

# Relationship of metabolic syndrome defined by IDF or revised NCEP ATP III with glycemic control among Malaysians with Type 2 Diabetes

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## Research

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# Abstract

**Background** The chronic complications of Type 2 Diabetes (T2D) such as macrovascular disease is amplified with the increase in the number of metabolic syndrome (MetS) risk factors. This research aims to study the relationship of MetS, diagnosed by the International Diabetes Federation (IDF) or revised National Cholesterol Education Programs Adult Treatment Panel III (NCEP ATP III) criteria, with glycemic control, Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), C-peptide, and insulin resistance in T2D patients.

**Methods** The study is a cross-sectional observational study which, involved 485 T2D patients who are receiving treatment at the University Kebangsaan Malaysia Medical Center (UKMMC), Kuala Lumpur, Malaysia. The MetS among the T2D patients was diagnosed based on IDF and revised NCEP ATP III criteria. C-peptide and HbA1c levels were determined by an automated quantitative immunoassay analyzer and high-performance liquid chromatography, respectively. The MetS factors; FBG, triglyceride, and high-density lipoprotein cholesterol were measured by spectrophotometer.

**Results** Application of the IDF and revised NCEP ATP III criteria respectively resulted in 73% and 85% of the T2D subjects being diagnosed with MetS. The concordance of these criteria in diagnosing MetS among T2D patients was low ( $\kappa = 0.33$ ,  $P < 0.001$ ). Both IDF and revised NCEP ATP III criteria indicated that T2D patients with 5 MetS factors had higher insulin resistance ( $P = 2.1 \times 10^{-13}$ ;  $1.4 \times 10^{-11}$ ), C-peptide ( $P = 1.21 \times 10^{-13}$ ;  $4.1 \times 10^{-11}$ ), FBG ( $P = 0.01$ ;  $0.021$ ), and HbA1c ( $P = 0.039$ ;  $0.018$ ) than those T2D patients without MetS, respectively.

**Conclusion** Although there is a low concordance between IDF and revised NCEP ATP III criteria in the diagnosis of MetS among T2D patients, both criteria showed that T2D patients with 5 MetS factors had higher insulin resistance, C-peptide, FBG, and HbA1c.

## Background

The burden of non-communicable disease in the developing countries is increasing, and leading to high mortality rates [1]. Nowadays Type 2 Diabetes (T2D) is pandemic. According to international diabetes federation report indicates that more than 415 million of people worldwide adults have diabetes and is expected to rise to 642 million by 2040 [2]. The metabolic syndrome (MetS) is complex with high socioeconomic impact due to its association with increased morbidity and mortality [3]. Metabolic syndrome has attracted increased attention due to its significant impact on cardiovascular diseases (CVD) and its high prevalence in T2D patients [4-9]. Metabolic syndrome can be defined as a cluster of interconnected cardio-metabolic dysfunctions which is characterized by the increase in fasting blood sugar, waist circumference, blood pressure, triglycerides (TG), and reduction in high-density lipoprotein cholesterol (HDLc) [10, 11].

Globally, 20-25% of the adult population has MetS and they are twice as likely to die from it; and they are three times more likely to have a heart attack or stroke compared with people without the syndrome [2, 12]. This increase in MetS globally is associated with

The burden of non-communicable diseases in developing countries is increasing and leading to high mortality rates [1]. Nowadays, Type 2 Diabetes (T2D) is pandemic. The International Diabetes Federation (IDF) estimated that more than 415 million people have diabetes, and this number is expected to reach 642 million by 2040 [2]. The metabolic syndrome (MetS) is a complex disorder with a high socioeconomic impact on global health due to its association with increased morbidity and mortality [3]. The MetS has attracted increased attention due to its significant impact on cardiovascular diseases (CVD) and its high prevalence in T2D patients [4-9]. The MetS can be defined as a cluster of cardio-metabolic dysfunctions which is characterized by the increase in fasting blood glucose (FBG), waist circumference (WC), blood pressure (BP), triglycerides (TG), and reduction in high-density lipoprotein cholesterol (HDL-C) [10, 11].

