Variability in Diagnostic Evaluation and Criteria for Gestational Diabetes

CAREN G. SOLOMON, MD
WALTER C. WILLETT, MD
JANET RICH-EDWARDS, MPH
DAVID J. HUNTER, MBBS
MEIR J. STAMPFER, MD
GRAHAM A. COLDITZ, MBBS
JOANN E. MANSON, MD

OBJECTIVE — To determine the frequency of screening for gestational diabetes mellitus (GDM) among a population receiving regular prenatal care and to assess the extent to which National Diabetes Data Group (NDDG) criteria for the diagnosis of GDM are used by practicing obstetricians.

RESEARCH DESIGN AND METHODS — We studied participants in the Nurses' Health Study II, a large prospective cohort study of 116,678 nurses aged 25–42 years in 1989. A total of 422 women who reported a first diagnosis of GDM between 1989 and 1991 were sent supplementary questionnaires regarding diagnosis and treatment, and medical records were requested for a subset of 120 to validate self-reported GDM and assess criteria used for diagnosis. A sample of 100 women who reported a pregnancy not complicated by GDM were sent questionnaires addressing GDM screening and prenatal care.

RESULTS — Among a sample of 93 women who reported a pregnancy not complicated by GDM and responded to the supplementary questionnaire, 16 (17%) reported no glucose loading test; 69% of unscreened women had one or more risk factors for GDM. Among a sample of 114 women who self-reported GDM in a singleton pregnancy and whose medical records were available for review, a physician diagnosis of GDM was confirmed in 107 (94%). Records and supplementary questionnaires indicated that oral glucose tolerance tests (OGTTs) were performed in 96 (86%) of these women. Of women with a physician diagnosis of GDM whose OGTT results were available, 25% failed to meet NDDG criteria for this diagnosis, although all had evidence of abnormal glucose homeostasis.

CONCLUSIONS — Screening for GDM is not universal, even among a group of health professionals in whom screening prevalence is likely to be higher than in the general population. Diagnostic criteria for GDM among obstetricians in practice remain nonstandard despite NDDG recommendations. Better understanding of the implications of differing degrees of glucose intolerance and of varying GDM screening and management strategies is required to make policy recommendations for appropriate and cost-effective care.

Gestational diabetes mellitus (GDM), defined as diabetes first detected in pregnancy, complicates 3–5% of pregnancies and is a significant cause of maternal and fetal morbidity (1). Because only one-half of GDM cases can be predicted by known risk factors for GDM such as obesity and advanced maternal age (2), universal screening for GDM has been recommended for all pregnant women by the American Diabetes Association (3) and for all pregnant women aged 30 or older (and younger women with known risk factors) by the American College of Obstetrics and Gynecology (4). However, the extent to which these recommendations are followed is unclear. Also, it is not clear whether or not the criteria for GDM endorsed by the National Diabetes Data Group (NDDG) (5) are consistently used by obstetricians in practice. We carried out an investigation of GDM screening and diagnosis among participants in the Nurses' Health Study II (NHS II), a prospective cohort study of U.S. female registered nurses of reproductive age.

RESEARCH DESIGN AND METHODS

— The NHS II is a prospective study of health outcomes in a cohort of 116,678 U.S. female nurses 25 to 42 years of age and residing in 1 of 14 U.S. states at the inception of the study in 1989. Participants complete biennial questionnaires on lifestyle factors and health events, including pregnancies. Among the 112,512 women without a history of GDM or other forms of diabetes on the baseline (1989) questionnaire, at the time this study was initiated, 12,277 women who returned the 1991 questionnaire reported at least one pregnancy lasting 6 months or more since 1989, and 422 of these women reported a first diagnosis of GDM during this 2-year interval.

