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The Effect of Metabolic Syndrome and its Components on Long Term Outcome in Patients with Cardiovascular Disease in Bangladesh

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Abstract **Original Research Article**

Background: The "Metabolic Syndrome" (MetS), a clustering of risk factors including abdominal obesity, poor glucose tolerance, hypertriglyceridemia, decreased high density lipoprotein (HDL) cholesterol, and/or hypertension. Cardiovascular disease (CVD) is the cause of 46.2% of non-communicable disease mortality, attracting attention on a global scale. One of the key reasons for early mortality and disability is CVD. According to the National Health and Nutritional Examination Survey (NHANES), approximately 30% of overweight and 60% of obese men and women are diagnosed with MetS. People with CVD have a greater rate of MetS than patients without the condition. ***Objective:*** The aim of the study is to assess the effect of Metabolic Syndrome and its components on long term outcome in patients with cardiovascular disease in Bangladesh. ***Methods:*** The study consisted of 415 persons who were aged between 35-84 years, during June 2020–May 2022. Data were collected through interview, clinical examination, and laboratory tests, and their survival status until April 2022 was ascertained. We defined MetS following the NCEP ATP III criteria, with minor modifications, i.e., presence of any three of the following: hypertension (BP ≥130/85 mm Hg); random blood glucose (RBG) level ≥7.0 mmol/L; hyper-triglyceridemia (≥2.28 mmol/L); low level of HDL-cholesterol (<1.04 mmol/L for men and <1.29 mmol/L for women); and BMI ≥25.0 kg/m2. Data were analysed with logistic regressions for the influential factors of MetS, and with Cox models for the association of MetS with the survival status. ***Results:*** MetSwas found in 137 (33.1%) participants and were older (57.9 ± 13.0) and primarily male (60.6%).Participants with MetS showed a greater prevalence of diabetes, hypertension, hypercholesterolemia, and overall worse management of risk variables at baseline, as predicted. The most common feature across all patients was raised fasting blood glucose (93.4%), followed by blood pressure (91.2%), elevated waist circumference (81.8%), elevated triglycerides (44.5%), and lowered HDL- cholesterol (27.7%).MetS was linked to an increased risk of a major cardiovascular event after numerous adjustments, with an OR of 1.18 (1.10–1.45). Furthermore, an increased risk of a severe cardiovascular incident was associated with elevated blood pressure, low HDL cholesterol, and raised triglycerides. ***Conclusion:*** After controlling for several possible confounders, it was discovered that MetS was independently linked with the incidence of CVD and death from CVD but not with myocardial infarction or TG. All of the study's outcomes were independently linked to specific MetS components in magnitudes comparable to those of the MetS itself. Additional study should look on the relationships between other MetS characteristic combinations and cardiovascular outcomes.

Keywords: Cardiovascular disease, metabolic syndrome.

INTRODUCTION

The connection between visceral obesity, hypertension, and atherosclerosis was established in 1765 by Joannes Baptista Morgagni in his seminal book 'De sedibus et causismorborum per anatomenindagatum' [1]. In the early 1920s, Hitzenberger, Richter-Quitner, and Kylin conducted more research on the co-occurrence of metabolic disorders such as hyperglycemia, hypertension, and other diseases such as

hyperuricaemia [2]. The "Metabolic Syndrome" (MetS), a clustering of risk factors including abdominal obesity, poor glucose tolerance, hypertriglyceridemia, decreased high density lipoprotein (HDL) cholesterol, and/or hypertension, was established as a result of these pioneering investigations [3, 4]. Insulin resistance played a key part in the initial conception of this disease, and it is obvious that this is a contemporaneous and linked trait. Traditional cardiovascular disease risk variables have been incorporated as the defining characteristics as the MetS has more recently been emphasized as an epidemiologic tool connected to cardiovascular disease risk. It is widely acknowledged that these co-morbidities represent a pathological state that significantly increases risk for the development of type 2 diabetes mellitus and atherosclerotic cardiovascular disease, even though the exact definition of what clinically constitutes the MetS has caused considerable debate [5].

