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Clustering of metabolic syndrome factors in Malaysian population: Asian Criteria revisited

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ABSTRACT

Introduction: Metabolic syndrome (MetS) had been known as clustering of risk factors for cardiovascular disease and diabetes. Over the years, clinical criteria had been revised to highlight importance of various risk factors in defining MetS. Studies had reported different clustering of factors based on different population characteristics.

Objective: Our study aimed to identify the clustering factors among our Malaysian population based on sexes and 4 major ethnic groups namely Malay, Chinese, Indian and other minor ethnic

Methods: A national cross sectional study was done covering both Peninsular and East Malaysia. Subjects' sociodemographic, body mass index (BMI), waist, hip and neck circumference, blood pressure, fasting triglycerides (TG) and HDL-cholesterol and glucose, urine microalbumin and serum insulin were taken. Principal component factor analysis with Varimax rotation was done to identify the clustering based on sex and ethnic groups.

Results: One thousand two hundred and sixty eight male and 2355 female subjects were recruited. Majority of subjects were Malays (63.0%) followed by Chinese (13.3%), Indian (7.4%) and other ethnic groups (13.8%) which followed the population composition in Malaysia. Four factors were identified for both men and women. The factors were anthropometry, glycemia, blood pressure and dyslipidemia given the cumulative percent of variance of 69.4 and 65.9 respectively. There are 4 factors identified for Malay, Chinese and Aborigines but 5 factors for Indian ethnic groups given cumulative percent of variance explained ranged from 65.1 to 77.7.

Discussion and Conclusion: BMI, neck circumference, blood pressure, Fasting TG and HDL had a high factor loading in both sexes suggesting that for field screening, diagnostic criteria would be adequate criteria. These factors also showed a similar pattern of loading by different ethnic groups. In conclusion, in Malaysian population, at least one measurement from each components namely anthropometric, blood pressure, glycemia and dyslipidemia is adequate to diagnose MetS.

Keywords: Metabolic Syndrome, Malaysia, factor cluster, sex, ethnic

Abbreviation

MetS: Metabolic Syndrome
BMI: Body mass index
TG: Triglyceride
HDL-C: High density lipoprotein – Cholesterol
2H PG: 2-hour Post-prandial glucose
FBG: Fasting blood glucose

Introduction

Over the decades,, the recognition of the clustering of factors as the risk factors for cardiovascular disease and diabetes continues to be discussed. Reaven had proposed the term "syndrome X" in 1988 Banting lecture which emphasized on insulin resistance as the main factor [1]. The World Health Organization (WHO) then formalized definition of metabolic syndrome which requires evidence of insulin resistance for diagnosis. Obesity, hypertension, high triglyceride (TG) level, reduced high-density lipoprotein cholesterol (HDL-C) level and microalbuminuria were listed as additional risk factors. [2]. Later in 2001, the National Cholesterol Education Program Adult Treatment Panel III (ATP III) established another criteria which did not require demonstration of insulin resistance for diagnosis but made the presence of 3 out of 5 factors as the basis for establishing diagnosis. The 5 factors are abdominal obesity given as waist circumferences by sexes, artherogenic dyslipidemia as high TG level and low HDL-C, raised blood pressure and elevated fasting glucose either impaired fasting glucose or type 2 diabetes mellitus [3]. In 2005, the International Diabetes Federation (IDF) [4] emphasizes on abdominal obesity as main factor for diagnosis. The differences in the diagnostic criteria lead to a joint interim statement to harmonize the MetS definition [5]. The common definition agrees that abdominal obesity should not be the prerequisite, and the presence of 3 out of 5 factors constitutes the diagnosis. Other factors such as neck circumference were also reported to have some predictive value [6]

The definitions were derived based on the evidence of the clustering of the factors. Factor analysis is one of the statistical methods that can group the quantitative measures based shared variance of a variable [7]. Studies on different ethnic groups had identified three to four factors based on factor analysis. Snehalatha *et al*, 2000 identified 4 factors and concluded that insulin resistance alone does not explain the clustering of CVD risk factors in south Indians [8]. Ghosh, 2004 reported central obesity and centralised subcutaneous fat had cumulatively explained 47% of the observed variance of metabolic syndrome among middle aged Bengalee Hindu men in Calcutta, India [9]. On the other hand, Wu *et al*, 2008, identified 3 factors among Chinese in Taiwan. The 3 subgroups were blood pressure which consisted of systolic and diastolic blood pressure, an insulin dimension which loaded mainly with steady state of plasma glucose and adiposity/glucose dimension which loaded in the same cluster with TG, waist hip ratio or fasting plasma glucose [10].

