Comparison of World Health Organization and National Diabetes Data Group Procedures to Detect Abnormalities of Glucose Tolerance During Pregnancy

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OBJECTIVE — To compare the one-step procedure proposed by the World Health Organization (WHO) with the two-step procedure proposed by the National Diabetes Data Group (NDDG) for the identification of abnormalities of glucose tolerance during pregnancy.

RESEARCH DESIGN AND METHODS — One hundred twenty-seven nondiabetic Pima Indian women had a 75-g 2-h glucose tolerance test (WHO criteria). Those with an elevated 1-h glucose concentration (≥7.8 mmol/l) were referred for a 100-g 3-h glucose tolerance test (National Diabetes Data Group criteria). The effectiveness of the two test procedures was determined by comparing the frequency of macrosomia and cesarean section as outcomes of pregnancy.

RESULTS — Of 42 women with 1-h plasma glucose concentrations ≥7.8 mmol/l, 13 had no 100-g test, 27 had a normal test, and 2 had an abnormal test. Both women (100%) with abnormal two-step 100-g tests also had abnormal one-step 75-g tests, but only 2 of the 11 women (18%) with an abnormal one-step test had an abnormal two-step test. Sixteen of the 127 women delivered babies weighing ≥4,000 g. Six of these women (38%) were correctly identified as abnormal using the one-step test and one (6%) using the two-step test. Of seven women delivering by cesarean section, four (57%) had abnormal one-step tests, but none had an abnormal two-step test.

CONCLUSIONS — The one-step WHO test for glucose tolerance during pregnancy was abnormal in a greater percentage of women with adverse outcomes than the more cumbersome two-step NDDG test. The one-step test has the added advantage of being directly comparable to the standard glucose tolerance test used in nonpregnant women.

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WHO, World Health Organization; NDDG, National Diabetes Data Group; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

Two sets of criteria are currently recommended by national or international organizations for the diagnosis of abnormalities of glucose tolerance during pregnancy. The World Health Organization (WHO) criteria (1) are based on a test utilizing a 75-g oral glucose load, the same load that is now accepted worldwide as the standard for the diagnosis of abnormal glucose tolerance in nonpregnant adults. The National Diabetes Data Group (NDDG) endorsed (2) an adaptation of the criteria proposed by O'Sullivan and Mahan in 1964 (3), which are based on a 3-h test following a 100-g load, administered fasting. A two-step procedure is commonly used in which the 100-g load is administered only to women who have a glucose concentration ≥7.8 mmol/l at 1 h after a 50-g glucose load, administered nonfasting. This two-step procedure, using the O'Sullivan and Mahan (3) criteria, has been endorsed by the American Diabetes Association (4) for areas not already using other criteria and by the American College of Obstetricians and Gynecologists (5), and it is in general use throughout the U.S. The WHO criteria, which define both diabetes (2-h plasma glucose ≥11.1 mmol/l) and impaired glucose tolerance (IGT, 2-h plasma glucose ≥7.8 mmol/l and <11.1 mmol/l) are used in most other parts of the world.

The NDDG criteria have a number of drawbacks that include the need for two tests, blood samples at four time points, a test duration of 3 h, a high glucose load that is often unpalatable to pregnant women, and no comparability with the 75-g test that is done on these same women in follow-up. These criteria have been criticized as not optimally predicting critical outcomes (6). Despite these drawbacks and the statement published as early as 1985 by the Second International Workshop-Conference on Gestational Diabetes (7) that the 75-g 2-h test "may eventually replace both the 100-g and 50-g tests," American obstetricians have been reluctant to adopt the

WHO criteria because of a lack of data on the 75-g load during pregnancy (7).

The purpose of this study is to present data from pregnant women who had both a 1-h and a 2-h glucose concentration measured after an oral 75-g load and who, if the 1-h glucose concentration was high, were referred for a fasting 100-g 3-h glucose tolerance test.

RESEARCH DESIGN AND METHODS

— The subjects of this study live in or near the Gila River Indian Community in southern Arizona, and most are Pima or Tohono O'odham Indians, who are Native Americans with a very high prevalence of non-insulin-dependent diabetes mellitus (8). Since 1965, a 75-g load has been administered to nonfasting women during pregnancy for the diagnosis of IGT and diabetes. Beginning in January 1992, a 1-h plasma glucose determination was added to the test, and women in whom this was ≥7.8 mmol/l were then tested after an overnight fast with a 100-g load. Because the glucose load makes little difference in the glucose concentration at 1 h in subjects with normal glucose tolerance (9–11), this cutoff point is comparable with a glucose concentration of 7.8 mmol/l following a 50-g load, the concentration above which the 100-g 3-h test is recommended under the NDDG criteria.

