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Association Of Metabolic Syndrome With Angiographic Severity Of Coronary Artery Disease

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Abstract
Introduction: *Metabolic syndrome (MetS) is considered one of the important factors that increases the cardiovascular risk. The objective of this study was to determine the relationship of metabolic syndrome in patients with coronary artery disease and to compare the frequency of severe coronary artery disease in patients with and without metabolic syndrome.*
Objective: *The aim of this study was to evaluate the relationship of metabolic syndrome (MetS) with angiographic severity of coronary artery dicence (CAD).*
Materials and Methods: *This was a cross-sectional observational study carried out in the Department of Cardiology, CMCH from October 2018 to September 2019. Two hundred fifty-two consecutive patients with coronary artery disease undergoing coronary angiography during the study period were included in the study as per inclusion and exclusion criteria. Lipid profile, fasting blood glucose, anthropometric and clinical parameters were analyzed. The severity of CAD on angiography was compared between the without etabolic syndrome group and with metabolic syndrome group. Severity of CAD was calculated by using Gensini score.* ***Results:*** *The mean ± SD of the age of study population was 53.12±10.57 years (range 30-80) and 181 (71.8%) were male. The study showed a significant positive correlation between presence of metabolic syndrome (MetS) and severity of coronary artery disease that counted by Gensini score (Spearman rho 0.424; p<0.0001). Multivariate regression analysis revealed that presence of metabolic syndrome (MetS) was an independent risk factor for the presence of severe CAD (OR=9.32, P<0.0001).*
Conclusion: *Metabolic syndrome is strongly related to the severity of coronary artery disease documented clinically and angiographically.*
Key words: *Coronary Artery Disease; Metabolic Syndrome (Mets); Correlation; Acute Myocardial Infarction; Coronary Angiography; Gensini Score.*

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I. Introduction

In developing countries coronary artery disease is an important worldwide health problem almost reaching an epidemic proportion. It is the principle cause of mortality in the whole world and also in our country. By year 2030, it has been projected that cardiovascular mortality will increase from 18.1 million in 2010 to 24.2 million. [1] Epidemiological transition from communicable disease to non-communicable disease in Bangladesh has observed. Metabolic syndrome (MetS) includes various cardio metabolic risk factors and is characterized by four essential components including intra-abdominal obesity, dyslipidemia, hypertension and impaired glucose tolerance [2,3] and associated to high risk of both type 2 diabetes and Coronary artery disease (CAD) and increased risk of cardiovascular events.[3,4] Despite significant controversy, majority of experts belief that the increased cardiovascular risk observed in these subjects is probably due to the clustering of risk factors.[5,6] Numerous epidemiological and clinical studies have confirmed the association between MetS and increased risk CAD.[7,8] Globally prevalence of metabolic syndrome in the adult population is on the rise with an estimated prevalence of 20–25% (IDF). South Asians are more prone to develop Met S because of their high percentage of body fat, central

obesity and insulin resistance. [2] A meta-analysis done by [9] has reported that overall prevalence of metabolic syndrome in Bangladeshi population is about 30%. Metabolic syndrome were defined according to International diabetes federation (IDF) criteria [10] as follows: Central obesity (waist circumference: Male ≥ 90 cm, female ≥ 80 cm) plus any two: Raised triglycerides (>150 mg/dl), reduced HDL cholesterol (< 40 mg/dl in men or < 50 mg/dl in women), raised blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or on treatment), or raised fasting plasma glucose (fasting plasma glucose ≥ 100 mg/dl or on treatment). The prevalence of the metabolic syndrome (MetS) has increased over the last few years in the world and by 2020, more than 300 million people will be affected by the cardiovascular disease risk factors that constitute the MetS, glucose intolerance, obesity, hypertension and dyslipidemia. The set of criteria to identifyMetS are some of cardio metabolic risk factors that occur together, including hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, central obesity and raised fasting blood glucose. Epidemiological studies have shown an increased rate of MetS both in urban and rural areas in Bangladesh [11,12] and this might be an important contributory factor for the increased prevalence of type 2 diabetes and cardiovascular disease (CVD) in the Bangladeshi population. The IDF estimated that 5.1 million Bangladeshi people are with diabetes. [13] WHO data published in 2011 reported that 14.31% of deaths are due to coronary heart disease in Bangladesh. The age-adjusted death rate reported was 109 per 100,000 of the population, ranking Bangladesh 104th in the world. [15] Hence, identification of the population at risk of these diseases is extremely important. In current years, changes in lifestyle and food behaviors extensively resulted in an increase in cardiovascular disease, diabetes and MetS worldwide, especially in developing countries [3] Among men 45 years and older and women 55 years and older, the MetS confers moderately high risk of CAD (10-year risk of 10%–20%).[16] The MetS has come as a major risk factor of CAD.[17,18,19] reported that patients with the MetS had a higher incidence of CAD and increased all-cause mortality than those without MetS. On development of CAD, MetS has an additive impact in addition to its individual components (e.g., hypertension, diabetes) is controversial. [20] Considering the above-mentioned evidence, early assessment of the risk and severity of CAD in patients with MetS is desirable because it could lead to improved patient or physician adherence to risk-reducing behaviors or interventions and improve clinical outcomes. The aim of the study is to determine the frequency of MetS in patients with CAD and to compare the angiographic severity of CAD with and without MetS.

