METABOLIC SYNDROME IN ACUTE CORONARY SYNDROME"

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ABSTRACT

Objective: To determine the frequency of metabolic syndrome in male patients presenting with acute coronary syndrome

Study design: A Descriptive study

Place and duration of study: Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi, from October 2007 to September 2008

Patients & Methods: Male patients with acute coronary syndrome (ACS) were included. Patients having angioplasty (PCI), coronary artery bypass surgery in the past and other co-morbid diseases were excluded. All patients were assessed for the presence of five components of metabolic syndrome including hypertension, HDL-Cholesterol and triglycerides, glucose intolerance and abdominal obesity. Systolic, diastolic blood pressures, waist circumference (WC) and body mass index (BMI) were measured. ECG, cardiac enzymes, fasting glucose and lipid profile were also done.

Results: A total of 135 male patients of ACS were studied with a mean age of 54.26±11 years. Metabolic syndrome (MS) was present in 55 (40.7%) patients. MS with all five components was documented in 4 (7.27%) while MS with four and three components was seen in 23 (41.81%) and 28 (50.90%) patients respectively. Only 24 (43.63%) patients with MS had diabetes mellitus, remaining 31(56.36%) were non diabetic. Frequencies of diabetes, hypertension and family history of CAD were significantly higher ($p<0.05$) in patients with metabolic syndrome as compared to patients with normal metabolic status.

Conclusion: Metabolic syndrome is fairly common and important risk factor in patients of IHD. Other risk factors like smoking, dyslipidemia, hypertension and diabetes were also frequently found. Public awareness to control the risk factors can reduce the prevalence of CAD in our country

Keywords: Acute coronary syndrome, coronary artery disease, metabolic syndrome, obesity.

INTRODUCTION

Cardiovascular disease (CVD) is becoming a major health burden in developing countries. In the year 2005, 58 million people died from CVD accounting for 30% of all deaths worldwide; more than half these deaths were in developing countries[1]. If the risk factors associated with CVD go unchecked, then by 2030, when the world population is expected to reach 8.2 billion, 33 percent (24.2 million) of all deaths will be due to CVD[2]. In South Asia, which represents more than a quarter of the developing world, a steady rise in incidence and prevalence of this disease is already showing a dangerous trend in CVD bringing a great challenge for health services[3].

Ever since the Framingham heart study in 1960s identified the important risk factors associated with CAD,[4,5] there has been a great stress to modify these risk factors to reduce the burden of CVD. Among the conventional risk factors of CAD, modifiable risk factors are diabetes, smoking, hypertension[6], hyperlipidemia[7], sedentary life style, obesity[8] stress and depression. Newly emerging risk factors include high-sensitivity C-reactive proteins (hsCRP)[9], homocysteine, lipoprotein(a), fibrinogen, D-dimers, Interleukin 6 and myeloperoxidases[10,11].

The metabolic syndrome (MS) is a cluster of lipid and nonlipid factors associated with insulin resistance that places a subject at a higher risk for diabetes and cardiovascular events[12,13]. According to National Cholesterol Education Program Adult Treatment Panel-III (NCEP ATP-III)[14] the diagnosis of MS be made when 3 or more of the following characteristics are present: abdominal obesity, high fasting glucose, high blood pressure, low HDL cholesterol, and high triglycerides. MS is

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associated with a greater risk of atherosclerotic disease than any of its individual components. Insulin resistance is a central pathophysiological process associated with MS[15]. Presence of MS increases the risk of Cordiovascular Disease (CVD) twice in next 5 to 10 years. It confers 5–fold increase in risk for developing type 2 Diabetes mellitus.[16] NCEP ATP III identified CAD as the primary clinical outcome of the MS.[17]

The aim of this study was to determine the frequency of MS and its various components in patients of acute coronary syndrome.