The present analysis was limited to 127 women without previously diagnosed diabetes who had a 1-h glucose measured during the 75-g glucose tolerance test during 1992 at a mean of 27 (range 15–38) weeks' gestation. Following delivery, medical charts were reviewed to determine the occurrence of two adverse outcomes known to be associated with hyperglycemia during pregnancy: macrosomia, defined as a birth weight of at least 4,000 g, and delivery by cesarean section. There are, of course, other causes of macrosomia, such as maternal obesity and genetic make-up, and rates of, and indications for, cesarean section vary from place to place. Thus, these pregnancy outcomes are not specific for, although often associated with, maternal hyperglycemia. The Indian Health Service follows the nationally recommended policy of treating gestational diabetes diagnosed by the NDDG criteria.

Table 1—*Results of 100-g 3-h OGTT (NDDG criteria) according to glucose concentration 2 h after a 75-g load (WHO criteria)*

	75-g 1-h glucose			
		≥7.8 mmol/l (referred for 100-g load)		
	<7.8 mmol/l	100-g test		
75-g 2-h glucose (mmol/l)	Not referred	No test done	Normal	Abnormal
<7.8	85	9	22	0
7.8–11.0	0	3	5	1
≥11.1	0	1	0	1
Total	85	13	27	2

Abnormal glucose was defined as plasma glucose concentration at ≥2 time points at or above respective standards: fasting, 5.8 mmol/l; 1 h, 10.6 mmol/l; 2 h, 9.2 mmol/l; and 3-h, 8.1 mmol/l.

RESULTS — Of the 127 women without previously known diabetes, the 42 (33%) who had a 1-h plasma glucose concentration ≥7.8 mmol/l were referred for the 100-g test. All those with a 1-h glucose concentration <7.8 mmol/l also had a 2-h glucose <7.8 mmol/l. Table 1 shows the results of the WHO (75 g) and NDDG (100 g) tests. Thirteen women had no follow-up test. According to the WHO criteria, 4 of these 13 women had an abnormal glucose tolerance test: 1 with a 2-h glucose concentration of 11.9 mmol/l had diabetes, and 3 with 2-h concentrations from 8.1 to 8.5 mmol/l had IGT.

Twenty-nine women with an abnormal 1-h glucose concentration were tested with the 100-g load. Of the 29, 27 had a normal test according to the NDDG criteria, i.e., no more than one glucose concentration above the respective cutoff concentration (see footnote in Table 1), but 5 did have IGT by the WHO criteria on the 75-g test. Two women met the NDDG criteria for gestational diabetes with at least two high glucose concentrations, and of these, one also had diabetes, and one had IGT by the WHO criteria.

Table 2—*Macrosomic deliveries (≥4,000 g) and cesarean sections by abnormal WHO or NDDG glucose tolerance tests in 127 women*

Outcome	*n*	Abnormal WHO test	Abnormal NDDG test
Macrosomia	16	6 (37.5)	1 (6.3)
Cesarean section	7	4 (57.1)	0 (0)
Either	17	6 (35.3)	1 (5.9)*

Data are *n* (%). Cesarean sections excluded the two done for clinical indications unrelated to hyperglycemia. *The one woman with an abnormal NDDG test was also abnormal by the WHO test. Thus, there were five discrepant results, and in each case, the WHO test was abnormal while the NDDG was not.

Table 2 shows the numbers of cases and the percentage with macrosomia and delivery by cesarean section in these 127 women. Sixteen women delivered babies weighing ≥4,000 g. Six (38%) had had an abnormal test by the WHO criteria, while only one (6%) was abnormal by the NDDG criteria. Four women did not receive the 100-g load. Nine cesarean sections were done, two of which were for indications not usually associated with hyperglycemia (twin and breech deliveries). Of the other seven, four cesareans (57%) had an abnormal WHO test. Two did not have the 3-h 100-g test, and in the five who did, this test was normal. Among the 127 women in this study, the WHO criteria identified as abnormal 38% of women delivering macrosomic infants and 57% of those delivering by cesarean section, while the NDDG criteria only identified 6.3% of macrosomic infants and no cesarean sections.

If the NDDG criteria are considered to be the "gold standard" for the di-

agnosis of gestational diabetes, then the WHO criteria, based on the glucose concentration 2 h after a 75-g load administered to nonfasting women, correctly identified both subjects with gestational diabetes. Although based on only two subjects, the estimated sensitivity was thus 100%. The WHO criteria also correctly identified 116 of the 127 subjects considered normal by the NDDG criteria (specificity = 93%). Conversely, if the WHO criteria are considered to be the "gold standard," only 2 of 11 women with abnormal glucose tolerance during gestation were identified by the NDDG criteria (sensitivity = 18%), and all other women would be considered normal by the NDDG test (specificity = 100%). Thus, there were nine discrepancies in diagnosis. In each of these discrepancies, a woman with an abnormal WHO test was considered normal or unknown by the NDDG test ($P = 0.0039$ by an exact binomial test for the hypothesis that there was no difference in abnormality rates between WHO and NDDG criteria).