Cardiovascular disease (CVD) is the cause of 46.2% of non-communicable disease mortality, attracting attention on a global scale [6]. One of the key reasons for early mortality and disability is CVD. According to the National Health and Nutritional Examination Survey (NHANES), approximately 30% of overweight and 60% of obese men and women are diagnosed with MetS [7]. In other words, the majority of obese people have a combination of risk factors that indicate an increased risk of cardiovascular disease. As a result, the MetS pandemic, which affects 20% of individuals in the Western world, is expanding concurrently with the obesity epidemic [8]. A vast range of vascular and cardiac diseases are produced by the MetS, each of which is a distinct risk factor for CVD [9]. In the following 5 to 10 years, patients with MetS are more likely than those without MetS to develop CVD, and the long-term risk is significantly greater [4]. MetS was also regarded as the second primary aim for CVD prevention according to the Adult Treatment Panel (ATP) III guidelines of the National Cholesterol Education Program (NCEP) [10].

People with CVD have a greater rate of MetS than patients without the condition. In hospitalized patients with acute myocardial infarction (AMI), the prevalence of MetS is 46%, which is comparable to the prevalence of acute coronary syndrome (43.4%) which showed that Mets is associated with CVD [11]. However, several researches have shown that MetS does not affect the mortality rate of CVD patients [12]. As a results, there are still controversy.

A study analyzed the prevalence of cardiovascular disease (CVD) in the adult population of Bangladesh using information from the available scientific literature. This research revealed that among Bangladeshi people, metropolitan regions had a higher weighted pooled prevalence of total CVD (8%) than rural regions (4%). Significant CVD prevalence and an upward trend were observed in the adult population of Bangladesh [13]. Another study was done to investigate the risk factors where a little over 30% of individuals had high blood pressure, 5% had diabetes, 20% were obese, 77% smoked or used smokeless tobacco, and 28% were physically inactive. The research showed that Bangladesh has a high incidence of CVD and that its risk factors, such as diabetes and hypertension, are on the increase, particularly among older people, women, and high-income groups [14].

MetS is a condition caused by several variables, and the primary diagnostic signs (components) include blood pressure, overweight and obesity, HDL-C, and fasting blood glucose [15]. Prevalence of Mets among Bangladeshi patients is 3-37% [16, 17]. However, no study was conducted in association with the metabolic syndrome effect on CVD patients.

OBJECTIVE

The aim of the study is to assess the effect of Metabolic Syndrome and its components on long term outcome in patients with cardiovascular disease in Bangladesh.

METHODS AND MATERIALS

The current research includes data on cohort participants with up to three years of follow-up. The cohort was established to evaluate the incidence of cardiovascular risk factors and metabolic syndrome, their correlation with indicators of subclinical atherosclerosis, and their influence on health outcomes among Bangladeshi patients attending Sheikh Hasina Medical College, Jamalpur. 588 individuals constituted a representative sample for the research (aged 35– 84 years). Minimum age (35 years) and outpatient and inpatients at attending Sheikh Hasina Medical College were requirements for study participation. Participants who had passed away and those who did not respond to repeated attempts at contact were eliminated from the research. Participant recruiting occurred between June and December of 2020. After application of inclusion and exclusion criteria, a total of 415 participants consented to the research and were monitored until April 2022. All individuals gave written informed permission and additional access to their medical records.

For the current investigation, we eliminated persons with significant CVD at baseline, including prevalent myocardial infarction and stroke, individuals who were lost to follow-up and COVID-19-positive patients.

MetS is defined according to the criteria outlined in the Third Report of the National Cholesterol Education Program Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in

Adults (NCEP ATP III) [18]. The NCEP ATP III requirements include at least three of the following elements: (1) fasting plasma glucose level of at least 110 mg/dL (6.1 mmol/L); (2) serum triglyceride level of at least 150 mg/dL (1.7 mmol/l) for men; (3) serum high-density lipoprotein (HDL) cholesterol level of at least 40 mg/dL (1.04 mmol/L) for men and at least 50 mg/dL (1.29 mmol/L) for women; (4) Blood Pressure of at least 130/85 mm Hg or controlled with antihypertensive treatment; and/or (5) waist circumference of more than 102 cm (Adult Treatment Plan III 2001). The NCEP ATP III definition does not define the presence of a specific component and suggests that if a person has many risk factors, even if they are not particularly severe individually, their combined effect may nevertheless significantly raise the risk of coronary heart disease.

MetS is characterized in this research as having any three of the following: 1) high blood glucose 7.0 mmol/L; 2) hypertriglyceridemia (triglyceride level 2.28 mmol/L); 3) low HDL cholesterol level (<1.04 mmol/L for men and <1.29 mmol/L for women); 4) BMI≥ 25.0 kg/m2; and 5) hypertension (systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg).

