

Screening for Gestational Diabetes Mellitus (GDM): Comparison between WHO 1999 and Modified O'Sullivan Criteria

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Abstract

Objectives: This study was aimed to compare the efficiency (concordance/discordance, sensitivity) of World Health Organization (WHO) 1999 and modified O'Sullivan criteria for diagnosis of gestational diabetes mellitus (GDM).

Methods: We screened 385 pregnant subjects for GDM (age: 26.4 ± 4.9 yrs, BMI: 25.3 ± 4.3 kg/m²; mean \pm SD) irrespective of gestational age and presence of risk factors under a cross-sectional pilot protocol. The study was done during December 2011 to June 2013 in the 'GDM Clinic' of Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU). All the mothers performed 75g oral glucose tolerance test (OGTT) for diagnosis of GDM following WHO 1999 criteria. They were asked for a 100g OGTT following modified O'Sullivan criteria after an interval of 3 to 5 days. Out of 385 performing 75g OGTT, 345 responded for the 100g OGTT. Abnormal glucose tolerance (AGT) detected by any or both the tests were considered as GDM. Plasma glucose was measured by glucose-oxidase method on the same day.

Results: Out of 345 subjects, 165 (47.8%) were found to have GDM considering both the criteria which were 36.6% (141/385) by 75g OGTT and 32.2% (111/345) by 100g OGTT respectively. BMI (mean \pm SD) of the attending mothers was relatively higher (25.3 ± 4.3 kg/m²). About half of the subjects (48.1%) had family history of diabetes, 33.5% had history of abortion and 53% were multigravida. Mean (\pm SD, yr.) age (yrs, 27.5 ± 5.0 vs. 25.3 ± 4.6) and BMI (kg/m², 26.5 ± 4.1 vs. 24.5 ± 4.0) were significantly higher in the GDM group than that of normal glucose tolerance (NGT) group ($p < 0.001$ for both). There was a fair agreement between the two criteria ($\kappa = 0.447$; $p < 0.0001$). About 15% (53/345) would escape GDM diagnosis by only 100g OGTT; conversely, 10% (34/345) would escape GDM diagnosis by only 75g OGTT. Holding combined result as gold standard, sensitivity of WHO criteria was 87.27% which for modified O'Sullivan criteria was 67.27%.

Conclusions: It is concluded that despite fair agreement, WHO recommended 75g OGTT encompasses AGT in pregnancy more efficiently in comparison to modified O'Sullivan 100g OGTT.

Keywords: GDM, WHO 1999 and O'Sullivan criteria

Introduction

For many years gestational diabetes mellitus (GDM) has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy though women found to have diabetes at initial prenatal visit should receive a diagnosis of overt diabetes not GDM (1). Screening for GDM is important as it is associated with adverse fetal and maternal outcomes and because these women and their children are at risk of developing diabetes mellitus (DM) in future (2,3,4). Female who have inherited genetic predisposition to type-2 DM, would be at higher risk of developing GDM during pregnancy (5). Specific risk factors and their degree of influence on GDM prevalence are difficult to quantify across populations. Recent data show that GDM prevalence has increased by ~10-100% in several race/ethnicity groups during the past 20 years (6). The variation may depend on difference in methodology of detection of GDM and study population across study. In Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, including 15 centers from different parts of the world, the overall frequency of GDM was 9.3 to 25.5% (7). In Bangladesh, a cross-sectional study done in rural population showed prevalence rate of 13.2% (8). Universal diagnostic criterion for screening GDM is still debatable (9). A number of different oral glucose tolerance tests (OGTTs) are used internationally, with the oral glucose load varying from 50g to 100g (2). There is more than one diagnostic test agreed upon gold standard and there are several threshold criteria for the tests that are currently being used; and no agreement on which criteria best identifies women at risk of poor outcomes is yet decided unanimously (10). The existence of performing different methods of glucose tolerance test has hindered the development of universal diagnostic criteria for GDM (11). One problem with the development of absolute diagnostic criteria is the lack of evidence that perinatal mortality is increased in pregnancies associated with mild degrees of hyperglycemia (11). In this context, a number of comparative studies between different diagnostic criteria are done in many countries including India, China etc. to find out diagnostic pick-up rate of individual criterion (3,11). In Bangladesh, there is a need for a simple, cheap, safe and effective test to diagnose GDM. Although there is no universal criterion for diagnosis of GDM, until recent modification of WHO criterion which is under evaluation for its quality of evidence and strength of recommendation (12), commonly used criteria are those of O'Sullivan and Mahan and the WHO 1999 criteria (11). This study

was aimed to compare the efficiency (concordance/discordance, sensitivity) of WHO 1999 and modified O'Sullivan criteria for diagnosis of GDM.

