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METABOLIC SYNDROME;

AGREEMENT BETWEEN METABOLIC SYNDROME DIAGNOSTIC CRITERIA AMONG TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT… Background: Metabolic syndrome and diabetes mellitus are the modifiable risk factors of cardiovascular diseases that double the chance of illness when occur together. Little work has been reported on the superlative criteria to diagnose metabolic syndrome among diabetics from the country. Therefore, the study was aimed to find the agreement between metabolic syndrome diagnostic criteria among type 2 diabetics. **Methods:** The retrospective data of 373 known type 2 diabetics who had reported history of taking antidiabetic medicines was analyzed. The new International Diabetes Federation definition, the World Health Organization criteria and the NCEP Adult Treatment Panel III criteria were used to diagnose metabolic syndrome. Data was analyzed by using Statistical Package for Social Sciences version 21. **Results:** Mean age of 373 diabetics was 49±10 years. Participants included 36.5% males and 63.5% females. Mean BMI, WC and BP were high in females; while HDL-C was low in males ($p < 0.05$). The frequency of MS by ATP III, IDF and WHO criteria were 88.2%; 87.4%; and 86.3%, respectively. Significant association was present between femininity, higher socioeconomic status and MS ($p < 0.05$). ATP III criteria diagnosed the maximum number of MS followed by IDF and WHO criteria. The highest agreement was found between ATP III and IDF criteria (k 0.487). More than 85.0% diabetics were diagnosed as true positive and true negative on all three criteria. The disagreement between the studied criteria ranged from 5.1% to 8.0%. **Conclusion:** The ATP III, IDF and WHO criteria can equally be used to diagnose metabolic syndrome among type 2 diabetics in the settings. However, ATP III and IDF criteria have an edge over WHO criteria. Increased rate of metabolic syndrome among diabetics have need of serious attention to reduce the risk of cardiovascular events.

Key words: Diabetes Mellitus Type 2, Metabolic Syndrome X, Obesity, Body Mass Index, Waist Circumference, Blood Pressure, Hypertriglyceridemia, Prevalence.

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INTRODUCTION

Metabolic syndrome (MS) is a group of disorders that includes abdominal obesity, dyslipidemia, insulin resistance and hypertension (HTN). Though all these components act as independent risk factors for cardiovascular diseases (CVD), but collectively these factors compound the risk to the higher level. Therefore diagnosing MS is necessary for its treatment and to prevent or delay CVD.[1] Type 2 diabetics have higher prevalence of MS than apparently healthy subjects; also diabetics with MS have increased risk of CVD than the diabetics without MS. Thus measuring prevalence of MS among T2DM patients is very crucial.[2]

Numbers of criteria for the diagnosis of MS are in practice worldwide. According to the new International Diabetes Federation (IDF) definition, a person presenting MS must have central obesity (waist circumference with ethnicity specific values) plus any two or more components.[3] Similarly World Health Organization (WHO) criteria also have a prerequisite i.e. Insulin Resistance/ Diabetes Mellitus plus any two or more of remaining components.[4] While the National Cholesterol Education Program - Adult Treatment Panel III (NCEP ATP III) criteria do not have a prerequisite and suggest a person with MS who have any three of the five components.[5] Depending on the criteria used, these differences may result in different prevalence rates of MS.

MS and DM are the modifiable risk factors of CVD that double the chance of illness when occur together. In Pakistan, several studies have measured frequency of MS among diabetics by using a single diagnostic criterion of their own choice.[6-10] And unfortunately, a little has been reported on the superlative criteria to diagnose MS among diabetics. Therefore, the study was designed with the hypothesis that new IDF definition is the better criterion than the WHO and ATP III criteria to diagnose MS among type 2 diabetics in the setting.

METHODS

Study type & Ethical approval

Ethical approval of this retrospective cross sectional study was obtained by the Institutional Ethical Review Board, Fatima Jinnah Medical University/ Sir Ganga Ram Hospital, Lahore on 5th January 2016 (No.26/ResProj/IERB).

Study population, Setting, Duration

The data of 373 known T2DM patients who had reported history of taking antidiabetic medicines and visited PHRC Research Centre specialized for Metabolic Diseases at Fatima Jinnah Medical University Lahore during the year 2012-13 was analyzed.

