

Gestational Diabetes Mellitus

Simplifying the International Association of Diabetes and Pregnancy diagnostic algorithm using fasting plasma glucose

MUKESH M. AGARWAL, MD, FCAP¹
 GURDEEP S. DHATT, FRCPATH²
 SYED M. SHAH, MD, PHD³

OBJECTIVE— To determine the impact of the International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria on 1) gestational diabetes mellitus (GDM) diagnosis compared with the American Diabetes Association (ADA) criteria and 2) the fasting plasma glucose (FPG) to predict GDM.

RESEARCH DESIGN AND METHODS— In 10,283 pregnant women undergoing a 75-g oral glucose tolerance test (OGTT) for universal screening of GDM, two FPG thresholds (of the OGTT) were used to rule in and to rule out GDM.

RESULTS— The IADPSG and ADA criteria identified GDM in 3,875 (37.7%) women and 1,328 (12.9%) women, respectively ($P < 0.0005$). FPG thresholds of ≥ 5.1 mmol/l ruled in GDM in 2,975 (28.9%) women with 100% specificity, while < 4.4 mmol/l ruled out GDM in 2,228 (21.7%) women with 95.4% sensitivity. FPG independently could have avoided the OGTT in 5,203 (50.6%) women.

CONCLUSIONS— The IADPSG criteria increased GDM prevalence nearly threefold. By circumventing a significant number of OGTTs, an initial FPG can greatly simplify the IADPSG diagnostic algorithm.

Diabetes Care 33:2018–2020, 2010

The scourge of gestational diabetes mellitus (GDM) is the lack of an international agreement on the screening and diagnosis among the pre-eminent diabetes, obstetric, and health care organizations (1). Therefore, without a globally accepted guideline, the diagnosis of GDM causes a great deal of clinical confusion (2). In March 2010, the International Association of Diabetes and Pregnancy Study Group (IADPSG) issued consensus guidelines to potentially attain a single approach for GDM diagnosis worldwide (3).

The inconsistency in GDM diagnosis is evident in the United Arab Emirates (UAE), which has the second highest prevalence of type 2 diabetes (18.7%) in

the world (4). GDM in the UAE varies from 7.9 to 24.9%, depending on which of the six well-accepted criteria are used for diagnosis (2). The popular American Diabetes Association (ADA) criteria (5) demonstrates a prevalence of 10.6–14.7% (2,6–8). In this population, multiple studies have confirmed that the initial fasting plasma glucose (FPG) result of the oral glucose tolerance test (OGTT) is excellent in determining the need to continue with the OGTT (6,9–10); however, its efficiency depends on the criteria used for GDM diagnosis (6). The aim of this study was to determine, in this high-risk population, the impact of the new IADPSG criteria on 1) the diagnosis of GDM compared with the ADA criteria

and 2) the FPG to predict GDM in order to decide whether to proceed with the OGTT.

RESEARCH DESIGN AND

METHODS— The subjects were pregnant women attending the routine antenatal clinics of two tertiary care hospitals. Due to a universal screening program, every pregnant woman underwent a 75-g OGTT scheduled at 24–28 weeks gestation. The data were collated from our four previous studies (2,6–8) between 2003 and 2008; a total of 10,283 pregnant women were available for analysis.

Plasma glucose was estimated by the glucose oxidase method (Beckman-Coulter, Brea, CA); the analytical standards for glucose were met (11). Previously, the gold standard was the ADA criteria (5) for the 75-g OGTT; the data were reanalyzed using the new IADPSG criteria (i.e., one or more plasma venous glucose values ≥ 0 h, 5.1 mmol/l; 1 h, 10.0 mmol/l; or 2 h, 8.5 mmol/l) (3).

The statistical analysis has been described earlier (6). A rule-in and rule-out algorithm (12) was used for the FPG to predict GDM. Briefly, this approach involves considering two FPG cutoff values. The higher threshold, with an inherently increased specificity, rules in GDM; the lower threshold, with its innate increased sensitivity, rules out GDM. Women who have FPG values in between these two thresholds are indeterminate and would need the diagnostic OGTT.

