Obstetric Medicine
Obstetric Medicine
6(3) 125–128

DOI: 10.1177/1753495X13482895
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Diagnostic effectiveness of 75 g oral glucose tolerance test for gestational diabetes in India based on the International Association of the Diabetes and Pregnancy Study Groups guidelines

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Abstract

Background: To determine the diagnostic effectiveness of the fasting and one-hour plasma glucose levels for gestational diabetes (GDM) based on International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria.

Methods: A Cross-sectional study that included 2348 pregnant women booked for antenatal care in 2011 at a tertiary care perinatal institute. Pregnant women underwent a 75 g oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation. Outcome measures include the incidence of GDM based on the IADPSG criteria and the diagnostic effectiveness of the recommended fasting and one-hour plasma glucose cut-off if used in isolation.

Results: The incidence of GDM was 21.81% ($n = 520$, 95% CI: 20.15, 23.57) with the IADPSG criteria. A fasting plasma glucose cut-off 92 mg/dL, in isolation, correctly classified 87.16% of GDM, with a specificity of 96.08%, clinically significant positive likelihood ratio (14.08) and a post-test probability of 79.71%. The one-hour 75 g test, in isolation, correctly classified 85.74% of GDM, had specificity of 99.68% and clinically significant positive likelihood ratio (111.12) and post-test probability of 96.87%. The application of the World Health Organization criteria would misclassify 11.91% (95% CI: 10.66, 13.26) of GDM as normal.

Conclusions: Additional testing of plasma glucose levels can be avoided for 18.25% ($n = 435$, 95% CI: 16.73, 19.84) if the IADPSG diagnostic criteria for GDM are applied with exit on a positive fasting or one-hour test result.

Keywords

gestational diabetes mellitus, IADPSG criteria, oral glucose tolerance test

Introduction

Approximately 79 million people are expected to have diabetes mellitus in India by the year 2030.[1] Gestational diabetes (GDM), a metabolic complication of pregnancy, has a reported prevalence that varies from 9.9% to 17.8% in India.[2] Hyperglycaemia in pregnancy has short- and long-term maternal and neonatal consequences although interventions for GDM can reduce adverse outcomes.[3–9] Accurate detection of GDM through a standardized test is essential to initiate interventions and to understand the wide variations in reported prevalence of GDM. Several methods have been used to diagnose GDM a 75 g oral glucose tolerance test (OGTT) at two-hours (World Health Organization [WHO] recommendation) and a three-hour 100 g OGTT based on the American Diabetic Association (ADA) guidelines.[10–12] Recently, a consensus guideline, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations, has been adopted to standardize the determination of GDM globally.[13] The IADPSG recommendations have two major changes compared with the WHO or ADA protocol. One, the IADPSG recommends a 75 g three test approach – a fasting plasma glucose determination and repeat plasma glucose determination at one- and two-hours after oral ingestion of 75 g glucose. Two, a pregnant woman is considered to have GDM if any of the three test values are higher than the recommended thresholds. Conversely, GDM is considered absent in a pregnant woman if all three test values are normal. The IADPSG guidelines were adopted for the detection of GDM at the Fernandez Hospital, an advanced tertiary care perinatal institute at Hyderabad, India, in 2011. The current study was designed to determine the impact of adopting the IADPSG guidelines at this institute focused specifically on (a) the changed incidence of gestational diabetes and (b) to determine the diagnostic effectiveness if we use only one of the fasting and one-hour test values (sequential testing) for the diagnosis of GDM.

Methods

Pregnant women booked for care at the study institute have a standardized antenatal care examination that includes details of medical, surgical and obstetric history, personal risk behaviours, clinical exams and investigations including trimester specific ultrasound exams and laboratory investigations. These details are entered into a medical record and transcribed into an electronic database. We used a retrospective design to retrieve information on pregnant women booked for antenatal care based on a study protocol that adhered to the tenets of the Declaration at Helsinki and protected patient privacy. Written informed consent from pregnant women is sought and documented after counselling at registration to use their medical records for research and education with complete protection of their privacy. Each woman re-assured that their clinical care will not be compromised or affected in any manner if they do not provide consent to

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use their medical records for educational or research purposes. The study protocol was approved by the institutional review board.

