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Original article

Comparison of glycated hemoglobin with fasting plasma glucose in definition of glycemic component of the metabolic syndrome in an Iranian population

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ABSTRACT

Aims: The aim of this study was to compare the utility of glycated hemoglobin (GHb) versus the fasting plasma glucose (FPG) in definition of glycemic component of the metabolic syndrome (MetS) in a non-diabetic Iranian population.

Methods: A cross-sectional study of first-degree relatives (FDRs) of patients with type 2 diabetes was conducted from 2003 to 2005. A total of 2410 non-diabetic FDRs of consecutive patients with type 2 diabetes 30–60 years old were examined. All subjects underwent a standard 75 g 2-h oral glucose tolerance test and GHb measurement. Consensus criteria in 2009 were used to identify MetS. Glycemic component of MetS was defined as either FPG $\geq$ 100 mg/dl or GHb $\geq$ 5.7%. The mean (SD) age of participants was 43.6 (6.5) years.

Results: The prevalence of MetS was 33.5% (95% confidence interval (CI): 31.6, 35.4) based on FPG criterion alone and 28.6% (95% CI: 26.8, 30.4) based on GHb criterion alone. Use of combination of both criteria increased the prevalence of MetS (36.7%; 95% CI: 34.8, 38.6). There was 88.7% (95% CI: 87.5, 90.0) agreement between the GHb and FPG when either was used to define MetS (κ coefficient = 0.737).

Conclusions: These data indicate that using GHb may be an acceptable surrogate of FPG to define glycemic component of MetS.

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1. Introduction

Metabolic syndrome (MetS), a clustering of factors that occur together more often than by chance alone, is an important clinical and public health problem worldwide and poses a significant risk for cardiovascular disease and type 2 diabetes [1]. Several clinical definitions have been proposed by different organizations over the past 15 years [2,3]. In 2009, a unified definition of MetS was proposed by several organizations [1] and consists of three of the five components, including elevated waist circumference, elevated triglycerides and reduced high density lipoprotein cholesterol (HDL), elevated blood pressure and fasting glucose, in which insulin resistance plays a key pathogenic role. This new definition considers that abdominal obesity is not an obligatory component of MetS. In 2010, the American Diabetes Association (ADA) has recommended the use of the glycated hemoglobin (GHb) to diagnose pre-diabetes and diabetes [4]. These changes in the definition of raised plasma glucose have prompted a few authors to use of a GHb criterion instead of the FPG in the definition of MetS. While use of GHb instead of FPG in definition of MetS has been described in only four studies from United States [5], Europe [6,7] and Asia [8], comprehensive data for Middle East populations have not been reported.

The objective of this study, therefore, was to assess the use of GHb instead of FPG in definition of glycemic component of the MetS in a non-diabetic Iranian population.

Racial disparities in GHb values and MetS exist [9–12]. The reason for ethnic differences are not clear but can be ascribed to differences in rates of obesity, hypertension, glucose intolerance, and body fat distribution patterns. Therefore, at an ethnological level, the study contributes by characterizing the occurrence of MetS based on FPG and/or GHb criteria in a specific population from central Iran.

2. Subjects and methods

Our sample comprised 3176 (818 men and 2358 women) first-degree relatives (FDRs) for a consecutive sample of patients with type 2 diabetes attending clinics in Isfahan Endocrine and Metabolism Research Center affiliated to Isfahan University of

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Medical Sciences, Iran, between 2003 and 2005. Participants with diabetes mellitus ($n = 504$) were excluded because there is controversy whether the diagnosis of MetS convey additional meaning in individuals with diabetes who should already be aggressively treated due to high cardiovascular risk. Those with no GHb measured ($n = 262$) were also excluded from the study; 2410 (620 men and 1790 women) subjects were included in analysis of the utility of GHb and FPG in definition of glycemic component of the MetS. The study protocol was approved by the Institutional Review Board of Isfahan University of Medical Sciences, Iran, and an informed consent form was signed by each participant.

2.1. Procedures

Details of the recruitment, anthropometric measurements and laboratory methods have been described in detail elsewhere [13,14]. In summary, the FDRs of patients with type 2 diabetes included siblings or children and reported to clinics in the morning after an overnight fast. Height and weight were measured with subjects in light clothes and without shoes using standard apparatus. Waist was measured midway between the lower rib margin and the iliac-crest at the end of a gentle expiration. Hip circumference was measured over the greater trochanters directly over the underwear. Body mass index (BMI) (weight/height^2 [kg/m^2]) is recognized as the measure of overall obesity. Resting blood pressure (BP) was measured after subjects had been seated for 10 min by using a mercury sphygmomanometer and appropriately sized cuffs, using standard techniques. Those participants with plasma glucose (PG) $\geq$200 mg/dl were considered as diabetic. If fasting plasma glucose (FPG) was $\geq$126 and $<$200 mg/dl, a second FPG was measured on another day. If the second FPG was also $\geq$126 mg/dl, participants were considered as diabetic. Subjects with FPG $<$ 126 mg/dl underwent a standard oral glucose tolerance test [OGTT (75 g glucose 2-h)] according to the ADA criteria [4]. Venous blood was sampled 0, 30, 60, and 120 min after oral glucose administration. Plasma glucose $\geq$200 mg/dl at 2 h in OGTT were also considered diabetic.