RESULTS— The current ADA criteria identified 1,328 (12.9%) women with GDM; however, by the new IADPSG criteria (applied to the same OGTT), 3,875 (37.7%) women would have GDM ($P < 0.0005$) (i.e., a 2.9-fold increase). The mean maternal age was (means \pm SD) 28.3 ± 6.1 years. The mean gestational age (at time of OGTT) was 25.6 ± 6.3 weeks. The women with GDM (with either the ADA or IADPSG criteria) were older with higher fasting, 1-h, and 2-h plasma glucose values ($P < 0.0005$). There were two main ethnic groups: 8,233 (80.1%) Arab women and 1,592 (15.5%) South-Asian women

From the ¹Department of Pathology, Faculty of Medicine, United Arab Emirates University, Al Ain, United Arab Emirates; the ²Department of Pathology, Tawam Hospital, Al Ain, United Arab Emirates; and the ³Department of Community Medicine, Faculty of Medicine, United Arab Emirates University, Al Ain, United Arab Emirates.

Corresponding author: Mukesh M. Agarwal, magarwal7@gmail.com.

Received 26 March 2010 and accepted 29 May 2010. Published ahead of print at <http://care.diabetesjournals.org> on 2 June 2010. DOI: 10.2337/dc10-0572.

© 2010 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Table 1—GDM diagnosis by IADPSG criteria (n = 10,283)

FPG at or above the threshold	4.2 mmol/l	4.4 mmol/l	4.7 mmol/l	5.0 mmol/l	5.1 mmol/l
No. of women at or above the threshold [n (%)]	9,478 (92.2)	8,055 (78.3)	6,000 (58.3)	3,701 (36.0)	2,975 (28.9)
False-negative rate (%)	1.7	4.6	11.1	19.5	23.2
Sensitivity (%)	98.3	95.4	88.9	80.5	76.8
PPV (%)	40.2	45.9	57.4	84.2	100.0
LR+	1.11	1.40	2.23	8.84	*
No. of women below the threshold [n (%)]	805 (7.8)	2,228 (21.7)	4,283 (41.7)	6,582 (64.0)	7,308 (71.1)
False-positive rate (%)	88.4	68.0	39.9	9.1	0.0
Specificity (%)	11.6	32.0	60.1	90.9	100.0
NPV (%)	92.0	91.9	90.0	88.5	87.7
LR–	0.14	0.15	0.18	0.21	0.23

Selected threshold values of the FPG with associated test sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, likelihood ratios of positive (LR+) and negative (LR–) test result; false-positive rate (1 – specificity) and false-negative rate (1 – sensitivity). *Not calculable.

(i.e., nationals of India, Pakistan, Bangladesh, and Sri Lanka). There was no significant difference in GDM diagnosis between Arabs and South Asians with IADPSG criteria ($P = 0.3$); nevertheless, with the ADA criteria the difference was significant ($P < 0.0005$).

The IADPSG criteria identified all women with GDM by the ADA criteria but categorized an additional 2,547 (24.8%) women as having GDM. The κ statistic for the agreement of GDM diagnosis (between IADPSG and ADA) was fair (39.4%). The area under the receiver-operating characteristic curve (AUC) for FPG using the IADPSG and ADA criteria was 0.907 (95% CI 0.899–0.914) and 0.871 (0.859–0.882), respectively. Table 1 lists selected threshold values for FPG with the associated test characteristics.

CONCLUSIONS— The IADPSG recommendation that every pregnant woman should undergo the OGTT is very demanding; it would severely overload the laboratory. An urgent, initial FPG result can assist in deciding if the pregnant woman should continue with her OGTT (6). In this study, using the two-cutoff approach, a higher FPG threshold of ≥ 5.1 mmol/l ruled in GDM in 2,975 (28.9%) women with 100% specificity (Table 1). A lower FPG threshold of < 4.4 mmol/l ruled out GDM in 2,228 (21.7%) women at an acceptable sensitivity of 95.4%; only 180 (4.6%) women with GDM were misclassified as healthy. In the Hyperglycemia and Adverse Pregnancy Outcome Study, risks of adverse outcomes were low when the FPG was ≤ 4.4 mmol/l (3). Thus, the initial FPG could circumvent the cumbersome OGTT in over half the pregnant women without compromising health care.

