Original Article

Metabolic Syndrome: Its Association with Acute ST-Elevation Myocardial Infarction and Its Clinical Outcome – A Study Done in the Tertiary Level Hospital in Bangladesh

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Abstract:

Background: Metabolic syndrome is a matter of immense public health concern. Based on ethnicity, its association and impact on ischemic heart diseases like myocardial infarction (MI) is a current topic of research. Objective: To evaluate the clinical impact of metabolic syndrome on patients with acute ST-elevation myocardial infarction (acute STEMI) in a Bangladeshi population. Methods: This prospective observational study was done in the Department of Cardiology of the National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, from July to December of 2013. A total 233 patient were selected for data collection; 109 were in group I (acute STEMI patients with metabolic syndrome), while 124 werein group II (acute STEMI patients without metabolic syndrome). Initial evaluation of the patients done by history and clinical examination was recorded in the preformed data collection sheet.Baseline investigations like ECG, CK(MB), lipid profile, fasting blood sugar, serum creatinine andechocardiography were done. Coronary angiogram (CAG) was done in the Cardiac Cath-Lab facility of the same hospital. The patients' outcomes were observed until they were discharged from the hospital. Results: Heart failure was significantly more in patients of group I than group II (46.79% vs. 20.97%; p<0.001). Among the patients who underwent coronary angiogram (CAG), the mean Friesinger score was 9.7±2.5 in group I and 7.1±3.3 in group II, which was statistically significant (p<0.05), and indicated more chances of severe coronary artery disease in group I patients. However, mortality rate was not statistically significant in between group I and group II (16.51% vs 12.09%; p=0.415). Both in heart failure and coronary artery disease, among all the components of metabolic syndrome, hyperglycemia had the strongest association followed by low HDL and high triglyceride (TG). However, raised BP had much less significant association with development of heart failure or coronary artery disease. Conclusion: Our data suggest that the acute ST-elevation myocardial infarction patients with metabolic syndrome have poor disease prognosis and in-hospital outcome than those without metabolic syndrome. However, the use of a simple risk score based on those biomarkers may identify a high-risk group to initiate preventive measures for cardiovascular health of the country's population.

Keywords: Myocardial infarction, metabolic syndrome, cardiovascular disease, clinical outcome.

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Introduction

The South Asian countries like India, Pakistan, Bangladesh, Sri Lanka and Nepal contribute to the highest proportion of the burden of the cardiovascular diseases (CVDs) compared to any other region¹⁻³. Estimates from the 'global burden of diseases study' suggests that by end of 2020, this part of the world will have more individuals with atherosclerotic cardiovascular disease than any other region⁴. The concept of metabolic syndrome

has been existing for near about 100 years intermingled with atherosclerotic cardiovascular disease⁵⁻⁷. The concept of the metabolic syndrome as a cluster of cardiovascular risk factors occurring in association with insulin resistance was brought to the wider scientific community in the American Diabetic Association (ADA) Scientific Sessions in 1988, through an informative lecture given by Reaven⁵. The frequent simultaneous presence of obesity, hyperlipidemia, diabetes mellitus and

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hypertension were first described in the late 60s, and subsequently highlighted in the late 70s by many researchers who coined the term "metabolic syndrome" and described its association with atherosclerosis^{6,7}. Today metabolic syndrome is a matter of immense public health concern for its atherosclerotic presentation. The syndrome may affect more than 50% of the elderly in the United States and even higher percentages in various ethnic groups around the world7. Metabolic syndrome is already one of the major public health problems around the world, which may be grievous when associated with any cardiac emergency like myocardial infarction (MI)^{4,7}. Its diagnosis is simple, mainly by using clinical information and biochemical tests which are available in any health care system. Several researcheshave been done in the Western countries to see the clinical behavior of metabolic syndrome in patients of acute ST-Elevation Myocardial Infarction(STEMI). However, there are only few reports in the literature in our country. Hence, the present study aims to see the clinical impact of metabolic syndrome on patients with acute STEMI in terms of disease prognosis and clinical outcome.