PATIENTS AND METHODS

This study was conducted at the Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi, a tertiary cardiac care center from October 2007 to September 2008. It was a descriptive study (case series) in which 135 male patients presenting with acute coronary syndrome for the first time at emergency department were included and purposive convenient sampling technique was used. Patients having lipid lowering drugs, percutaneous coronary intervention (PCI), coronary artery bypass surgery in the past and patients with other co-morbid conditions like heart failure, valvular heart disease, renal failure, chronic liver disease and any other chronic diseases were excluded from the study. All patients were informed about the study and an oral consent was obtained from them.

Acute coronary syndrome (ACS) was diagnosed on the basis of ECG changes and rise in cardiac enzymes and further classified into ST elevation Myocardial Infarction (STEMI), Non-ST elevation Myocardial Infarction (NSTEMI) and unstable angina.

Demographic data and presence of known risk factors like hypertension, diabetes mellitus, smoking and dyslipidemia were obtained, along with level of physical activity of at least 30 min daily or 5 days a week. Intake of any antihypertensive drugs, hypoglycemics and lipid lowering drugs was documented. Subjects were assessed for the five components of metabolic syndrome. Blood pressure was measured by using a standard mercury sphygmomanometer after the subject's pain and anxiety were relieved and the mean value of two measurements taken at least 15 minutes apart was used in the analysis. Waist circumference was measured at highest point of iliac crest by measuring tape by the same observer. Body mass index was also calculated. Fasting blood samples were drawn for glucose and lipid profile in first 24 hours after acute coronary insult. Metabolic syndrome was defined by the presence of 3 or more out of 5 components (Table 01): central obesity (waist circumference ≥ 90 cm (men); fasting plasma glucose ≥ 100 mg/dl; triglycerides ≥ 150 mg/dl; high density lipoprotein cholesterol <40 mg/dl (men); systolic BP ≥130 or diastolic BP ≥ 85 mmHg.[18]

The data was collected on a pre-designed proforma and variables were entered on SPSS version 15. Frequencies and percentages were computed for qualitative variables and variables compared by Chi square test. Mean and standard deviation were calculated for quantitative variables and mean were compared between two groups (metabolic syndrome and normal metabolic status) by using independent sample t-test. P-value of 0.05 was considered as significant.

RESULTS

A total of 135 patients of ACS were studied with a mean age of 54±11.60 years (range 28 to 80 years). Maximum number of patients, 41 (31.9%), were seen in the age group 51-60. STEMI was diagnosed in 96 (71.1%) persons, NSTEMI was present in 12 (8.9%) while unstable angina was seen in 27 (20%).

Data presented is either mean value ± standard deviation (SD) or numbers along with their percentages in parentheses depending on the type of variable M I= myocardial infarction, BMI= body mass index, TRG = triglycerides

A total of 55 (40.7%) patients fulfilled the criteria for metabolic syndrome (Table 2) and 80 (59.25) were having normal metabolic status (NMS). Out of these 55 patients, five components of MS were present only in 4 (7.27%) patients; four components were seen in 23 (41.81%) patients while 28 (50.90%) patients had only 3 components present. Only 24 (43.63%) patients having MS had Diabetes Mellitus while remaining 31(56.36%) subjects were non diabetic (Table 3). In patients with

MS, STEMI was seen in 27 (49.09%) while NSTEMI was seen in 12 (21.81%) and 16 (29.09%) had unstable angina.

As far as five components of MS were concerned individually among all 135 patients, their respective frequency is given in table 3.

Among 135 patients of ACS, frequency of smoking, hypertension, diabetes, family history of premature CAD, level of physical activity and different grades of BMI are given in detail in table 2.

A total cholesterol (TC) level of >200 mg/dl was observed in 29 (21.48%) patients. LDL cholesterol (LDL-C) above 100 mg/dl was seen in 54 (40.0%). A TC/HDL ratio of >5 was seen in only 21 persons (15.5%). No significant association was seen among various qualitative variables when Chi square tests were applied. Frequencies of diabetes, hypertension and smoking status among patients with MS and NMS were compared using chi square test. Mean of age, systolic, diastolic BP, TC, HDL, LDL, TG, BMI and WC were compared among patients with MS and NMS using student's t test. The significant differences ($p < 0.05$) between these two groups were found in systolic BP (p=0.005), diastolic BP (p=0.009), triglycerides (p=0.001), BMI (p=0.001) and WC (p= 0.04). Significant differences were also seen in frequencies of diabetes (p=0.013), hypertension (p=0.016)and family history of CAD (p=0.017).

