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Metabolic syndrome and cardiovascular risk in diabetic subjects

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Summary
There are divergent criteria for the identification of metabolic syndrome (MetS), but all the definitions agree that obesity, insulin resistance, dyslipidemia and hypertension are core components of this syndrome. The MetS is associated with an increased risk of cardiovascular disease events in general populations. Well-designed prospective studies in Asian populations are very limited. This study characterizes nine parameters of the MetS in a population of diabetic patients without a history of cardiovascular disease in Bangladesh, and defines the influence of MetS on peripheral vascular disease. A total of 100 patients with diabetes who visited the outpatient department of BIRDEM for routine diabetic follow-up were included in this study. The prevalence of MetS was 66%. Sixty-seven percent of patients had a waist circumference above normal, 89% hypertriglyceridemia, and 87% a low HDL-C level, while elevated systolic blood pressure was found in 46% and diastolic blood pressure in 55%, according to IDF criteria. Peripheral vascular disease defined by a low ankle-brachial index (<0.9) was identified in 24% of patients with no history of a cardiovascular event.

Introduction

Metabolic syndrome

The metabolic syndrome (MetS) is a clustering of metabolic abnormalities that have been associated with an increased risk of coronary heart disease, stroke, and cardiovascular mortality compared to the presence of an individual component. Metabolic abnormalities associated with MetS include obesity, microalbuminuria, and abnormalities in fibrinolysis and coagulation.

The prevalence of the metabolic syndrome has varied markedly between different studies, most likely because of the lack of accepted criteria for the definition of MetS [1]. Insulin resistance and central obesity are significant risk factors contributing to the underlying cause of MetS.

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The three most important widely recognized recent attempts to define the metabolic syndrome include the WHO report from 1991 [2], The European Group for the study of Insulin Resistance (EGIR) in 1999, and the US National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) in 2001.

More recently, the American College of Endocrinology (ACE) released a position statement on what it refers to as the insulin resistance syndrome [3], and in 2005 the International Diabetes Federation (IDF) [4] published new criteria for identifying persons with metabolic syndrome. The new IDF definition addresses both clinical and research needs, providing an accessible, diagnostic tool suitable for worldwide use [5].

Metabolic syndrome and cardiovascular risk

Each criterion of the MetS is related to an increased risk of developing cardiovascular disease (CVD). Metabolically several risk factors tend to cluster in middle-aged adults, including elevated levels of high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides, blood glucose, body mass index (BMI), and systolic blood pressure.

Some risk factors are related to a greater risk of coronary heart disease (CHD). The presence of three or more metabolic risk factors leads to a 2-fold increased risk for CHD in men and a 5-fold increased risk for women [5]. The prevalence of metabolic syndrome depends on age, ethnic background, and sex [6]. The Atherosclerosis Risk in Communities Study revealed that a parental history of diabetes and a parental history of hypertension were associated with the development of MetS, and a parental history of both diabetes and hypertension was associated with a further increased risk of MetS [7].

The metabolic syndrome is associated with an increased risk of cardiovascular disease events in general populations. Timely lifestyle and dietary interventions could decelerate the progression of diabetes and the various components of MetS, reduce the rate of development of cardiovascular complications, and reduce the costs associated with treatment and rehabilitation. However, well-designed prospective studies in Asian populations are very limited.

Metabolic syndrome and peripheral vascular disease

The prevalence of peripheral vascular disease (PVD) is increased in persons with the metabolic syndrome [8]. Assessment of peripheral pulses and measurement of the ankle–brachial index (ABI) are tools for evaluating PVD. The ABI, the ratio of the ankle-to-brachial systolic blood pressure, is the gold standard for the diagnosis of peripheral vascular disease and is a highly specific method for the assessment of vascular risk in otherwise asymptomatic patients. The measurement of ABI by palpation in the setting of primary care in patients at intermediate cardiovascular risk is a sufficiently sensitive method to consider its use as a screening test for the exclusion of PAD [9]. In the present study, we measured ABI using palpation to diagnose PVD, because handheld Doppler was not available. An ABI in the range of $\geqslant$0.91 to $\leqslant$1.30 is considered normal, and an ABI $\leqslant$0.90 identifies the presence of PVD [10].