Methods

This prospective observational study was done in the Department of Cardiology of the National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, which is one of the largest specialized tertiary level cardiovascular treatment facility of the country. It was done between July and December of 2013. The study population were the patients with acute STEMI, with metabolic syndrome (group I) and without metabolic syndrome (groupII), who were admitted in NICVD Hospital into that period of time. We adopted the Convenience Sampling technique. The sample size determined was at least 95 sample in each group. Sample size was determined by the formula for estimating the difference between the twopopulation proportions with level of significance 5% and power 80% for one-sided test.

Inclusion criteria:

Group I:

 Acute STEMI (the diagnosis of acute ST-Elevation Myocardial Infarction was done according to the 'third universal definition of myocardial infarction')⁸ patients admitted into the hospital within 12 hours of onset of chest discomfort,

- 2) Who fulfilled the criteria of 'International Diabetic Federation (IDF) definition of metabolic syndrome'9, and
- 3) Received streptokinase therapy after admission.

Group II:

- 1) Acute STEMI patients admitted into the hospital within 12 hours of onset of chest discomfort,
- 2) Having no evidence of metabolic syndrome, and
- 3) Received streptokinase therapy.

Exclusion criteria:

- 1) Acute STEMI patients who arrived >12 hours of onset of chest discomfort,
- 2) History of previous myocardial infarction (MI),
- 3) History of Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG),
- 4) Patients having cardiomyopathy, congenital heart disease, or valvular heart disease,
- 5) Patients with acute infections, neoplastic disease, chronic renal insufficiency and other severe chronic diseases.

Data collection was done after taking written informed consent from each patient or from his/ her legal guardian who fulfilled the criteria. Total 233 patient were selected for data collection; in group I, 109 and in group II, 124 patients were included. Initial evaluation of the patients done by history and clinical examination was recorded in the preformed data collection sheet. Demographic profile, pulse, blood pressure, body weight, waist circumference and ECG report at emergency room were recorded. Risk factors like history of hypertension, smoking, dyslipidemia, diabetes mellitus and obesity were also noted. Detailed drug history was taken. Those who were previously hypertensive and taking antihypertensive drugswere counted as hypertensive patients. For the rest the highest blood pressure value on the second and third day were also taken for the record. Baseline investigations like ECG (done by the Fukuda Denshi-FX-2111 EKG Machine, made in Japan), CK(MB), lipid profile, fasting blood sugar, serum creatinine andechocardiography (done by the GE Vivid S5 Ultrasound Machine, made in USA)were done. Besides, patients who were taking lipid lowering agent were counted

as dyslipidemic. Fasting lipid profile on the next morning after admission was taken for highdensity lipoproteins (HDL) and triglyceride (TG). Serum level of triglyceride and HDL was measured by enzymatic method, while LDL cholesterol was measured by Friedewald formula. Previously diagnosed type II diabetic patients were counted as patients with raised fasting glucose. For the rest, the fasting blood glucose was done on the next morning. Fasting blood glucose was measured by enzymatic method. All the blood samples were analyzed within 2 hours of collection. Coronary angiogram (CAG) was done in the Cardiac Cath-Lab facility of the same hospital. For the patients undergone coronary angiogram, their angiographic severity of coronary artery disease assessment was done by using 'Friesinger score' 10. We also observed the patients' outcome until discharge from the hospital.Data was analyzed by using SPSS (Statistical Package for Social Science) version 16.0.Comparison between groups was doneby unpaired t-test, while categorical data was analyzed with Chi-square (χ 2) test.