II. Methods

Type of study: Cross-sectional observational study.
Place of Study: Department of cardiology, Chittagong Medical College Hospital, Chattogram, Bangladesh.
Study period: One year from October 2018 to September 2019.
Study population: Coronary artery disease patients undergoing coronary angiography during the study period and fulfilling the inclusion and exclusion criteria.
Sampling Technique: Consecutive sampling.
Sample Size: The sample size will be determined by the following formula:

$$n = \frac{Z^2 pq}{d^2}$$
$$= 252$$

Inclusion Criteria:

- Patients underwent coronary angiography for coronary artery disease

Exclusion Criteria:

- Previous history of revascularization (PCI, CABG)
- Renal failure.
- Liver failure.
- Acute infection
- Malignant diseases.
- Pregnancy.
- Those unwilling to give consent.

Study procedure: This is a hospital based study that will include 252 consecutive acute coronary syndrome patients (both STEMI, NSTEMI and unstable angina) who was subsequently undergo coronary angiography. After selection, the aim, objectives and procedure of the study was explained in details to the subjects. An informed written consent was taken from all study patients. History was taken and clinical examination was performed following standard procedure of clinical methods. Data on demographic profile of the patient which includes age, diabetes, hypertension, dyslipidemia, and smoking, prior CAD, medication history (anti- hypertensive and anti-diabetic) was required. The body height was measured in the standing position without shoes. Weight was

measured similarly without shoes and heavy dresses. Waist circumference (WC) was measured at the mid-point between the distal border of the ribs and the top of the iliac crest with subjects standing at the end of a normal expiration. With all aseptic precautions 5ml of fasting blood sample was drawn by lab assistant with the subject in sitting position, with limited use of tourniquet and was sent to laboratory for analysis. Fasting lipid profile, fasting plasma glucose was determined on the day of blood collection. If not, sample after centrifugation was store at 4°C for up to 4 days.

Patients was divided into two groups with and without MetS according to IDF criteria. Coronary Angiography was performed by percutaneous femoral or radial approach. Coronary angiograms was obtained for each coronary vessel in ≥2 projections. Analysis of the coronary angiograms was performed visually by an experienced operator. The severity of the CAD was assessed by vessel score and Gensini score. Vessel score; Significant coronary artery disease is defined as > 70% stenosis in any of the three major epicardial coronary arteries or a left main coronary artery stenosis > 50%. Patients will be grouped as having single vessels disease (SVD), double vessel disease (DVD) and triple vessel disease (TVD) according to the number of vessel involvement. Gensini score; It grades narrowing of the lumen of the coronary artery and scores it with numerical values with the following method; score 1 for 1–25% narrowing, 2 for 26–50% narrowing, 4 for 51–75%, 8 for 76–90%, 16 for 91–99%, and 32 for a completely occluded artery. This score is then multiplied by a factor that represents the importance of the lesion's location in the coronary artery system: 5 for the left main coronary artery; 2.5 for the proximal left anterior descending coronary artery or proximal circumflex artery; 1.5 for the mid left anterior descending coronary artery; 1 for the proximal right coronary artery, distal left anterior descending coronary artery, obtuse marginal artery or posterior lateral artery; and 0.5 for other stenosis. The severity of disease is expressed as the sum of the scores for the individual lesions.

Data collection tool: All demographic, clinical, angiographic and laboratory data were recorded in a pre-designed data collection sheet.

Data analysis: The statistical analysis was carried out by using Statistical Package for Social Sciences (SPSS-25). To test the distribution pattern, the Kolmogorov–Smirnov test was used. Continuous variables were presented as mean ± standard deviations (SDs) and compared by Student's t-test between two parameters and analysis of variance (ANOVA) test when parameters were more than two. All non-parametric data were analyzed by Chi-square test. Risk factors of patients having severe CAD were evaluated by odds ratio. Statistical significance and confidence interval were set at $p<0.05$ and 95% level respectively.

III. Results

The present cross sectional study intended to investigate the relationship of MetS with angiographic severity of CAD patients. The study patients were divided into two groups (without MetS and with MetS) according to presence of MetS and another two groups (Gensini score <20 and Gensini score ≥20) according to coronary artery disease severity. The findings obtained from data analysis are presented below:

Table I: Distribution of age and MetS of the patients (n=252)

Age (in years)	Without MetS		With MetS		Total		P value	X^2	Range
	n	%	N	%	n	%	0.277* (ns)	1.183	30-80
<40 years	11	12.2 %	13	8%	24	9.5%			
≥40 years	79	87.8 %	149	92%	228	90.5%			
Total	90	100%	162	100%	252	100%			
Mean ± SD	51.89 ±10.997		53.80 ±10.308		53.12 ±10.577				

SD = Standard deviation.

*=P-value was derived by chi-square test; ns= statistically non-significant.