To assess screening for GDM among pregnant NHS II participants, we mailed supplementary questionnaires to a computer-generated random sample of 100 of the women who reported a pregnancy but no diagnosis of GDM between 1989 and 1991. Information we requested included whether the participant had in fact had a nondiabetic pregnancy during this time period, whether or not an oral glucose challenge test or other glucose screening test was performed, and the frequency of prenatal visits and urine screening, and the infant's birthweight was categorized as <6 lb (2.7 kg), 6–7.9 lb (2.7-<3.6 kg), 8–9.4 lb (3.6-<4.3 kg), or ≥9.5 lb (4.3 kg).

We also mailed supplementary questionnaires to all women reporting a first diagnosis of GDM during this time

From the Channing Laboratory (J.E.M., J.R.-E., D.J.H., M.J.S., G.A.C., W.C.W.), Section for Clinical Epidemiology, Division of General Medicine, Endocrine-Hypertension Division (C.G.S.), Division of Preventive Medicine (J.E.M.), and Department of Medicine, Brigham and Women's Hospital, Harvard Medical School; and the Departments of Nutrition (M.J.S., W.C.W.) and Epidemiology (D.J.H., M.J.S., G.A.C., W.C.W.), Harvard School of Public Health, Boston, Massachusetts.

Address correspondence and reprint requests to Caren G. Solomon, MD, Section for Clinical Epidemiology, Division of General Medicine, Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115. E-mail: cgsolomon@bics.bwh.harvard.edu.

Received for publication 15 March 1995 and accepted in revised form 16 August 1995.

GDM, gestational diabetes mellitus; NDDG, National Diabetes Data Group; NHS II, Nurses' Health Study II; OGTT, oral glucose tolerance test.

Table 1—Comparison of women who did or did not undergo screening for GDM with a 1-h 50-g glucose screening test

	Screened	Not screened
n	(77)	(16)
Age (years)	30.5	31.1
BMI (kg/m^2)	23.0	23.6
Family history of diabetes (%)	16.9	12.5
Primigravidas (%)	33.8	37.5
Nonwhite ethnicity (%)	2.6	0

Family history indicates diabetes in a first-degree relative. None of these differences was statistically significant.

period, inquiring again whether or not GDM was physician-diagnosed and requesting details of diagnosis and therapy. In addition, to validate these diagnoses and to assess the diagnostic criteria used by physicians, we requested medical records for a subset of 120 women, chosen from those women who returned the supplementary questionnaire corroborating that they had had a physician diagnosis of GDM and agreeing to medical record review.

Definite GDM was defined by any one of the following criteria: *1*) documented 3-h oral glucose tolerance test (OGTT) results meeting NDDG criteria for this diagnosis, i.e., two or more glucose levels greater than the following: fasting 105 mg/dl (5.8 mmol/l), 1-h 190 mg/dl (10.6 mmol/l), 2-h 165 mg/dl (9.2 mmol/l), or 3-h 145 mg/dl (8.1 mmol/l); 2) requirement for insulin; or 3) two fasting blood glucose levels ≥140 mg/dl (7.8 mmol/l). While lesser degrees of fasting hyperglycemia would be considered abnormal in pregnancy, the above threshold was chosen for a diagnosis of definite GDM insofar as it is an accepted definition for diabetes outside of pregnancy. Probable GDM was defined by any of the following: *1*) a documented physician diagnosis of GDM; or 2) OGTT results consistent with GDM by modified criteria for the diagnosis recommended by Carpenter and Coustan (6) (i.e., two or more glucose levels greater than the following: fasting 95 mg/dl (5.3 mmol/l), 1-h 180 mg/dl (10 mmol/l), 2-h 155 mg/dl (8.6 mmol/l), or 3-h 140 mg/dl (7.8 mmol/l). Possible GDM was defined by *1*) an elevated 1-h glucose screening test ≥135 mg/dl (7.5 mmol/l) or 2) other evidence of abnormal but nondiagnostic glucose tolerance (including elevated fasting glucose ≥105 mg/dl [5.8 mmol/l], 1-h postprandial ≥140 mg/dl [7.8 mmol/l], 2-h postprandial ≥120 mg/dl [6.7 mmol/l], and elevated HbA_{1c} above the reported laboratory normal range). A threshold of 135 mg/dl was used for the 1-h screening test to increase sensitivity for potential GDM cases; it has been reported that >10% of GDM cases may be missed using a threshold of 140 mg/dl (7). GDM was considered absent if there was no evidence in the medical record to suggest deviation from normal glucose tolerance. For those patients who initially received insufficient information from the obstetrician, we mailed a directed questionnaire to the physician asking specifically whether or not the patient was considered to have GDM, impaired glucose tolerance, or normal glucose tolerance and the test results on which the diagnosis was based.