Results

The mean age of the patients in group I was 54.59±10.44 and that of group II was 53.24±9.40 years. There was no statistically significant mean age difference (p>0.05), as shown in Table 1. Both group I and group II havealmost similar sex distribution (male-67.80% vs. 68.54%; female-32.11% vs. 31.45%). The common risk factors for ischemic heart disease (IHD) at admissionwere shown in Figure 1.It was found that 34.86% of the patients in group I were hypertensive in contrast to 25.8% of those in group II. Diabetes mellitus was found 41.28% in group I and 14.51% in group II. Besides, 22.01% and 16.93% patients were dyslipidemic in group I and group II respectively. 51.37% of group I and 58.06% of group II were current smoker/had history of smoking. Family history of cardiovascular disease was present in 19.26% and 16.12% in group I and group II respectively. All common risk factors were statistically nonsignificant (p>0.05), except diabetes (p=0.007). The mean waist circumference in male patients was 96±4.9 cm in group I and 84±5.6 cm in group II, and in female patients was 84±3.5 cm and 74±5.5 cm respectively. Differences of waist circumference were statistically significant between group I and group II in both males and

females(p<0.01), as shown in Table 2.It was also observed that high level of triglycerides (TG) was the most frequently present metabolic syndrome components in group I followed by a lowlevel of high-density lipoproteins(HDL), hyperglycemia and raised blood pressure (BP). High TG (>150 mg%) was more evident in group I thangroup II (88.07% vs. 68.55%;p<0.001). Group Ipatients also had low HDL (<40mg% in male, <50mg% in female) than group II patients (86.23% vs. 66.13%; p<0.001). Similarly, group I patients were more hyperglycaemic (fasting serum glucose \geq 5.6mmol/L) than that of group II (62.38% vs. 40.32%; p<0.001). Raised blood pressure (≥130/85mmHg) was more evident in group I, too (51.37% vs. 27.41%; p<0.01) (Table 3).

As we observed the clinical consequences of the patient as shown in Table 4, the incidence of heart failure (as described by Hasdai et al.)11was significantly more in patients of group I than those of group II (46.79% vs. 20.97%; p<0.001). Among the heart failure patients 62.33% was male and 37.67% was female, whereas among no heart failure patients 71.15% was male and 28.85% was female. Heart failure was more among females than males(39.18 vs 30.19%; p=0.024).A total of 112 patients underwent coronary angiogram (CAG), 53 from group I and 59 from group II. The mean Friesinger score of those patients were 9.7±2.5 and 7.1±3.3 in group I and II respectively, and the difference was ultimately statistically significant (p<0.05). It indicated more chances of severe coronary artery disease in group I patients. It was also found that the mortality was 16.51% in group I and 12.09% in group II, which was not statistically significant (p=0.415).

We tried to find the association of metabolic syndrome with those outcomes of the patients. Table 5shows thathyperglycemia had the strongest association in development of heart failure in those patients, followed by low level ofhigh-density lipoproteins (HDL) and high triglyceride (TG). However, raised blood pressure had much less significant association with development of heart failure. Similarly, in Table 6, hyperglycemia showed the strongest association for development of significant coronary artery disease, followed by low HDL and high TG. However, raised blood pressure had much less significant association in this event as well.

Table 1. Distribution of the patients by age (n=233).

A :	Group I		GROUP II		P value
Age in years	n	%	n	%	
30 – 39	14	12.84	14	11.24	$^{\rm a}0.654^{\rm NS}$
40 - 49	26	23.85	36	29.03	$^{a}0.134\mathrm{^{NS}}$
50 – 59	29	26.60	31	25.0	$^{\rm a}0.966^{\rm NS}$
60 - 69	32	29.35	35	28.22	$^{\mathrm{a}}0.755^{\mathrm{NS}}$
> 69	8	07.33	8	06.45	$^{\mathrm{a}}0.553^{\mathrm{NS}}$
Total	109	100.0	124	100.0	
Mean±SD	54.59±1	0.44	53.24±9.4	10	^b 0.550 ^{NS}

Group I: Patients with metabolic syndrome; Group II: Patients without metabolic syndrome;

NS=Non-significant; a: p value determined by χ^2 test; b: p value determined by unpaired t-test.