The primary outcome of the study was a combination of myocardial infarction, stroke, and cardiovascular- related death. Secondary outcomes were myocardial infarction, stroke, cardiovascular mortality, and all-cause death. Deaths from cardiovascular causes included ischemic heart disease, heart failure, sudden cardiac death, stroke, peripheral vascular disease, and other cardiovascular causes.

Statistical Analysis

For continuous variables, descriptive analyses included mean and standard deviations (SD). Prevalence and frequency are indicated as percentages. The chi-square statistic was used to compare categorical variables. Logistic regression was performed to investigate MetS-related variables. The Kaplan-Meyer survival analysis was used to investigate the link between MetS and its various components and survival for up to five years. In addition, the Cox model was used to calculate the hazard ratio for MetS mortality. All analyses were carried out with the help of the statistical program SPSS Statistics version 23 for Windows.

RESULTS

Table 1 displayed the baseline characteristics of study participants (n=415) based on the NCEP ATP III diagnosis of metabolic syndrome. MetS was found in 137 (33.1%) of the participants (overall 50.6% of males and 49.4% of women). People with MetS were older (57.9 ± 13.0) and primarily male (60.6%) as compared to participants without MetS. Participants with MetS showed a greater prevalence of diabetes, hypertension, hypercholesterolemia, and overall worse management of risk variables at baseline, as predicted. The most common feature across all patients was raised fasting blood glucose (93.4%), followed by blood pressure (91.2%), elevated waist circumference (81.8%), elevated triglycerides (44.5%), and lowered HDL-cholesterol (27.7%).

Table 1: Baseline characteristics of study participants, according to the definition of metabolic syndrome in the (NCEP ATP III) n=415

Characteristics	No MetS n=278	MetS n=137	P value
Age, year	55.2 ± 12.9	57.9 ± 13.0	0.002
Sex Male Female	 127(45.6%) 151 (54.3%)	 83 (60.6%) 54 (39.4%)	 <0.001
BMI	24.3 ± 2.2	28.3 ± 2.9	<0.001
Risk factors			
Weight, kg	71 ± 10.1	80 ± 12.9	<0.002
Waist circumference, cm	82 ± 10	109 ± 17	
BP Systolic BP, mm HG Diastolic BP, mmHG	 125 ± 18 73 ± 9	 147 ± 13 89 ± 10	 0.000
Fasting blood glucose, m/dL	90 ± 14	119 ± 29	0.002
Total cholesterol, mg/dL	199 ± 29	230 ± 41	0.002
LDL cholesterol, mg/dL	127 ± 36	134± 37	0.000
HDL cholesterol, mg/dL	66 ± 19	59 ± 17	0.003
TG, mg/dL	92 ± 41	150 ± 121	<0.001
CVD			
Diabetes	39 (14.1%)	72 (52.6%)	0.001
Hypertension	77 (27.7%)	58 (42.3%)	<0.002
Hypercholesteremia	98 (35.3%)	101 (73.7%)	0.003

Heart failure	27 (9.7%)	19 (13.9%)	0.002
MetS trait			
Elevated waist circumference	119(42.8%)	112 (81.8%)	0.000
Elevate BP	105 (37.8%)	125 (91.2%)	0.000
Elevate FBG	31 (11.2%)	128 (93.4%)	0.000
Reduced HDL-cholestrol	18 (6.5%)	38 (27.7%)	<0.002
Elevated TG	21 (7.6%)	61 (44.5%)	<0.001

MetSwas linked to an increased risk of a major cardiovascular event after numerous adjustments, with an OR of 1.18 (1.10–1.45). Furthermore, an increased risk of a severe cardiovascular incident was associated with elevated blood pressure, low HDL cholesterol, and raised triglycerides. MetS was not linked to a greater risk of myocardial infarction but was substantially related with a higher mortality from cardiovascular disease 0.89 (95% CI, 0.56-1.42) for secondary endpoint events. Additionally, elevated tg is not linked to an increased risk of CVD mortality. Table 2 displays the full outcomes of the relationship for the primary and secondary endpoints.

