ORIGINAL PAPER

Predictive value of Metabolic Syndrome components in detecting the syndrome in patients with type 2 Diabetes Mellitus

*H. Chanda[1], P. Kelly[2], B. Andrews[3], S. Siziya[4] S. Lakhi[1]

[1]*Department of Internal Medicine, University Teaching Hospital, private bag RW1X, Lusaka, Zambia.*
[2]*Tropgan Research group, University Teaching Hospital, Lusaka, Zambia.*
[3]*Vanderbelt University*
[4]*Department of Public Health, School of Medicine, University of Zambia, P.O. Box 50110, Lusaka, Zambia*

ABSTRACT

Background: Metabolic Syndrome (MetS) is a constellation of clinical features that increase cardiovascular morbidity and mortality in individuals. Up-to-date, there is no cheap, single surrogate test for MetS and current diagnostic criteria for the syndrome use scoring systems which are laborious, and the associated blood lipid tests are expensive and thus not adaptable to low resource countries such as Zambia.

Objective: The aim of the current study was to determine the predictive value of individual components of MetS in detecting the syndrome in patients with type 2 DM so as to explore simpler and cheaper alternative diagnostic approaches.

Materials and Methods: This was a cross-sectional hospital based study of 400 medical outpatients with type 2 DM. The National Cholesterol Education Program Adult Treatment Panel III (ATP III) was used as the standard diagnostic test and components of MetS that were measured included waist circumference, blood pressure, fasting blood sugar, fasting serum triglycerides and HDL cholesterol. We defined abdominal obesity as waist circumference $\geq$ 94cm for men and $\geq$80cm for women. The sensitivity, specificity, predictive values and likelihood ratios of individual components of MetS were determined.

Results: The prevalence of MetS using ATP III was 73% (91% in women and 50% in men; $p<0.001$).The presence of a large waist circumference had sensitivity and specificity of 90% with likelihood ratio of 9 and positive and negative predictive values of 96% and 78% respectively in predicting type 2 DM patients with MetS. Hypertension had sensitivity of 94% and poor specificity of 56% and thus a low likelihood ratio of 2. The positive and negative predictive values were 85% and 78% respectively. Both hypertriglyceridemia and low serum HDL levels had poor sensitivities of 42% and 28% but had high likelihood ratios (11 and 14 respectively) due to high specificities (96% for hypertriglyceridemia, 98% for low HDL). The negative and positive predictive values for hypertriglyceridemia were 97% and 38% respectively whereas low HDL had 98% and 33% as positive and negative predictive values for MetS. The presence of a high BMI had sensitivity of 56%, specificity of 80%, likelihood ratio of 3 and positive and negative predictive values of 88% and 40% respectively.

***Conclusions*:** In Zambian patients already suffering from type 2 DM, a large waist circumference is a fairly sensitive (90%) and specific (90%) test in predicting MetS with negative and positive predictive values of 96% and 78% respectively. And a type 2 DM patient with a large waist circumference

***Corresponding Author**
Humphrey Chanda,
Department of Internal Medicine
Private Bag RW 1X,
Lusaka, Zambia
humphreychanda@gmail.com

Key words: *Metabolic Syndrome, Type 2 Diabetes Mellitus, Predictive value.*

is 9 times more likely to have MetS than one with normal waist circumference, with a posttest probability of 96%. Therefore, simple waist circumference measurement can be used alone as an alternative cheaper surrogate test to detect MetS in patients with type 2 DM.

INTRODUCTION

Metabolic syndrome (MetS) is the clustering of three or more risk factors for cardiovascular disease in one individual. These risk factors include type 2 diabetes mellitus (DM), high blood pressure, high serum triglycerides, low levels of High Density Lipoprotein cholesterol (HDL) and abdominal obesity[1,2,3,4,5]. Each individual component of the MetS carries a high risk for cardiovascular disease and a combination of three or more in one person has an additive effect[6]. Therefore, recognizing MetS in patients is important because it acts as a clinical tool for identifying individuals at high risk of cardiovascular morbidity and mortality so as to initiate lifestyle and medical interventions early enough to avert complications[7].

