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ORIGINAL ARTICLE

Comparison of ADA and WHO Criteria in Detecting Pattern of Glucose Disorders in a Population-Based Study: Tehran Lipid and Glucose Study

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Many studies have been performed to compare WHO and ADA criteria for detection of diabetic patients. This study aims to compare these two criteria in a community-based epidemiological survey in an urban population of Tehran, Iran.

Materials and Methods: Subjects were chosen from among 15005 urban individuals, 3 years old and over, selected by cluster random sampling in the cross-sectional phase of a longitudinal study conducted in the east of Tehran; there were 3870 men and 5359 women aged 20 years and over. Those with known diabetes were excluded. Blood samples were taken after 12-14 hours overnight fast and 2 hours post 75gr glucose taken orally. Prevalence of glucose tolerance categories and the level of agreement (κ statistic) were obtained using WHO and ADA criteria.

Results: Based on WHO criteria 6.0% (0.95 CI, 5.5-6.5) had type-2 diabetes and 13.0% (12.3-13.7) had IGT (Impaired glucose tolerance). Using ADA, 3.3% (2.9-3.7) had type-2 diabetes and 4.8% (4.4-5.2) had IFG (Impaired fasting glucose); p<0.05 and <0.001 for diabetes and IGT, respectively and 7355 (84%) had concordance with both criteria. Among 7105 normal subjects classified according to WHO criteria, 153 (2.2%) had IFG or diabetes by ADA, whereas from 8068 normal subjects according to ADA criteria, 1116 (13.8%) had IGT or diabetes based on WHO criteria. The level of agreement (κ statistic) between the two criteria was 35% (p<0.001). Sensitivity and specificity of ADA criteria were 45.5 and 100%, respectively, considering WHO as the gold standard.

Conclusion: Our data shows a low level of agreement between WHO and ADA diagnostic criteria for detection of diabetes. Patients with unknown diabetes, glucose disorders are detected more frequently using WHO criteria.

Key Words: Diabetes mellitus, Impaired glucose tolerance, Impaired fasting glucose, WHO criteria, ADA criteria, Tehran Lipid and Glucose Study.

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Introduction

The diagnosis and classification of diabetes through the years has been controversial. In 1979 to some extent, worldwide consensus was achieved.[1] Although the American National Diabetes Data Group (NDDG) and World Health Organization (WHO)[2,3] were still recommending slightly different criteria, the American Diabetes Association (ADA) proposed a revised classification and diagnostic criteria in 1997.[4] Based on epidemi-

ologic surveys, ADA changed the diagnostic criteria, lowering the fasting plasma glucose (FPG) criterion to ⩾ 7.0 mmol/L (⩾ 126 mg/dL); the hope was that these changes would make the diagnosis easier and thus more likely to be made. For clinical diagnosis, the ADA recommends that the diagnosis should be comfirmed by a second test, while for epidemiological studies, they recommended the single use of FPG ⩾7.0 mmol/L alone. The WHO study group gave both fasting and 2-hour glucose criteria for diagnosis, but for epidemiological and screening purposes they stated that the 2-hour assessment could be used alone; a recommendation followed in most epidemiological studies.[4,5] There have been many studies in recent years comparing ADA and WHO criteria for detection of diabetic patients[6-8] and many have found great discrepancies between the two criteria. In order to investigate this issue in an Iranian population, we compared WHO and ADA diagnostic criteria in the categorization of glucose tolerance in a representative sample of an urban population living in the east of Tehran. Possible discordance of diagnostic categories and level of agreement between both diagnostic criteria were computed.

Subjects and Methods

The Tehran Lipid and Glucose Study (TLGS) is a study conducted to determine the risk factors for atherosclerosis among Tehran's urban population and to develop population-based measures to change the life-style of the population and ultimately to prevent the rising trend of diabetes mellitus and dyslipidemias.[9] The design of this study encompasses two major components: phase 1 is a cross-sectional prevalence study of coronary artery disease (CAD) and associated risk factors and phase 2 is a prospective interventional study for 20 years. A cluster random sampling technique was used to recruit 15005 people, aged 3 years old and over, from the urban district 13 of Tehran, the capital of the Islamic Republic of Iran. All 9229 individuals, aged 20 years and over [3870 (41.9%) males and 5359 (58.1%) females] participating in the cross sectional phase of the TLGS from 1998-2001 entered this study. Comparison between the two criteria was performed excluding known cases of diabetes mellitus.