Statistical analysis

We calculated the frequency of women who underwent GDM screening and the frequency of women meeting defined criteria for diagnosis of GDM. We compared characteristics of women who did or did not undergo glucose screening in pregnancy using the Wilcoxon's rank-sum test for continuous variables and the χ^2 test for discrete variables. $P < 0.05$ was considered statistically significant.

RESULTS

GDM screening

Of the sample of 100 women reporting a pregnancy not complicated by GDM, 97 (97%) responded to the supplementary questionnaire. After exclusion of two women whose pregnancies had in fact occurred outside of the defined time period, one woman who reported on the supplementary questionnaire that she had GDM (and had apparently erred in completing the original questionnaire), and one woman who could not recall if a 1-h 50-g glucose screening test was done, we had information on 93 women; 89 returned the mailed questionnaire and 4 were later reached by phone. Among subjects completing the mailed questionnaire, which asked about frequency of prenatal visits and urine testing, all (100%) reported five or more prenatal visits and two or more urine glucose screens during pregnancy (i.e., the most frequent regimens offered as response choices).

Of the 93 women, 77 (83%) reported having a 1-h 50-g glucose screening test. The women who reported this test did not differ significantly from women without such screening ($n = 16$) in age, BMI, family history of diabetes, gravidity, or ethnicity (Table 1). Of the 16 women who were not screened with this test, 11 (69%) had one or more of the following traditional risk factors for GDM: age ≥30 years ($n = 9$), obesity (defined as BMI ≥27.3 kg/m^2) ($n = 3$), or family history of diabetes in a first-degree relative ($n = 2$). Extreme obesity, i.e., weight >200 lb (91 kg), may have increased the likelihood of screening; four (5%) women in the screened group but none (0%) in the unscreened group had a weight in this range (NS). The frequency of macrosomia, defined as infant's weight ≥4.3 kg, was comparable among screened and unscreened women (7% in each group).

GDM diagnosis

Of 422 women reporting a first diagnosis of GDM between 1989 and 1991, 389 (92%) responded to the supplementary questionnaires or to telephone follow-up. Fifteen women (3.9%) reported that this was not in fact their first diagnosis of GDM, and another 15 women (3.9%) gave a different response than their response on the initial questionnaire and denied the diagnosis of GDM. Of the latter group, only two women clearly seemed to have erred in completing the initial questionnaire, while four women provided additional information on glucose levels suggestive of abnormal glucose tolerance, and the remainder did not provide adequate information to determine whether or not the initial report of GDM was truly in error. Of the responders, 359 (92%) corroborated on the supplementary questionnaire that a first physician diagnosis of GDM had been made in the preceding 2

Table 2—Validation of self-reported GDM

	n (%)
Self-reported GDM diagnosed 1989–1991	422
Supplementary questionnaire returned	389 (92)
GDM on supplementary questionnaire	359 (92)
Medical records requested	120
Medical records received	117 (97)
Singleton pregnancies with self-reported GDM	114
Definite GDM	73 (64)
Diagnostic OGTT (NDDG criteria)	67
Insulin (with nondiagnostic OGTT)	5
Fasting hyperglycemia	1
Probable GDM	34 (30)
OGTT with modified criteria	10
Physician diagnosis only	24
Possible GDM	7 (6)
Disconfirmed GDM	0 (0)

OGTT denotes a 3-h 100-g OGTT. See METHODS section for details.

years; 304 (85%) of these women consented to medical record review.