Most of the study population (90.5%) was in the ≥40 years of age group. The average mean age of the patients was 53.12 ± 10.577 years (range: 30-80 years). Mean ± SD age was 51.89 ± 10.997 in without MetS group and 53.80 ± 10.308 in with MetS group. No significant difference in presence of MetS among the age groups was found in the present study (Table I).

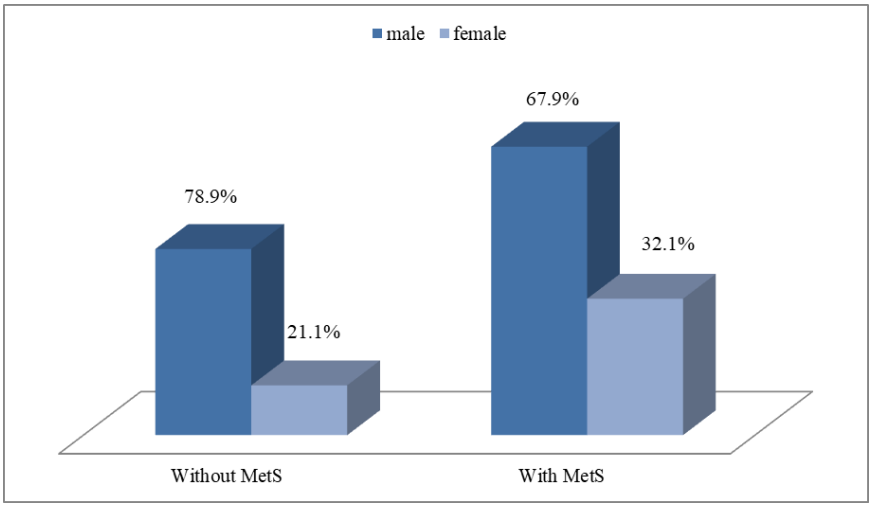

Figure-1: Distribution of gender and MetS of the patients (n=252)

Bar diagram shows the gender distribution of the study patients and it depicts that, there was male predominance, total 181 (71.8%) with male to female ratio about 2.55:1. In without MetS group, 71 (78.9%) were male and in with MetS group 110 (67.9%) were male. There was no significant differences in presence of MetS concerning gender.

Table II: Association between presence of MetS and Anthropometric profile of the patients(n=252)

Variable	Without MetS		With MetS		Total		P value
	N	%	n	%	N	%	
BMI, in kg/m^2							
Under weight (<18.5)	03	3.3%	01	0.6%	04	1.6%	<0.0001* (vhs)
Normal (18.5-22.9)	40	44.4%	32	19.8%	72	28.6%	
Over weight (≥23)	13	14.4%	35	21.6%	48	19%	
Obese (≥25)	34	37.8%	94	58%	128	50.8%	
Total	90	100%	162	100%	252	100%	
Mean ± SD	23.9081 ± 3.496		25.8837 ± 3.944		25.1781 ± 3.9		
Range	17.10-54.80						
Waist circumference (cm)							
Mean ± SD	90.277 ± 4.971		92.966 ± 7.079		92.006 ± 6.524		0.002# (hs)
Range	65.00-157.00						

SD = Standard deviation; BMI= Body mass index.

*=P-value was derived by chi-square test; ns= statistically non-significant.

#=P-value was derived by t-test; hs= statistically highly significant; vhs= statistically very highly significant.

Prevalence of obesity by different anthropometric tools is described in Table II. It shows that as per BMI cut off value for Asian, 19.0% patients were overweight and 50.8% were obese. There was very highly significant association between BMI and presence of MetS. Average mean ± SD waist circumference was 92.006 ± 6.524 cm. Waist circumference also had highly significant association with presence of MetS.

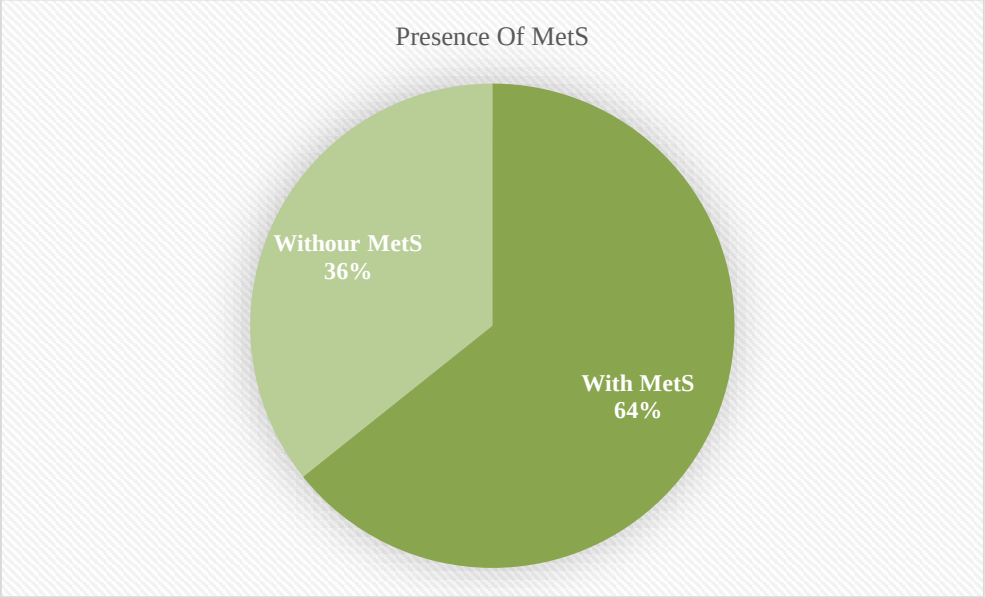

Figure-2: Distribution of MetS in the study population (n=252)

Pie diagram shows the distribution of MetS in study population and it depicts that, there was 64.3% with MetS and 35.7% without MetS.