Metabolic Syndrome Diagnostic Criteria

The new International Diabetes Federation (IDF) definition[3], the World Health Organization (WHO) criteria[4] & the National Cholesterol Education Program - Adult Treatment Panel III (NCEP ATP III) criteria[5] were used to diagnose metabolic syndrome. Detailed description of the criteria used in the study shown in Table-I.

STATISTICAL ANALYSIS

Data was analyzed by using Statistical Package for Social Sciences (SPSS) version 21. Qualitative variables were presented as number (percentage) and quantitative variables as mean (standard deviation). Chi Square and Student's t-test were used for the comparison of qualitative and quantitative variables, respectively. Cross tabulation and kappa statistics were used to find agreement between diagnostic criteria for MS. P value <0.05 was considered significant.

RESULTS

Demographic Characteristics

Mean age of 373 type 2 diabetics was 49 ± 10 years. Patients included 36.5% males; 63.5% females; 54.4% illiterate; and 10.5% cigarette smokers. Monthly income of 59.5% patients was less than 100 USD. Mean duration of diabetes was 08 ± 06 years. No relationship was found between MS and the variables age, education, cigarette smoking and duration of diabetes. However, significant association was present between MS and the variables gender female and higher socioeconomic status ($p<0.05$).

	IDF[a] Criteria	WHO[b] Criteria	ATP[c] III Criteria
MS[d]	Central Obesity *plus* Any other two or more components	Diabetes Mellitus *plus* Any other two or more components	Any three or more components
Obesity (cm)	WC[e]	WHR[f]	WC
	Men ≥90	Men ≥0.90	Men ≥102
	Women ≥80	Women ≥0.85	Women ≥88
DM[g] (mg/dl)	Rx or ≥100 (FPG[h])	Rx or ≥110 (FPG)	Rx or ≥100 (FPG)
HTN[i] (mm/Hg)	Rx or ≥130/85	Rx or ≥140/90	Rx or ≥130/85
HDL-C[j] (mg/dl)	Men <40	Men <35	Men <40
	Women <50	Women <39	Women <50
HTG[k] (mg/dl)	≥150	≥150	≥150

Table-I. Description of Criteria Used to Diagnose Metabolic Syndrome

[a]IDF: International Diabetes Federation; [b]WHO: World Health Organization; [c]ATP III: National Cholesterol Education Program - Adult Treatment Panel III; [d]MS: Metabolic Syndrome; [e]WC: Waist Circumference; [f]WHR: Waist-to-hip ratio; [g]DM: Diabetes Mellitus; [h]FPG: Fasting Plasma Glucose; [i]HTN: Hypertension; [j]HDL-C: Low HDL-Cholesterol; [k]HTG: Hypertriglyceridemia.

Anthropometry & Biochemical Assay

Mean BMI, waist circumference and blood pressure levels were significantly higher in females (p <0.05). Mean HDL-C levels were significantly low in males (p <0.001). Mean triglycerides levels were raised among both genders (p 0.953) Table-II.

MS Prevalence Rate

The rates obtained by ATP III, IDF and WHO criteria were 88.2%; 87.4%; and 86.3%, respectively. It was seen that ATP III criteria identified the maximum number of diabetics with MS, while WHO criteria identified the minimum. According to IDF and ATP III criteria, gender female had significantly higher MS prevalence rate than males (p <0.001), but it was insignificant when WHO criteria was used (p 0.091). When compared to other two criteria, it was the WHO criteria that reported the highest MS rate (82.4%) among males; and the lowest rate (88.6%) among females Table-III.

MS Components

Obesity was the most prevalent MS component especially in females. It was found in more than 90% patients by IDF & WHO criteria. But its occurrence was reduced upto 67% patients by ATP III criteria. A large number of males evaluated as obese by IDF & WHO criteria were normal on ATP III criteria. The second most prevalent component was low HDL-C. Its incidence rate was significantly higher in females. The frequency of low HDL-C (34.3%) by WHO criteria was less than half of the frequencies determined by IDF & ATP III criteria. The prevalence of HTN was ranked at number three among MS components. The prevalence of HTN by WHO criteria (57.4%) was the lowest frequency when compared to the frequencies determined by other two studied criteria. No gender difference was observed for HTN except in WHO criteria (p <0.001). Hypertriglyceridemia was the least prevalent component by all three criteria and was equally present among both genders Table-III.