It is estimated that 20-25% of the world's adult population suffers from MetS. People with MetS have a 3-fold increase in the risk of coronary heart disease and stroke and a 2-fold increased risk of mortality from cardio- and cerebrovascular disease compared with people without the MetS [2, 12]. This global increase in MetS is associated with the worldwide epidemic of obesity and T2D. Obesity and physical inactivity are the driving force for MetS, and a person with MetS has a 5-fold relative risk to develop T2D [6, 13-15]. Overweight and obesity lead to adverse metabolic effects on BP, HDL-C, TG, and impaired glucose tolerance (IGT) [16].

The National Cholesterol Education Programs Adult Treatment Panel III (NCEP ATP III) proposed a simple set of diagnostic criteria for MetS based on WC, TG, HDL-C, BP, and FBG levels [17]. In 2005, the IDF modified the MetS definition, which stated that WC is necessary for the diagnosis of MetS along with two or more of the other MetS parameters, including the treatment of the above MetS parameters [18]. In the same year, the American Heart Association and the National Heart, Lung, and Blood Institute revised the NCEP ATP III criteria and affirmed its overall utility and validity and proposed that it continued to be used with minor modifications and clarifications [19] (Table 1).

In 2009, a meeting between several organizations: International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity attempted to unify criteria [20]. In this meeting, the IDF criteria were modified, and it was agreed that WC should not be an obligatory component for the diagnosis of MetS, and three abnormal

findings out of 5 would qualify a person for the MetS. However, there is no consensus on the definition of MetS worldwide. Studies revealed that the impact of different definitions of MetS on the risk of future CVD and T2D is discrepant [21, 22].

Several studies have assessed the MetS among normal individuals in different populations, while few studies evaluated the MetS among T2D patients. Taking into consideration, T2D patients who had MetS also have cardiovascular risk factors. Therefore, the diagnosis of MetS in those T2D patients is very important for the detection, prevention, and treatment of the underlying risk factors [23, 24]. This research aims to study the relationship of MetS, diagnosed by the IDF or the revised NCEP ATP III criteria, with glycemic control (FBG, HbA1c, C-peptide, and insulin resistance) in T2D patients.

In the worldwide epidemic of obesity and diabetes. Obesity and physical inactivity are the driving force for MetS and a person with MetS has 5-fold relative risk to develop diabetes [6, 13-15]. Overweight and obesity lead to adverse metabolic effects on blood pressure, HDL cholesterol, TG and impaired glucose tolerance (IGT) [16].

The National Cholesterol Education Programs Adult Treatment Panel III (NCEP-ATPIII) proposed a simple set of diagnostic criteria for MetS based on waist circumference, TG, HDL-C, blood pressure, and fasting glucose level [17]. In 2005, the International Diabetes Federation (IDF) modified the MetS definition, which stated that waist circumference is necessary for the diagnosis of MetS along with any two of the other MetS parameters that were suggested by NCEP while IDF included the treatment of the above parameters as well [18]. In the same year the American Heart Association and the National Heart, Lung, and Blood Institute revised the NCEP criteria and affirmed its overall utility and validity and proposed that it continued to be used with minor modifications and clarifications [19] (Table 1).

**Table 1:** Diagnostic criteria of metabolic syndrome

Parameters	Revised NCEP	IDF
Definition	Any three of the following 5 features	Increased waist circumference
Elevated waist circumference	≥102 cm in men ≥ 88 cm in women	men ≥ 90 cm, women ≥ 80 cm along with any 2 of following features
Triglyceride	≥1.7 mmol/l or TG treatment	
HDL cholesterol	Men <1.03 mmol/l or women <1.29 mmol/l or HDL cholesterol treatment	
Blood pressure	Systolic ≥ 130 mmHg or Diastolic ≥85 mmHg or hypertension treatment or previously diagnosed hypertension	
Glucose	≥5.6 mmol/l or treatment for elevated glucose or previously diagnosed type 2 diabetes	

<sup>a</sup>Sub-Saharan Africans, Eastern Mediterranean and Middle East (Arab) populations use European and Ethnic South and Central Americans Use South Asia.