Table III: Association between presence of MetS and risk factors (n= 252)

Variable	Without MetS		With MetS		Total		P value
	n	%	N	%	n	%	
HTN							
No	46	51.1%	30	18.5%	76	30.2%	<0.0001*
Yes	44	48.9%	132	81.5%	176	69.8%	(vhs)
Total	90	100%	162	100%	252	100%	
DM							
No	69	76.7%	83	51.2%	152	60.3%	
Yes	21	23.3%	79	48.8%	100	39.7%	<0.0001*
Total	90	100%	162	100%	252	100%	(vhs)
Dyslipidemia							
No	39	43.3%	51	31.5%	90	35.7%	
Yes	51	56.7%	111	68.5%	162	64.3%	0.060*
Total	90	100%	162	100%	252	100%	(ns)
Smoking							
No	44	48.9%	75	46.3%	119	47.2%	
Yes	46	51.1%	87	53.7%	133	52.8%	0.693*
Total	90	100%	162	100%	252	100%	(ns)

HTN= Hypertension; DM= Diabetes mellitus.

*=P-value was derived by chi-square test; ns= statistically non-significant; vhs= statistically very highly significant.

Table represents the univariate analysis of presence of MetS in comparison to risk factors. Hypertension and Diabetes mellitus showed very high significant with presence of MetS. No significant difference in presence of MetS among smoking and dyslipidemia were found in the present study.

Table IV: Association between lipid profile and FBS with presence of MetS (n=252)

Parameters	Without MetS Mean ± SD	With MetS Mean ± SD	Total Mean ± SD	P value
Fasting blood glucose (gm/dl)	82.644 ± 27.917	106.985 ± 28.443	98.292 ± 30.526	<0.0001#(vhs)
Range		14.80-216.00		
Total cholesterol (mg/dl)	181.1 ± 46.588	186.24 ± 46.215	184.40 ± 46.321	0.40#(ns)
Range		21.00-350.00		
LDL (mg/dl)	113.38 ± 43.233	116.49 ± 30.736	115.38 ± 35.65	0.55#(ns)
Range		40.00-393.00		
HDL (mg/dl)	42.43 ± 14.067	36.63 ± 9.906	38.70 ± 11.87	<0.0001#(vhs)

Range		21.00-149.00		
Triglyceride (mg/dl)	183.27 ± 110.345	241.86 ± 105.644	220.94 ± 110.76	<0.0001[#](vhs)
Range		40.00-891.00		

SD = Standard deviation; HDL= High density lipid; LDL= Low density lipid.
[#]=P-value was derived by t-test; vhs= statistically very highly significant; ns= statistically non-significant.

Association between presence of MetS and different biochemical variables are described in Table IV. It shows that, there was statistically very highly significant association were observed between presence of MetS and fasting blood sugar, triglyceride and HDL levels. In contrast, no significant association were found for presence of MetS, and total cholesterol and LDL levels.

Table V: CAG findings of the study population (n=252)

Parameter	Frequency	Percentage
Significant CAD		
No	46	18.3%
Yes	206	81.7%
Number of vessel involved		
No vessel involved	26	10.3%
Single vessel	81	32.1%
Double vessel	68	27.0%
Triple vessel	77	30.6%
Diagnosis		
UA	67	26.6%
NSTEMI	64	25.4%
STEMI	121	48.0%
Gensini score		
<20	64	25.4%
20-40	74	29.4%
>40	114	45.2%

CAD= Coronary artery disease; UA= Unstable angina; NSTEMI= Non ST elevated myocardial infarction; STEMI= ST elevated myocardial infarction.

Extent, diagnosis and severity of the CAD of the studied patients demonstrated by CAG is described in the Table V. It shows that, most of the patients had single and triple vessel disease, significant CAD, STEMI and gensini score >40.