Our Malaysian population is multiracial with different prevalence of MetS [11, 12]. We thus, would like to study the different pattern of clustering in our population based on sex and the four major ethnic groups.

Methodology

This is a nationwide cross sectional study involving both Peninsular Malaysia and East Malaysia with 6 institutions collaboration. Household were selected using multistage enumeration block sampling used by the Department of Statistics Malaysia [13] to divide the country into contiguous geographical areas. One house occupant was selected per household using World Health Survey KISH Table. Single proportion formula was used to estimates the required sample size for the prevalence study based on study by Tan *et al*, 2004 in Singapore [14] with 5% precision giving the estimated sample required was 870 subjects from each zone with the total number of 4350 subjects. Details of the study methodology were described in previous publication [11]. Briefly, subjects' socio-demographic and clinical data were taken using a standard case report form. Blood pressure, body mass index (BMI), waist circumference, hip circumference, and neck circumference were measured by trained research assistant. Neck circumference was measured in the midway of the neck, between mid-cervical spine and mid-anterior neck. In men with a laryngeal prominence (Adam's apple), it was measured just below the prominence.

Venous blood samples for fasting triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), insulin, fasting glucose and urine microalbumin were taken. All subjects except the known diabetics were given an oral glucose tolerance. A two-hour post glucose challenge plasma glucose level (2H PG) was taken.

The study protocol was approved by the Medical Research and Ethics Committee of the Ministry of Health as well as from the ethics committee of each participating institute. Informed consent was obtained from all participants prior to data collection.

Analysis methodology

For the purpose of this study, the Kadazan-Dusun, Bajau, Murut plus several other ethnic minorities were categorized as the 'other ethnic group'. Insulin resistance (HOMA IR) was computed as fasting blood glucose (mmol/l) x fasting insulin (µmol/ml) / 22.5 [15]. Clinical and biochemical characteristics in men and women were presented as mean (sd) based on exclude cases listwise method.

Factor analysis was performed to describe sex and ethnic specific cluster of MetS variables. Factor analysis was done using principal component analyses with Varimax rotation. Variables with factor loadings of at least 0.4 were used in interpretation. Waist circumference and fasting insulin were taken as representative of central obesity and insulin resistance.

Result

Out of 4335 subjects recruited, to avoid potential effect of medications on metabolic values, 712 were excluded from the factor analysis because they were taking medication for hypertension, diabetes or dyslipidemia. Of those excluded, 16.5% or 250 were males and 16.4% or 462 were female leaving 1268 male and 2355 female for the factor analysis. By ethnic groups, there were 2286 (63.0%) Malays, 484(13.3%), Chinese, 270 (7.4%), Indian and 500 (13.8%) other ethnic including the indigenous group.

Women were found to have higher BMI and hip circumference compared to men. However other anthropometric parameters, i.e. waist and neck circumference and waist –hip ratio were higher in men. Men also found to have higher blood pressure reading. There are no significant different of glucose and insulin parameters between both sexes (Table 1).

Anthropometric measurements were found to have significant correlation (r >0.3). Systolic and diastolic blood pressure as well as fasting plasma glucose and 2H PG correlated to each other but not to other factors. Fasting TG, HDL-C and microalbuminuria did not correlate to any factors (Table 2).

Four factors were identified for both men and women. The factors were anthropometry, glycemia, blood pressure and dyslipidemia given the cumulative percent of variance of 69.4 and 65.9 respectively. BMI showed the highest factor loading for anthropometric measurement for both sexes. In men, microalbuminuria clustered with TG and HDL-C. In women, insulinemia clustered with TG and HDL but microalbuminuria was not significantly loaded (Table 3).

There were 4 factors identified for the Malays, Chinese and other ethnic groups. In contrast, 5 factors were identified for the Indians with cumulative percent of variance ranging from 65.1 to 77.7. Hyperinsulinemia is not loaded significantly in the Malays, but clustered with anthropometric measurement in Chinese and with dyslipidemia variables in the Indians and other ethnic group (Table 4).