In 2009, a meeting between several organization: International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity attempt to unify criteria [20]. In this meeting, the IDF criteria was modified and it was agreed that waist circumference should not be an obligatory component and three abnormal findings out of 5 would qualify a person for the MetS. However, there is no consensus on the definition of MetS worldwide. Studies revealed that the impact of different definitions of MetS on the risk of future CVD and diabetes is discrepant [21, 22].

Several studies have assessed the MetS among normal individual in different populations whereas few studies assessed the MetS among T2D. Taking into consideration, diabetic patients who had MetS also have cardiovascular risk factors, therefore the diagnosis of MetS in those patients is very important for detection, prevention, and treatment of the underlying risk factors and for the reduction of the cardiovascular disease burden in the general population [23, 24]. This research aims to study the relationship of metabolic syndrome, diagnosed by International Diabetes Federation or the revised National Cholesterol Education Programs (NCEP-R) criteria, with glycemic control including fasting glucose, glycated hemoglobin, C-peptide and insulin resistance in T2D patients.

## Methods

### Study design and subjects

The current study was cross-sectional observation study. Four hundred and eighty-five previously diagnosed T2D patients aged between 30 and 70 years attending the University Kebangsaan Malaysia Medical Center, Kuala Lumpur, Malaysia were randomly recruited into the study after obtaining their informed consent. Ethical approval was obtained from the National University of Malaysia Research and Ethics committee.

### **Sample and data collection**

Waist circumference was measured midway between the lower rib margin and the superior iliac spine at the end of gentle expiration in a standing position. Blood pressure (BP) measurements were taken from each patient's right arm in the seated position by using an Omron IntelliSense Automatic Blood Pressure Monitor after 10 min rest in a quiet room. Two to three successive BP readings were obtained at 5 minutes intervals and averaged. Fasting blood (5ml) was collected from each subjected and divided into two tubes, EDTA tube for HbA1c measurement and plain tubes for biochemical investigations. The plain tubes were centrifuged for 10 minutes at 3000 × g within 30 minutes of blood collection and the serum from each sample was separated into two Eppendorf tubes and immediately kept at -20°C until analysis. The treatment for each participant was collected from the patient data record at the University Kebangsaan Malaysia Medical Center,

### **Biochemical analyses and Glycated hemoglobin (HbA1c) measurements**

Kits for the measurement of glucose, triglyceride and HDL cholesterol (reference number 10260, 10724, 10028 and 10018 respectively) were purchased from Human Company (Human GmbH, Wiesbaden, Germany). Human company elevated control sera (Humatrol P Reference number 13512) was used as quality control for these parameters. C-peptide was measured in an automated quantitative immunoassay analyzer (Immulite, DPC, Los Angeles, USA) using IMMULITE C-peptide kit (catalogue number LKPE1). Glycated hemoglobin (HbA1c) levels were determined by high performance liquid chromatography (VARIANT Hemoglobin A1c Reorder Pack, catalog no. 270-0003, Bio-Rad Laboratories, Inc., Richmond, California, USA) with lyphochek diabetes Bi-level controls (Catalogue number 740) as quality control. Insulin resistance was calculated using the Homeostasis Model Assessment (HOMA2) Calculator v2.2 available from Oxford Center for Diabetes, Endocrinology and Metabolism. This program used fasting C-peptide or insulin and blood glucose levels to calculate insulin resistance.

### **Assessment of metabolic syndrome**

Metabolic syndrome was diagnosed based on the IDF and NCEP-R criteria. All subjects included in this study were previously diagnosed with T2D and therefore blood glucose was excluded from the five MetS criteria. The MetS in T2D was diagnosed according to NCEP-R that included two or more of the following abnormalities:

1. Central obesity: waist circumference  $\geq 102$  cm for men or  $\geq 88$  cm for women

2. Raised blood pressure: systolic blood pressure  $\geq 130$  mmHg or diastolic blood pressure  $\geq 85$ mmHg or treatment of previously diagnosed hypertension
3. Raised triglyceride level:  $\geq 7$  mmol/l or specific treatment for this lipid abnormality
4. Reduced HDL cholesterol: men  $<1.03$  mmol/l, women  $<1.29$  mmol/l or HDL cholesterol treatment.

