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A Rapid, Inexpensive and Non Invasive Screening for Metabolic Syndrome, Type 2 Diabetes Mellitus and Coronary Artery Disease in a Malaysian Population

Aye M[1]*, Cabot JSF[1] and Razak MSA[2]

[1]*Department of Medicine, UniKL Royal College of Medicine, Perak, Malaysia*
[2]*State Health Department, Ministry of Health, Perak, Malaysia*

Abstract

Introduction: The development of rapid, non-invasive and inexpensive tools to screen individuals at risk of developing metabolic syndrome and its consequences of type 2 diabetes and coronary artery disease is important from an epidemiologic and public health view.

Method: A cross sectional analysis was performed with 398 patients from January to November 2011 from records of an outpatient department of a district hospital in rural Malaysia, comprising all races, for prevalence of Metabolic Syndrome (MetS) according to different published criteria.

Result: The prevalence of MetS by different criteria was 49.0% by Hypertensive-Waist (HW), 32.7% Hyper triglyceridaemic-Waist (HTGW), 55.3% by International Diabetes Federation (IDF), 55.3% by Harmonized NCEPATP111 (HNCEPATP111), and 61% by Modified WHO (MWHO). Prevalence of type 2 Diabetes Mellitus (DM) by different criteria was 53.3, 55.4, 55.5, 56.3, 70.3 % respectively and that of Coronary Artery Disease (CAD) was: 21.0, 23.1, 22.7, 23.3 and 23.3% respectively. The agreement of IDF with HW, HTGW, Harmonized NCEPATP111, MWHO using Kappa index was 0.744, 0.560, 0.870 and 0.494 respectively.

Conclusion: HW is able to screen MetS better than HTGW and has better concordance with IDF, although its ability to screen for DM and CAD is somewhat less than HTGW. HW is therefore an excellent screening test for MetS as it is immediately available, non-invasive, requires no laboratory tests, has no appreciable cost, has better concordance with IDF than HTGW and is comparable to IDF and HNCEP for screening DM and CAD.

Keywords: Hypertensive-waist; Hypertriglyceridemic-waist; IDF; NCEPATPIII; Modified WHO; Metabolic syndrome

Introduction

Metabolic Syndrome (Mets) is a condition that substantially increases Coronary Artery Disease (CAD) and is characterized by a cluster of several metabolic abnormalities; centrally distributed obesity, decreased high density lipoprotein cholesterol (HDL-C), elevated triglycerides, hypertension, and hyperglycaemia [1-3]. Abdominal obesity is common in south Asians who, even in non-obese subjects, have a high percentage of body fat, thick subcutaneous adipose tissue, low muscular mass, hyperinsulinaemia and insulin resistance, a combination conducive to development of MetS even in the absence of hyperglycemia and elevated low density lipoprotein cholesterol [4-6]. 'Hypertriglyceridemic-Waist (HTGW) index', has been proposed as a simple and inexpensive tool to identify individuals at risk of developing CAD [7]. High concordance between IDF and HTGW was expected as both use values for waist circumference and fasting triglycerides levels. Gomez Huelgas et al. reported that HTGW showed a moderate agreement with metabolic syndrome defined by IDF and National Cholesterol Education Programme Adult Treatment Panel 111(Ncepatpiii) criteria [8]. The prevalence of MetS by HTGW was 19% in a Quebec cohort, 26.2% in France 11% in 137 American postmenopausal women and 19.7% in a Malaysian study [9-12]. The Malaysian study reported that it had a good correlation with IDF [12]. Prevalence of individual risk factors of MetS varies with ethnicity, with hypertension the most common chronic disease and co-morbidity in Malaysia and obesity also common in Malaysia population [13,14]. Hypertension appears to be a more frequent abnormality among the risk factors for MetS in Asian populations, than in Caucasians [15-18]. We studied Hypertensive-Waist (HW) in a Malaysian population as: 1) a tool to screen MetS, CAD and DM and compare HW with other established definitions of MetS such as IDF, Harmonised NCEPATP111 (HNCEPATP111), Modified World Health Organisation (MWHO), HTGW (Appendix); 2) compare the agreement of HW and other criteria to IDF [12].