Since its first official definition by the World Health Organization (WHO) in 1999[1,5,8,9] the diagnostic criteria for MetS has undergone a lot of modifications[2]. Despite these efforts, diagnostic criteria for MetS use scoring systems such as the harmonized[5] criteria and ATP III[1,10] which are laborious and the associated blood lipid tests are expensive and thus may delay diagnosis and treatment of the MetS. Type 2 DM patients are particularly at risk with about 75% to 80% estimated to have the MetS. There is growing evidence that simple waist circumference measurement may be used alone to diagnose MetS.[11,12,113] Previous studies[11,12,13] have assessed the predictive value of MetS components for insulin resistance compared to ATP III but there is a subsection of patients that do not have insulin resistance but have MetS and these studies were done in asymptomatic whites. Furthermore, the expressivity of MetS varies across populations[8] and study findings elsewhere may not apply to Zambia. To the best of our knowledge previous studies have not assessed the predictive value of individual components of MetS among Zambian patients suffering from type 2 DM.

The aim of the current study was to determine the predictive value of individual components of MetS in detecting the MetS in patients that already have type 2 DM so as to explore simpler and cheaper alternative diagnostic approaches.

RESEARCH DESIGN AND METHODS

This cross sectional study recruited 400 medical outpatients at the University Teaching Hospital (UTH), Lusaka, Zambia. These were patients already confirmed to have type 2 DM by the attending physicians. Written consent was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZAREC) and individual patients. Patients were identified using file review as they were waiting to be attended to.

Demographic data and past medical and drug history focused on diabetes and hypertension were obtained from each patient. Thereafter, a physician examined the patient to determine waist circumference, blood pressure, height, weight and to exclude confounders such as ascites, abdominal masses and pregnancy.

Waist circumference was measured in centimeters using a tape measure at the level of the umbilicus without top garments in the supine position. Height was measured in meters without head dress or footwear and weight was measured in kilograms without footwear. Body mass index was calculated by dividing height squared into the weight. Blood pressure was measured using a mercury sphygmomanometer after a patient had rested for at least 10 minutes. For each patient two blood pressure readings were taken 5 minutes apart, one in the sitting position and the other in the supine position and the final reading was the average of the two readings. To exclude inter-observer bias all clinical examinations were done by the same physician. For each patient, blood sugar, serum triglycerides and HDL were measured. Epi Info version 3.3.2 was used for data entry and analysis.

Metabolic syndrome definition

Since all study participants had type 2 DM only two of the following ATP III criteria were needed to establish the diagnosis of MetS,

1. Abdominal obesity with waist circumference for men $\geq$94cm and for women $\geq$80 cm,
2. Blood pressure > 130 systolic and/or >85mmHg diastolic on at least two or more occasions or drug treatment for elevated blood pressure.
3. Fasting triglycerides $\geq$ 1.7mmol./L, or drug treatment for elevated triglycerides.

4. Fasting HDL-cholesterol <0.9mmol/L in males and <1.0mmol/L in females or drug treatment for reduced HDL cholesterol.

Statistical analysis

Clinical and biochemical data was summarized by computing means ± standard deviation (SD) for continuous variables and percentages for categorical variables. Each patient was evaluated for the presence of MetS using the data obtained on blood pressure, waist circumference and fasting serum levels of triglycerides and HDL cholesterol. Unpaired student t-test was used to determine the differences in the distribution of continuous variables between males and females and the level of statistical significance was set at the 0.05 level. Using the ATP III as the standard test, we computed sensitivity, specificity, positive predictive values, negative predictive values, likelihood ratios and posttest probabilities for each attendant component of MetS so as to determine their predictive value in identifying type 2 DM patients with the syndrome.

RESULTS

Out of the 400 patients recruited into the study 222(56%) were women. The age range was 38- 96 years with a mean of 59.30±11.13 (SD) years. On average women were older and had larger waist circumferences than men. There was no significant gender difference in terms of height, weight and BMI. And all hypertensive patients in the study were already on antihypertensive drugs probably contributing to the mean systolic BP of 133±24 reported.

Table 1: Participants' clinical and biochemical characteristics

	Pooled (n=400)	Women (n=222)	Men (n=178)	P value
Age (Years)	.....	60.60 ± 10.35	57.70 ± 11.86	0.009
Height (m)	1.63 ± 0.23	1.61 ± 0.30	1.65 ± 0.06	0.115
Weight (Kg)	67.50 ± 14.84	65.80 ± 11.72	69.50 ± 17.82	0.014
SBP (mmHg)	133.10 ± 24.22	133.00 ± 24.83	133.30 ± 23.51	0.915
DBP (mmol./L)	82.90 ± 13.70	82.70 ± 12.34	83.10 ± 15.28	0.795
BMI (Kg/m^2)	25.70 ± 5.21	25.90 ± 4.71	25.50 ± 5.78	0.450
Waist circumference (cm)	90.90 ± 14.84	93.10 ± 13.36	88.10 ± 16.12	<0.001
Fasting blood sugar (mmol./l)	8.97 ± 3.80	9.06 ± 3.30	8.85 ± 4.36	0.586
Serum Triglycerides (mmol./L)	1.77 ± 1.61	1.81 ± 1.82	1.71 ± 1.30	0.583
Serum HDL (mmol./L)	1.30 ± 0.87	1.38 ± 0.99	1.21 ± 0.68	0.058