Discussion

The main ethnic groups in Peninsular Malaysia are Malays, Chinese and Indian while the main ethnic groups in Sabah are the Kadazan-Dusun, Bajau and Murut. The study subjects' distribution follows the distribution of Malaysia's ethnic population where majority were Malays, followed by Chinese and Indians.

This study were aimed to determine which MetS factors that contributes the most in the development of MetS, considering the possibility of variation between sexes and ethnicity. We have excluded those who were on medication to avoid the effect of the medication on the metabolic parameters. We believed that detection of MetS should be simplified to the easiest method not requiring high technology laboratory test and suitable to be used by healthcare personnel at periphery level. Simplifying the diagnostic criteria will further facilitate the intervention at early stage without requiring highly trained health personnel. Factor analysis is a multivariate approach that reduced a set of variables into factors based on inter-item correlation. The factor loading of each variable tells the percentage of variance explained by the variables to explain the factor, which in this case, how much the metabolic variables explained the MetS. Studies had used this statistical tool to identify two to four clustering factors in different populations [8-10].

Generally, for both men and women, there were four components identified i.e. anthropometric measurements, blood pressure, glycemia and dyslipidemia. In anthropometric measures, BMI had the highest factor loading of all 4 measurements. BMI is known to be related to insulin resistance, although waist-hip ratio explained more on central obesity. A study among southern Indian population also noted a common link between BMI with other factors in both men and women [8]. Neck circumference was also found to load high in both men and women. This is similar to the reports by Laakso, 2002 [6] who reported a high correlation between neck circumference and BMI. These findings suggested that, for

field screening, diagnostic criteria using BMI and neck circumference which is the easiest to measure would be an adequate criteria.

The clustering effect of both systolic and diastolic blood pressures had always been reported by other studies as a separate factor. We found that the blood pressure was loaded high in both sexes indicating the importance of these factors in metabolic syndrome cluster. This is in line with finding from a study on impact of treatment on insulin sensitivity where gender was reported to be independent factor for metabolic syndrome intervention [16] On the other hand, fasting blood glucose was loaded slightly higher than 2H PG suggesting that FBG which was easier to perform, can be used as a measurement for glycemia in diagnosing MetS. Similarly, TG and HDL-C were loaded high for both sexes supporting their role in MetS diagnosis. Fasting insulin is only loaded for women and microalbuminuria for men. Thus, these two factors may just be optional variables in MetS.

By ethnicity, relatively similar clustering pattern was seen. BMI was still the anthropometric measure that loaded the highest for all 4 ethnic groups. Glycemia and blood pressure were loaded separately as seen in the sex group pattern except for FBG which loaded lower than 2H PG in the Chinese. Wu et al, 2008 [10] also noted low communality of FPG and steady state plasma glucose among normal Chinese in Taiwan but noted increasing communality among those with impaired glucose and diabetes among. We found that among the Indians, TG loaded relatively low compared to other ethnic groups but microalbuminuria loaded high, clustering together with insulin. The Bengalese study [9] also noted similar clustering of TG with glycemia variables. However, the study did not include microalbuminuria as one of the factors.

In conclusion, in the Malaysian population, at least one measurement from each components namely anthropometric, blood pressure, glycemia and dyslipidemia is adequate to diagnose MetS. Microalbuminuria and fasting insulin can be the supportive criterias especially in the Indian group.

Conclusion

In multiracial population of Malaysia, simple metabolic syndrome features is adequate for early detection of MetS at primare care setting.

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Table 1: Clinical and biochemical characteristics in men and women