Data presented is either mean value ± standard deviation (SD) or numbers along with their percentages in parentheses depending on the type of variable. MI= myocardial infarction, BMI= body mass index, TG = triglycerides WC = waist circumference, MS = Metabolic Syndrome, NMS = Normal metabolic status, FPG=fasting plasma glucose, C=cholesterol, CAD= coranry artery disease.

DISCUSSION

Metabolic Syndrome was initially defined by World Health Organization (WHO) consultation group in 1998[19] .This definition of MS emphasized insulin resistance as the major underlying risk factor and required evidence of insulin resistance for diagnosis. However, other major criteria came from NCEP ATP III in 2001 14 that did not require demonstration of

Table 1: Diagnostic Criteria for Metabolic Syndrome[23]

Measure	Cut off value
Elevated waist circumference	≥90 cm 35.5 in (Men) ≥80 cm 31.5 in (women)
Elevated TG	≥150 mg/dL or on drugs for elevated TG
Reduced HDL-C	<40 mg/dL (men) < 50 mg/dL (women) or on drugs for reduced HDL-C
Elevated BP	130 mmHg systolic BP or 85 mmHg diastolic BP on drug for hypertension
Elevated fasting glucose	≥100 mg/dL or on drugs for high glucose

(at least any 3 out of 5 components should be present for diagnosis)
TG= triglycerides, BP= blood pressure, in=inches, HDL-C=HDL cholesterol

Table 2: Baseline Characteristics of Patients with Acute Coronary Syndrome (n = 135)

Variables	Values
Age(yrs)	54.26 ± 11.60
Diabetics	34 (25.2 %)
Hypertensive	50 (37 %)
Smokers	60 (44 %)
Ex smokers	22 (16.3%)
Family history of CAD	24 (17.8%)
Age Groups	
≤ 40 years	18 (13.4%)
41-50 years	38 (28.1%)
51-60 years	43 (31.9%)
> 61 years	36 (26.6%)
Types of M I	
ST elevation MI	96 (71.1)
Non ST elevation MI	12 (8.9%)
unstable angina	27 (20%)
Plasma glucose fasting (	123 ± 55.7
mg/dl)	162.69 ± 36.06
Total cholesterol (mg/dl)	41.06 ± 6.74
HDL (mg/dl)	89.88 ± 31.68
LDL (mg/dl)	158.39 ± 69.34
TRG (mg/dl)	3.90 ± 0.8
TC:HDL	51 (37.8%)
BMI 25- 29.9 (kg/m²)	22 (16.3%)
BMI > 30	55 (40.7%)
Metabolic Syndrome	64(47.4%)
Physically active	

Table 3: Frequency of Components of Metabolic Syndrome (N=135)

Component of MS	No.(Percentage)
Waist circumference ≥90 cm (35.5 in)	85 (62.96)
TG ≥150 mg/dL or on drugs for elevated	71 (52.59)
Reduced HDL-C (<40 mg/dL)	56 (41.48)
Elevated SBP 130 mmHg on drug for hypertension	66 (48.88)
Elevated DBP 85 mmHg (on drug for hypertension)	59 (43.70)
Elevated fasting glucose ≥100 mg/dL (or on drugs for high glucose)	69 (51.11)

(at least any 3 out of 5 components should be present for diagnosis)
MS= metabolic syndrome, TG= triglycerides, BP= blood pressure, C= cholesterol