While according to the IDF criteria, MetS was defined by the presence of central obesity (waist circumference in Asian male  $\geq 90$  cm and female  $\geq 80$  cm) together with one of the other MetS criteria which includes; blood pressure, triglyceride, and HDL cholesterol with the same cut off point as NCEP-R.

### Statistical analysis

The analyses were assessed by SPSS version 11.5 software (SPSS, Inc, Chicago, USA). The fasting blood glucose, glycated hemoglobin, C-peptide, and insulin resistance were log transformed as they were not normally distributed. Mean and 95% confidence intervals were transformed back and reported. The Cohen's Kappa ( $\kappa$ ) test was used to evaluate the concordance between the IDF and NCEP-R criteria. The general linear model adjusted for age, sex, race and history of diabetes (as covariates) was used to study the correlation of MetS with glycemic control; fasting blood glucose, glycated hemoglobin, C-peptide and insulin resistance (as a set of dependent variables).

## Results

Four hundred and eighty-five previously diagnosed T2D subjects agreed to participate in this project. These patients were on insulin and/or oral antidiabetic medications (98%) followed by antihyperlipidemic agents (65%) and antihypertensive medications (64.5%). Three hundred fifty-six (73%) and 415 (85%) out of the 485 T2D had MetS when defined by the of IDF and NCEP-R criteria respectively (Table 2). Application of the harmonizing definition of the metabolic syndrome on T2D resulted in more than 97% of T2D with metabolic syndrome, thus this definition could not be included in this study.

**Table 2:** Concordance of International Diabetes Federation and reversed National Cholesterol Education Program criteria in the diagnosis of metabolic syndrome among type 2 diabetes

	No	% prevalence of metabolic syndrome in type 2 diabetes		Concordance ( $\kappa$ , P-value)
		NCEP-R	IDF	
Total	485	85	73	0.33, P<0.001
men	206	84	62	0.31, P<0.001
women	279	87	82	0.34, P<0.001
Malaysian Malays	253	88	74	0.35, P<0.001
Men	113	88	63	0.35, P<0.001
women	140	89	81	0.33, P<0.001
Malaysian Chinese	143	81	67	0.32, P<0.001
Men	65	85	57	0.25, P=0.01
Women	78	78	76	0.42, P<0.001
Malaysian Indians	89	85	83	0.24, P=0.024
Men	28	68	64	0.28, P=0.13
Women	61	93	92	0.08, P=0.54

The IDF and NCEP-R criteria concurred the diagnosis of MetS in 331 (68%) T2D, while 25 (5%) were diagnosed as MetS by the IDF but not by NCEP-R and 84 (17%) by NCEP-R criteria but not by IDF ( $\kappa$  0.33, P<0.001). NCEP-R criteria showed that not much differences in the prevalence of MetS between diabetic women (87%) and diabetic men (84%); while IDF criteria showed that the prevalence of MetS was higher in diabetic women (82%) than in diabetic men (62%). NCEP-R criteria showed that the highest prevalence of MetS was found in Malay (88%) followed by Malaysian Indian (85%) and Malaysian Chinese (81%); whereas IDF criteria showed that the highest prevalence of MetS was found among Malaysian Indians (83%) followed by the Malays (74%) and the lowest was among the Malaysian Chinese (67%). Both criteria showed higher prevalence's of MetS among women than men within the three races with low concordance particularly among the Malaysian Indian women ( $\kappa$  =0.08, P=0.54) table (2).