Medical records were requested for a sample of 120 (39%) of these 304 women and were obtained for 117 (97%) of the 120 women. We excluded three women because medical record review revealed molar pregnancy (one woman) or multiple gestation (two women). Of the remaining 114 subjects, 107 (94%) were considered by medical record review to have definite or probable GDM.

GDM was considered definite in 73 (64%) women. Of these women, 67 had documented OGTT results diagnostic of GDM by NDDG criteria (see METHODS). Five women with no or nondiagnostic OGTT results were documented to require insulin during pregnancy; an additional 10 women whose OGTT results were diagnostic of GDM also required insulin. One woman (whose OGTT results were not diagnostic of GDM and who did not require insulin) had two documented fasting blood glucose levels >140 mg/dl (7.8 mmol/l), diagnostic of GDM. Another 34 women (30%) were considered to have probable GDM on the basis of a recorded physician diagnosis of GDM; 10 of these women met modified OGTT criteria for GDM. The remaining seven (6%) women had possible GDM, as defined by an abnormal glucose test nondiagnostic of GDM in the absence of a documented physician diagnosis of GDM. No woman who reported GDM had evidence of completely normal glucose tolerance in pregnancy (Table 2).

Review of medical records documented 3-h OGTTs in only 93 (82%) of the 114 women. An additional three women with a confirmed physician diagnosis of GDM (on medical record review) but without medical record documentation of OGTT reported on their supplementary questionnaires that they had an OGTT; even including these women, 18 women (16%) self-reporting GDM apparently did not undergo recommended testing for this condition as endorsed by the American College of Obstetrics and Gynecology. In addition, of 89 women with a documented physician diagnosis of GDM for whom precise OGTT results were available, 22 (25%) failed to meet NDDG criteria for the diagnosis. While one of these women was documented to require insulin and thus presumably had other blood glucose levels consistent with diabetes, diagnosis of GDM in the remaining 21 (24%) women appeared to be based on the abnormal but nondiagnostic OGTT results. In only 1 of these 21 women was the 1-h 50-g glucose screening test result >200 mg/dl (11.1 mmol/l), a result that some clinicians would consider virtually diagnostic of GDM.

Nonetheless, all women self-reporting GDM demonstrated some derangement of glucose tolerance. In addition to the 67 women who had diagnostic OGTT results by NDDG criteria, 15 (17%) of the 89 women whose precise OGTT results were available had one abnormal value on this test, and 10 (11%) (six of whom had one abnormal value by NDDG criteria) met modified criteria for GDM; the three women meeting none of these criteria had elevated 1-h screening tests and one abnormal value on an OGTT by modified criteria. In addition, results of OGTTs were documented to be abnormal in another three women whose precise results were unavailable. Of the 22 women either who did not undergo an OGTT or for whom no OGTT results were documented, 4 had evidence of definite GDM (insulin requirement in three and fasting hyperglycemia [≥7.8 mmol/l on more than one occasion] in one), and the remaining 18 women all had evidence of abnormal glucose homeostasis, including abnormal 1-h glucose screening tests ≥7.5 mmol/l (n = 13), elevated postprandial (n = 3) or fasting (≥5.8 mmol/l [n = 1]) glucose levels, and/or elevated HbA_{1c} level (n = 1).

CONCLUSIONS— Routine screening for GDM has been recommended by diabetologists (3) and obstetricians (4). However, data from the NHS II indicate that even among a population of well-educated and motivated female health professionals receiving regular prenatal care, such screening for GDM is not universal, even in women older than 30. Among a random sample of pregnant women in our cohort between 1989 and 1991, 17% were not screened in this manner, despite the presence of one or more well-recognized GDM risk factors in more than two-thirds of unscreened women. This estimated prevalence of screening is likely to be higher than that in a general population because of the medical background and high level of prenatal care among this cohort.

