Prevalence and Clinical Characteristics of Metabolic Syndrome among Malaysian Hypertensive Subjects using the International Diabetes Federation Definition

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ABSTRACT

Individuals with metabolic syndrome are at increased risk for developing cardiovascular disease and diabetes mellitus. This study was carried out to determine the prevalence of metabolic syndrome and clinical characteristics in hypertensive patients according to the criteria of the new International Diabetes Federation (IDF) definition. Hypertensive patients were recruited from the Medical Out-Patient Department, Kuantan Hospital. The five components of metabolic syndrome were examined which included blood pressure (≥130/85 mmHg), fasting glucose (≥5.6mmol/L), fasting triglycerides (≥1.7 mmol/L), high-density lipoprotein (HDL) cholesterol level (<1.03mmol/L in males and <1.29mmol/L in females), and abdominal obesity (waist circumference: men>90cm; women>80cm). Out of 139 hypertensive patients, there were 113 met all the selection criteria consisted of 61 male and 52 female subjects. The participants' age ranged from 21 to 91 years (51.9±16.8 years; mean±SD), and body mass index 13.5-42.3 kg/m^2 (27.5±4.9 kg/m^2). According to the IDF criteria, the prevalence of central obesity was 67.2% in men and 84.6% in women. Among the 113 hypertensive subjects over 21 years of age, 51 subjects or 45.1% had metabolic syndrome. The present data revealed that there was high prevalence of metabolic syndrome in Malaysian hypertensive subjects. This finding was supported by the fact of high prevalence of central obesity among the study subjects.

KEYWORDS: clinical characteristics, prevalence, metabolic syndrome, hypertension

INTRODUCTION

The metabolic syndrome (MetS) is a cluster of 3 out of five of the following medical conditions abdominal (central) obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density cholesterol (HDL) levels.[1-4] MetS is also a disorder of energy utilization and storage, and demonstrated in combination of comorbid diseases in the same patients. Patients with MetS are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.[4,5] It is also associated with increased risk of developing cardiovascular disease (CVD), particularly heart failure and diabetes.

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There are various definitions and criteria used for identifying individuals with MetS which includes the definition by the World Health Organisation (WHO), National Cholesterol Education Program-Third Adult Treatment Panel (NCEP ATP III) and the International Diabetes Federation (IDF).[6-8] In 2005, the IDF formulated a new, clinically accessible worldwide definition of the MetS in a global consensus statement built on earlier definitions.[8,9] It is estimated that around a quarter of the world's population have MetS.[10] Some studies have shown the prevalence in the USA to be an estimated 34% of the adult population[11] and the prevalence increases with age. The fact that MetS is quite prevalence, it has been observed in many ethnic groups worldwide, including Malaysia.[12-17]

CVD as the major contributor towards this non communicable diseases epidemic is of global health concern. Similarly in Malaysia, in the National Health and Morbidity Survey (2006),[18] it was found that CVD is the leading cause of mortality in both genders.[19] As for hypertension, it has recognized as one of the major risk factors of CVD. It confers an increased risk of cardiovascular-related death.[20, 21] This risk is more pronounced when the MetS itself is

present among hypertensive patients. The prevalence of hypertension according to the new criteria of blood pressure (BP) (BP>140/90 mmHg) varies between 15-35% in urban adult populations of Asia.[22] In Malaysia, the prevalence of hypertension amongst adults were 14% in a small survey in 1980s,[23] and 14.4%, 33%, 42.6%, 32.7% and 30.3% in nationwide surveys in 1986, 1996, 2006, 2011 and 2015, respectively.[24-28] This indicates that the prevalence of hypertension has rapidly increased in Malaysia in the past 30 years.

Risk factors of CVD such as dyslipidemia, diabetes, and obesity are found more commonly in association with hypertension than normotension. Multiple sources have revealed the increased prevalence of these risk factors in patients with hypertension, with varying degrees of certainty and uniformity.[29-31] The clinical importance lies in the fact that a hypertensive patient is likely to have not only hypertension, but also many other risk factors. Factors associated with an increased risk of developing CVD that tend to cluster in individuals include older age, high blood pressure, a low level of HDL, a high triglyceride level, a high plasma glucose concentration and obesity.[32]

This is also the case in the Malaysian adult population.[26,33-35] Based on the reports, there is a high possibility that the MetS is potentially prevalence in hypertensive subjects. To date, there were several reports on the prevalence of MetS among Malaysian adult population.[16,17]

However, there is no specific data on prevalence and clinical characteristics of MetS among hypertensive patients. The fact that understanding patient's clinical background is essential, further evaluation on comorbid diseases certainly would benefit medical practitioners in clinical and therapeutic management. Given the recognized global epidemic of hypertension, it is valuable and timely to assess the prevalence and clinical characteristics of MetS in the Malaysian population among hypertensive subjects.