Pregnant women undergo a 75 g OGTT test between 24 and 28 weeks of gestation as part of a universal screening protocol. The OGTT test involves measurement of plasma glucose levels after an overnight fast (8 hours), followed by oral consumption of 75 g glucose, and plasma glucose measurement at one and two hours. A plasma fasting blood glucose >126 mg/dL in a pregnant woman is considered as overt diabetes (after confirmation) even if there is no prior history of diabetes. Gestational diabetes is defined as a fasting plasma glucose value >92 mg/dL or a one-hour plasma glucose value >180 mg/dL or a two-hour plasma glucose value >153 mg/dL. Gestational diabetes is considered absent if a pregnant woman has normal values at all three test intervals. We excluded pregnant women with overt diabetes mellitus (prior history and/or a fasting plasma glucose level >126 mg/dL) and women who did not complete the OGTT test from the study. We defined hypertensive disorders in pregnancy based on the working group recommendations of high blood pressure in pregnancy.[14] We defined a preterm delivery as <37 weeks of gestation and macrosomia as a birth weight >4 kg. A trained neonatologist determined the postdelivery fetal growth using Lubchenco charts and categorized babies as small for gestational age, average for gestational age and large for gestational age.

We analysed the data using the statistical software STATA version 9.0 (College station, TX, USA). We determined the prevalence and 95% confidence intervals (CI) of GDM based on the IADPSG and the WHO recommendations. The determination of GDM based on the IADPSG criteria involves any one of three positive values and requires three blood draws and test that may not be feasible in resource poor settings with busy obstetric practices. We explored to check if the testing can be limited using a sequential approach in such situations, thus, limiting further testing if the fasting plasma glucose value was >92 mg/dL or one-hour plasma glucose value was >180 mg/dL. We tested this using tests of diagnostic effectiveness sensitivity, specificity and likelihood ratios, and area under receiver operator characteristic curve (AUROC) of the different cut-off values of fasting and one-hour OGTT test, using the values in isolation and in comparison with GDM diagnosed based on the WHO criteria. We looked at the likelihood ratios as they are more useful than predictive values to apply in clinical practice. A positive likelihood ratio >10 is considered clinically significant.

Table 1 Characteristics of the 2384 women who participated in the study.

Characteristic	*N* (%)
Maternal age ≥35 years	105 (4.40%)
Primigravid	1073 (45.01%)
Body mass index >30	428 (17.95%)
Body mass index 25–30	512 (21.48%)
Normal body mass index	1205 (50.53%)
Body mass index <18.5	239 (10.03%)
Gestational hypertension	73 (3.67%)
Pre-eclampsia	57 (2.39%)
Chronic hypertension	36 (1.51%)
Screen positive hypothyroid	84 (3.52%)
Mean (SD) gestational age at delivery (weeks)	37.71 (2.95)
Preterm <37 weeks gestation	279 (11.70%)

SD = standard deviation.

Table 2 Incidence of gestational diabetes using the different IADPSG criteria.

Criteria	Incidence, % (95% CI)
Fasting plasma glucose >92 mg/dL	15.10 (13.71, 16.58)
1-hour plasma glucose >180 mg/dL	8.05 (7.01, 9.20)
2-hour plasma glucose >153 mg/dL	9.19 (8.08, 10.40)
Fasting *and* 1-hour plasma glucose positive	4.91 (4.09, 5.83)
Fasting *or* 1-hour plasma glucose positive	18.25 (16.73,19.84)
Fasting *and* 1-hour *and* 2-hour plasma glucose positive	0.38 (0.18, 0.69)
Any one of Fasting, 1-hour or 2-hour plasma glucose positive (IADPSG criteria)	21.8 (20.15, 23.57)

IADPSG = International Association of the Diabetes and Pregnancy Study Groups.