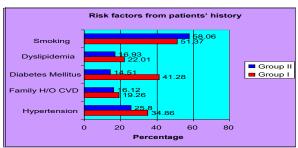


Figure 1: Distribution of common risk factors of Ischemic Heart Disease (IHD) (n=233).

Table 2.Mean waist circumference (n=233).

Waist circumference (cm)	Group I	Group II	P value
Male	96±4.9	84±5.6	0.002**
Female	84±3.5	74±5.5	0.003**

** = Significant at the level of p<0.01; p value was determined by unpaired t-test.

Table 3.Distribution of components of metabolic syndrome (n=233).

Components	Group I		Group II		n 1
of metabolic syndrome	n	%	n	%	- P value
Hyperglycemia	68	62.38	50	40.32	0.0001***
Raised blood pressure	56	51.37	34	27.41	0.007**
High TG	96	88.07	85	68.55	0.0001***
Low HDL	94	86.23	82	66.13	0.0001***

NS = Non-significant; * = Significant at the level of p<0.05;** = Significant at the level of p<0.01; *** = Significant at the level of p<0.001; p value was determined by χ^2 test.

Table 4. Clinical outcome of the patients (n=233).

Clinical outcome	Group I		Group II		P Value
_	n	%	n	%	_
Death	18	16.51	15	12.09	a0.415 ^{NS}
Heart failure	51	46.79	26	20.97	a0.001***
MeanFriesinger score	53	9.7±2.5	59	7.1±3.3	^b 0.036*

NS = Non-significant; ***= Significant at the level of p<0.001; ** = Significant at the level of p<0.01; * = Significant at the level of p<0.05; a: p value reached from $\chi 2$ test test; b: p value reached from Unpaired t-test.

Table 5. Association between components of metabolic syndromes and heart failure.

Components of metabolic syndrome	Risk ratio (RR)	95% CI
Hyperglycemia	4.88	2.71-8.78
Low HDL	1.76	1.16-2.67
High Triglyceride	1.46	1.06-2.47
Raised blood pressure	1.36	0.84-2.20

Table 6. Association between components of metabolic syndromes and coronary artery disease.

Component of metabolic syndrome	Risk ratio (RR)	95% CI
Hyperglycemia	3.16	0.63-15.56
Low HDL	2.83	0.12-3.56
High Triglyceride	1.37	1.67-2.98
Raised blood pressure	1.12	0.76-8.20

Discussion

Metabolic syndrome is associated with an increased risk of cardiovascular disease¹². Of all the acute STEMI patients with discomfort in the chest <12 hours duration admitted in Coronary Care Unit (CCU) of NICVD, Dhaka, Bangladesh, from July to December of 2013, a total of 233 were included in this study. Among them, 109 patients with metabolic syndrome were taken as group I, while the other 124 patients without metabolic syndrome were taken as group II. Patients were included in this study by convenience sampling technique after considering all the inclusion and exclusion criteria.

There was no significant difference of age and sex distribution among the group I and group II. The mean age of group I and group II patients

