is not only metabolic syndrome, but its individual components have emerged as an important risk factor for ischemic stroke. Early diagnosis and treatment of patients at risk may avert the development of ischemic stroke. Caring physicians should look for metabolic syndrome in their patients and important measures should be taken for their treatment to reduce the incidence of ischemic stroke. The metabolic syndrome cannot be taken as the sole risk for ischemic stroke because other risk factors like age, sex, smoking and LDL cholesterol levels are not included in the constellation.

CONCLUSION:

This study clearly shows that metabolic syndrome is an important risk factor for acute ischemic non-embolic stroke. Frequency of metabolic syndrome in ischemic stroke was higher in female patients as compared to males. Hypertension and low HDL levels were more frequently found components of metabolic syndrome in our study

MetS can become a useful and simple tool to identify the patients at risk of ischemic stroke and supports the potential for preventive efforts.

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