Table VI: Association between presence of MetS and CAG findings of the patients (n=252)

Parameters	Without MetS		With MetS		Total		P value
	n	%	N	%	n	%	
Significant CAD							<0.0001[*] (vhs)
No	34	37.8%	12	7.4%	46	18.3%	
Yes	56	62.2%	150	92.6%	206	81.7%	
Total	90	100%	162	100%	252	100%	
Number of vessel involved							
No vessel involved	25	27.8%	1	0.6%	26	10.3%	<0.0001[*] (vhs)
Single vessel	35	38.9%	46	28.4%	81	32.1%	
Double vessel	19	21.1%	49	30.3%	68	27%	
Triple vessel	11	12.2%	66	40.7%	77	30.6%	
Total	90	100%	162	100%	252	100%	
Diagnosis							
UA	36	40%	31	19.1%	67	26.6%	0.001[*] (hs)
NSTEMI	23	25.6%	41	25.3%	64	25.4%	
STEMI	31	34.4%	90	55.6%	121	48%	
Total	90	100%	162	100%	252	100%	
Gensini score							
<20	47	52.2%	17	10.5%	64	25.4%	<0.0001[¥] (vhs)
≥20	43	47.8%	145	89.5%	188	74.6%	
Total	90	100%	162	100%	252	100%	

Mean ± SD	25.56 ± 24.468	49.76 ± 28.971	41.12 ± 29.759	
Range		0.00-141.00		

SD = Standard deviation; CAD= Coronary artery disease; UA= Unstable angina; NSTEMI= Non ST elevated myocardial infarction; STEMI= ST elevated myocardial infarction; ¥=P-value was derived by spearman correlation analysis; *=P-value was derived by chi-square test; hs= statistically highly significant; vhs= statistically very highly significant.

Association between presence of MetS with the angiographic severity, diagnosis and extent was described in the Table VI. It shows that, presence of MetS had very highly significant association with the extent, diagnosis and severity of CAD as assessed by the Gensini score.

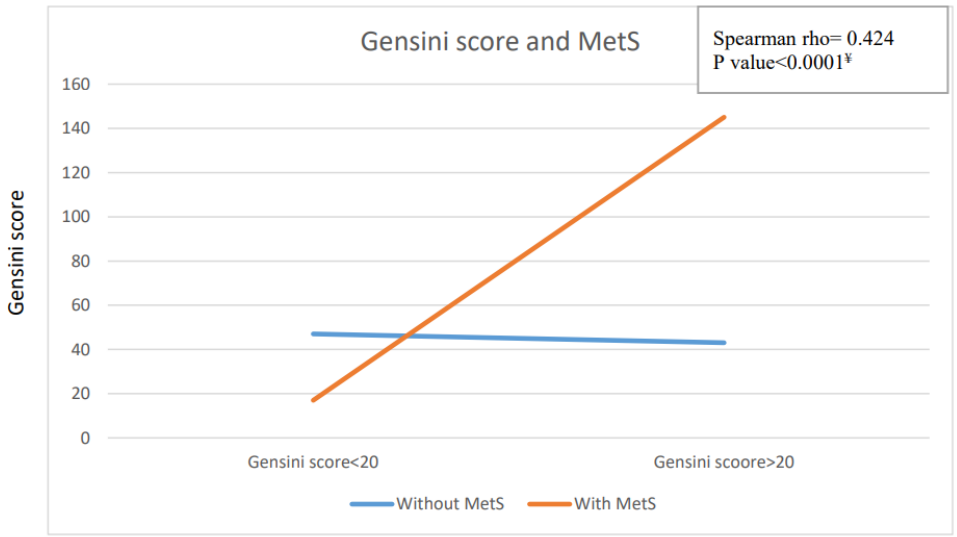

Figure-3: Correlation presence of MetS and Gensini score of the study patients (n=252)

Line diagram shows correlation between presence of MetS and Gensini score. Both the variables were positively correlated and the degree of association was very highly strong (Spearman rho 0.424; p<0.0001).

Table VII: Univariate association between demographic and risk factor variables and severity of CAD (N=252)

Variable	Severity of CAD		P value
	Gensini score <20(n=64)	Gensini score ≥20 (n=188)	
Age (in years)	50.08 ± 9.385	54.15 ± 10.782	0.005#(s)
Male gender	36 (56.3%)	145 (77.1%)	0.001*(hs)
Presence of HTN	39 (60.9%)	137 (72.9%)	0.072*(ns)
Presence of DM	15 (23.4%)	85 (45.2%)	0.002*(hs)
Smoker	26 (40.6%)	107 (56.9%)	0.024*(s)
Presence of dyslipidemia	33 (51.6%)	129 (68.6%)	0.014*(s)
BMI (kg/m^2)	25.69 ± 3.545	25.00 ± 4.007	0.220#(ns)
Waist circumference (cm)	91.77 ± 5.690	92.08 ± 6.797	0.716#(ns)

CAD= Coronary artery disease; HTN= Hypertension; DM= Diabetes mellitus; BMI=Body mass index; #=P-value derived by t-test. *=P-value was derived by chi-square test; s= statistically significant; ns= statistically non-significant; hs= statistically highly significant.

Table VII describes the association between different demographic and risk factors related variables of the patients with the severity of CAD. It shows that, there were highly significant association between gender and diabetes mellitus. Male gender, elderly patients, patients with DM, patients with dyslipidemia and smokers were more likely to had severe CAD in comparison to their counterpart. On the other hand HTN, BMI and waist circumference had no significant association with the severity of CAD.