MATERIALS AND METHODS

Study Population

A cross-sectional study was carried out among hypertensive patients who attended the Out-Patient Department and Medical-Out Patient Department, Kuantan General Hospital, Pahang, Malaysia from 2005 till 2007. Eligible subjects were: (1) Aged more than 21 years old; (2) Seated systolic blood pressure (SBP)^3 140 mmHg and/or seated diastolic blood pressure (DBP)^3 90mmHg; (3) Newly diagnosed, untreated, or treated hypertension; (4) Hypertension with or without other diseases; and (5) Stable body weight over the past 3 months.

Study Procedures

The study was conducted according to the declaration of Helsinki. The protocol was approved by the Ethical Committee of the Kulliyyah of Medicine, International Islamic University Malaysia (IIUM), Kuantan Pahang Malaysia. All participants were required to submit written informed consent form prior to the study. This study comprised two visits: First visit for the screening purposes and followed by blood sampling in the second visit. During the first visit, the subjects underwent a physical examination with full medical history and had a series of baseline measurements including blood pressure, heart rate, height, weight, systemic examination, and electrocardiography.

Subjects who met the selection criteria were subsequently reviewed in the following visit. In the second visit, they were requested to fast overnight (after 2200 h) for the purpose of blood sampling. For treated hypertensive subjects who were on antihypertensive drugs or on other drugs, they were requested to take the medication(s) after the blood sampling. Blood sampling was performed after the above assessment was completed.

Blood Pressure Measurements

Blood pressure was recorded by using an automated sphygmomanometer TM-2551p (Vital sensor product of A&D Company, Limited). Each participant was seated in a chair with his/her back supported. Three readings were taken 1 minute apart in the seated position after being rested for at least 10 minutes. The initial reading was disregarded and the last 2 readings were averaged. Patients were asked to refrain from smoking or ingesting caffeine during the 30 minutes preceding the measurement. Blood pressure was measured consistently with the same arm in the both visits. A standard cuff with a bladder size 12 to 13 cm by 35 cm was used. A larger bladder size was used for larger arms.

Laboratory Measurements

All patients were required to fast overnight before the blood sampling procedure. For biochemistry measurements, heparinized plasma was the sample of choice. Five ml of blood were drawn and put into vacutainer (heparin) tubes. The samples were stored on ice between the time of sampling and centrifugation. The samples were centrifuged on the same day within 2 to 4 hours after the blood sampling. Freshly taken samples were centrifuged at 5000 rpm at 4^{o}C.

The plasma fraction was separated and transferred into a labeled test tube for analysis. All plasma samples were stored at 2^{o}C to 8^{o}C and stabilized for 14 days, or stored at -20^{o}C and stabilized for 6 months. Serum blood glucose was determined by the glucose hexokinase method (Bayer diagnostic glucose (HK) reagent with the express plus clinical chemistry

analyzer). Lipid profile includes total cholesterol, triglyceride, high density lipoprotein cholesterol (HDL) and low density lipoprotein cholesterol (LDL) were measured by using enzyme calorimetric end point technique on spectrophotometer (Bayer Express Plus, Germany)

Metabolic Syndrome Criteria

In this study, the IDF criteria was used for a person to be defined as having the MetS.[7] They must have:

(1) Central obesity defined as waist circumference ≥ 90 cm for South-Asian men and ≥ 80cm for South-Asian women;
(2) Plus any two of the following four factors:
(a)raised fasting triglyceride level (≥ 1.7 mmol/L or ≥ 150mg/dL), or specific treatment for this lipid abnormality;
(b)reduced high density lipoprotein cholesterol (HDL) level (<1.03mmol/L in males and < 1.29mmol/L in females), or specific treatment for this lipid abnormality;
(c)raised blood pressure: SBP ≥ 130 or DBP ≥ 85 mmHg, or treatment of previously diagnosed hypertension; (d) raised fasting plasma glucose (≥ 5.6mmol or ≥ 100 mg/dL) or previously diagnosed type 2 diabetes mellitus.

Statistical Analysis

Descriptive summaries were used to analyze the characteristics of study subjects. All data were presented as means±standard deviation (± SD). The normality of the distribution of all variables was assessed by the Kolmogorov-Smirnov test.

The differences between two groups in continuous data which had a normal distribution were evaluated by Student's t test; for continuous variables which had a skewed distribution, Mann-Whitney U test was used. Pearson's correlation coefficients were used to calculate correlations between parameters. Statistical significance was defined as a two-tailed P value < 0.05. The SPSS version 11.0 software was used for the data analysis.

RESULTS

In the period of 15 months, 139 hypertensive patients (73 males, 66 females) were recruited. Out of 139 hypertensive patients, only 113 met all the selection criteria which consisted of 61 male and 52 female subjects.