All data are means ± SD

Based on the ATP III criteria, prevalence of MetS was 73 % and was more common in women than in men (91% and 50% respectively, P< 0.001). All components of MetS were significantly more prevalent in women than men except for serum triglycerides.

Table 2: Prevalence of MetS and its components among type 2 DM patients.

	Pooled (n=400)	Women (n=222)	Men (n=178)	P Value
MetS	290 (73)	201 (91)	89 (50)	<0.001
Large WC*	273 (68)	183 (82)	90 (51)	<0.001
Hypertension	321 (80)	204 (92)	117 (66)	<0.001
Hypertriglyceridaemia	125 (31)	78 (35)	47 (31)	0.061
Low HDL	82 (21)	57 (26)	25 (14)	0.004

All data are n (%)
*Waist circumference

A combination of type 2 DM + large waist circumference + hypertension was the most common (68%) diagnostic triad for MetS and the prevalence of this triad was significantly higher in women than in men just like a combination of type 2 DM + low HDL + large waist circumference and type 2 DM + hypertension + low HDL. This is illustrated in table 3 below.

Table 3: Diagnostic triads of MetS among Zambians with type 2 DM

	Pooled	Women	Men	P value
Type2 DM + Large WC * + hypertension	248(62)	169(68)	79(44)	<0.001
Type 2 DM + Large WC * + Hypertriglyceridaemia	95(24)	59(27)	36(20)	0.138
Type 2 DM + Large WC * + low HDL	59(15)	43(19)	16(9)	0.004
Type 2 DM + Hypertension + Hypertr iglyceridaemia	107(27)	70(32)	37(21)	0.016
Type 2 DM + Hypertension + low HDL	67(17)	50(23)	17(10)	<0.001
Type 2DM + Hypertriglyceridaemia + low HDL	44(11)	24(11)	20(11)	0.893

All data are n (%)
*Waist circumference

Predictive value of MetS components in detecting the MetS in patients with type 2 DM

A large waist circumference had a sensitivity of 90% (90% in women, 92% in men) and specificity of 90% (86% in women, 91% in men) with positive and negative predictive values of 96% (98% in women, 91% in men) and 78% (47% in women, 92% in men) respectively in detecting MetS in type 2 DM patients. The posttest probability for waist circumference was 96% (94% in women, 97% in

men) and a type 2 DM patient with a large waist circumference is 9 times more likely to have the MetS than one with a normal waist circumference.

Table 4 Predictive value of MetS components in identifying the syndrome in patients with type 2 DM

MetS component		Sensitivity %	Specificity %	Positive predictive value%	Negative predictive value%	Likelihood Ratio	Posttest probability %
Large WC*	Pooled	90	90	96	78	9	96
	Male	92	91	91	92	10	97
	Female	90	86	98	47	6	94
Hypertension	Pooled	94	56	85	78	2	85
	Male	93	62	71	90	2	87
	Female	95	33	93	39	1	79
Hypertriglyceridaemia	Pooled	42	96	97	38	11	97
	Male	48	96	92	65	12	53
	Female	38	100	100	15	Infinite	100
Low HDL	Pooled	28	98	98	33	14	97
	Male	26	98	92	57	13	97
	Female	28	100	100	13	infinite	100
High BMI	Pooled	56	80	88	40	3	88
	Male	62	84	80	69	4	91
	Female	52	57	92	11	1	77

*Waist circumference

Hypertension had a sensitivity of 94% (95% in women, 93% in men), specificity of 56% (33% in women, 62% in men) and thus the low likelihood ratio of 2 observed. The positive and negative predictive values were 71% (93% in women, 71% in men) and 91% (39% in women, 90% in men) respectively, with posttest probability of 85% (79% in women, 87% in men).