Table VIII: Univariate association between biochemical parameters and severity of CAD (N=252)

Variable	Severity of CAD		P value
	Gensini score <20(n=64)	Gensini score ≥20(n=188)	
Fasting blood sugar (mg/dl)	89.05 ± 25.794	101.44 ± 31.422	0.002#(hs)
Total cholesterol (mg/dl)	185.36 ± 39.428	184.08 ± 48.538	0.833#(ns)
LDL (mg/dl)	109.64 ± 29.508	117.34 ± 37.383	0.096(ns)
HDL (mg/dl)	40.36 ± 9.622	38.14 ± 12.515	0.197#(ns)
Triglyceride (mg/dl)	196.50 ± 101.232	229.25 ± 112.871	0.032#(s)

CAD= Coronary artery disease; HDL= High density lipid; LDL= Low density lipid.
#=P-value was derived by t-test; s= statistically significant; hs= statistically highly significant; ns= statistically non-significant.

Table VIII describes the association between different biochemical parameters of the patients with the severity of CAD. It shows that, fasting blood sugar and triglyceride levels were significantly higher among the patients with severe CAD in comparison to their counterpart.

Table IX: Adjusted Odds Ratio for Risk of Patients having severe CAD by CAG (N=252)

Variable	Adjusted OR	95% CI	
		Lower	Upper
Elderly patients	1.24	0.49	3.13
Male gender	2.62	1.34	4.69
DM	2.69	1.41	5.14
Smoking	1.93	1.09	3.44
Dyslipidemia	2.05	1.51	3.67
Fasting blood sugar	2.07	1.16	3.67
Triglyceride	1.79	0.99	3.24
Metabolic syndrome	9.32	4.86	17.87

CI = Confidence interval; OR = Odds Ratio

To further evaluate the correlation between presence of MetS and severity of CAD a multivariate analysis was performed. Variables which were found to have significant association in univariate analysis were entered in the model (Table IX). Besides presence of MetS, male gender, history of DM, history of smoking, history of dyslipidemia and fasting blood sugar levels were also independenly associated with severity of CAD (Gensini score ≥20).

IV. Discussion

Numerous previous studies evaluating the relation between MetS and angiographic CAD have been limited because of the relative lack of clinical data about the patient from Bangladesh. In the present study, 252 patients were investigated who had been admitted for routine CAG for symptoms and signs consistent with a diagnosis of AMI (STMI, NSTMI and unstable angina). The purpose of the study was to evaluate the relationship of metabolic syndrome (MetS) with severity of coronary artery disease (CAD). It has been reported that MetS is a marker of cardiovascular disease risk, but not above and beyond the risk associated with its individual components.[21,22] Therefore, the number of markers of MetS may be more useful than MetS per se to predict the severity of CAD, and it has been used instead of a binary definition of MetS in several studies .[23,24] In this cross sectional study group of selected patients with AMI, the multivariate analysis revealed an independent association between MetS and severity of CAD. A number of scores have been described in the past for grading the severity of coronary artery disease on angiography like Gensini score, Jenkins score, syntax score and Friesinger score etc. The Gensini scoring system [25] was used in this study for assessing the coronary atherosclerotic disease burden. Gensini score was chosen because of its simplicity and widely accepted as aCAD burden marker and its prognostic value has been demonstrated in different clinical situations. The study population was divided into two groups depending upon the Gensini score, non-severe CAD (score <20) and severe CAD (score ≥20) group. In the present study, more than half of the patients (64.3%) showed presence of MetS(Figure-4). Adults with metabolic syndrome are twice as likely to die from and are three times as likely to have a heart attack or stroke compared with people without the metabolic syndrome (.[26,27,28,29] In addition, they have a five-fold greater risk of developing type 2 diabetes.[30] Similarly among 192 patients, 125 (65%) patients fulfilled the criteria of MetS.[31] A total of 327 (62%) patients had the MetS among 527 patients who underwent their first coronary angiography.[32,33] found 47% patient was with MetS. Of the 632 patients studied, 283 (44.8%) were diagnosed with MetS.[34] Coronary angiographic finding revealed that, most of the patients had single (32.1%) and triple (30.6%) vessel disease, significant CAD (81.7%), STEMI (48.0%) and gensini score >40 (45.2%) (Table-VI). Presence of MetS had very highly significant association with the extent, diagnosis and severity of