Multivariate analysis of covariance in both IDF and NCEP-R criteria revealed a significant relationship for metabolic syndrome,  $\Lambda' = 0.865$  and  $0.855$  P=  $4.8 \times 10^{-10}$  and  $4.7 \times 10^{-11}$  with powers to detect relationship were at 0.99998 and 0.99997 respectively. Type 2 diabetic patients with 5 MetS factors defined by IDF or



NCEP-R criteria had significantly higher FBG ( $P= 0.01, P=0.021$ ) than T2D without metabolic syndrome (Table 3 and 4). While both criteria did not show statistical difference between T2D with 4 or 3 MetS parameters and T2D without metabolic syndrome. HbA1c was higher in T2D with five criteria of MetS than T2D without metabolic syndrome ( $P= 0.039, P= 0.018$ ) in both IDF and NCEP-R criteria. Whereas IDF criteria showed that T2D patients with 5 criteria of MetS had a significantly higher HbA1c than T2D with 4 or 3 criteria of MetS ( $P= 0.034, P= 0.005$  respectively).

**Table 3:** The relationship of metabolic syndrome diagnosed by International Diabetes Federation criteria with glycemic control among type 2 diabetes

Parameters	Diabetes without metabolic Syndrome (n=129)	Diabetes with 3 criteria of metabolic syndrome (n=68)	Diabetes with 4 criteria of metabolic syndrome (n=146)	Diabetes with 5 criteria of metabolic syndrome (n=141)
Fasting glucose (mmo/L)	7.7 (7.24-8.20)	8.0 (7.33-8.71)	7.9 (7.48-8.39)	8.6 (8.15-9.16)
p-value		0.516	0.526	<b>0.01</b> , ( <sup>b</sup> 0.042)
Glycated hemoglobin (%)	7.7 (7.40-8.0)	7.6 (7.18-8.02)	7.6 (7.28-7.83)	8.2 (7.85-8.47)
p-value		0.69	0.507	<b>0.039</b> , ( <sup>a</sup> 0.034, <sup>b</sup> 0.005)
C-peptide (pmol/l)	489 (441-542)	569 (493-656)	667 (605-735)	809 (735-893)
p-value		0.096	<b><math>2.33 \times 10^{-5}</math></b>	<b><math>1.21 \times 10^{-13}</math></b> , ( <sup>a</sup> $7.1 \times 10^{-5}$ , <sup>b</sup> 0.006)
Insulin resistance	2.4 (2.23-2.54)	2.6 (2.39-2.85)	2.9 (2.69-3.03)	3.4 (3.16-3.56)
p-value		0.110	<b><math>7.65 \times 10^{-5}</math></b>	<b><math>2.1 \times 10^{-13}</math></b> , ( <sup>a</sup> $5.9 \times 10^{-5}$ , <sup>b</sup> 0.0002)

The result presented as geometric mean and 95% confidence interval of mean adjusted to age, sex, race and history of diabetes. <sup>a</sup>, Diabetes with 5 criteria of metabolic syndrome versus 3 criteria of metabolic syndrome; <sup>b</sup>, Diabetes with 5 criteria of metabolic syndrome versus diabetes with 4 criteria of metabolic syndrome.

**Table 4:** The relationship of metabolic syndrome diagnosed by reversed National Cholesterol Education Program criteria with glycemic control among type 2 diabetes

Parameters	Diabetes without metabolic Syndrome (n=70)	Diabetes with 3 criteria of metabolic syndrome (n=136)	Diabetes with 4 criteria of metabolic syndrome (n=196)	Diabetes with 5 criteria of metabolic syndrome (n=82)
Fasting glucose (mmo/L)	7.8(7.03-8.23)	8.0(7.54-8.5)	8.0(7.62-8.42)	8.8(8.11-9.49)
p-value		0.395	0.356	<b>0.021</b>
Glycated hemoglobin (%)	7.6(7.25-8.07)	7.5(7.24-7.82)	7.7(7.49-7.98)	8.4(7.96-8.80)
p-value		0.624	0.747	<b>0.018</b> , <sup>a</sup> 0.001, <sup>b</sup> 0.009
C-peptide (pmol/l)	443(385-509)	569(515-628)	688(633-747)	857(752-975)
p-value		<b>0.004</b>	<b>1.5×10<sup>-7</sup></b> , ( <sup>c</sup> 0.004)	<b>4.1×10<sup>-11</sup></b> ( <sup>a</sup> 1.4×10 <sup>-6</sup> , <sup>b</sup> 0.005)
Insulin resistance	2.3 (2.01-2.49)	2.6(2.46-2.79)	2.9(2.77-3.07)	3.5(3.21-3.78)
p-value		<b>0.01</b>	<b>3.1×10<sup>-6</sup></b> , ( <sup>c</sup> 0.01)	<b>1.4×10<sup>-11</sup></b> ( <sup>a</sup> 7.6×10 <sup>-8</sup> , <sup>b</sup> 0.0003)