The IADPSG criteria increased GDM prevalence almost threefold compared with the ADA criteria; this would further add to the health expenditure due to the additional antenatal visits, further laboratory work up, and medications, if needed. However, using these more liberal criteria does have many advantages. In the short term, as confirmed by the recent trials, attaining glucose targets by diet, exercise, or drugs would decrease adverse outcome in index pregnancy. In the long term, a significantly greater number of women would be identified to be at risk for type 2 diabetes; this fact is most evident in Australia (13), because the Australasian criteria are the most inclusive among the six major criteria for GDM diagnosis (2). Thus, these new criteria could be of real benefit; targeting the “extra” women with GDM after delivery may help to forestall the ongoing epidemic of type 2 diabetes.

The current guidelines for GDM have numerous shortcomings: they have often been developed from tenuous data, frequently the result of expert opinion, sometimes economically driven, and at times convenience oriented (1). Finally, the long-awaited, single-guideline—based on sound scientific data—is available. In many other areas of medicine, standardization has been attained with fruitful results (14); such consistency is crucial for GDM. Despite the constraints, this unique opportunity for one global approach to GDM should not be missed.

Acknowledgments— We gratefully acknowledge the invaluable help of all the technologists of the Al Ain and Tawam

hospital laboratories for their technical excellence.

No potential conflicts of interest relevant to this article were reported.

M.M.A. conceptualized the idea, collated the data, carried out the statistical analysis, and wrote the manuscript. G.S.D. contributed to the idea, the presentation, and discussion and edited the manuscript with several constructive criticisms. S.M.S. contributed/checked the statistics substantially and reviewed the manuscript.

References

1. Agarwal MM. Evolution of screening and diagnostic criteria for GDM worldwide. In *Gestational Diabetes During and After Pregnancy*. Kim C, Ferrara A, Eds. Dordrecht, Springer, 2010, p. 33–47
2. Agarwal MM, Dhatt GS, Punnoose J, Koster G. Gestational diabetes: dilemma caused by multiple international diagnostic criteria. *Diabet Med* 2005;22:1731–1736
3. International Association of Diabetes and Pregnancy Study Groups. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33:676–682
4. International Diabetes Federation. *Diabetes e-Atlas, 4th Edition*. Brussels, Belgium, International Diabetes Federation, 2009. Available at <http://www.eatlas.idf.org>. Accessed 21 March 2010
5. American Diabetes Association. Diagnosis and classification of diabetes mellitus (Position Statement). *Diabetes Care* 2010;33(Suppl. 1):S62–S69
6. Agarwal MM, Dhatt GS, Punnoose J. Gestational diabetes: utility of fasting plasma glucose as a screening test depends upon the diagnostic criteria. *Diabet Med* 2006;23:1319–1326
7. Agarwal MM, Dhatt GS, Safrdou MF. Gestational diabetes: using a portable glucometer

- to simplify the approach to screening. *Gynecol Obstet Invest* 2008;66:178–183
8. Agarwal MM, Dhatt GS, Othman Y, Gupta R. Gestational diabetes: fasting capillary glucose as a screening test in a multi-ethnic, high-risk population. *Diabet Med* 2009;26:760–765
 9. Agarwal MM, Hughes PF, Punnose J, Ezimokhai M. Fasting plasma glucose as a screening test for gestational diabetes in a multi-ethnic, high-risk population. *Diabet Med* 2000;17:720–726
 10. Agarwal MM, Dhatt GS, Punnose J, Koster G. Gestational diabetes in a high-risk population: using the fasting plasma glucose to simplify the diagnostic algorithm. *Eur J Obstet Gynecol Reprod Biol* 2005;120:39–44
 11. Sacks DB, Bruns DE, Goldstein DE, McClaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2002;48:436–472
 12. Henderson AR. Assessing test accuracy and its clinical consequences: a primer for receiver operating characteristic curve analysis. *Ann Clin Biochem* 1993; 30:521–539
 13. Cheung NW, Byth K. Population health significance of gestational diabetes. *Diabetes Care* 2003;26:2005–2009
 14. Gibler WB, Blomkalns AL. Achieving standardization in clinical research: changing cacophony into harmony. *Ann Emerg Med* 2004;44:213–214