A policy of universal screening for GDM in fact remains controversial. While some investigators have noted no identifiable risk factors in >40% of women with GDM identified by universal screening (2), others have reported a low risk of GDM in the absence of established risk factors (8). Furthermore, the reliability of GDM screening tests has been questioned (9). Noting the suboptimal reproducibility and economic costs of screening, as well as the paucity of randomized controlled trial data showing a benefit for treatment of GDM once identified, the Canadian Task Force on the Periodic Health Examination did not recommend universal screening for GDM (10), in contrast to the policies recommended by the

American Diabetes Association (3) and American College of Obstetricians and Gynecologists (4). Moreover, the inconvenience and discomfort associated with glucose tolerance testing may have a role in physicians' failure to screen universally; neither HbA_{1c} (11) nor fructosamine (12) measurements have thus far proven sufficiently sensitive to replace this more cumbersome screening strategy.

Among the present cohort of women, self-reporting of physician diagnosis of GDM was quite accurate. Medical record review confirmed a physician diagnosis of GDM in 94% of self-reported cases and indicated some impairment of glucose tolerance in all of the remaining cases.

Of note is the observation that one-quarter or more of women accurately reporting a physician diagnosis of GDM did not actually meet NDDG criteria for this diagnosis. Indeed, appropriate diagnostic criteria for GDM remain controversial. Complications associated with GDM are increased among women meeting the less stringent modified OGTT criteria recommended by Carpenter and Coustan (6) and also among women with only one abnormal glucose level by NDDG criteria (13); in this cohort, 86% of women whose precise OGTT results were available met modified criteria for GDM, and 93% had at least one abnormal value on this test.

Record review indicated that a physician diagnosis of GDM was in many cases based on a high 1-h 50-g glucose screening test result, in the absence of other diagnostic testing. Some physicians empirically consider a glucose level ≥200 mg/dl on the 1-h 50-g glucose screening test, in the absence of an OGTT, to be diagnostic of GDM. Only two women in this cohort not meeting NDDG criteria for the diagnosis of GDM (one with no available OGTT results, another with one abnormal value on OGTT) had screening test results in this range; the woman with no available OGTT results required insulin and thus met the criteria for definite GDM on this basis. While it is conceivable that medical records available for review may have been incomplete and that further screening beyond the 1-h test may have been performed, screening beyond that documented in the available medical records was suggested by the nurses' supplementary questionnaires in only three cases; incomplete documentation is thus unlikely to have introduced significant misclassification.

Only 15–20% of women with abnormal results on the 1-h 50-g glucose screening test meet diagnostic criteria for GDM on the OGTT, although this frequency increases with higher screening test results (6). However, even in the absence of abnormal OGTT results, elevated glucose levels on the 1-h screen may be markers for abnormal glucose homeostasis. Insulin resistance typically increases as pregnancy progresses (14); women with an abnormal screening test and initially normal OGTT have a significantly higher risk of developing frank glucose intolerance with progression of pregnancy than do women with a normal screening test result (15), and appropriate diagnosis may depend on retesting, which is rarely done in practice. Furthermore, women who have abnormal 1-h screening test results, but do not have two abnormal values on a 3-h OGTT, have been reported to have increased risk of perinatal morbidity characteristically associated with diabetes (16).

To our knowledge, only one other published study has evaluated the prevalence of screening for GDM in the U.S. Based on responses of physicians to a mailed questionnaire, Landon et al. (17) reported universal screening for GDM by 90% of maternal-fetal subspecialists and 77% of obstetricians, most commonly but not in all cases by 50-g glucose loading tests. The criteria used by physicians to diagnose GDM were not assessed in that study. The data of Landon et al., as well as our own data, support the observation made in other settings that practice guidelines may influence but are unlikely to wholly guide clinical practice (18).