The result presented as geometric mean and 95% confidence interval of mean adjusted to age, sex, race and history of diabetes. <sup>a</sup>, Diabetes with 5 criteria of metabolic syndrome versus diabetes with 3 criteria of metabolic syndrome; <sup>b</sup>, Diabetes with 5 criteria of metabolic syndrome versus diabetes with 4 criteria of metabolic; <sup>c</sup>, diabetes with 4 metabolic syndrome criteria versus diabetes with 3 criteria of metabolic syndrome.

C-peptide was significantly higher in T2D having five MetS factors ( $P= 1.21 \times 10^{-13}$ ,  $P= 4.1 \times 10^{-11}$ ) or four MetS factors ( $P= 2.33 \times 10^{-5}$ ,  $P= 1.5 \times 10^{-7}$ ) than those who were T2D without metabolic syndrome using both IDF and NCEP-R criteria respectively (Table 3 and 4). The NCEP-R criteria showed that T2D with three MetS factors had a significantly higher C-peptide than T2D without metabolic syndrome ( $P= 0.004$ ), whereas the IDF criteria showed no difference ( $P= 0.096$ ). Both IDF and NCEP-R criteria showed a significantly higher C-peptide in T2D who had 5 MetS factors than those who had 4 ( $P= 0.006$ ;  $0.005$ ) or 3 factors of metabolic syndrome ( $P= 7.1 \times 10^{-5}$ ;  $1.4 \times 10^{-6}$ ).

Type 2 Diabetes with five MetS factors had higher insulin resistance than T2D without metabolic syndrome ( $P= 2.1 \times 10^{-13}$ ;  $1.4 \times 10^{-11}$ ), and those who had three ( $P= 5.9 \times 10^{-5}$ ;  $7.6 \times 10^{-8}$ ) or four MetS factors ( $P= 0.0002$ ,  $P= 0.0003$ ) when IDF or NCEP-R criteria were applied respectively. Both, IDF and NCEP-R

criteria showed that insulin resistance was significantly higher in T2D with 4 MetS factors ( $P= 7.65 \times 10^{-5}$ ;  $3.1 \times 10^{-6}$ ) than T2D without metabolic syndrome respectively. NCEP-R criteria showed that T2D with 3 factors of MetS had higher insulin resistance than T2D without metabolic syndrome ( $P= 0.01$ ) while application of IDF criteria did not show a significant association ( $P= 0.110$ ).

## Discussion

In the present study, the prevalence of MetS among T2D was higher according to NCEP-R criteria compared to IDF and the concordance between these two criteria was low. However, in German Type 2 diabetes, IDF criteria showed more MetS than NCEP-R with a higher concordance (0.69) [25]. Whereas in United Kingdom the modified NCEP Criteria (BMI 28.8 kg/m<sup>2</sup> used instead of waist circumference) showed a higher prevalence than IDF with 0.60 concordance between these criteria [26]. Recent study among Ethiopians showed that NCEP criteria was higher than IDF (70% vs 60% with moderate concordance  $K=0.54$ ) [27]. The low agreement between the IDF and revised NCEP criteria in this study is essentially explained by differences in the contribution of waist circumference to the definition of these two criteria. The IDF stated that waist circumference is necessary for the diagnosis of MetS along with two other MetS factors; while revised NCEP defined MetS as any three MetS factors. The difference in concordance between the MetS diagnostic criteria in different populations is probably due to ethnic characteristics, dietary habits, and lifestyle, thus making it difficult to use a single diagnostic criterion for all populations.