Medical history and clinical examination

All invited participants, after giving informed written consent, were studied by trained physicians according to a uniform protocol. Demographic and lifestyle information were obtained using a standard and validated questionnaire.

For measuring blood pressure, the participants remained seated for 15 minutes, when a qualified physician measured blood pressure according to standard protocol, two times after one more measurement for determining peak inflation level using a standard mercury sphygmomanometer, calibrated by the Iranian Institue of Standards and Industrial Researchs. Anthropometic measurements were taken with shoes removed and the participans wearing lightweight clothing. Weight and height were measured according to the standard protocol. Waist circumference was measured at the level of the umbilicus and hip circumference was measured over light clothing at the widest girth of the hip. Body mass index was calculated by dividing the weight in kilograms to the square of height in meters.

Serum glucose analysis

A blood samples was drawn between 7:00 and 9:00 AM from all study participants after 12-14 hours overnight fast, and 82.5g glucose monohydrate solution (equivalent to 75g anhydrous glucose; Cerestar EP, Spain) was then administered orally. Blood samples were obtained 120 minutes after the ingestion of glucose load, taken in sitting position according to the standard protocol and centrifuged in 30-50 minutes after collection. All blood glucose analyses were carried out at the TLGS research laboratory on the day of blood collection by selectra 2-auto analyzer (vital scientific, Spankern, Netherlands). Glucose was

Table 1. Distribution of glucose status according to WHO and ADA criteria in various age groups of Tehranian adults, excluding known diabetic patients

	n	WHO*			ADA†		
Age (years)		Normal	IGT	DM	Normal	IFG	DM
20-29	1825	96.5‡	3.1	0.4	98.6	1.0	0.3
30-39	2457	89.4	8.5	2.1	96.5	2.6	1.0
40-49	1790	76.9	15.7	7.4	90.0	6.1	3.9
50-59	1338	69.4	19.7	10.9	85.4	8.1	6.5
60-69	1053	63.3	23.1	13.6	84.4	8.1	7.5
⩾ 70	320	56.6	28.4	15.	80.9	12.2	6.9
Total	8783	80.9	13.0	6.0	91.9	4.8	3.3

* WHO criteria, 2hPG: normal <140,IGT 140-199, DM ⩾ 200 mg/dL
† ADA criteria, FBG: normal < 110, IFG 110-125, DM ⩾ 126 mg/dL
‡ Numbers show percent

measured using the enzymatic colorimetric method with the glucose oxidase technique. Assay performance was monitored every 20 test intervals using the glucose control serum, percinorm (normal range) and percipath (pathologic range) whenever applicable (Boehringer Mannheim, Germany; cat. No 1446070 for percinorm and 171118 for percipath. Glucose standard (c.f.a.s. Roche, Germany; cat. No 759350) was used to calibrate the selectra 2 auto analyzer each day of laboratory analysis. All samples were analyzed when internal quality control met the acceptable criteria. Inter and intra-assay coefficients of variations were both 2.2%. According to WHO criteria, subjects were classified as normal (2hPG < 140 mg/dL), IGT (Impaired Glucose Tolerance, 140 ≥ 2hPG > 140), or diabetic (2hPG ≥ 200 mg/dL), and according to ADA criteria subjects were normal (FBS < 110 mg/dL), IFG (Impaired Fasting Glucose, 110 < FBS ≤ 125), and diabetic (FBS ≥ 126 mg/dL).[3,4,10]

Statistical analysis

Prevalence of different glucose status according the two criteria was computed. The level of agreement of the diagnostic categories between WHO and ADA criteria was examined using κ statistics. $p<0.05$ was considered to be statistically significant. This research was approved by the appropriate Research Ethics Committee.

Results

According to WHO criteria, 6.0% (0.95 CI, 5.5-6.5) of the urban residents of Tehran, aged 20 years and over, had newly diagnosed diabetes and 13.0% (12.3-13.7) had IGT. The prevalence of known DM, new DM, and IGT increased steadily by age (Fig. 1).

