

Research Article**Study of Prevalence of Metabolic Syndrome in Coronary Artery Disease and Cerebrovascular Accident Patients****Sumit Pal Singh Chawla¹, Tarsempal Singh², Jaswant Singh³, Sarabjot Kaur⁴, Ravinder Garg^{5*}, Dr Shaminder Kaur⁶**¹Sr. Resident, ⁴PG Resident, ⁵Associate Professor, ⁶Assistant Professor, Department of Medicine, GGS Medical College & Hospital, Faridkot, Punjab, India²Professor, ³Associate Professor, Department of Medicine, Govt. Medical College, Amritsar, Punjab, India
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Abstract: Metabolic syndrome is characterized by clustering of metabolic abnormalities which includes insulin resistance, glucose intolerance, central obesity, dyslipidemia and hypertension. This study was carried out to analyse the prevalence of metabolic syndrome and its individual components in 200 patients, 100 each of coronary artery disease (CAD) and cerebrovascular accident (CVA). Subjects attending the Medicine out-patient and in-patient departments of Guru Nanak Dev Hospital, Amritsar were taken and data was analysed using the standard statistical methods (Chi-Square tests and 'p value' for level of significance). It was observed that 58% of CAD and 46% of CVA patients had metabolic syndrome. Overall, 52% of total patients had this syndrome. This study concluded that metabolic syndrome patients are at an increased risk of CAD and CVA and calls for early identification of these individuals. Aggressive management of modifiable risk factors like diabetes, hypertension, dyslipidemia and obesity can halt this epidemic and hence reduce the burden of cardiovascular and cerebrovascular diseases.**Keywords:** Metabolic syndrome, Cerebrovascular disease, Cardiovascular disease, Dyslipidemia, Risk factors, Hypertension

INTRODUCTION

Metabolic syndrome refers to a cluster of metabolic abnormalities related to a state of insulin resistance which is often associated with obesity. The major characteristics include insulin resistance, abdominal obesity, elevated blood pressure and lipid abnormalities (elevated levels of triglycerides and low levels of high density lipoprotein cholesterol).

Abdominal obesity presents clinically as increased waist circumference. Leptin deficiency or resistance leads to tissue deposition of fat. This ectopic distribution of fat (triglycerides) particularly its visceral or central component causes insulin resistance. Visceral adipocytes are metabolically more active and excess adipose tissue lipolysis leads to increased plasma concentrations of free fatty acids (FFA) [1].

In the setting of insulin resistance, the vasodilatory effect of insulin is lost, but the renal effect on sodium reabsorption is preserved. Insulin also increases the activity of the sympathetic nervous system [2]. These factors along with endothelial dysfunction that

manifests as blunting of the biologic effect of a potent endothelium-derived vasodilator, nitric oxide, and increased production of vasoconstrictors such as angiotensin II, endothelin-1, cyclooxygenase and lipooxygenase products of arachidonic acid metabolism, contribute to elevated blood pressure.

Metabolic syndrome is associated with a proinflammatory and prothrombotic state that may include elevated levels of C-reactive protein (CRP), endothelial dysfunction, hyperfibrinogenemia, increased platelet aggregation, increased levels of plasminogen activator inhibitor type 1 (PAI-1), elevated uric acid levels, microalbuminuria and a shift towards small, dense particles of low density lipoprotein cholesterol [3]. This proinflammatory and prothrombotic state plays an important role in the pathogenesis of atherothrombosis.

The prevalence of metabolic syndrome is estimated to be around 20–25 per cent of the population [4]. The prevalence increases with age, affecting less than 10 percent of people in their 20s and 40 percent of people

in their 60s [5]. It is higher in females than in males. Generally, there is higher prevalence of metabolic syndrome in Non-European groups, South Asians, Black Africans, Caribbeans, Hispanics and significantly lower prevalence in European white and Chinese [6, 7].

Aims and Objectives

- To study the association of central obesity, dyslipidemia, hypertension, and diabetes with metabolic syndrome
- To assess the prevalence of metabolic syndrome in CAD patients
- To assess the prevalence of metabolic syndrome in CVA patients

MATERIALS AND METHODS

This study was carried out in 200 patients, 100 each of coronary artery disease and cerebrovascular accident attending the Medicine outpatient and indoor department at Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. Informed consent was obtained from each patient.