Our data indicate heterogeneity in present patterns of screening for and diagnosing GDM, which may reflect either a lack of awareness of guidelines or controversy regarding what is appropriate. Further studies evaluating the risks and implications of GDM and comparing costs and efficacy of different screening and management strategies are needed to define appropriate and cost-effective approaches to this common complication of pregnancy.

Acknowledgments— This research was supported by Research Grants CA-50385 and DK-36798 from the National Institutes of Health. C.G.S. is also supported by an American Heart Association Clinician Scientist Award. J.E.M. is also supported by a Merck/Society for Epidemiological Research Clinical Epidemiology Award.

References

1. Magee MS, Walden CE, Benedetti TJ, Knopp RH: Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity. *JAMA* 269:609–615, 1993
2. Coustan DR, Nelson C, Carpenter MW, Carr SR, Rotondo L, Widness JA: Maternal age and screening for gestational diabetes: a population-based study. *Obstet Gynecol* 73:557–560, 1989
3. Gestational diabetes mellitus (Position Statement). *Diabetes Care* 13:5–6, 1990
4. American College of Obstetricians and Gynecologists: Management of diabetes mellitus in pregnancy. *ACOG Tech Bull* 92:1–2, 1986
5. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
6. Carpenter MW, Coustan DR: Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol* 144:768–773, 1982
7. Sacks DA, Salim A-F, Karten GJ, Forsythe AB, Hackett JR: Screening for gestational diabetes with the one-hour 50-g glucose test. *Obstet Gynecol* 70:89–93, 1987
8. Dietrich ML, Dolnicek TF, Rayburn WF: Gestational diabetes screening in a private, Midwestern American population. *Am J Obstet Gynecol* 156:1403–1408, 1987
9. O'Sullivan JB, Mahan CM: Glucose tolerance test variability in pregnant and nonpregnant women. *Am J Clin Nutr* 19:345–351, 1966
10. Canadian Task Force on the Periodic Health Examination: Periodic Health Examination 1992 update. I. Screening for gestational diabetes mellitus. *Can Med Assoc J* 147:435–442, 1992
11. Loke DF, Chua S, Kek LP, Thai AC, Ratnam SS: Glycosylated hemoglobins in pregnant women with normal and abnormal glucose tolerance. *Gynecol Obstet Invest* 37:25–29, 1994
12. Roberts AB, Baker JR, Metcalf P, Mullard C: Fructosamine compared with a glucose load as a screening test for gestational diabetes. *Obstet Gynecol* 76:773–775, 1990
13. Langer O, Brustman L, Anyaegbunam A, Mazze R: The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. *Am J Obstet Gynecol* 157:758–763, 1987
14. Kuhl C: Insulin secretion and insulin resistance in pregnancy and GDM: implica-

tions for diagnosis and management. *Diabetes* 40:18–24, 1991
15. Benjamin F, Wilson SJ, Deutsch S, Seltzer VL, Droesch K, Droesch J: Effect of advancing pregnancy on the glucose tolerance test and on the 50 g oral glucose load screening test for gestational diabetes. *Obstet Gynecol* 68:362–365, 1986
16. Tallarigo L, Giampietro O, Penno G, Miccoli R, Gregori G, Navalesi R: Relation of glucose tolerance to complications of pregnancy in non-diabetic women. *N Engl J Med* 315:989–992, 1986
17. Landon MB, Gabbe SG, Sachs L: Management of diabetes mellitus and pregnancy: a survey of obstetricians and maternal-fetal specialists. *Obstet Gynecol* 75:635–640, 1990
18. Lomas J, Anderson GM, Domnick-Pierre K, Vayda E, Enkin MW, Hannah WJ: Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. *N Engl J Med* 321:1306–1311, 1989