Materials and Method

A cross sectional study of 398 patients was performed using the Epi Info version 6 (CDC) for population surveys. Sampling was selected by a clustered systematic randomized sampling with fifteen patients recruited every Thursday from the outpatient clinic. All ethnic groups (Malay, Indian and Chinese) were included, with age 20 years and above. Patients with known causes of hypertension, obesity and dyslipidemia such as Cushing's and Pseudo-Cushing's syndrome, chronic renal failure, nephrotic syndrome and hypothyroidism were excluded, as were smokers. HW had been reported comparable to IDF in detecting MetS and defined as systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or history of treated hypertension; plus a waist circumference ≥ 80 cm for women and ≥ 90 cm for men (we used 90 cm in lieu of 94 cm in reference as outlined under Material and Methods) [19,20]. We chose IDF to validate other definitions of MetS because: 1) it is ethnic specific; 2) WC is used as required criteria by IDF as it is for HW; 3) to have comparable data since most of local and other studies used IDF as a gold standard for agreement criteria [20].

***Corresponding author:** Aye M, Department of Medicine, UniKL Royal College of Medicine, Perak, Malaysia, E-mail: mraaye@hotmail.com

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The research purpose was explained to and consent obtained from all patients. Patients were interviewed and examined by the investigators and measurements of BMI (kg/m^2), Waist Circumference (WC) by cm and blood pressure (mmHg) were carried out by the same assigned staff nurse trained to measure WC. WC measurement was standardized using a measuring tape at the midpoint between the lower costal cartilage and the highest point of iliac crest at full expiration. Blood samples for fasting plasma sugar (FPG) (mmol/L), serum triglycerides (mmol/L) (TG) and high-density lipoprotein cholesterol (mmol/L) (HDL), total Cholesterol (TC). Low Density Lipoprotein-C (LDL-C) was taken in early morning after an overnight fast. Period of study was from January 15 to June 30, 2011. Cut-off points for definitions were adopted by the criteria of a Malay study in Appendix: Male waist circumference (WC) ≥ 90 cm, female ≥ 80 cm were assessed for MetS by IDF criteria when they had at least one of the following three criteria: BP ≥ 130/85 mmHg; TG ≥ 1.7 mmol/ L; HDL ≤ 1.29 mmol/ L for females and ≤ 1 mmol/ L for males and FBS ≥ 5.6 mmol/L [12]. Any three out of the five criteria for IDF was defined as MetS for HNCEPAPT111. Elevated FPG cut-off point for MWHO was >6.1mmol/L or DM and this plus any two of following : body mass index (BMI) ≥ 30 kg/m^2 , blood pressure 140/90 mmHg , HDL <I mmol /L for males and <0.9 mmol/L for females , high TG ≥ 1.7 mmol/L was defined as MetS according to MWHO criteria. The cut-off points for hypertension, WC and triglycerides and low HDL-C for HTGW, HW and IDF were the same. Fasting plasma glucose ≥ 7 mmol/L was defined as DM. Coronary Artery Disease (CAD) was defined by patients' record: coronary angiography, angioplasty, CABG, symptoms of angina or unstable angina plus ECG changes, cardiac biomarkers with or without echocardiogram changes and response to coronary vasodilators. Cut-off points for high TC and LDL-C were >5.2 mmol / L and 2.5 mmol /L respectively according to hospital protocol where the study was carried out. MetS was defined for different criteria adopting the Table 1. WC was ≥ 90 cm for men and ≥ 80 cm for women in all definitions of MetS in this study [12]. Cut-off points for TG, HLD-C, systolic and diastolic BP, elevated fasting plasma glucose are the same in all criteria except WHO where cut-off points for systolic BP, diastolic BP, HDL-C were higher.