CAD as assessed by the Gensini score (Table-VI). MetS and Gensini score were positively correlated and the degree of association was very highly strong (Spearman rho 0.424; p<0.0001) (Figure-5). Similarly, [34] described that patients with MetS had severer CAD as assessed by the Gensini score compared to patients without MetS (23.3 ± 29.2 vs. 15.5 ± 23.4, p = 0.002). Metabolic syndrome was significantly (p<0.05) associated with CAD.[35] There was highly significant (p<0.001) and significant (p-0.004) association with acute coronary artery disease and Gensini score, with presence of MetS.[31,32] revealed the frequency of CAD and multi-vessel disease was higher in patients with the MetS compared with those without it (60% vs 32%, P < 0.001; 34% vs 16%, P < 0.001, respectively). Most of the study population (90.5%) was in the ≥40 years of age group. The average mean age of the patients was 53.12 ± 10.577 years (range: 30-80 years). Mean ± SD age was 51.89 ± 10.997 years in without MetS group and 53.80 ± 10.308 years in with MetS group. Mean ± SD age was 50.08 ± 9.385 years in <20 Gensini score group and 54.15 ± 10.782 years in ≥20 Gensini score group. No significant difference in presence of MetS among the age groups was found in the present study (Table-I). Elderly patients were more likely to had severe CAD. Similarly, MetS score was positively associated (p<0.001) with age.[32] There were no significant differences in age between the without MetS and with MetS groups. Mean ± SD age were 61.0 ± 10.8 years and 61.0 ± 10 years in without MetS and with MetS group respectively.[34] There was no difference in the mean age between without MetS and with MetS groups.[32] A Global case-control study of risk factors for cases of acute myocardial infarction reported that the mean age (51.9 years) for the occurrence of AMI among Bangladeshi population was the lowest amongst all South Asians and it was 6 years lower compared with non-South Asians (58.8 years).[36] Average mean ± SD age was 65.00 ± 11.00 years among the patients, reported by [37] but in their observation patients without MetS were significantly older than MetS group (P<0.001). The gender distribution of the study patients and it depicts that, there was male predominance, total 181 (71.8%) with male to female ratio about 2.55:1. In without MetS group, 71 (78.9%) were male and in with MetS group 110 (67.9%) were male. Number of male patient was 36 (56.3%) in <20 Gensini score group and 145 (77.1%) in ≥20 Gensini score group. There was no significant differences in presence of MetS concerning gender (Figure-3). But highly significant association was found between gender and severity of CAD (table-VII). The current study also showed a similar trend of sex ratio like those of [38] that out of 100 patients 56 (56 %) patients were male and 44(44%) patients were female. Male to female ratio was 1.27: 1. There was overall male predominance in the study done by.[33] There were no significant differences in sex between the without MetS and with MetS groups.[34] As per BMI cut off value for Asian present study shows, 19.0% patients were overweight and 50.8% were obese. Average mean ± SD BMI was 25.1781 ± 3.9 kg/m^2. There was very highly significant association between BMI and presence of MetS. Mean ± SD BMI were 25.69 ± 3.545 kg/m^2 and 25.00 ± 4.007 kg/m^2, in non-severe and severe CAD groups respectively. BMI had no significant association with the severity of CAD (Table-VII). Similar result found in the study conducted by [32] that was, mean ± SD BMI (kg/m²) were 23.7 ± 2.8 and 26.0 ± 2.9 in without MetS and with MetS groups respectively (p< 0.001). Mean ± SD BMI (kg/m2) were 24.2 ± 2.8 and 26.5 ± 2.6 in without MetS and with MetS groups. There was high association between BMI and presence of MetS (p< 0.001). [34] BMI (kg/m2) were 29.3 and 25.8, in with and without MetS respectively. [39] Average mean ± SD waist circumference was 92.006 ± 6.524 cm. In without MetS and with MetS groups mean ± SD waist circumference were 90.277 ± 4.971 and 92.966 ± 7.079 cm respectively. Waist circumference also had highly significant association with presence of MetS (Table-II). Mean ± SD were 91.77 ± 5.690 and 92.08 ± 6.797, in non-severe and severe CAD groups respectively. Waist circumference had no significant association with the severity of CAD.[32] found MetS score was positively associated with waist circumference (p<0.001). Mean ± SD waist circumference (cm) were 84.1 ± 8.5 and 92.7 ± 8.1 in without MetS and with MetS group respectively. Average mean ± SD waist circumference (cm) was 98.00 ± 11.00. Mean ± SD waist circumference (cm) were 102.0 ± 10.00 and 92.00 ± 9.00 in without MetS and with MetS groups. Waist circumference was significantly different in subjects with MetS compared to those free of MetS (P< 0.001). [37] Mean ± SD waist circumference (cm) were 97.7±8.9 and 88±9.6 in with MetS and without MetS groups with p <0.0001. [33] Average WC (cm) was 94.8 (13.4) with range 32-165 reported by. [39] Hypertension and Diabetes mellitus showed very high significant with presence of MetS. No significant difference in presence of MetS among smoking and dyslipidemia were found in the present study. Patients with DM, patients with dyslipidemia and smokers were more likely to had severe CAD. On the other hand HTN had no significant association with the severity of CAD (Table-III). Among patients with MetS, hypertension (HTN) (71%), and diabetes (DM) (56.8%) were positively associated (p<0.001).[37] About 52.5% were diagnosed with DM and 24.8% with HTN, the prevalence of HTN, and DM was significantly higher in the patients who met the MetS criteria.[40] Presence of MetS was significantly associated with HTN and DM with a p value <0.001.[32,34] Prevalence of dyslipidemia (%) was 28.7.[41] Smoking frequency (%) were 70 (35) and 106 (32) in without MetS and with MetS groups with no significant association (p-0.054).[32] Smoking frequency (%) were 151 (43%) and 131 (47%) in without MetS and with MetS groups with no significant association (0.401).[34] There was no statistical significant of smoking with MetS (p-0.9). Smoking frequency (%) was 71 (8.5%) and 12 (8.7%), in wit and without MetS groups. [39] Smoking habit was significantly (p=0.02) associated with CAD.[35] Regarding association of lipid profile and fasting blood sugar with presence of MetS,