Methods

Study subjects

This study was intended to screen 385 pregnant subjects for GDM (age: 26.4±4.9 yrs, BMI: 25.3±4.3 kg/m²; mean ± SD) by 02 sample 75g (WHO 1999 criterion) as well as 04 sample 100g (O'Sullivan criterion) OGTT at an interval of 3 to 5 days to find out agreement (concordance/discordance) between two criteria. 345 subjects completed both the tests. They were recruited from antenatal clinic of BSMMU irrespective of trimester and presence of risk factors. Women with prior history of GDM or DM were excluded from the study.

Study design

It was a cross-sectional study carried out at the 'GDM clinic' of BSMMU from December 2011 to June, 2013. Prior to commencement of this study the research protocol was approved by the Institutional Review Board (IRB). All the mothers were done both 75g and 100g OGTT at an interval of the mentioned period. Pregnant women were given an appointment after matching the inclusion and exclusion criteria and were advised to come after overnight fast of at least 8 hours. Preliminary list of patients were documented in a diary. The preceding evening they were reminded over telephone. In the morning of OGTT, written consent was taken from each mother after discussing the study procedure. A 75g two-hour OGTT was done following WHO 1999 criteria for GDM screening. A new list of patients who had

WHO 1999 OGTT criterion for GDM	Modified O'Sullivan criterion
00 hr plasma glucose (FPG): ≥ 7.0 mmol/L	≥ 5.3 mmol/L
01 hr plasma glucose (01h PG): None	≥ 10.0 mmol/L
02 hr plasma glucose (02h PG): ≥ 7.8 mmol/L	≥ 8.6 mmol/L
03 hr plasma glucose (03h PG): None	≥ 7.8 mmol/L

In WHO 1999 criterion, test is positive if one or both cut-off value satisfy
In O'Sullivan criterion, test is positive when two of the values satisfy

completed 75g OGTT was made and they were asked to come within 3 to 5 days in similar manner with the same preparation (as for 75g OGTT) for 100g 3-hour OGTT that followed modified O'Sullivan criteria. Abnormal glucose tolerance (AGT) detected by any or both the tests were considered as GDM. Clinical evaluation including estimation of height, weight, BMI (kg/m²) and BP

(mmHg) were measured by calibrated instruments.

Analytic method

The sample was transported to laboratory in pre-labeled test tubes. Plasma glucose was assayed by glucose-oxidase method on the same day in automated analyzer (RA-50 analyzer (Dade Behring, Germany). Report was immediately collected and preserved. Samples of different subjects were run on different days in different assay runs (149 runs). A fixed known concentration for low level (5.21 mmol/l) as well as high level (16.1 mmol/l) was used in every assay run. Inter-assay Coefficient variance (CV) for low level was 5.36%, and for high level were 5.59%.

Statistical analysis

All data were processed by utilizing SPSS program (Version 22.0) and expressed as frequencies or percentages as well as mean (\pm SD/SEM) as applicable. Comparison between the frequencies for agreement of detecting GDM by two test methods was done by Kappa-test. Sensitivity of individual criteria was calculated in light of the total frequency of GDM considering both the criteria of diagnosis for each individual. P values \leq 0.05 were considered significant statistically.

Results

Though 385 subjects were recruited for the purpose, finally 345 mothers completed both the OGTT. It seems

that BMI (mean \pm SD) of the mothers was relatively higher (25.3 \pm 4.3, kg/m²). About half of the subjects (48.1%) had family history of diabetes, 33.5% had history of abortion and 53% were multigravida (Table-I). As shown in Table-II, considering both the criteria 165 (47.8%) out of 345 subjects were found to have GDM which were 36.6% (141/385) by 75g OGTT and 32.2% (111/345) by 100g OGTT (Fig-1). Mean (\pm SD, yr.) age (yrs, 27.5 \pm 5.0 vs. 25.3 \pm 4.6) and BMI (kg/m², 26.5 \pm 4.1 vs. 24.5 \pm 4.0) were significantly higher in the GDM group ($p < 0.001$ for both).