Statistical analyses were performed using the SPSS version 11.5 (SPSS Inc, Chicago, Il, USA). Student's t test was used to determine means; Chi Square test was used to determine association; Kappa index was used to determine agreement. Data were considered statistically significant with p-value < 0.05.

Results

194 males and 204 females were evaluated. The overall prevalence of MetS defined by HW = 44.8%; HTGW = 40.5%; IDF = 55.3%; HNCEPATPIII = 61.6%, MWHO = 38.9%. By gender and IDF criteria, males = 40% and females = 60%; by HNCEPATP111 and MWHO criteria = 44.5% and 55.5%, by HTGW criteria = 41.5% and 58.5% and by HW criteria = 40.5% and 59.5%. By ethnicity, highest prevalence of MetS was Indian by IDF criteria (43.2%); Malays by MWHO criteria (47.7%) and in Chinese by HNCEPAT111 criteria (18.4%). The prevalence of MetS was approximately equal among Malays and Indians with Chinese having the lowest prevalence by all criteria. By age MetS was highest in the age group 50-59 followed by age group ≥ 60, 40-49, 30-39 and 20-29 by all criteria definitions. Thus, there is a steady increase in the MetS prevalence with age up to 50-59 (Table 1).

Table 2 shows prevalence and association of DM and CAD by different definitions. DM by MWHO criteria was highest, followed by HNCEPATP111, IDF, HTGW and HW. This is because MWHO uses DM or elevated FPG was a major diagnostic criterion for MetS, and therefore MWHO criteria has highest odds ratio followed by the others.

Variable	Total Number (%)	IDF	HNCEP	Modified WHO	HTGW	HW
Metabolic syndrome	398	220 (55.3)	245(61.6)	155 (38.9)	130 (32.7)	195(49.0)
Age						
20-29		9 (4.1)	10 (4.1)	6 (3.9)	5 (3.8)	9 (4.6)
30-39		17 (7.7)	20 (8.2)	11 (7.1)	9(6.9)	13 (6.7)
40-49		53 (24.1)	56 (22.9)	36(23.2)	31 (23.8)	49 (25.1)
50-59		82 (27.3)	92 (37.6)	63(40.6)	49 (37.7)	73 (37.4)
≥ 60		59 (26.9)	67 (27.3)	39(25.2)	36 (27.7)	51 (26.2)
Gender						
Male	194 (48.8)	132 (60.0)	109 (44.5)	69(44.5)	54 (41.5)	79 (40.5)
Female	204 (51.2)	88 (40.0)	136 (55.5)	86(55.5)	76 (58.5)	116 (59.5)
Ethnicity						
Malay	139 (39.2)	88 (40.0)	101 (41.2)	74(47.7)	58 (44.6)	84 (43.1)
Indian	136 (38.3)	95 (43.2)	99 (40.4)	60(38.7)	50 (38.5)	79 (40.5)
Chinese	80(22.5)	37 (16.8)	45 (18.4)	21(13.5)	22 (16.9)	32 (16.4)

IDF: International Diabetes Federation; NCEPATP111: National Cholesterol Education Prevention Adult Treatment Panel 111; HTGW: high Triglyceride Waist; HW: Hypertensive Waist; HNCEP: HarmonizedNCEPATP111

Table 1: Distribution of demographic factors in study population with Metabolic Syndrome by different definitions (percentage in parenthesis).

	IDF	HNCEP	Modified WHO	HTGW	HW
DM	122 (55.5) 4.44(2.85-6.91)	138 (56.3) 7.29(4.38-12.1)	109 (70.3) 8.70 (5.49-13.8)	72 (55.4) 2.50(1.63-3.84)	104 (53.3) 2.93(1.93-4.44)
CAD	50 (22.7) 1.89(1.11-3.22)	57 (23.3) 2.43(1.35-4.35)	36 (23.3) 1.63(0.98-2.71)	30 (23.1) 1.53(0.91-2.57)	41 (21.0) 1.37(0.83-2.28)

IDF: International Diabetes Federation; NCEPATP111: National Cholesterol Education Prevention Adult Treatment Panel 111; HTGW: High Triglyceride Waist; HW: Hypertensive Waist; HNCEP: Harmonizedncepatp111; CAD: Coronary Artery Disease; Figures In The Brackets Are Percentages, HNECPATP Is The Most Sensitive To Screen For Mets, DM And CAD

Table 2: Prevalence DM & CAD in patients with MetS and their association with MetS defined by different definitions.