Inclusion Criteria

- Patients with Electrocardiography (ECG) or Echocardiography (ECHO) suggestive of CAD.
- Patients with clinical & CT scan findings of CVA.
- Already known dyslipidemic, hypertensive & diabetic.
- Patients with family history of dyslipidemia, Diabetes, Hypertension, CAD & CVA.

Exclusion Criteria

- Valvular heart disease
- Patients less than 30 years of age
- Patients on antipsychotics, antiretroviral therapy
- Patients on oral contraceptives
- Meningitis
- Systemic malignancy
- Nephrotic syndrome
- Vasculitis

The diagnosis of CAD was established on the basis of clinical and ECG or ECHO findings and that of CVA by clinical and CT scan findings. Detailed history was elicited from patients or relatives regarding nature of illness and thorough general & systemic examination was done.

Metabolic syndrome in study subjects was diagnosed as per International Diabetes Foundation (IDF) 2005 criteria² which required:

Central obesity: defined as waist circumference (adjusted for South Asians): Male ≥ 90 cms, Female ≥ 80 cms

Plus any two or more of the following:

- Raised TG level: ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes.

Screening for parameters of Metabolic Syndrome Waist Circumference

Waist circumference was measured using a non stretchable plastic measuring tape. The participants were asked to stand erect and one layer of clothing was accepted. At the end of expiration, waist circumference was measured at the mid-point of lowermost border of 12th rib and uppermost point of iliac crest.

Blood Pressure

Blood pressure was recorded in right arm supine position after making the patient to rest for 10 minutes. Two readings were taken five minutes apart using a mercury sphygmomanometer and the average was taken into consideration. Each patient was asked for previously diagnosed hypertension and response recorded.

Fasting Plasma Glucose

Fasting plasma glucose was measured (in mg/dL) from venous blood sample drawn in morning following at least 8 hours of fasting. Each patient was asked for previously diagnosed diabetes mellitus and response recorded.

Triglyceride and HDL

Triglyceride and HDL levels were measured (in mg/dL) from venous blood sample drawn in morning following at least 8 hours of fasting. Each patient was asked for previously diagnosed lipid abnormality for which treatment was being taken and response recorded.

Analysis of the data

Data for the above mentioned parameters were statistically analysed for their significance. The patient characteristics were analysed using the “Chi-Square tests” and p value was determined to evaluate the level of significance. If p value is less than 0.05, it is considered significant.

RESULTS

A total of 200 cases, 100 each of CAD and CVA, were taken for the study and they were divided into 2 groups based on their age distribution.

Individuals aged 30 to 60 years formed one group while the other group comprised of those more than 60 years of age.

The study revealed that 54% of CAD and 50% of CVA patients were in age group of >60 years. Overall 52% of all patients were aged >60 years. 54% of CAD and 55% of CVA patients were males. Overall, males constituted 54.5% of total cases.

Central obesity was found in 65% patients of CAD and 55% patients of CVA. Overall, 60% of all patients were obese (Fig. 1).

61% of CAD and 64% of CVA patients were either known hypertensive or had BP \geq 130/85 mm of Hg. Overall, 62.5% of all patients were either known hypertensive or had BP \geq 130/85 mm of Hg.

51% and 43% patients of CAD and CVA respectively were either known diabetic or had FPG \geq 100 mg/dl. Overall, 47% of all patients were either known diabetic or had FPG \geq 100 mg/dl.

54% and 47% of CAD and CVA patients respectively had high TG levels. Overall, 50.5% of total patients had hypertriglyceridemia. 50% of CAD and 46% of CVA patients had low HDL levels. Overall, 48% of total patients had low HDL levels.

58% of CAD and 46% of CVA patients had Metabolic Syndrome. Overall, 52% of total patients had Metabolic Syndrome (Table 1, Fig. 2). There was no statistically significant difference between prevalence of Metabolic Syndrome in CAD and CVA patients (p value of 0.089).