The patients' age ranged from 21 to 91 years old (52.0±16.8 years; mean+SD), and body mass index ranged from 13.5 to 42.3 kg/m^2 (27.5±5.0 kg/m^2). The detail of clinical characteristics and biochemical profiles of the study participants are as shown in Table I.

Table I: Clinical characteristics and biochemical values of study subjects

Variable	Mean ± SD
Total subjects	113
Male : Female	61:52
Race Malay:Chinese:Indian	85:24:4
Age (years)	52.0 ± 16.8
Height (m)	1.61 ± 0.08
Weight (kg)	71.08 ± 15.08
BMI (kgm^{-2})	27.5 ± 5.0
Waist circumference (cm)	92.8 ± 11.9
Duration of hypertension (month)	92.1 ± 91.5
SBP (mmHg)	145.3 ± 20.2
DBP(mmHg)	90.7 ± 8.8
Heart rate (beats/minute)	75.7 ± 6.8
Glucose (mmol/L)	6.52 ± 2.81
Total cholesterol (mmol/L)	5.77 ± 1.22
HDL cholesterol (mmol/L)	1.44 ± 0.55
LDL cholesterol (mmol/L)	3.39 ± 1.00
Triglyceride (mmol/L)	1.85 ± 1.12
Creatinine (μmol/L)	111.81 ± 42.08
Uric acid (μmol/L)	387.8 ± 109.7

According to the IDF criteria, the prevalence of central obesity among hypertensive patients was 76.1% (86 out of 113 patients) which includes 48.9% in men and 51.1% in women.

Out of 86 hypertensive patients with obesity, only 51 patients or 45.1% had MetS involving 24 men (47.1%) and 27 women (52.9%). Waist circumference, triglyceride and fasting glucose levels were significantly higher in patient with MetS (P<0.001 for waist circumference; P<0.05 for triglyceride and fasting glucose levels). Other variables were found to be not significantly different between the two groups (P>0.05).

The detail of clinical and metabolic characteristics of the study subjects with and without MetS is as shown in Table II. Among hypertensive subjects who have no MetS, 36 out of 62 had no other diseases (58.1%). The remaining 26 hypertensive subjects had at least one or more other diseases.

Whereas, among hypertensive subjects with positive MetS, 21 out of 51 had no other diseases (41.1%). The remaining 30 hypertensive subjects had at least one combination with other diseases (Table II).

Table II: Clinical and metabolic characteristics of the subjects with and without Metabolic syndrome

Variable	Negative MetS (n=62)	Positive MetS (n=51)
Sex (Male:Female)	37:25	24:27
Age (years)	52.7 ± 17.0	51.1 ± 16.6
Height (m)	1.61 ± 0.08	1.61 ± 0.08
Weight (kg)	69.0 ± 15.3	73.7 ± 14.5
BMI (kgm^{-2})	26.8 ± 5.2	28.4 ± 4.6
Waist circumference (cm)	88.8 ± 11.2	97.6 ± 10.9**
Duration of hypertension (month)	97.7 ± 88.5	85.4 ± 95.5
SBP (mmHg)	144.3 ± 20.6	146.4 ± 20.0
DBP(mmHg)	90.4 ± 8.1	91.0 ± 9.7
Heart rate (beats/minute)	76.4 ± 6.6	74.8 ± 7.0
Glucose (mmol/L)	5.76 ± 1.94	7.45 ± 3.39*
Total Cholesterol (mmol/L)	5.63 ± 1.21	5.94 ± 1.22
HDL Cholesterol (mmol/L)	1.46 ± 0.54	1.42 ± 0.57
LDL Cholesterol (mmol/L)	3.33 ± 0.99	3.46 ± 1.23
Triglyceride (mmol/L)	1.57 ± 1.02	2.20 ± 1.14*
Creatinine (µmol/L)	113.68 ± 49.89	109.63 ± 30.98
Uric Acid (µmol/L)	392.6 ± 94.1	382.5 ± 125.8
Diagnosis:		
Hypertension alone	36	21
Hypertension with 1 disease[a]	15	19
Hypertension with 2 diseases[a]	10	9
Hypertension with 3 diseases[a]	1	2

[a] Other diseases include ischaemic heart disease, diabetes mellitus, hyperlipidemia, gout
* P < 0.05
** P < 0.001

The co-morbid diseases found among study participants include ischaemic heart disease, diabetes mellitus, hyperlipidemia, and gout. In terms of prevalence of MetS in different age group of hypertensive patients, there were 56%, 40%, and 44.7%, in less than 40 years old, 40 to 60 years old, and more than 60 years old, respectively (Table III).