The prevalence of CAD was highest by HNCEPATP111 and MWHO followed by HTGW IDF and HW. However, only HNCEPATP111 and IDF had significant association with CAD.

Table 3 shows mean: age, BMI, WC, Systolic BP (SBP), Diastolic BP (DBP), FPG, TG, HDL-C, TC, and LDL-C by all definitions.

Mean WC was highest with HW, and lowest with HNCEPATP 111. Mean systolic and diastolic BP was highest with HW definition with all other definitions having lower systolic and diastolic pressures than HW definition.

TG (normal value; 1.7 mmol/L for male and female) was highest by HTGW, followed by MWHO, HNCEPATP111, IDF, and lowest by HW. HDL-C (normal value: 1.30 mmol/L for females and normal value: 1.0 mmol for male) was lowest by MWHO, gradually increased by HNCEPATP111, IDF and highest by HW.

FPG (normal: 7 mmol/L) was highest by MWHO (as a required major criteria), followed by HTGW and comparable in the remaining three definitions.

TC mmol/L and LDL-C mmol/L was highest by HNCEPATP111 and HW and lower and comparable in the remaining three definitions.

Table 4 shows prevalence of MetS factors in different definitions of the syndrome. WC prevalence was high in HW, HTGW and IDF (as a required criterion) to diagnose MetS; and lower in MWHO and NCEPATP111.

Highest prevalence of elevated FPG was seen in MWHO (as a required criterion), followed by HNCEPATP111, IDF, HTGW, and HW.

Prevalence of high TG was highest in HTGW (as a required major criterion), followed by MWHO, IDF and HNCEPATP111 and HW.

Prevalence of low HDL-C was highest in MWHO, followed by HNCEPATP111 and IDF, HW and HTGW.

Hypertension prevalence was highest in HW (as a required criterion), followed by MWHO, HNCEPATP111 and IDF and HTGW.

Table 5 shows sensitivity and specificity, Kappa index and p values of MetS defined by HNCEPATPIII, MWHO, HTGW and HW vs. IDF.

	Hypertensive -waist	Hypertriglyceridemic-waist	IDF	H-NCEPATP 111	Modified WHO
Age	52.0 ± 12.6	53.1 ± 11.3	52.7 ± 11.4	52.9 ± 11.8	53.1 ± 11.3
BMI	31.1 ± 6.49	29.6 ± 5.79	30.4 ± 6.56	29.8 ± 6.55	30.6 ± 7.06
WC	101 ± 10.8	99.4 ± 9.85	100 ± 10.7	98.4 ± 11.4	98.8 ± 11.5
SBP	148 ± 13.7	143 ± 18.0	142 ± 16.7	142 ± 16.7	145 ± 14.0
DBP	87.4 ± 8.63	84.7 ± 9.83	85.2 ± 10.1	85.4 ± 9.96	86.7 ± 9.22
TG	1.81 ± 7.12	2.81 ± 2.04	2.15 ± 1.77	2.14 ± 1.71	2.30 ± 1.68
HDL-C	1.10 ± 0.39	1.04 ± 0.36	1.05 ± 0.34	1.04 ± 0.337	1.02 ± 0.33
FPG	7.41 ± 2.74	7.90 ± 3.15	7.73 ± 2.89	7.72 ± 2.80	8.53 ± 2.92
T C	5.59 ± 1.66	5.04 ± 1.32	5.09 ± 1.34	5.24 ± 1.53	5.04 ± 1.32
LDL-C	3.38 ± 1.51	3.14 ± 1.32	3.33 ± 1.33	3.35 ± 1.31	3.14 ± 1.24

BMI: Body Mass Index; WC: Waist Circumference; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TG: Triglycerides; HDL-C: High Density Lipoprotein-Cholesterol; FPG: Fasting Plasma Glucose; T:Total Cholesterol: LDL-C: Low Density Lipoprotein -Cholesterol

Table 3: Comparison of the baseline characteristics in subjects with MetS according to IDF, NCEPATPIII, MWHO, HTGW and HW.