Hypertriglyceridemia was 42% sensitive (38% in women, 48% in men), 96% specific (100% in women, 96% in men) with positive predictive value of 97% (100% in women, 92% in men) and negative predictive value of 38% (15% in women, 65% in men). The likelihood ratio was 11 with a posttest probability of 97% (100% in women, 53% in men).

Low HDL levels were 28% sensitive (28% in women, 26% in men), 98% specific (100% in women, 98% in men) with positive and negative predictive values of 98% (100% in women, 92% in men) and 33% (13% in women, 57% in men) respectively in identifying study participants with the MetS. A Zambian type 2 DM patient is 14 times likely to have MetS than one with high fasting serum HDL levels. The posttest probability for low HDL was 97% (100% in women, 97% in men).

For BMI, the sensitivity was 56% (52% in women, 62% in men) and specificity was 80% (57% in women, 84% in men) with likelihood ratio of 3. The positive and negative predictive values for MetS were 88% (92% in women, 80% in men) and 40% (11%in women, 69% in men) respectively, with a posttest probability of 88% (77% in women, 91% in men).

DISCUSSION

Diagnostic criteria for MetS use scoring systems which are laborious and the associated blood lipid tests are expensive and thus may delay diagnosis and treatment of the MetS. Type 2 DM patients are particularly at risk with about 75% to 80% estimated to have the MetS.[1] The main objective of the current study was to determine the predictive value of MetS components in detecting the syndrome among patients already suffering from type 2 DM so as to find an alternative single surrogate test that is simpler and cheaper than counting MetS components.

In this study of black Zambians, the ATP III criteria were used as the standard test and our findings confirm that a large waist circumference is a fairly sensitive (90%) and specific (90%) test to identify type 2 DM patients with the MetS as defined by ATP III. Even though hypertriglyceridemia and low levels of HDL cholesterol have higher likelihood ratios (11 and 14 respectively) due to better specificity, they suffer poor sensitivity (42% for hypertriglyceridemia, 28% for low HDL) and negative predictive values (38 for hypertriglyceridemia, 33% for low HDL) and above all they are more expensive to assess than waist circumference. Hypertension had higher sensitivity (94%) than a large waist circumference (90%) but it had poor specificity (56%) and thus a low likelihood ratio (2). A type 2 DM patient with a large waist circumference is nine times likely to have MetS compared to one with normal waist circumference, with a posttest probability of 96%. Most tests in medicine have likelihood ratios for a positive result between 1.5 and 20.[1] Higher values are associated with tests that are more accurate at identifying patients with disease, with values of 10 or greater of particular note.[1] Even though women had larger waist circumferences than men and probably contributing to the higher prevalence of MetS observed in women, the specificity of a large waist circumference is lower in women (86%) compared to men (91%) and thus the lower likelihood ratio observed in women. And this may be due to the fact that the abdominal circumference in women may be increased during pregnancy and may remain as such even way after they have delivered and thus giving false positive results for abdominal obesity and subsequently MetS. For this reason, a diabetic man with a large waist circumference is more likely to have the MetS than a diabetic woman with a large waist circumference (likelihood ratio 10 in men, 6 in women).

Previous studies

Even though the exact cause of the MetS is not known, both abdominal obesity and insulin resistance (IR) are believed to play a central role[1, 14, 15, 16,17,18,19]. A study in Cameroon [13] has even suggested that the prevalence of MetS in sub Sahara Africa may be driven by abdominal obesity which is diagnosed by simple waist circumference measurement.

Previous studies [11,12,13] have compared the diagnostic accuracy of MetS components with ATP III criteria in detecting IR. For example a study by Justo et al[11] among asymptomatic white patients in Minnesota, USA, reported that measuring waist circumference alone provided greater diagnostic accuracy than counting metabolic syndrome components as advocated for by ATP III.[15] Two other similar studies[12,13] before had reported similar findings that measures of obesity and dyslipidaemia have good predictive value for IR. But there is a subsection of patients without IR that have MetS. Furthermore, these earlier studies had used BMI as a measure of obesity instead of waist circumference and they were done among asymptomatic whites. To the best of our knowledge, the predictive value of MetS components in detecting the MetS in type 2 DM patients, as defined by ATP III, was not assessed in previous studies.

Study limitations

Even though we met the main objective of the study, the results may only apply to black Zambians with type 2 DM. Therefore, there is need to conduct a similar study in non diabetics and non black Zambians.