The prevalence of MetS in our Malaysian T2D defined by IDF was similar to that reported in Ethiopians [28], Nepalese [29], Iranian [30], sub-Saharan Africans [31], and White American (70%) but higher than the Black (65%) and Mexican Americans (62%) [32] even though NCEP criteria were used in their study. On the other hand, a lower prevalence of MetS was reported from India 45.8, 57.7 and 28% using NCEP-ATP III, WHO and IDF criteria respectively [9] and Ghana 43.83% with NCEP-ATP III, 63.58% with WHO, and 69.14% with IDF criteria [34]. Similarly, lower prevalence of MetS was reported in recent studies from Ethiopia 53.5% in IDF whereas 66.7% in the NCEP-ATP III criteria [35] and from Sri Lanka 28.9%, 43.8%, and 70.6% using NCEP-ATP III, IDF, and WHO criteria, respectively [36]. A previous study reported higher prevalence of MetS in Malaysia Type 2 diabetics 96.1% and 84.8% according to NCEP ATP III and IDF definitions, respectively [37].

The increased waist circumference was more frequent in women (89% and 59%) than men (68% and 23%) when defined by IDF and NCEP-R respectively resulting in a higher prevalence of MetS in women than men, which is in agreement with previous studies [26, 29, 36, 38, 39]. According to a large population survey conducted, female diabetics were more obese compared to male diabetics (13% and 10%, respectively) [40]. In addition, diabetic women are more likely than men to have hypertension, low levels of HDL cholesterol and high levels of triglycerides [41]. Higher prevalence of MetS in females may be due to the higher HDL cut-off and lower waist circumference cut-off values in females as compared to males. Hence, more females than males can be recognized as having metabolic syndrome.

In general, IDF and NCEP-R criteria are the most applicable for epidemiological studies and clinical diagnosis of MetS. However, the concordance between these two criteria was low for the diagnosis of MetS among Malaysian T2D. NCEP-R criteria utilized American data while IDF criteria based on accumulated international data. There is an ethnic difference in waist circumference, which was considered by IDF. Although IDF and NCEP-R criteria were in low concordance for the diagnosis of MetS among Malaysian patients with Type 2 diabetes, there was a similar relationship of MetS particularly in the patients with 5 criteria, as defined either by IDF or NCEP-R, with glycemic parameters (insulin resistance, C-peptide, blood glucose and HbA1c). Type 2 diabetic patients with MetS have higher central obesity, which is associated with higher insulin resistance and higher blood pressure [16]. Accumulation of lipids in the liver and muscle of T2D has been shown to aggravate the insulin resistance [42]. This resulted in increased glucose production by the liver and less glucose conversion into glycogen by muscles. Consequently, beta cells compensated the insulin resistance via increased insulin production.

## Conclusion

The relationship of metabolic syndrome, as defined by either IDF or NCEP-R criteria, with insulin resistance and poor glycemic control were similar with a low concordance between IDF and NCEP-R criteria in the diagnosis of MetS among T2D. Based on the finding of our study as well as many other studies, it is clear that the different definitions of MetS give rise to different prevalence. In fact, the difference between the two criteria is in the definition of MetS which requires more consideration as chronic complication of T2D is amplified with metabolic syndrome.

## Abbreviations

IDF: International Diabetes Federation; NCEP-ATPIII: The National Cholesterol Education Programs Adult Treatment Panel III; NCEP-R: Revised National Cholesterol Education Programs; WHO: World Health Organisation; T2D: Type diabetes; MetS: Metabolic syndrome; CVD: Cardiovascular diseases; BP: Blood pressure; HDL: High-density lipoprotein; TG: Triglycerides; FBG: Fasting plasma glucose; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

## Declarations

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### Contributions

RSA and WZWN participated in study design, sample collection, experimental tests, conducted statistical analyses, interpreted results, and wrote the draft of the manuscript. NAK sample collection and study

design, MA and SAA critically revised and edited the manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

The data are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

The study was approved by National University of Malaysia Research and Ethics committee. Written informed consent was obtained from each participant before the sample collection.

## Consent for publication

Not applicable.

## Competing interests

The authors declare no conflict of interest.

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