Table 2: Association cardiovascular events with metabolic syndrome and its components

MetS traits	**Cardiovascular events OR (CI 95%)**			
	Primary outcome	**Secondary outcome**		
	MI, Stroke, mortality from CVD	**MI**	**Stroke**	**Mortality**
Metabolic syndrome	*1.18 (1.10–1.45)*	1.10 (0.68–1.79)	1.23 (1.02, 1.58)	0.89 (0.56–1.42)
Elevated waist circumference	*1.32 (1.01–1.74)*	1.15 (1.09–1.82)	1.16 (0.76–1.76)	*1.64 (1.03–2.60)*
Elevated blood pressure	*1.45 (1.17–1.80*	1.26 (0.72–2.21)	0.90 (0.50–1.61)	1.22 (0.99–1.51)
Elevated fasting blood glucose	*1.68 (1.01–2.78)*	1.37 (1.02–1.83)	1.37 (1.02–1.83)	*1.42 (1.06–1.92)*
Reduced HDL-cholesterol	*1.67 (1.04–2.66)*	*1.76 (1.09–2.84)*	*1.35 (1.07–1.70)*	*1.38 (1.02–1.85)*
Elevated triglyceride	-1.13 (− 8.20, 5.94)	1.34 (0.82–2.20)	*1.63 (1.12–2.35)*	1.22 (0.99–1.51)

DISCUSSION

In the cohort research of 415 middle-aged adult participants with a 3-year follow-up, our goal was to prospectively explore the prevalence and risk estimations of MetS and its components with major cardiovascular events. After adjusting for many factors, we discovered that MetS was linked to a greater incidence of the study's primary outcome, a composite of myocardial infarction, stroke, and cardiovascular-related death. Additionally, higher CVD was linked to equal magnitudes of increased blood pressure, decreased HDL cholesterol, and raised triglycerides, suggesting that MetS was not above the level explained by the existence of its individual components.

We discovered a strong correlation between the incidence of major CVD and MetS. The strength of the connection was less than the twofold rise in risk that was reported in the greatest meta-analyses of metabolic syndrome and cardiovascular risk. Additionally significant correlations for myocardial infarction, stroke, CVD mortality, and all- cause death were identified by the authors in this meta-analysis [19]. Our results are consistent with other research, which found a weak or nonexistent relationship between MetS and CVD outcomes [12, 20, 21].

In our study, the prevalence of MetS was 33.1%; however, prior data from other studies indicated a lower prevalence, e.g., the Botnia study in Finland and Sweden found a prevalence of 22.6% [22] and the Risk Factors and Life Expectancy Study (RIFLE) study in Italy found a prevalence of 12% [23]. Depending on the criteria used to define the MetS, varying prevalence rates have been reported in recent research from developing nations. Depending on sex, the prevalence of MetS in Iran was estimated to range between 24 and 30 percent using NCEP criteria [24].

In our study, participants with MetS showed a greater prevalence of diabetes, hypertension, hypercholesterolemia, and overall worse management of risk variables at baseline, as predicted. The most common feature across all patients was raised fasting blood glucose (93.4%), followed by blood pressure (91.2%), elevated waist circumference (81.8%), elevated triglycerides (44.5%), and lowered HDL-cholesterol (27.7%).

There is evidence that Asian Indians have low HDL [25, 26], and >90% of Asian Indians have low levels of HDL 2b, the most protective component of HDL [27]. In a group of hypertensive women aged 20–79 years from Bangladesh, the prevalence of low HDL cholesterol was greater than 90 percent [28]. 65% of Bangladeshi rural women aged 18 and older, according to a separate research [29], had poor HDL cholesterol levels. Bangladeshis have the highest frequency of low HDL (52%) among South Asians, almost double that of Pakistanis (30%) and three times that of Indians (17%). In an African group of individuals with MetS, the prevalence of dyslipidemia (TG >150 mg% or HDL cholesterol 40 mg %) was 92% [30].

The economic and social implications of this burden will be substantial, especially considering that many developing nations continue to struggle with ailments connected to poverty, such as malnutrition, infectious diseases, and inadequate health care facilities. Desirable is the identification of MetS warning indicators, which would provide early education and intervention among these individuals. Additional prospective long-term studies are necessary to discover the MetS components that more accurately predict who would acquire type 2 diabetes and/or cardiovascular disease.

CONCLUSION

After controlling for several possible confounders, it was discovered that MetS was independently linked with the incidence of CVD and death from CVD but not with myocardial infarction or TG. All of the study's outcomes were independently linked to specific MetS components in magnitudes comparable to those of the MetS itself. Additional study should look on the relationships between other MetS characteristic combinations and cardiovascular outcomes.

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