In summary, a large waist circumference is a fairly sensitive (90%) and specific (90%) test in predicting MetS with negative and positive predictive values of 96% and 78% respectively. And a type 2 DM patient with a large waist circumference is 9 times more likely to have MetS than one with normal waist circumference, with a posttest probability of 96%. Therefore, simple waist circumference measurement can be used alone as an alternative cheaper surrogate test to detect MetS in patients with type 2 DM.

ACKNOWLEDGEMENTS

We would like to thank the ministry of health for sponsorship, Dr Brown Kamanga for his support, the UTH biochemistry laboratory and clinic 5 staff for their support and last but not the least all the patients; without their participation the research would not have been possible.

REFERENCES

1. Fauci, A.S., Braunwald, E., Kasper, D.L., Hauser S.L, Longo D.L, Jameson J.L. *et al.* HARRISON'S principles of INTERNAL MEDICINE.2008. 17th Edition. *McGraw-Hill.* 1509-1514.
2. Reaven, G. The metabolic syndrome or insulin resistance syndrome? Different names, different concepts, and different goals. *Endocrinol Metab clin North Am* 2004; 33: 283-303
3. Reaven G : The metabolic syndrome. *J Insur Med* 2004; 36: 132-142
4. Kahn, R., Ruse, J., Ferrannini, E., Stern, M.. The metabolic syndrome: time for a critical appraisal: Joint statement from the American Association and the European Association for the study of Diabetes. *Diabetes care.*2005; 28:2289-304.[Pub Med].
5. Alberti K.G, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet 2005; 366: 1059-62.
6. Adediran, O.S., Edo, A.E., Jimoh, A.K, Ohwovoriole, A.E. Prevalence of metabolic syndrome among Nigerians with type 2 diabetes. *Diabetes International, African Edition* 2007; 15(1): 13-14.
7. Mathew, G.K, Praveen A. MEDICINE-Prep' Manual for undergraduates.2008.3rd Edition. 747-8.
8. Onyemelukwe, G.C., Bakari, A.G. The metabolic syndrome among Nigerians with type 2 diabetes. *MERA. 2006; 26:21-23.*
9. World Health Organization. Prevention of diabetes mellitus. Technical Report Series no. 844. *WHO, Geneva,* 1994
10. Expert panel on Detection, Evaluation, and Treatment of high blood Cholesterol in Adults: Executive summary of the Third Report of the National Cholesterol Education program (NCEP) Expert panel in Adults (Adult treatment panel III). *JAMA 285:2486-2497, 2001.*
11. Justo S.J, Bruce D.J, Thomas G.A, Kent R.B, Gary L.S, Stephen T.T. Correspondence between the Adult Treatment Panel III Criteria for Metabolic Syndrome and Insulin Resistance.2006. Diabetes Care 29:668-672.
12. Liao Y, Kwon S, Shaughnessy S, Wallace P, Huho A, Jenkins AJ *et al.* Critical evaluation of adult treatment panel III criteria in identifying insulin resistance with dyslipidaemia. *Diabetes care 2004; 27: 978-983.*
13. Cheal K.L, Abbasi F, Lamendola C, Mclaughlin T, Reaven G.M, Ford E.S; Relationship to insulin resistance of the Adult Treatment panel III diagnostic criteria for identification of the metabolic syndrome. Diabetes 2004; 53: 1195-200.
14. Anthonia, O. Prevalence of the metabolic syndrome. *Diabetology and Metabolic Syndrome* 2010; 2:1
15. Fezeu, L., Balkau B, Kengne A.P, Sobyngwi E, Mbanya J.C. Metabolic syndrome in a sub-Saharan African setting: central obesity may be the key determinant. *Atherosclerosis* 2007, 193(1):70-76.
16. National Institutes of Health. Third report of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III). *Bethesda: NHI,* 2001.
17. Hu, G., Qiao, Q., Tuomilehto, J. Plasma insulin and cardiovascular mortality in non diabetic European men and women: a meta-analysis of data from eleven prospective studies. *Diabetologia* 2004; 47: 1245-56.
18. Carr, D.B., Utzschneider, K.M., Hull, R.L. Intra-abdominal fat is a major determinant of the National Cholesterol Education program Adult treatment panel III criteria for the metabolic syndrome. *Diabetes 2004; 53(8): 2087-94.*
19. Anthonia, O. Prevalence and gender distribution of metabolic syndrome. *Diabetology and Metabolic Syndrome* 2010; 2:1.