Objectives

The primary objective of the present study was to determine the prevalence of the key parameters of the metabolic syndrome in a population of Bangladeshi patients with diabetes and no history of CVD. The secondary objective was to determine whether the metabolic syndrome influences the presence of peripheral vascular disease in this population.

Material and methods

This study was conducted in the Outpatient Medical Department at the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) in Dhaka, Bangladesh. The study protocol was approved by the Ethical Review Committee of BIRDEM.

Inclusion criteria: Consecutive patients with diabetes between the ages of 40 and 80 years visiting the clinic for routine follow-up, and no history of a cardiac event or intervention.
Exclusion criteria: Patients >80 years old, prior history of a cardiac event or intervention, pregnancy, and comorbid diseases.

Study patients

Using convenience sampling, 100 patients visiting the clinic for routine follow-up of their diabetes were interviewed and examined. Each study patient was examined and completed a questionnaire regarding their medical history, family history of cardiovascular disease, treatment for hypertension or diabetes, physical activity and exercise, smoking habits, and alcohol intake. Each patient was briefed about the study and informed consent was obtained.

Clinical examination

In the present study, the IDF criteria were used to define the presence of the metabolic syndrome. Parameters measured at baseline include height, weight, BMI, and waist circumference. Blood pressure was measured using a standard sphygmomanometer with the patient in the supine position after resting for at least 5 min. The palpated peripheral vessels were the arteria dorsalis pedis (ADP), posterior tibial artery (PTA), and femoral artery.

Ankle systolic blood pressure was measured by palpation. ABI was measured manually, because handheld Doppler was not available in our tertiary care hospital. The arteria dorsalis pedis was localized and palpated. A standard sphygmomanometer was placed around the ankle and the systolic blood pressure was recorded using auscultation. This ankle systolic blood pressure was divided by the brachial systolic pressure to determine the ABI. An ABI $\leqslant$0.90 was considered abnormal.

Table 1.1 Clinical characteristics of study patients.

Socio-demographic variables	*N* = 100 (%)
Women	47 (47%)
Men	53 (53%)
Age (years)	
Mean (±SD)	51.30 (±9.29)
Smoker (no.)	17 (17%)
Alcohol (no.)	1 (1%)
Family history cardiovascular event	16 (16%)

Table 1.2 Clinical and biochemical characteristics of study patients.

Anthropometric and biochemical parameters	*N* = 100 (mean ± SD)
BMI (kg/m^2)	24.20 ± 3.01
Waist circumference (cm)	89.68 ± 7.18
FPG (mmol/L)	8.12 ± 2.53
TG (mg/dL)	244.84 ± 10.19
Total cholesterol (mg/dL)	202.64 ± 36.66
LDL-C (mg/dL)	126.86 ± 25.51
HDL-C (mg/dL)	36.75 ± 5.09
Diastolic BP (mmHg)	80.65 ± 7.37
Systolic BP (mmHg)	127.25 ± 15.59

BMI, body mass index; FPG, fasting plasma glucose; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; and BP, blood pressure.

Results

Clinical and biochemical characteristics of study patients

The mean age of the patients was 51.3 years, and 47% were women (Tables 1.1 and 1.2). Of the 100 study patients, 17% were smokers and 1% consumed alcohol. A family history of a cardiovascular disease event was present in 16% of patients. The mean BMI was 24.20 kg/m^2. The mean fasting plasma glucose was 8.12 mmol/L, and the mean waist circumference was 89.68 cm.

Regarding the lipid profile, the mean values were triglycerides 244.84 mg/dL, total cholesterol 202.64 mg/dL, low-density lipoprotein cholesterol (LDL-C) 126.86 mg/dL, and HDL-C 36.75 mg/dL. The mean systolic and diastolic blood pressures were 127 mmHg and 81 mmHg, respectively.