Results

The study included 2384 pregnant women booked for antenatal care with a mean age (SD) of 27.18 (3.95) years (range 18–45 years). The characteristics of these 2384 women are presented in Table 1. The prevalence of GDM was 17.20% ($n = 410$, 95% CI: 15.68, 18.71) based on the WHO criteria and increased to 21.81% ($n = 520$, 95% CI: 20.15, 23.57) with the IADPSG criteria. One hundred and seventy-four (7.30%, 95% CI: 6.31, 8.40) pregnant women are false-positives and 284 (11.91%, 95% CI: 10.66, 13.26) are false-negatives if we use the WHO criteria for the diagnosis of GDM with the IADPSG criteria considered as the gold standard. Table 2 presents the different identification rates if we use the IADPSG cut-off values in isolation or as several combinations.

The diagnostic effectiveness of different fasting plasma glucose levels and the one-hour 75 g OGTT, if used in isolation was explored in comparison with the WHO criteria as the gold standard. The diagnostic effectiveness of fasting plasma glucose >92 mg/dL (AUROC 0.81, 95% CI: 0.78, 0.83) was better but did not differ significantly from the one-hour 75 g OGTT value (AUROC 0.76, 95% CI: 0.73, 0.78) to discriminate between pregnant women with and without GDM. The number of pregnant women needing one-hour 75 g OGTT could be reduced by 15.10% ($n = 360$, 95% CI: 13.67, 16.54) if we exclude pregnant women with fasting plasma glucose levels >92 mg/dL from further testing. The number of pregnant women needing two-hour 75 g OGTT could be reduced by an additional 3.71% ($n = 75$, 95% CI: 2.89, 4.53) if we exclude pregnant women with one-hour 75 g OGTT plasma glucose levels >180 mg/dL from further testing. Overall, additional testing of plasma glucose levels can be avoided for 18.25% ($n = 435$, 95% CI: 16.73, 19.84) if the IADPSG diagnostic criteria for GDM are applied with exit on a positive fasting or one-hour test result.

We did not find significant associations with outcomes of pregnancy; however, these data are not discussed as the study did not have enough power to explore for associations of GDM with outcomes of pregnancy.

Discussion

Gestational diabetes is an emerging problem among pregnant women in India.[15] The wide variation in reported incidence of GDM in India indicates the need for a reliable, standardized and replicable diagnostic or screening test.[2] More than one in five pregnant women in this study was determined to have GDM based on the IADPSG criteria. We found that fasting and one-hour 75 g OGTT using the IADPSG cut-offs has good diagnostic properties in this population and that additional testing can be reduced for nearly one in five pregnant women if test results are applied with exit on a positive test result at fasting or

one hour. These results may suggest that exit based on a fasting or one-hour OGTT can result in a substantial saving in terms of tests done as well as waiting period for pregnant women. However, further studies are necessary on associations of GDM with clinical outcomes of pregnancy in this population, prior to any recommendations to exit the OGTT on a positive fasting or one-hour result.

The application of the test and the consequences of a false-positive or a false-negative result determine the choice of a diagnostic or screening test. The preferred cut-off values that determine the accuracy of a test depend on a relative benefit-harm ratio if we misclassify pregnant women as false-positives or false-negatives. If we consider maternal and neonatal adverse events associated with GDM, the misclassification of a normal pregnant woman as having GDM, although not ideal, is relatively less serious than the consequences of missing a pregnant woman with GDM.

The two-hour cut-off with the IADPSG criteria is much higher than the two-hour cut-off with the WHO criteria. However, the inclusion of a fasting or a one-hour cut-off for the diagnosis of GDM with the IADPSG criteria leads to a higher incidence of GDM as a proportion of previously normal pregnant women are now categorized as GDM. We found that the application of the WHO criteria would have led us to misclassify 11.91% (95% CI: 10.66, 13.26) of pregnant women with GDM as normal. Evaluating the effectiveness of using only the fasting and one-hour 75 g OGTT values assume great significance in resource poor settings.