Agreement Analysis

The highest agreement was achieved between IDF & ATP III criteria (k 0.487; p <0.001). Overall 89.0% patients were identified on both criteria; 82.3% diabetics with MS and 6.7% without MS. A moderate agreement was estimated between IDF & WHO criteria (k 0.366; p <0.001). Total patients identified on both criteria were 85.5%; of which 79.6% diabetics were with MS and 5.9% without MS. The lowest agreement was evaluated between ATP III & WHO criteria (k 0.361; p <0.001) and total 85.8% patients were recognized on both criteria; There were 80.2% diabetics with MS; and 5.6% without MS. Overall more than 85.0% diabetics were screened as true positive and true negative on all three criteria. The disagreement between the studied criteria ranged from 5.1% to 8.0%. It was the lowest between ATP III & IDF criteria; and the highest between ATP III & WHO criteria Table-IV.

	All (n=373)	Male (n=136)	Female (n=237)	P value
Age (years)	49±10	52±10	47±09	<0.001
Weight (Kg)	70±13	72±11	69±14	0.030
Height (cm)	158±12	168±08	152±11	<0.001
Body Mass Index	28±07	25±04	30±07	<0.001
Waist Circumference (cm)	101±13	97±11	104±13	<0.001
Hip Circumference (cm)	102±11	98±09	105±12	<0.001
Waist-to-hip ratio	0.99±0.07	0.99±0.06	0.99±0.08	0.414
Glucose Fasting (mg/dl)	176±78	167±71	180±82	0.111
HDL-Cholesterol (mg/dl)	40±07	38±06	42±08	<0.001
Triglycerides (mg/dl)	213±131	212±127	213±134	0.953
Systolic Blood Pressure (mm/Hg)	135±18	131±17	136±18	0.008
Diastolic Blood Pressure (mm/Hg)	84±11	82±11	85±11	0.036

Table-II. Comparison of anthropometric measurements and biochemical assays

		IDF[a]	ATP III[b]	WHO[c]
MS[d]	All	326(87.4%)	329(88.2%)	322(86.3%)
	Male	103(75.7%)	106(77.9%)	112(82.4%)
	Female	223(94.0%)	223(94.0%)	210(88.6%)
	P value	<0.001	<0.001	0.091
Obesity	All	337(90.3%)	**252(67.6%)**	351(94.1%)
	Male	108(79.4%)	**36(26.5%)**	123(90.4%)
	Female	229(96.6%)	**216(91.1%)**	228(96.2%)
	P value	<0.001	<0.001	0.023
HDL-C[e]	All	287(76.9%)	287(76.9%)	**128(34.3%)**
	Male	83(61.0%)	83(61.0%)	37(27.2%)
	Female	204(86.1%)	204(86.1%)	91(38.4%)
	P value	<0.001	<0.001	0.028
HTN[f]	All	263(70.5%)	263(70.5%)	**214(57.4%)**
	Male	94(69.1%)	94(69.1%)	61(44.9%)
	Female	169(71.3%)	169(71.3%)	153(64.6%)
	P value	0.655	0.655	<0.001
HTG[g]	All	249(66.8%)	249(66.8%)	249(66.8%)
	Male	90(66.2%)	90(66.2%)	90(66.2%)
	Female	159(67.1%)	159(67.1%)	159(67.1%)
	P value	0.857	0.857	0.857

Table-III. Frequency distribution of metabolic syndrome and its components

[a]IDF: International Diabetes Federation; [b]ATP III: National Cholesterol Education Program - Adult Treatment Panel III; [c]WHO: World Health Organization; [d]MS: Metabolic Syndrome; [e]HDL-C: Low HDL-Cholesterol; [f]HTN: Hypertension; [g]HTG: Hypertriglyceridemia.

		ATP III[c]			
		MS	Non- MS		
IDF[a]	MS[b]	307(82.3%)	19(5.1%)	326(87.4%)	<0.001 (Kappa=0.487)
	Non- MS	22(5.9%)	25(6.7%)	47(12.6%)	
Total		329(88.2%)	44(11.8%)	373(100%)	
		WHO[d]			
		MS	Non- MS		
IDF	MS	297(79.6%)	29(7.8%)	326(87.4%)	<0.001 (Kappa=0.366)
	Non- MS	25(6.7%)	22(5.9%)	47(12.6%)	
Total		322(86.3%)	51(13.7%)	373(100%)	
		WHO			
		MS	Non- MS		
ATP III	MS	299(80.2%)	30(8.0%)	329(88.2%)	<0.001 (Kappa=0.361)
	Non- MS	23(6.2%)	21(5.6%)	44(11.8%)	
Total		322(86.3%)	51(13.7%)	373(100%)	

Table-IV. Agreement analysis between MS diagnostic criteria

[a]IDF: International Diabetes Federation; [b]MS: Metabolic Syndrome; [c]ATP III: National Cholesterol Education Program - Adult Treatment Panel III; [d]WHO: World Health Organization.