Of these patients with Metabolic Syndrome, 54.8% were aged >60 years and 45.2% belonged to age group of 30 to 60 years. 44.2% were males and 55.8% were females (p= 0.002; significant). Central obesity was observed in 100% cases in accordance with IDF criteria for Metabolic Syndrome. However, 16.7% patients of study were obese but did not have Metabolic Syndrome. 82.7% patients were either known hypertensive or having BP \geq 130/85 mm of Hg (Fig. 3). 58.7% were either known diabetic or had raised FPG \geq 100 mg/dl. 75% patients had high TG levels and 60.6% had low HDL levels.

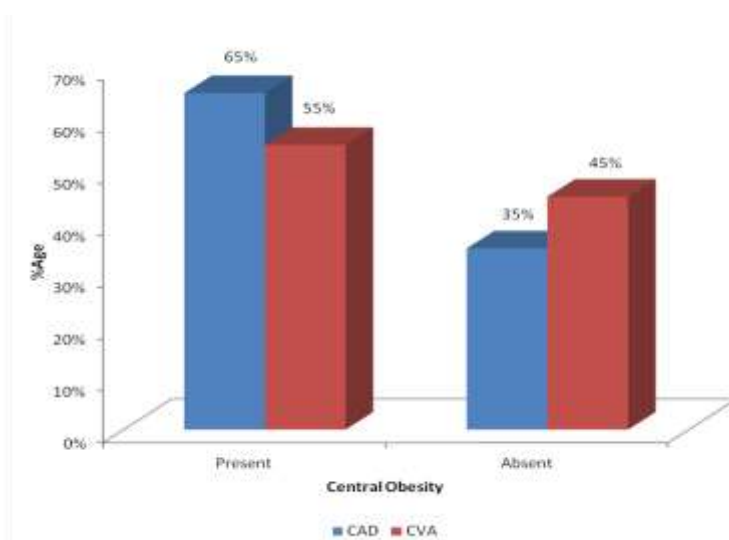


Fig. 1: Showing Association of Central Obesity in CAD and CVA Patients

Central obesity was defined in terms of waist circumference as per the IDF guidelines. It was observed that 65% patients of CAD and 55% patients of CVA had central obesity. In total, 60% of all patients

participating in the study were obese. Central obesity is a risk factor for both CAD and CVA. p value was 0.149 which was insignificant (p>0.05).

Table 1: Showing prevalence of metabolic syndrome in CAD and CVA patients

Metabolic Syndrome	CAD		CVA		Total	
	No. of Cases	% age	No. of Cases	%age	No. of Cases	%age
Present	58	58%	46	46%	104	52%
Absent	42	42%	54	54%	96	48%
Total	100	100%	100	100%	200	100%

$X^2=2.885$; $df=1$; $p=0.089$; Not Significant

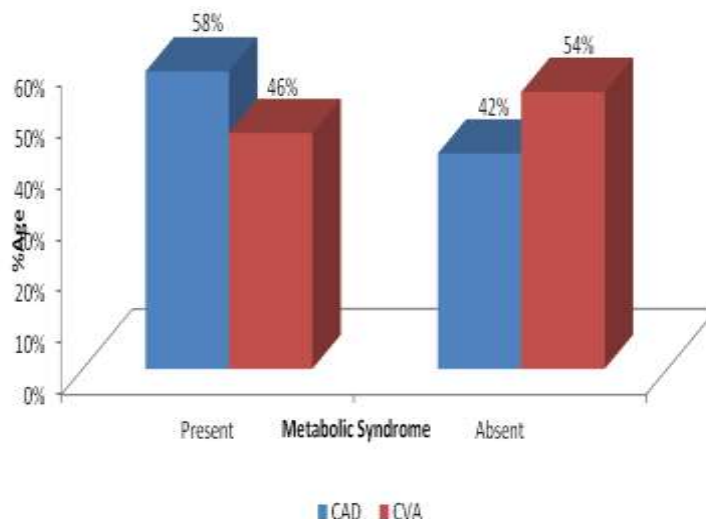


Fig. 2: Showing prevalence of metabolic syndrome in CAD and CVA patients

Among CAD patients, 58% and among CVA patients, 46% had metabolic syndrome. In total, 52% of patients participating in the study had metabolic syndrome. p value was 0.089 which was insignificant.

Hence no statistically significant difference was observed between prevalence of metabolic syndrome in CAD and CVA patients.