Variables	Men (n=1268) Mean(sd)	Women (n=2355) Mean(sd)	p-value
Age (years)	48.5 (15.54)	47.5 (13.92)	<0.001
BMI (kg/m^2)	25.3 (4.83)	26.3 (5.37)	<0.001
Waist circumference (cm)	88.4(12.32)	85.2 (13.13)	<0.001
Neck Circumference (cm)	37.7 (3.42)	34.1(3.17)	0.001
Hip Circumference (cm)	97.2(9.62)	98.2(11.06)	0.001
Waist hip ratio (WHR)	0.91 (0.085)	0.87 (0.122)	<0.001
Systolic Blood pressure (mmHg)	135.0(21.66)	131.1(22.85)	<0.001
Diastolic Blood pressure (mmHg)	79.4(11.65)	77.9(11.38)	0.852
Fasting blood glucose (mmol/l)	5.6(2.63)	5.6(2.64)	<0.001
2 Hour post challenge glucose (mmol/l)	6.8(3.73)	7.6(3.68)	0.559
Fasting insulin (µmol/ml)	12.1(11.9)*	12.6(11.7)*	0.918
HOMA of Insulin resistance	2.49(2.82)*	2.63(2.85)*	0.696
Microalbuminuria	7.5(20.43)*	8.1(19.3)*	0.696
Total Cholesterol	5.8(1.32)	5.79(1.26)	0.911
Fasting triglyceride	1.7(1.11)	1.4(1.01)	<0.001
High density lipoprotein (HDL-C)	1.2(0.32)	1.4(0.37)	<0.001
Low density lipoprotein (LDL)	3.5(1.12)	3.6(1.13)	0.899

*median (IQR)

Table 2: Correlation coefficients of metabolic syndrome variables in both men and women

	BMI	WC	NC	HC	WHR	SBP	DBP	FPG	2H PG	FTG	HDL	MA	FI	HOMAIR
BMI		0.786	0.534	0.810			0.324							
WC	0.786		0.610	0.594	0.656									
NC	0.534	0.610		0.532										
HC	0.810	0.594	0.532											
WHR		0.656												
SBP							0.756							
DBP						0.756								
FPG									0.700					0.387
2H PG								0.700						
FTG														
HDL														
MA														
FI														0.897
HOMAIR													0.897	

All correlation coefficients were statistically significant with $p<0.05$

Table 3: Clustering of metabolic syndrome variables in men and women

	Men				Women			
Variables	**1 anthropometry**	**2 glycemia**	**3 BP**	**4 dyslipidemia**	**1 anthropometric**	**2 glycemia**	**3 BP**	**4 dyslipidemia**
BMI (kg/m^2)	0.905				0.908			
Waist circumference (cm)	0.898				0.815			
Neck circumference(cm)	0.827				0.785			
Hip circumference (cm)	0.891				0.839			
Fasting blood glucose		0.898				0.903		
2Hours post challenge BG		0.890				0.865		
Fasting insulin								0.543
Systolic blood pressure			0.920				0.906	
Diastolic blood pressure			0.889				0.891	
Fasting TG				0.638				0.622
HDL-C				-0.727				-0.709
microalbuminuria				0.488				
Cumulative % of variance	**33.55**	**48.49**	**60.03**	**69.38**	**32.17**	**45.91**	**57.16**	**65.92**

*BP: Blood pressure

Table 4: Clustering of metabolic syndrome variables among 4 major ethnic groups

	Malay				Chinese				Indian					Other ethnic group			
Variables	**1 A**	**2 G**	**3 BP**	**4 L**	**1 A**	**2 BP**	**3 G**	**4 L**	**1 A**	**2 G**	**3 BP**	**4 L**	**5 I**	**1 A**	**2 BP**	**3 G**	**4 L**
BMI (kg/m^2)	0.903				0.874				0.940					0.941			
Waist circum (cm)	0.823				0.788				0.858					0.904			
Neck circum (cm)	0.696				0.561				0.498			0.545		0.734			
Hip circum (cm)	0.845				0.768				0.844					0.946			
FBG		0.912					0.697			0.902						0.873	
2Hours PG		0.891					0.790			0.892						0.823	
Fasting insulin					0.532								0.596				0.419
SBP			0.913			0.905					0.938				0.905		
DBP			0.899			0.902					0.932				0.841		
Fasting TG				0.620				0.717		0.515		0.424	0.447				0.638
HDL-C				-0.813				-0.736				-0.847					-0.812
Micro albuminuria							0.596						-0.702		0.513		
Cumulative % of variance	**30.53**	**45.42**	**56.85**	**65.39**	**32.89**	**46.02**	**56.03**	**65.06**	**27.14**	**44.23**	**60.16**	**69.11**	**77.687**	**33.94**	**47.414**	**59.434**	**69.482**

A: Anthropometric; G: Glycemia; BP blood pressure; L lipidemia; I insulinemia