We found that the use of only a fasting plasma glucose cut–off >92 mg/dL could correctly classify 87.16% of pregnant women with GDM (using the WHO criteria as the gold standard). This cut-off has a very high specificity (96.08%) and a clinically significant positive likelihood ratio (14.08). Both the specificity and the positive likelihood ratio indicate that the fasting plasma glucose cut–off >92 mg/dL is a clinically useful cut-off. The high specificity of the test can also be used to rule in the disease of interest, in this instance, GDM. The disease or condition can be ruled in if a test with a high specificity gives a positive test result. The positive likelihood ratio of 14.08 tells us that a positive test result is 14 times more likely to come from a pregnant woman with GDM compared with a pregnant woman without GDM. The one-hour 75 g test, used in isolation, correctly classified 85.74% of pregnant women with GDM (using the WHO criteria as the gold standard), but had a higher specificity (99.68%) and clinically very significant positive likelihood ratio (111.12). A positive test result with the one-hour 75 g OGTT (>180 mg/dL) thus rules in GDM and indicates that the pregnant woman is 111 times more likely to have GDM compared with a pregnant woman without GDM.

Diagnostic test parameters can be translated into clinical practice to optimally utilize the test results for clinical management. A positive test result should increase the post-test probability of the disease to lead to a diagnosis. We can determine the post-test probability based on the prevalence of the disease and the positive likelihood ratio of the test criteria. We found that a positive fasting plasma glucose >92 mg/dL increased the probability of disease from 21.81% (95% CI: 20.15, 23.57) to 79.71% (95% CI: 78.04, 81.28). A positive one-hour 75 g plasma glucose value >180 mg/dL increased the probability of disease even further from 21.81% (95% CI: 20.15, 23.57) to 96.87% (95% CI: 96.56, 97.16). These results indicate that the use of fasting plasma glucose >92 mg/dL or a one-hour 75 g plasma glucose value >180 mg/dL, in isolation, is also useful to discriminate pregnant women with and without GDM.

Intuitively, these results indicate that we can limit the two-hour test to pregnant women considered normal with the fasting and the one-hour 75 g OGTT. We could also consider limiting the complete OGTT to persons with a fasting plasma value >85 mg/dL to ≤92 mg/dL or a one-hour plasma glucose value >160 mg/dL to ≤80 mg/dL using the sensitivity to rule out a disease and the likelihood ratios. The post-test probabilities for GDM are 36.04% with a fasting plasma glucose value of >85 mg/dL and 53.95% with a one-hour plasma glucose value >160 mg/dL. Limiting the complete OGTT to these subgroups provides a major advantage in terms of resources and logistics, and waiting time and convenience including blood draws for pregnant women. However, this relative advantage has to be balanced against clinical outcomes of pregnancy and potential associations of the three values (in isolation and combination) with such outcomes. A previous study has reported the differential risk for adverse outcomes of pregnancy associated with different combinations of abnormal glucose values.[16] Pregnant women with elevated postglucose load levels and normal fasting glucose levels were more likely to have preterm deliveries, hypertensive disorders in pregnancy or a neonate with hyperbilirubinemia.[16] Pregnant women with elevated fasting glucose levels but normal postglucose load levels were more likely to have a large for gestational age baby.[16] We did not have sufficient power to explore for and comment on such associations. Additionally, non-pharmacological and pharmacological interventions are provided to women with GDM and the potential beneficial effects of these interventions on associations with outcomes have to be considered.

In summary, the IADPSG criteria have good specificity, positive likelihood ratio and post-test probabilities for GDM in this population. The consistent use of IADPSG criteria may help standardize the determination of GDM in India and provide comparable estimates within India and across the world. However, the cost-effectiveness of the test has to be ascertained prior to widespread use.

Acknowledgments

None

Declaration of Conflicting Interests

None.

Funding

The study was supported by the Fernandez Hospital Educational and Research Foundation, Hyderabad.

Ethical approval

The study was approved by the Institutional Review Board of Fernandez Hospital Pvt Ltd, Hyderabad, India 500001

Guarantor

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Contributorship

IN was involved with the design of the study, data collection, interpretation of results and writing of the manuscript, TS was involved with the design, interpretation and writing of the manuscript. PKN was involved with the design, data analysis and interpretation of results and writing of the manuscript.

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