Metabolic risks	Hypertensive -waist	Hypertriglyceridemic- waist	IDF	Harmonized NCEPATP111	Modified WHO
High WC	158 (100 %)	130 (100%)	220 (100%)	217 (88.6%)	134 (86.5%)
Raised FPG	112 (70.9%)	102 (78.5%)	174 (79.1%)	196 (80%)	152 (98.1%)
High TG	75 (47.5%)	130 (100%)	127 (57.7%)	144 (58.8%)	105 (67.2%)
Low HDLC	106 (67.1%)	89 (68.5%)	155 (70.5%)	175 (71.4%)	116 (74.8%)
High BP	158 (100%)	104 (80.0%)	186 (84.5%)	208 (84.9%)	137 (88.4%)

Table 4: Prevalence of metabolic risk factors of MS in the study cohort (n=398).

Definition	IDF Index					
	MetS	Normal	Sensitivity	Specificity	Kappa Index	p-Value
HW						
MetS (%)	182(93.3)	13 (6.7)	82.7%	92.6%	0.744	0.00
Normal (%)	38(18.7)	165(81.3)				
HTGW						
MS (%)	129(99.2)	1 (8)	58.6%	99.4%	0.560	0.00
Normal (%)	91(34.0)	177 (66.0)				
HNCEPATPIII						
MetS (%)	220 (89.8)	25 (10.2)	100%	85.9%	0.871	0.00
Normal (%)	0 (0)	153 (100)				
Mod. WHO						
MetS (%)	136(87.7)	19(12.3)	61.8%	89.3%	0.494	0.00
Normal (%)	84(34.6)	159 (65.4)				

Table 5: Agreement with IDF of other definitions which define metabolic syndrome.

Sensitivity and specificity of IDF vs. HNCEPATP111 was 100% and 85.9%; HW 82.7 and 92.6%, MWHO 61.8% and 89.3% and HTGW 58.6 and 99.4%.

The agreement (kappa index) between IDF definition and HNCEPATP111 was 0.817, MWHO was 0.494; HTGW was 0.560 and HW was 0.744 ($p < 0.01$) respectively. Therefore, there was excellent agreement between IDF and HNCEPATP111, good agreement with HW, and moderate agreement with HTGW and MWHO.

Discussion

Being hospital based, this study possibly may show a higher prevalence of MetS than the general population. In this cohort, the highest prevalence of MetS was defined by HNCEPATPIII, followed by IDF, HW, MWHO and HTGW. Since HNECPATP111 does not include high WC, it diagnoses a somewhat different MetS group than does IDF. This finding is consistent with a report of a Korean study and others who claim WC should not be mandatory in definition of MetS as there are subjects without abdominal obesity who may still be at greater future risk of DM or CAD by having clustering of other risk factors [21,22]. This is also applicable to MWHO where elevated FPG is a required criterion to define MetS and therefore having lower prevalence of MetS in this and other Malaysian studies [12,21-23]. The prevalence of MetS is higher in IDF than NCEPATP111 in these studies possibly because of higher cut-off points of WC in two local studies to define NCEPATP111 [12,21-23]. In CURES-34 study IDF criteria was most sensitive to detect MetS followed by MWHO and NCEPATP111 [23-25].

IDF has very good agreement HNCEPATP111, moderately good agreement with HW and moderate agreement with HTGW and MWHO in our study, consistent with other studies [12,23,24]. The very good agreement with IDF and HNCEPATP111 is that both criteria have common risk factors for diagnosis of MetS, consisting of hypertension, elevated FPG, low HDLC and high TG.