The metabolic syndrome: characteristics of criteria and diagnosis

Among the study patients, 67% had a waist circumference above normal (>80 cm for women and >90 cm for men), 89% had hypertriglyceridemia, 87% had low HDL-C, and 46% and 55% had elevated systolic and diastolic blood pressures, respectively (Table 2). All patients had elevated fasting plasma glucose; all had been diagnosed before study entry as having either impaired glucose tolerance, impaired fasting glucose, or diabetes.

Using the IDF criteria, 66% of the study patients were determined to have the metabolic syndrome. The age-adjusted prevalence using the IDF criteria was 43.4% of study patients, 34% of whom were over 50 years old. The age-adjusted prevalence of NCEP ATP III defined MetS was 24.5% in the present study. This is very close to the age-adjusted prevalence of MetS in US adults (24%), based on the NCEP ATP III and WHO definitions.

Peripheral vascular disease in study patients

All study patients were screened for peripheral vascular disease, by examining peripheral pulses and measuring the ABI. Patients in whom a peripheral pulse was absent or the ABI could not be measured were categorized as having an abnormal ABI (<0.9). An abnormal ABI was found in 24% of the study patients (Table 3).

Discussion

The concept of the metabolic syndrome conferring increased risk of incident type 2 diabetes and cardiovascular disease has been around for more than a couple of decades. It is reasonable to consider that identifying the presence of the MetS based on standard criteria, resulting in action by the clinician and patient to reduce risk factor levels, will likely lead to improved outcomes, to an extent similar to that if a more refined estimate of future disease probability had been made.

A primary observation regarding the clustering of metabolic disorders is the association with increased cardiovascular risk. It is well established that multiple risk factors confer greater risk than a single risk factor. The more components of MetS that are present the greater the cardiovascular risk [11]. In the present study, the most commonly increased risk factors are an above-normal waist circumference, hypertriglyceridemia, and low HDL-C.

The metabolic abnormalities of MetS and diabetes are associated with atherosclerosis, including coronary artery calcification [12], and involvement of other peripheral vessels. A large cohort study found that a low ankle-brachial index was associated with an increased risk of cardiovascular events and mortality [13]. In the present study, 24% of patients, who had no history of a cardiovascular event, had peripheral vascular disease as defined by an ankle—brachial index less than 0.9. Because of the small number of patients in this study diagnosed with peripheral vascular disease, no statistically significant association with cardiovascular disease was found.

Table 2 Characteristics of the metabolic syndrome parameters in among study patients.

Total no.	Waist circumference above normal	Hypertriglyceridemia	Dysglycemia or raised fasting glucose	Elevated systolic blood pressure	Elevated diastolic blood pressure	Low HDL-C
100	67%	89%	100%	46%	55%	87%

Table 3 Ankle—brachial index in study patients.

Ankle—brachial index	Frequency	Percent
>0.9	76	76
<0.9	24	24
Total (n)	100	100

It is reasonable to consider that the prevalence of peripheral vascular disease may have been higher if measured more accurately using a Doppler study, compared to the manual measurement used in this study. Also to be considered is that it is known that the ABI may be falsely raised in diabetic patients who have severe disease in smaller arteries (communication accessed at http://www.simond-odds.com/Arterial/Investigations/ABPI_FAQ.htm).

Conclusion

This study provides some insights into the prevalence of the various parameters of the metabolic syndrome in Bangladeshi patients with diabetes, and the prevalence of peripheral vascular disease. An above-normal waist circumference, hypertriglyceridemia, and low HDL-C were the most prevalent risk factors for the metabolic syndrome in this population. Further, the presence of the metabolic syndrome did not influence the occurrence of peripheral vascular disease. The prevalence of the metabolic syndrome was high as defined by the IDF criteria, even on age-adjusted basis, and was similar to the prevalence in the United States on age-adjusted basis using the NCEP ATP III and WHO definitions. In patients with diabetes, effective strategies to reduce central obesity, dyslipidemia, and hypertension could reduce the prevalence of the metabolic syndrome and thereby reduce the occurrence of cardiovascular events.

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