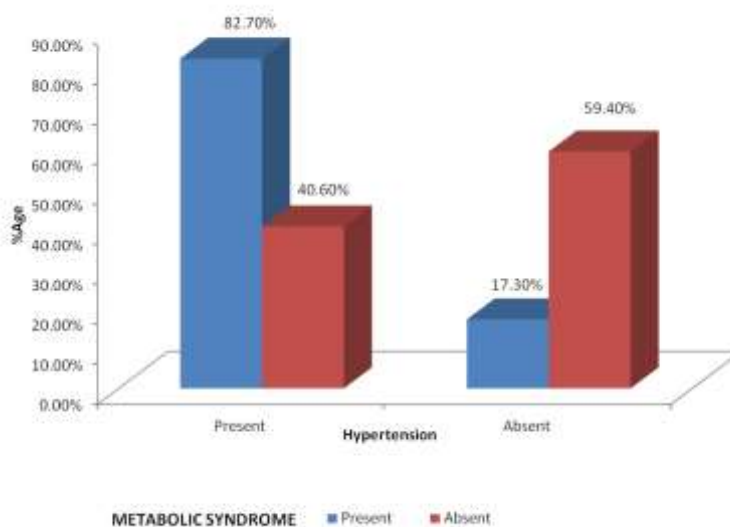


Fig. 3: Showing association of hypertension with metabolic syndrome

Among cases of metabolic syndrome, 82.7% were either known hypertensives or had BP \geq 130/85 mmHg. 17.3% cases of metabolic syndrome were normotensive. p value was <0.001 which is highly significant.

DISCUSSION

Metabolic syndrome consists of multiple, interrelated risk factors of metabolic origin that appear to directly promote the development of cardiovascular and cerebrovascular diseases. The metabolic risk factors consist of central obesity, atherogenic dyslipidemia (elevated triglycerides and low HDL cholesterol

concentrations), elevated blood pressure and elevated plasma glucose.

This study showed significant prevalence of obesity in the patients suffering from CAD (65%) and CVA (55%). Obesity is considered to be the link between insulin resistance and metabolic abnormalities which includes diabetes, hypertension and dyslipidemia, all of which are risk factors for CAD and CVA [8]. The visceral fat stored beneath the muscles and wrapped around the internal organs is considered to be the most ‘atherogenic’, ‘diabetogenic’, and ‘hypertensinogenic’ fat depot of the human body.

Prevalence of hypertension in CAD and CVA patients was 61% and 64% respectively in this study. These findings highlight the importance of hypertension as a potential risk factor for both cardiovascular and cerebrovascular events. Among patients with metabolic syndrome, those having hypertension were as high as 82.7%, further signifying the potential contribution of hypertension to causation of metabolic syndrome and resultant morbidity and mortality.

51% of CAD and 43% of CVA patients participating in this study were found to have either diabetes mellitus or impaired fasting glucose. 61% patients of metabolic syndrome were either diabetic or had impaired fasting glucose.

High levels of triglyceride were noted in 54% cases of CAD and 47% cases of CVA. Low HDL levels were observed in 50% and 46% cases of CAD and CVA respectively. Their respective contribution in causation of metabolic syndrome was highly significant ($p < 0.001$).

An increase in TGL, in addition to high LDL levels, significantly increases the risk for CVD while low HDL is considered to be a particularly key risk factor for CVD in both non-diabetic and diabetic individuals, as confirmed in epidemiological studies [9] and in the Lipid Research Clinics Prevalence Study [10].

In a case control study conducted on 76 patients, with an age range of 40-70 years by Immanuel Sin [11], consisting of 38 post ischemic stroke patients and 38 controls, HDL levels were significantly lower in stroke patients as compared to control subjects ($p < 0.05$). The study concluded that low HDL-cholesterol level is a risk factor for ischemic stroke.

In another cohort study of 10 years follow up, by Kurth T *et al.* [12] in 27,937 US women aged > 45 years, to evaluate the association between various lipid parameters and the risk of ischemic stroke, it was seen that low HDL, LDL, Total cholesterol & TC/HDL ratio were significantly associated with increased risk of ischemic stroke.