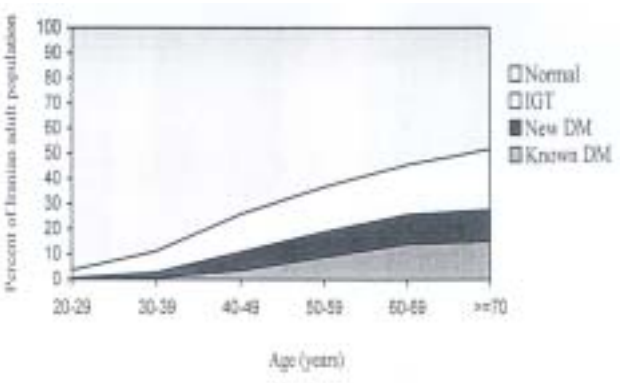

Fig.1. The trend in prevalence of diabetes and impaired glucose tolerance in age groups

Based on ADA criteria 3.3% (2.9-3.7) had diabetes and 43.8% (4.4-5.2) had IFG. Prevalence of glucose disorders detected by WHO criteria was at least two times higher than that of ADA criteria. Prevalence of glucose disorders increased steadily with age by WHO criteria but using ADA criteria there was a decline in IFG prevalence in the 60-69 year old age group (Table 1).

The two criteria were concordant in 7355 (84.0%) of subjects. Among 153 discordant individuals classified as normal by WHO criteria, 140 (91.5%) were classified as IFG by ADA, whereas from 1116 discordant normal individuals by ADA criteria, 967 (86.6%) had IGT using WHO criteria. On the other hand, of 992 individuals classified as IGT, 967 (97.5%) were categorized as normal by ADA and from 270 IFG individuals, 140 (51.8%) were classified as normal using WHO criteria, the rest (45.2%) were diagnosed as having diabetes (Table 2). The level of agreement between the two diagnostic criteria was low (κ=0.35, p<0.001).

In order to compare the two criteria from the point of view of biological characteristics, we considered age, BMI, WHR, FBS, 2-hPG, mean systolic and diastolic blood pressure and lipid profiles (Table 3 and 4). Concordant diabetic (n=250) and "high-risk" group (IGT, or IFG, n=153) had significant higher age, BMI, WHR, FBS, 2hPG, and mean systolic and diastolic blood pressure (p<0.001). After adjustment for age and sex, all individuals who were normal by WHO criteria and abnormal (IFG or diabetes) by ADA criteria (153) showed higher fasting glucose and lower 2-hPG than those who were normal by

Table 2. The number of Tehranian adults according to glucose tolerance status by WHO and ADA criteria

	ADA			
WHO	**Normal**	**IFG**	**DM**	**Total**
Normal	6952	140	13	7105
IGT	967	153	25	1145
DM	149	130	250	529
Total	8068	423	288	8779

Table 3. Mean values of age, WHR, BMI, fasting and 2-h plasma glucose systolic blood pressure (SBP) and diastolic blood pressure (DBP) of Tehranian adults by diagnostic criteria

WHO/ADA	**n**	**Age (years)**	**BMI (Kg/m^2)**	**WHR**	**FBS (mg/dL)**	**2-hPG (mg/dL)**	**SBP (mm/Hg)**	**DBP (mm/Hg)**
Normal/Normal	6909	40.0 (39.8-40.4)	26.3 (26.2-26.4)	0.86 (0.85-0.86)	88.1 (87.9-88.3)	121.9 (103.4-140.0)	116.4 (116.0-116.7	76.6 (76.3-76.8)
IGT/IFG	153	52.7* (50.7-54.7)	30.3* (29.4-31.2)	0.92* (0.90-0.93)	115.6* (114.8-116.3)	161.5* (153.0-17.0)	131.5* (128.2-134.7)	82.5* (80.8-84.2)
DM/DM	250	54.4* (53.0.55.7)	29.6* (29.0-30.0)	0.95* (0.94-0.96)	168.2* (162.2-174.2)	273.8* (257.2-290.3)	136.7* (133.7-139.7)	84.9* (83.4-86.5)
Normal/ IFG,DM	153	47.2* (45.1-49.4)	28.0* (27.3-28.7)	0.90* (0.89-0.92)	116.4* (114.5-118.3)	115.3* (60.9-169.6)	124.0* (120.8-127.2)	79.5* (77.8-81.2)
IGT, DM/ Normal	1116	50.7* (49.9-51.5)	28.5* (28.3-28.8)	0.90* (0.90-0.91)	94.7* (94.2-95.2)	149.6* (146.5-152.7)	129.5* (128.3-130.7)	81.9* (81.3-82.6)

Data are point values (95% CI).