were 54.59±10.44 years and 53.24±9.40 years respectively. Zaher et al.¹³ found the mean age in similar patients 49.85±9.89 years in Bangladeshi population, which supports the findings of the present study. Male-female ratio was 2.15:1. Group I and II have almost similar sex distribution (male-67.80% VS. 68.54%; female-32.11% vs. 31.45%) without any statistical difference. However, this result is discordant to the findings of Zaher et al.¹³, where the sex ratios were 8.04:1. Among the components of metabolic syndrome, hyperglycemia was found to have the strongest association for development of heart failure in our study, followed by low HDL and high triglyceride. However, raised BP has much less significant association here. Hyperglycemia was also found to be the strongest associated factor for development of heart failure in the study conducted by Zeller et al.14, followed by low HDL and high TG respectively. Triglycerides in blood became an associated factor for heart failure which may be explained by the genetic abnormalities for TG regulation that was found in the Asian Indian population as described by Deedwania& Singh¹⁵ and Lee et al. 16 Several studies have shown that high prevalence of small dense low density lipoprotein (LDL), together with the increased triglyceride (TG) and decreased HDL levels, forms the "atherogenic lipoprotein phenotype", a potent risk factor for coronary heart disease (CHD), are prevalent in South Asian and may partly explain the excess CAD risk in this population¹⁵. The lipid profile of our study is also consistent with the general South Asian profile. The study done by Bhopal et al.¹⁷ revealed similar findings in South Asians. Even in a study conducted on European population by Zeller et al.14 found that 80% of the acute MI patients with metabolic syndrome had low HDL and 57% had high TG in comparison to non-metabolic syndrome patients (i.e. 22% and 14% respectively).

We found that heart failure was much more in patients with metabolic syndrome than the other group (46.79% vs. 20.97%; p<0.001). It was also evident in previous study that metabolic syndrome itself is an independent predictor of heart failure in men >50 years, as studied by Ingelsson et al. 18, in large population of 2314 with a long term follow

up of 20 years. Heart failure group had more patients in the range of 11-15 (55% vs. 45%).Luz et al.¹⁹ observed Friesinger score 0 in 19.0%, score 1-4 was 17.9%, score 5-10 was 36.1% and score 11-15 was 27.0% in suspected cases of coronary artery disease. In contrast, Bampi et al.20 found Friesinger score 0 in 37.0%, score 1-4 was 07.0%, score 5-10 was 32.0% and score 11-15 was 24.0% in their study patients. The findings of Luz et al.¹⁹ and Bampi et al.²⁰ more or less support our study results. In hospital mortality, one of the primary clinical outcomes of this study, was similar in group I and group II, though the patients with metabolic syndrome had a trend to have more mortality (16.51% vs. 12.09%; p= 0.415). This may be significant with larger sample size. A sample size more than 541 is needed to provide such evidence. Zeller et al.14 found an initial significantly high mortality among the patients with acute MI and metabolic syndrome(10.7% vs. 3.8%; p<0.001). But after evaluating the effect of confounder by multivariate analysis, metabolic syndrome did not remain an independent predictor in hospital mortality. However, they concluded that there is a high prevalence of metabolic syndrome among patients with acute MI and highlights the detrimental impact of metabolic syndrome on short-term outcomes, particularly heart failure. Post-hoc analysis of GISSI-Prevenzione Trial database (reported by Levantesi et al.)21 revealed that patients of metabolic syndromewith history of MI has increased mortality in long term (42 months) follow up in comparison to those without metabolic syndrome (8.5% vs.7.4%; p=0.002).

Limitations of the study

As the sample size was small and the study subjects were selected purposively, it is difficult to generalize the findings to the reference population. Actual prevalence of metabolic syndrome in acute STEMI could not be detected as all consecutive patientswere not evaluated. Limited follow up of the patients was done and long term follow up was avoided due to time constraint of the study. All the patients of the study were not available for coronary angiogram due to financial problems and some patients refused to undergo the procedure and few died before the procedure. Evaluation of the angiography was evaluated by

the visual estimation, so there might be chances of inter observer and intra observer variation in interpretation of the severity of the arterial stenosis.

Conclusion

Our data suggests that the acute ST-elevation myocardial infarction patients with metabolic syndrome have poor disease prognosis and inhospital outcome than those without metabolic syndrome. However, the use of a simple risk score based on those biomarkers may identify a highrisk group (vulnerable to cardiovascular disease or emergency) to initiate preventive measures for cardiovascular health of the country's population.

Conflict of interest: The authors declare no conflict of interest.

Ethical approval issue: The study was approved by the Ethics Review Committee of Bangladesh College of Physicians and Surgeons (BCPS), Dhaka, Bangladesh.

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