there was statistically very highly significant association were observed between presence of MetS and fasting blood sugar, triglyceride and HDL levels. In contrast, no significant association were found for presence of MetS, and total cholesterol and LDL levels. The association between different biochemical parameters of the patients with the severity of CAD shows that, fasting blood sugar and triglyceride levels were significantly higher among the patients with severe CAD in comparison to other components (Table-IV). Similarly, the mean serum levels of FBG and cholesterol ($P < 0.001$), TG ($P < 0.0001$) and LDL-C ($P < 0.001$) in CAD patients with MetS were significantly higher, and HDL-C levels ($P < 0.001$) were significantly lower than in those without MetS.[42] Among patients with MetS, low HDL-C (95%) was the most frequent component followed by elevated FBS (76%), and elevated TG (39%). The frequency of MetS components in all the subjects was as follows: Low HDL-C (80%) and elevated TG (26%). Similar to the MetS group, low HDL-C was the most frequent finding (80%) in all the cases without MetS.[37] Lipid profile and fasting blood sugar levels showed significantly positive association with MetS.[34] Triglyceride, HDL and FBG showed highly significant ($p<0.001$) association while total cholesterol showed significant (p-0.013) with MetS. On the other hand LDL showed no significant association.[32] Multivariate analysis was performed to further evaluate the correlation between presence of MetS and severity of CAD. Besides presence of MetS, male gender, history of DM history of smoking, history of dyslipidemia and fasting blood sugar levels were also independenly associated with Gensini score ≥20 (severe CAD) (Table-VII). On multiple logistic regression analysis, the MetS, age, HTN, DM, smokings were independently associated with angiographic CAD.[32] After adjusting for sex, based on multivariable linear regression analysis, the high WC ($\beta = 0.63$, $P < 0.0001$), high BP ($\beta = 0.19$, $P < 0.05$), high FBG ($\beta = 0.14$, $P < 0.01$), high TG ($\beta = 0.19$, $P < 0.01$) and low HDL- C ($\beta = 0.20$, $P < 0.0001$) were found as significant predictors of MetS in CAD patients.[42] Although a diagnosis of MetS was associated with the CAD severity assessed by the Gensini score, MetS per se did not predict the presence of CAD. Individually, high FBG was the only predictive factor for CAD in univariate analysis OR 2.070, 95% CI 1.371-3.124, $p = 0.001$). Adjustment for other demographic features,LDL- C, and individual MetS constituents did not diminish this association (OR 1.973, 95% CI 1.297-3.000, $p = 0.002$). Low HDL-C, high BMI, high BP, and high TG were not predictive of CAD in univariate and multivariate analyses. High BP as a companion increased the OR significantly to 2.579. The other single trait of significance was low HDL-C. Among the triads the cluster with high BP and low HDL-C was the highest risk (OR 3.731). Among the quartets, only combinations including high BP and low HDL-C were associated with increased risk (OR 3.256 and 3.167). The OR for the quintet was not significantly increased (OR 1.769, 95% CI 0.572-5.471, p= 0.322). High FBG, high BP, and low HDL-C are significant contributors to CAD risk.[34] Clinically, this study might indicate that presence of MetS is a useful marker for predicting sever CHD and that more attention should be paid to MetS management in such patients. Clinical implications of the present study are that in the patients who had conventional cardiovascular risk factors with MetS, more severe CAD may be found, and the global cardiovascular risk may be increased. Thus, suggestion can be given that when assessing this risk in a CAD patient, presence of MetS should be considered. The identification of high risk in CAD patients might be useful in clinical practice, leading to more intensive treatment of modifiable cardiovascular risk factors and early and frequent diagnostic checks.

V. Conclusion

Positive association between presence of metabolic syndrome and CAD was found in this study. Metabolic syndrome is strongly related to the severity of ACS presentation, documented clinically and angiographically. The predictive abilityof metabolic syndrome for CAD can be used for early management. In conclusion, the findings of this study approve the effectiveness of evaluation of metabolic syndrome to predict the severity of coronary artery disease. It was also disclosed that detection of metabolic syndrome should be performed in patients with CAD before other invasive procedures. Further multicenter study on large number of population selected randomly can ensure the generalization of the result.

VI. Limitations

This study results should be interpreted considering the following limitations:

- Single centered study.
- Randomization was not done, which might be subjected to selection bias.
- Patients with acute coronary syndrome was the study population. So, the results may not be applied to the common healthy people.
- Data collection period was short, so accuracy of result may be insufficient.

VII. Recommendations

Detection of metabolic syndrome can be recommended as substitute of coronary angiography at low resource setting to predict the severity of the coronary artery disease that can be performed. So the relationship of metabolic syndrome to severity of CAD has been revealed solely by cross-sectional statistical associations.

Prospective studies of prophylactic intervention may be recommended with large sample size, long duration, multicenter design, evaluation of lifestyle and metabolic syndrome components, utilizing complete Gensini score and other angiographic scores.

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