Table III: Prevalence of hypertensive patients with and without Metabolic Syndrome by gender and age group

		Without Metabolic Syndrome, n (%)	With Metabolic Syndrome, n (%)
Total hypertensive patients		62 (54.9)	51 (45.1)
Gender	Male	37	24
	Female	25	27
Age	< 40	11 (44.0)	14 (56.0)
	40 - 60	30 (60.0)	20 (40.0)
	> 60	21 (55.3)	17 (44.7)

DISCUSSION

In the present study the new IDF criteria was used as the definition to identify hypertensive patient with MetS. We found that there were 45.1% (51 study subjects) of hypertensive subjects over 21 years of age had MetS. This is consistent with previous reports from earlier studies in other parts of the world.[36-38] The high prevalence of MetS in this study is supported by the fact that the prevalence of central obesity among hypertensive patients were significantly high, which was 76.1% (86 out of 113 patients). This may suggest that individuals with hypertension tend to have more clustering of other metabolic abnormalities than the general population. Consistent with previous studies involving local populations, the prevalence of overweight and obesity continued to increase from 4.4% in 1996 to 14.0% in 2006 and further increased to 19.5% in 2011.[39,40,41] In the latest National Heath and Morbidity Survey (NHMS), these prevalence of overweight and obesity were reported to be 27.2% and 30.6%, in 2011 and 2015, respectively.[27,28] The WHO and IDF definitions of MetS both include abdominal or central obesity.[5,7] According to the new IDF definition, it needs to be first identified among the study patients. It takes into account the mounting evidence that abdominal adiposity is common to each of the components of the MetS. Thus, an increased waist circumference is well accepted proxy measurement for abdominal adiposity and it is a necessary requirement for the diagnosis of the MetS. This indicates that though the pathogenesis of the MetS and its components is complex, abdominal obesity is a key causative factor.

The MetS was introduced as a diagnostic category to identify individuals that satisfy three of five relatively arbitrarily chosen criteria. The aim is to initiate lifestyle changes with the goal of decreasing risk of CVD[42] and to improve patient management. In the present study, hypertensive patients with positive MetS are warrant to be treated vigorously and to be followed up more frequently. This is

based on the fact that they are more prone to develop CVD than those without MetS. Its primary goal is not to make a diagnosis but to increase understanding of why a hypertensive patient with positive MetS is prone to develop more complications than those without MetS. It appears that making the diagnosis of the MetS does not bring with it much in the way of pathophysiologic understanding had contributed to it.[42]

It is worth to mention here that the primary value of the concept of insulin resistance is merely related to pathophysiology of those abnormalities. Insulin resistant or hyperinsulinemic individuals are at greatly increased risk of being glucose intolerant, with a dyslipidemia characterized by a high plasma triglyceride and low HDL concentration, and an increase in blood pressure. Insulin resistance is also the major determinant of CVD in overweight or obese individuals.[43]

Obesity itself is known to promote insulin resistance, although not all insulin-resistant individuals are overweight. In addition to the importance of obesity in the MetS definition criteria, we should remember that patients of normal weight can also be insulin resistance. In the present study, the common abnormalities showed by the participants defined by IDF were high glucose and triglyceride levels among hypertensive patients with MetS. These findings were profoundly in agreement with the underlying pathophysiology that constitutes a diagnosis of MetS. Moreover, insulin resistance is the central feature that accounts for all of the component of different version of the MetS and a predisposition to multiple diseases.[1,44]

There are some concerns in using these criteria for diagnosing MetS. A central obesity is most easily measured by waist circumference using the guidelines in IDF criteria which are gender and ethnic-group specific. Therefore, it is strongly recommended that for epidemiological studies and, example for case detection, ethnic group specific cut-points should be used for people of the same ethnic group. Thus, the same understanding was applied in the present study, whereby the IDF criteria are best suit for South Asian candidates. This is in agreement with previous MetS study finding on prevalence of MetS among Malaysians.[41]

Several limitations of this study should be noted. First of all, it is a cross-sectional study. Hence, a causal relationship could not be defined from the study populations. Secondly, any relevant factors which may contribute to the obesity and hypertension were not included. Among those relevant parameters include dietary habits, physical activity and genetic factors. Thirdly, study population was relatively small and concentrated among hypertensive patients in Kuantan population. This limits the generalizability of the findings. Despite of the limitations, this study manages to provide relevant findings on the prevalence of MetS and clinical characteristics among local hypertensive patients which is worrying and required serious attention.

As a conclusion, our present study showed a high prevalence of MetS among local hypertensive subjects. In order to further reduce risk of developing CVD, this group of patients has to be managed and counselled. Hence, there is an urgent need to screen all hypertensive patients for features of MetS at the time of diagnosis. This will form a comprehensive patient management that includes patient's lifestyle modification with or without pharmacotherapy and proper follow up.

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