DISCUSSION

Diabetics with MS have increased risk of CVD than the diabetics without MS. For the reason, it was important to determine MS prevalence rate among T2DM patients. Asma et al.[11] used ATP III, IDF and WHO criteria to determine the prevalence rates of MS among Pakistani diabetics, and found pretty similar rates as obtained in the study. By using same three diagnostic criteria, Pokharel et al.[12] yielded frequencies among Nepali diabetics were slightly lower. In contrast to the above findings, Yadav et al.[13] reported percentages

among Indian diabetics were nearly half. Gender was significantly associated with MS and females had higher prevalence rate of MS than males.[11-13] Same significant association and high prevalence rate was achieved in present study.

Several studies had used a single criterion to diagnose MS among diabetics. The MS rates calculated in the study were a little higher but comparable to the other rates reported from Pakistan i.e. 85.8% (ATP III) by Mohsin et al.[7]; 77.0% (ATP III) by Tariq et al.[8]; 76.0% (IDF) by Ahmed et al.[9]; and 70.0% (WHO) by Khuwaja et al.[10] However rates 25.2% (WHO) from Nigeria[14]; and 24.0% (IDF) from Ghana[15] were amazingly low. These rates were about 3 times lesser than the MS rates reported among Pakistani diabetics. Few studies had used ATP III & IDF criteria to diagnose MS among diabetics. The prevalence rates (ATP=85.1%; IDF=87.2%) among Turkish diabetics[2] were same as of present study. However, rates (ATP=75.4%; IDF=76.8%) from Iran[16]; and (ATP=60.4%; IDF=71.7%) from Africa[17] were comparatively smaller.

Obesity was the most prevalent MS component especially in females. Likewise present study, other studies also reported obesity as the most frequently occurring MS component with gender association.[10,12] Obesity was found in more than 90% patients by IDF & WHO criteria; but was markedly reduced upto 67% patients by ATP III criteria. This significant difference seems because of ATP III criteria that do not recommend ethnic specific values for waist circumference.[5] Hypertension was the second least prevalent component in the study. Approximately similar ranking was achieved by Pokharel et al.[12] who found it the least prevalent component. Oppositely, Alebiosu et al.[14] found it as the most prevalent MS component.

The frequencies of MS (88.2%, 87.4%, and 86.3%) obtained in the study were slightly increased but comparable to other frequencies ranging 70.0% to 91.9% reported from Pakistan[7-10]; however greatly differed with the frequencies reported from India, Ghana and Nigeria.[13-15] It was established that ATP III criteria identified the maximum number of diabetics with MS, while WHO criteria identified the minimum. Similarly, the highest rates of MS by ATP III criteria and the lowest by WHO criteria were reported by other studies from Pakistan.[7-11] But studies from Turkey[2], India[13], Iran[16], and Africa[17] showed that it was the IDF criteria that reported the highest rate followed by ATP III criteria. The studies had reported the highest degree of agreement between IDF & ATP III criteria; and the lowest between IDF & WHO criteria.[11-13] Similar highest agreement for the same two criteria was obtained in the present study. But the lowest agreement was observed between ATP III & WHO criteria.

The ATP III, IDF and WHO criteria determined nearly equivalent frequencies and propose that these criteria can equally be used to measure frequency of MS in type 2 diabetics. However, the highest agreement was found between ATP III and IDF criteria; and had an edge over WHO criteria. By using ethnic specific values for waist circumference, ATP III criteria can further improve its agreement with IDF definition. The rates obtained in the studied population were very high and have need of serious attention by the physicians to screen diabetics for MS to reduce the risk of cardiovascular events.

Conflicts of Interest

It is stated that all the authors meet authorship criteria; assure you that the manuscript contains an original data of T2DM patients; is neither published nor under consideration for publication in any other journal; and there are no conflicts of interest. Also, all the authors have read and approved the manuscript.

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PREVIOUS RELATED STUDY

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