Table 4: Comparing CAD Risk factors in MS and NMS

No	Risk factors	MS n=55	NMS n=80	P value
1	Smoking	25 (45.4%)	35 (43.7%)	0.845
2	Hypertension	27 (49%)	23 (28%)	0.016
3	Diabetes Mellitus	35 (63.6%)	66 (82%)	0.013
4	CAD history	15 (27.2%)	9 (11.2%)	0.017
5	Physically active	28 (50.9%)	36 (45%)	0.499
6	Age	54.80 ± 12.36	53.89 ± 11.11	0.65
7	Systolic BP	129 ± 27.22	117 ± 20.30	0.005
8	Diastolic BP	82 ± 16.18	76 ± 13.13	0.009
9	Total Cholesterol (mg/dl)	170 ± 33.53	165 ± 33.64	0.33
10	LDL- C (mg/dl)	90 ± 28.70	93 ± 28.09	0.60
11	HDL- C (mg/dl)	40 ± 8.53	41 ± 3.2	0.38
12	TG (mg/dl)	180 ± 69.98	142 ± 51.29	0.001
13	WC (cm)	98 ± 10.62	93 ± 8.93	0.001
14	BMI	26 ± 3.61	24 ± 3.55	0.04
15	F P G (mg/dl)	130 ± 55.97	117 ± 55.87	0.16

insulin resistance or any other single factor mandatory for diagnosis of MS. In 2005, the the International Diabetes Federation(IDF) dropped the WHO requirement for insulin resistance but made abdominal obesity a madatory as 1 of 5 factors required in the diagnosis of MS,[20] the remainder of the criteria being essentially identical to those provided by NCEP ATP III. NCEP ATP III criteria does not mandate abdominal obesity as an essentially required component for the diagnosis MS.

Patients with the metabolic syndrome are at high risk of having adverse cardiovascular events. Metabolic syndrome and Diabetes Mellitus are associated with systemic inflammation[21] and a procoagulant state. Metabolic Syndrome associated endothelial inflammation may promote destabilization of pre-existing coronary artery plaque thus leading to plaque rupture and thrombosis[22] causing cardiovascular events.

In our study patients frequency of MS was 40.07% (55 subjects) as compared to women ischemia syndrome study (WISE study) where 25% of the IHD cohort had MS. The difference was most likely attributable to gender difference. The same study, however, showed 76% of WISE study subjects were overweight (BMI >25) compared to 54% in our study. Out of total 55 patients with MS, 27 (49.09%) had STEMI, 12 (21.81%) had NSTEMI, while 16 (29.09%) had unstable angina. In a local study by Yasmin et al 100 patients of IHD were studied to document MS. Frequency of

metabolic syndrome was 32% in men and 28% in women. The highest rate of metabolic syndrome was in men diagnosed as STEMI[23]. This is consistent with our results of STEMI and MS. However, in this study upper limit for WC for males was taken as 102 cm (males) and 88 cm (females), however WHO and NCEP ATP-III recommends that upper limit of WC for Asians is 90 cm (males) and 80 cm (female). In our study number of patients with MS is higher (40.07%) as comparared to Yasmin et al. the reason for this higher frequency of MS in our study is due to lower cut off value used for waist circumference. The use of this lower value for WC brought (WC) two third subjects of this study into the range of abdominal obesity. Another study by Marroquin et al, studying the MS in IHD found that presence of MS is associated with angiographically significant CAD and cardiovascular risk in women with suspected IHD. Furthermore, women with the metabolic syndrome and angiographically significant CAD had a lower 4-year survival and high rate of cardiac events as compared with women with normal metabolic status[24]. Another sub-study by Kip et al concluded that MS but not BMI predicts future cardiovascular risk. It is vital to recommend weight loss in overweight and obese and control of all modifiable risk factors to prevent transition to the metabolic syndrome[25].

CONCLUSION

Frequency of metabolic syndrome is very high among our patients with IHD. Majority of patients had higher fasting blood glucose levels and triglycerides along with increased waist circumference. In our study TC and LDL-Cholesterol levels were not significantly raised however high TG levels and low HDL show that metabolic syndrome and its components may be an important culprit in the etiology of IHD. Public awareness to control metabolic syndrome related risk factors is vital to control the rising incidence of IHD in our population.

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