* Statistically significant differences (p<0.05) comparing the mean values (reference group normal subjects by both criteria)

Table 4. Mean values of lipid profiles categorized by diagnostic criteria

WHO/ADA	n	Total cholesterol (mg/dL)	LDL-C (mg/dL)	HDL-C (mg/dL)	Triglyceride (mg/dL)
Normal/Normal	6952	204 (202-205)	131 (130-131)	42.4 (42.2-42.7)	155 (153-157)
IGT/IFG	153	230* (222-238)	144* (137-151)	41.2* (39.6-42.9)	224* (199-249)
DM/DM	250	244* (237-250)	152* (147-158)	40.9* (39.6-42.0)	273* (248-297)
Normal/ IFG,DM	153	222* (214-229)	144* (137-151)	40.5* (38.8-42.3)	213* (183-242)
IGT, DM/ Normal	1116	227* (225-230)	145* (143-147)	42.1* (41.5-42.8)	212* (205-220)

Data are point values (95% CI).
* Statistically significant differences ($p<0.05$) comparing the mean values (reference group normal subjects by both criteria)

ADA criteria and abnormal (IGT, or diabetes) by WHO criteria (n=1108) ($p<0.001$). No significant difference were observed between these two discordant groups according to anthropometric indices, whereas abnormal subjects by WHO criteria showed higher systolic and diastolic blood pressure than abnormal subjects by ADA ($p<0.001$). Both of these sets of discordant groups showed higher cardiovascular risk factors than concordant (n=6909) normal subjects ($p<0.001$).

Discussion

The main reason to test for high blood glucose concentration in people who have no symptoms of diabetes is to prevent complications of hyperglycemia, mainly death.[11,12] Overall, the prevalence of diabetes mellitus and "at risk of diabetes" categories were highly underestimated when using ADA criteria in the present study. The use of fasting plasma glucose for diagnosis of glucose disorders, failed to detect about forty percent of the diabetic patients and more than fifty percent of the IGT patients. Our results are concordant with the results of other population based studies in Brazil, United States, and sub-Saharan Africa.[13-15] Published data on this issue reported differences in both directions; the ADA ciriteria produced both higher and lower diabetes prevalence estimates.[16-22] In 1997, the American Diabetes Association published updated criteria for the diagnosis of diabetes and states of glucose intolerance.[4] Its recommendation that the oral glucose tolerance test not be routinely used to identify people with either diabetes or IGT, has fueled considerable controversies regarding the importance of such testing in either a clinical or epidemiological context.[23.24] Most reports have pointed out that a fasting plasma glucose level alone will underestimate the prevalence of diabetes and/or underestimate the prevalence of IGT. These observations have been cited to support a co-evaluation of ADA recommendation and retention of oral glucose tolerance test (OGTT) for routine use.[25.26]

Analyzing the impact of revising the diagnostic criteria, we found that the overall change in the prevalence of diabetes was 2.7%. Another and far more important consequence of the adopatation of the ADA criteria is that the diabetic status of a large number of individuals will be changed. This disagreement in classification goes in both directions, from diabetes to normal and from normal to diabetes. The probability of the disagreement in classification depended on age and body mass index. Moreover, our results revealed higher mean systolic and diastolic blood pressure and also higher plasma lipid levels in individuals with glucose disorders according to WHO criteria. This discrepancy was also reported in similar studies in Korea and Brazil.[13,27]

There is a progressive trend in the prevalence of glucose disorders in all age groups, irrespective of ADA and/or WHO criteria. In middle-aged individuals with normal BMI and WHR, the agreement between ADA and WHO is high. The poor agreement between IFG and IGT is evident. Since WHO criteria are clearly more accurate in detection of IGT and diabetes in general population, the ADA criteria are not recommended for detection glucose disorders in an Iranian population.

In conclusion, the present study shows that due to significant underestimation of glucose disorders by ADA criteria, WHO criteria, despite the cost and inconvenience, are more accurate to detect individuals with glucose disorders.

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