Glycated hemoglobin (GHb) (measured by ion-exchange chromatography), total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol (measured using standardized procedures), and low-density lipoprotein (LDL) cholesterol (calculated by the Friedewald equation [15]: LDL = (total cholesterol − HDL − triglyceride)/5, for total triglycerides less than 400 mg/dl) were assessed.

Cases of MetS were identified according to the consensus criteria released in 2009 [1], which was the same as the third report of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) [12]. It was considered present when at least three of the following characteristics were observed: central obesity, defined using ethnic-specific cut points of waist (waist circumference $\geq$102 cm in men and $\geq$88 cm in women); triglycerides $\geq$ 150 mg/dl; HDL $<$ 40 mg/dl in men and $<$50 mg/dl in women; blood pressure (BP) $\geq$130/85 mmHg or on antihypertensive medication, or raised plasma glucose, defined as FPG $\geq$ 100 mg/dl. We compared the use of GHb $\geq$ 5.7% versus the FPG $\geq$ 100 mg/dl in the definition of the glycemic component of MetS. With the use of GHb in definition of glycemic component of the MetS, we follow the ADA recommendations that established a cut-off point of $\geq$5.7% [16]. Agreement between two definitions was the percentage of individuals who were classified the same under both definitions.

2.2. Statistical analysis

Statistical methods used included the Student's t-test; chi squared test, analysis of variance or Kruskal–Walis tests for normally or non-normally distributed continuous variables respectively and general linear model. Age-, gender-adjusted means were calculated and compared using general linear models with Bonferroni correction for multiple comparisons. The κ statistic was calculated as a measure of agreement between the two definitions of the MetS using the FPG and/or GHb, respectively. Analyses were performed using SPSS version 13 for Windows (SPSS Inc., Chicago, IL, USA). All tests for statistical

Table 1
Age and age-, gender-adjusted mean and proportion characteristics of non-diabetic first-degree relatives of patients with type 2 diabetes by diagnosis of metabolic syndrome according to fasting plasma glucose, glycated hemoglobin or both.

Characteristic	No MetS using either FPG or GHb	MetS using FPG only	MetS using GHb only	MetS using both FPG or GHb
Number (%)	1526 (63.3)	808 (33.5)	690 (28.6)	885 (36.7)
Age (yr.)	42.2 (0.17)	44.4 (0.23)	44.4 (0.25)	44.5 (0.22)***
Height (cm)	159.2 (0.15)	159.7 (0.20)	160.0 (0.22)	159.7 (0.19)*
Weight (kg)	70.1 (0.29)	79.4 (0.39)	80.1 (0.42)	79.1 (0.38)***
Waist circumference (cm)	85.6 (0.22)	94.4 (0.29)	94.9 (0.32)	94.2 (0.28)***
Hip circumference (cm)	105.4 (0.22)	111.4 (0.30)	111.6 (0.33)	111.2 (0.29)***
Waist-to-hip ratio	0.81 (0.001)	0.85 (0.002)	0.85 (0.002)	0.85 (0.002)***
Body mass index (kg/m^2)	27.7 (0.10)	31.2 (0.14)	31.3 (0.15)	31.0 (0.13)***
Fasting plasma glucose (mg/dl)	93.2 (0.29)	100.3 (0.40)***[a]	96.9 (0.43)	99.3 (0.38)***
Plasma glucose 30 min (mg/dl)	137.7 (0.82)	151.6 (1.12)**[a]	147.1 (1.22)	150.0 (1.08)***
Plasma glucose 60 min (mg/dl)	137.7 (1.05)	161.2 (1.44)	157.5 (1.55)	159.7 (1.38)***
Plasma glucose 120 min (mg/dl)	111.5 (0.83)	123.5 (1.13)	121.4 (1.22)	123.1 (1.08)***
Glycated hemoglobin (%)	4.9 (0.02)	5.2 (0.03)	5.4 (0.03)***[b]	5.3 (0.03)***
Cholesterol (mg/dl)	195.5 (1.00)	204.7 (1.35)	203.4 (1.46)	203.8 (1.29)***
LDL (mg/dl)	121.1 (0.89)	122.0 (1.21)	120.9 (1.32)	121.5 (1.16)
HDL (mg/dl)	48.7 (0.28)	40.8 (0.38)	40.0 (0.41)	41.0 (0.36)***
Triglyceride (mg/dl)	132.4 (2.72)	220.1 (3.67)	223.5 (4.00)	216.7 (3.51)***
Systolic BP (mm Hg)	110.6 (0.41)	122.6 (0.56)	123.7 (0.60)	121.9 (0.53)***
Diastolic BP (mm Hg)	71.3 (0.31)	80.2 (0.41)	81.4 (0.45)	80.0 (0.40)***
Obesity (BMI $\geq$ 30), no. (%)	352 (23.5)	467 (58.1)	408 (59.7)	492 (56.0)***
Women, no. (%)	1123 (73.7)	621 (76.9)	527 (76.4)	667 (75.4)

Age-, gender adjusted means were calculated using general linear models with Bonferroni correction for multiple comparisons. Data are express as mean (SE) or number (%). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ comparison across all four groups. [a]***$P < 0.001$, [a]**$P < 0.01$ the difference in the mean of the variables compared FPG-alone group with GHb-alone. [b]***$P < 0.001$. The difference in the mean of the variables compared GHb-alone group with FPG-alone. IGT: impaired glucose tolerance, LDL: low density lipoprotein cholesterol, and HDL: high density lipoprotein cholesterol.

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