Our study would suggest that it seems best to have fluid major criteria for the diagnosis of MetS. It also indicates that HNCEPATP111 appears suitable to diagnose MetS for Southeast Asians. This finding is consistent with reports from India, Sri Lanka and Korea [21,26,27].

The reason for reduced agreement of IDF with MWHO is probably because MWHO uses DM and/or raised fasting plasma glucose, greater cut off levels for systolic/diastolic blood pressures and low HDL to define MetS than the other definitions, accounting for reduced sensitivity of MWHO for MetS definition and hence the lowest detection rate. Likewise, the reason for reduced agreement with HTGW is that high TG is the least common risk factor among other definitions for developing MetS (Table 4). Therefore, when this risk factor and high WC are used to define MetS, it has lower sensitivity of MetS and poor agreement (second lowest agreement) with IDF, consistent with other reports of populations in Malaysia, Quebec, France and USA [9-12]. We agree that HTGW is not a good screening tool for MetS in Malaysia population.

There are very few studies that compare HW ability to screen for consequences of MetS such as DM and CAD with other definitions [28]. That study was also different from ours by use of different targets of study, higher cut-off points of WC and use of IDF to define MetS. HW has the ability to screen MetS, and has good agreement with IDF and HNCEPATP111. As MetS is associated with three fold higher risk of Type 2 DM and two to three fold higher risk of CAD, we believe HW to be a very simple, no cost, screening tool for DM for CAD [3]. Others report show WC is independently associated with hypertension and DM in African American women [28,29].

The lower prevalence of CAD and DM by HW than other definitions could be explained by several factors. IDF defined MetS cut-off point of WC for men as ≥ 94 cm, different from our study and Framingham Risk Score was used to define CVS risk in the study another [28]. Also there are many risk factors for developing CAD other than hypertension, especially dyslipidemia and elevated FPG, not measured by HW. The pattern of clustering of MetS factors varies among ethnic groups [13,14]. In South East Asias, hypertension and increased WC are the most common risk factor for developing MetS, with elevated TG the least associated risk factor [14,30,31]. Definitions that include high TG or elevated FPG as criteria to define MetS by HTGW and MWHO respectively would result in screening for a higher prevalence of DM and CAD. Low HDL-C and high TG lipid disorder is a virtual marker for DM, so HTGW gives a higher prevalence of DM and CAD [32]. HTGW is comparable to HNCEPATP111 and IDF and better than HW to screen for DM and CAD in this and other studies [8,33,34]. However in other studies, cut-off points for TG were lower than our study and thus the ability of HW as a tool to predict DM and CAD appears not less than HTGW which is claimed as a good tool to predict DM and CVS risks [8,33,34].

In our study HW was better than HTGW to detect MetS and has better agreement with IDF, and like HTGW, is comparable to IDF and HNCEPATP111 to screen DM and CAD. We agree with others that MetS and its components are associated with type 2 diabetes but have weak or no association with vascular risk in elderly populations, suggesting that attempts to define criteria that simultaneously predict risk for both cardiovascular disease and DM are not helpful [35]. Clinical focus should assess the optimum risk for each disease.

Therefore, we assert that HW is cheaper, easier, non-invasive and a more sensitive screening tool for MetS than HTGW. However, this may be applicable only in similar ethnic groups with similar clustering pattern of metabolic risk factors for MetS [13].

The prevalence of MetS was highest using the criteria of HNCEPATP111. IDF definition had very good agreement with HNCEPATPIII, and good agreement with HW. HW is a better screening test than HTGW for MetS, having comparable prevalence of DM and CAD with IDF and HNCEPATPIII and most importantly requires no blood work or time to identify most MetS patients who can then be more fully screened for potential complications. The screening and definition for MetS should be based on clustering pattern of metabolic risks in the study population. This is true of all ethnic Malaysians and should be confirmed in other ethnic groups as a good screen, especially in developing countries.

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