Table-III delineates the agreement/disparity between the two criteria. There was fair agreement between the two criteria ($\kappa = 0.447$; $p < 0.0001$). However, it was observed that 15.4% (53/345) would not be diagnosed as GDM by 100g if 75g OGTT was not done. Conversely, 9.9% (34/345) would escape diagnosis of GDM by 75g if they did not carry out 100g OGTT indicating better impact of 75g OGTT. As judged holding combined result as the gold standard, sensitivity for WHO 1999 criterion was 87.27% which was 67.27% for modified O'Sullivan criterion (Table-IV).

32 subjects, not diagnosed GDM by 75g OGTT, exerted FPG < 7.0 mmol/L but > 5.2 mmol/L and 02h value OGTT < 7.8 mmol/L. 15 of them were AGT by cut-offs in 100g OGTT, mostly 01h and 02h values; but none exclusively by 03h value and only 3 exclusively by 01h value.

53 NGT by 100g were found AGT by 75g OGTT. None had FPG > 6.9 mmol/L, all diagnosed as GDM by the 02h

Table-I: Characteristics of studied subjects (N=385)

Characters/variables	All subjects
N	385
Age (mean \pm SD, yr)	26.4 \pm 4.9
Body mass index (BMI, mean \pm SD, kg/m ²)	25.3 \pm 4.3
Family history of DM	185 (48.1)
History of abortion	129 (33.5)
Gravida:	
Primigravida	181 (47.0)
Multigravida	204 (53.0)
Occupation:	
Service / others	146 (37.9)
Housewife	239 (62.1)

(Within parenthesis are percentages over column total)

40 subjects denied performing 100g oral glucose tolerance test.

Table-II: Age and BMI of subjects detected as GDM and NGT			
Characters/variables	GDM	NGT	p
N	165	180	
Age (mean ± SD, yr)	27.5±5.0	25.3±4.6	<0.001
BMI (mean ± SD, kg/m ²)	26.5±4.1	24.5±4.0	<0.001
Systolic BP (mean±SD,mmHg)	103±11	98±11	<0.001
Diastolic BP (mean±SD,mmHg)	67±8	64±8	<0.005
Family history of DM	95 (57.9)	77 (42.8)	0.006
History of abortion	56 (33.5)	55 (30.6)	0.502
Gravida:			
Primigravida	50 (30.3)	67 (37.2)	0.176
Multigravida	115 (69.7)	113 (62.8)	

(Within parenthesis are percentages over column total)

Glycemic status determined on the basis of combined status determined by both 75g and 100g OGTT.

BMI: body mass index GDM: gestational diabetes mellitus

NGT: normal glucose tolerance.

Table-III: Agreement/Disagreement of two tests for diagnosis			
75 gm OGTT (WHO)	100 gm OGTT (O'Sullivan)		Total
	GDM	NGT	
GDM	77 (22.3)	53 (15.4)	130 (37.7)
NGT	34 (9.9)	181 (52.5)	215 (62.3)
Total	111 (32.2)	234 (67.8)	345

(Within parentheses are percentages over grand total) by Kappa test, $k=0.447$; $p<0.0001$

OGTT: oral glucose tolerance test GDM: gestational diabetes mellitus NGT: normal glucose tolerance.

Criteria	Sensitivity
WHO	87.27%
O'Sullivan	67.27%

Calculated over 345 subjects all of whom carried out both the 75g and 100g OGTT

OGTT: oral glucose tolerance test GDM: gestational diabetes mellitus NGT: normal glucose tolerance.

Table-IV: Sensitivity of WHO 1999 criteria and O'Sullivan Criteria			
Status by OGTT	WHO criteria	O'Sullivan Criteria	Combined
GDM	144	111	165
NGT	201	234	180
Total	345	345	345

(Groups are not mutually exclusive)

As the combined inference of glycemic status is dependent on the result of both the criteria, specificity of any of the criteria is thus cent percent.

value that exceeded 7.7 mmol/L. On 100g OGTT, 17 of them had 02h cut-off >7.8 mmol/L, but only 8 had values exceeding 8.5 mmol/L and the rest 9 had 02h value between 7.8 to 8.5 mmol/L; and none fulfilled criteria by the help of fasting or 01h value or 03h value for GDM.