Prevalence of metabolic syndrome in CAD patients was 58% and in CVA patients it was 46%. Overall prevalence including both types of cases was found to be 52%.

In a study done on 1209 Finnish men aged 42-60 years, the 10-year CVD (cardiovascular disease) risk was increased 2.1- and 2.5- fold with the ATP III and WHO MS definitions, respectively. The same study found that the risk of death from CVD was increased by 2.63-2.96 times and the risk of death from any cause was increased 1.87-2.11 times with the presence of the MS. The MS alone predicted ~25% of all new-onset

CVD [13]. The DECODE study reported that the presence of MS increased all-cause and CVD mortality by 1.2-2.8 times [14].

In a cohort study done by Kurl S *et al.* [15] in 1131 men, patients with the metabolic syndrome had a 2.05-fold risk for all strokes and 2.41-fold risk for ischemic stroke, after adjusting for socioeconomic status, smoking, alcohol and family history of coronary heart disease.

In a prospective cohort study done by Koren-Morag N *et al.* [16] in 14,284 patients with atherosclerotic cardiovascular disease to find relation between the metabolic syndrome and ischemic stroke or transient ischemic attack, 3703 (26%) had metabolic syndrome without diabetes and 3500 (25%) had frank diabetes alone. The study showed that all components of the metabolic syndrome were associated with increased risk for ischemic stroke or TIA, but impaired fasting glucose and hypertension were the strongest risk predictors.

A case control study, conducted in 214 South Indian patients with first acute ischemic stroke in Sri Chitra Trunal Institute, Trivandrum showed that high fasting blood sugar was associated with 4 fold stroke risk and metabolic syndrome with 6 fold stroke risk than community control group [17].

Enas *et al.* [18] in his study found that South Asians develop metabolic abnormalities at a lower body mass index and waist circumference than other groups, conventional criteria underestimate the prevalence of MS by 25% to 50%. South Asian-specific waist circumference recommended by the International Diabetes Federation appear to be more appropriate in this population. So in our study waist circumference was adjusted for the south Asians.

There was a significant difference in the prevalence of metabolic syndrome between males and females. It was significantly higher in females (58%) as compared to males (46%). Metabolic syndrome was more prevalent in patients more than 60 years of age than in patients of lesser age. In patients of age more than 60 years, prevalence of metabolic syndrome was 57% and in patients less than/equal to 60 years, it was 47%.

In a study done by Lee *et al.* [19] using the Asia-Pacific criteria for abdominal obesity based on waist circumference (≥ 90 cm in men, ≥ 80 cm in women), prevalence rates of metabolic syndrome were 10.9% (9.8% male, 12.4% female).

In South East Asia, prevalence of diabetes, premature coronary artery disease and dyslipidemia are higher than the rest of the world though partly attributed due to genetic predisposition. Diabetes and premature coronary artery disease are occurring about 10 years earlier in South East Asia than rest of the world

population. In India, mortality attributable by cardiovascular disease is expected to rise by 103% in men and by 90% in women from 1985 to 2015 [20]. So, there is an overwhelming moral, medical and economic imperative to identify individuals with metabolic syndrome early so that lifestyle interventions and treatment may prevent the development of diabetes, cardiovascular and cerebrovascular diseases.

CONCLUSION

- Central obesity is a risk factor for both CAD and CVA.
- Hypertension is an important contributing factor for causation for CAD and CVA.
- Diabetes Mellitus or pre-diabetes also contribute to CAD and CVA although to a lesser extent than central obesity and hypertension.
- Hypertriglyceridemia and Low HDL levels are more prevalent in CAD patients than in CVA patients.
- Metabolic Syndrome patients are at increased risk of CAD and CVA.
- Metabolic Syndrome is more prevalent in females than in males.
- Central obesity, Diabetes Mellitus, Hypertension, dyslipidemia: all these factors significantly contribute to the Metabolic Syndrome.

There is an urgent need to explore nutrition and physical activity and their role in the prevention and treatment of disorders directly or indirectly related to the metabolic syndrome. Early diagnosis and aggressive management of modifiable risk factors like diabetes, hypertension, dyslipidemia, obesity can halt this epidemic and hence reduce the burden of cardiovascular and cerebrovascular diseases.

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