Discussion

The present comparative study was carried out to find out agreement (concordance/discordance) between WHO 1999 and modified O'Sullivan criteria. It is noteworthy that WHO has already updated the criteria for GDM in September 2013, but the quality of evidences and strength of recommendation is yet under evaluation (12). Our study clearly observed that the frequency of GDM is very high (47.8% considered on combined results) which was 36.6% by WHO 1999 criteria and 32.2% by modified

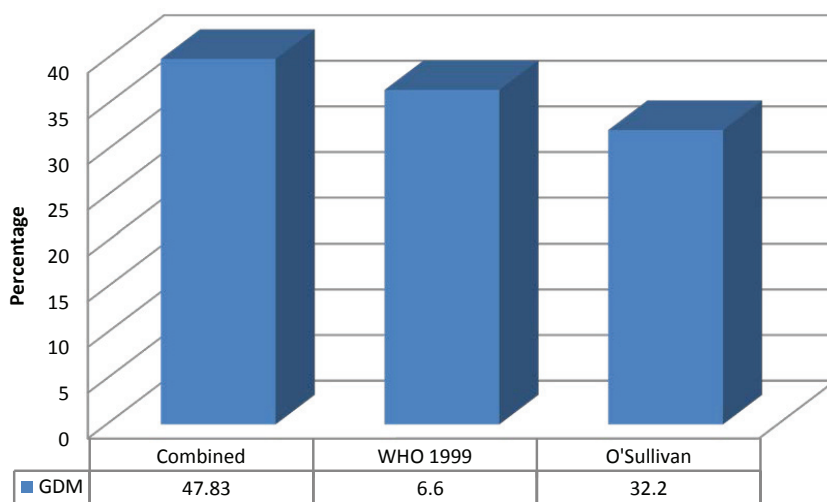


Fig-1. Frequency of GDM by WHO 1999, O'Sullivan criteria

O'Sullivan criteria. Of the two diagnostic criteria, WHO recommended criterion was more efficient for detecting GDM. In the context of concordance/discordance between the two criteria it was observed that 15.4% subjects would have been missed their diagnosis of GDM if evaluated by only 100g OGTT; conversely, only 9.9% would have been missed if only 75g OGTT done.

Sahu et al. (2009) observed that diagnostic pick-up was five times more with WHO 1999 criteria than that of ADA criteria using the same cut-off value as adapted in modified O'Sullivan criteria (3). The repetition of this fact happened in another study by Seshiah et al. where diagnostic pick-up rate was approximately four times greater with WHO 1999 criteria than with modified O'Sullivan criteria (13). Higher FPG value of WHO 1999 criteria could influence its sensitivity to be low; but here only one positive value is enough for diagnosis and 2-hour post load value is set at lower level while in O'Sullivan criteria two positive glucose values are needed though FPG level is relatively low. In our study, 32 subjects who were not diagnosed as GDM by 75g OGTT, exerted FPG <7.0 mmol/L but >5.2 mmol/L and 02h glucose value after 75g OGTT <7.8 mmol/L. Among them, 15 were diagnosed as GDM due to exceeding other cut-offs in 100g OGTT, mostly 01h and 02h values; none exclusively only 03h value and 3 exclusively 01h value. Thereby, importance of 03h glucose value as well as 01h value is a bit diluted. On the other hand, 53 mothers who were not GDM by 100g were found AGT by 75g OGTT. It is interesting to observe that, none of them had FPG

>6.9 mmol/L; therefore, all must have been diagnosed as GDM by the 02h value that exceeded 7.7 mmol/L by the WHO 1999 criteria. On the day of 100g OGTT, 17 of them showed 02h cut-off >7.8 mmol/L. But only 8 persons had values exceeding 8.5 mmol/L and the rest 9 had 02h value between 7.8 to 8.5 mmol/L; and none virtually fulfilled criteria by the help of fasting or 01h value or 03h value. Thereby neither excess load of 100g instead of 75g glucose nor low-set FPG or 01h and 03h values seem to be much important in the context of screening procedure than usual 75g 02h OGTT. Rather relatively low set and stringent 02h value of 75g OGTT may be more contributing in discriminating AGT in pregnancy. As a matter of fact, better sensitivity and efficiency has been observed in our study when the outcome of two tests was compared. But it must be mentioned that our study is tertiary care centre based, and the number of subjects may not be satisfactory enough for a conclusive remark.

In the Asian context, insulin resistance is the most important factor for GDM and their postprandial glucose level is higher than Caucasians (14). Therefore, greater sensitivity of WHO criteria is explainable in spite of higher FPG value. As a result, in light of calculation for sensitivity, the WHO 1999 OGTT criterion was found to be more sensitive than modified O'Sullivan criteria.

Conclusions

In conclusion, the frequency of GDM observed in our population is quite high. Despite fair agreement, WHO recommended 75g OGTT is more sensitive than that of

100g modified O'Sullivan criteria for diagnosis of GDM.

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The whole is more than the sum of its parts.

— ARISTOTLE