CONCLUSIONS — The nonfasting 2-h post 75-g glucose concentration strongly predicts adverse outcomes for the mother and her offspring in the Pima Indians (12–19). This study suggests that the standard WHO criteria are more likely to identify abnormal outcomes in pregnant women than are the NDDG criteria currently used in most of the U.S. Many women in this population had been tested for diabetes with oral glucose tolerance tests (OGTTs) at ~2-year intervals. Those with known diabetes at the time of pregnancy did not undergo diagnostic tests. Thus, women with known preexisting diabetes were not included in this study. In a population tested only during pregnancy, a high proportion of women with undiagnosed preexisting diabetes would have been identified as cases of gestational diabetes. Inclusion of such women in the population tested would have had the effect of increasing the sensitivity of the NDDG procedure to some degree, but such women would also be correctly identified as having diabetes by the WHO procedure.

Although the 75-g load is larger than the 50-g screening load originally recommended by O'Sullivan (3), previous studies (9–11) have shown that in subjects with normal glucose tolerance, the glucose load makes little difference in the glucose concentration measured during a glucose tolerance test. Thus, the 75-g load would not be expected to result in higher glucose concentrations at 1 h than would the 50-g load. However, in subjects with abnormal glucose tolerance, there appears to be a glucose load dosage effect (9), and such subjects, with a slightly elevated glucose concentration 1 h after a 50-g load, might have an even higher concentration after a 75-g load. It is unlikely, however, that a woman would have had a lower 1-h glucose concentration using 75 g instead of 50 g. Thus, the group of women who had glucose concentrations ≥7.8 mmol/l 1 h after a 75-g glucose load would include all who would have been so identified using a 50-g load.

There is a strong argument for not requiring an overnight fast before the initial glucose tolerance test and very little to recommend it. Pregnant women often experience nausea when fasting and may refuse, or be unable, to fast until the test. It may be unreasonable to expect a woman to get up, possibly with morning sickness, travel to the clinic, and then wait an additional 3 h before eating. Because glucose concentrations during the glucose tolerance test are affected little by the time since the last meal (20), fasting, or the fasting glucose, adds little to the glucose tolerance test but makes the testing procedure more cumbersome and may account for much of the difficulty encountered in administering this test to pregnant women.

The purpose of these tests is to identify women with abnormal glucose tolerance that is associated with adverse outcomes in pregnancy. Women who have normal glucose concentrations following an oral glucose load obviously have an adequate insulin response and sensitivity to insulin action. In addition, pregnant women tend to have fasting glucose concentrations that are low (21–23). Thus, if an elevated fasting glucose concentration is encountered in the face of an otherwise normal glucose tolerance test, the possibilities of laboratory error or of an inaccurate history that the woman is fasting need to be considered. In the present series, there was no instance in which the only elevated glucose concentration was the fasting glucose. The fasting glucose is, therefore, probably unnecessary.

The NDDG test, in addition to requiring that women fast, requires women with abnormal screening tests to have a second test. Because not all women who needed the follow-up diagnostic test appeared for the test, no direct comparison of the two glucose loads is possible. The test using the 100-g load is unpalatable, lasts 3 h, and requires four blood samples. The fact that 13 of the 42 women (31%) in this study who had an abnormal 1-h glucose did not return for the fasting 100-g test may reflect some of these problems. Compliance will vary from practice to practice, and so this will be less of a concern in some populations and more of a concern in others. Although a universal diagnostic test (rather than a screening test) may not be deemed necessary in all settings, if it can be done with a minimum of disruption, it would be useful.

The NDDG criteria currently recommended are not systematically applied. Investigators have attempted to improve the sensitivity by lowering the cutoff value on the screen (24,25), changing the timing for screening or testing (26), reducing the number of abnormal values required for diagnosis of abnormality (27), or lowering the definitions of abnormal (24,25,27).

Among residents of the Gila River Indian Community, a population with

high rates of abnormal glucose tolerance during pregnancy, the WHO criteria did not miss either of the two women who met the NDDG criteria for gestational diabetes and classified as abnormal some who were considered normal by the NDDG criteria, including some with adverse outcomes often associated with hyperglycemia. Admittedly, because of the small numbers, this is an unstable estimate of sensitivity. In the unlikely event that the next woman had a 2-h glucose <7.8 mmol/l by WHO criteria but >9.2 mmol/l (along with at least one other high glucose) by NDDG criteria, the sensitivity would be 67%. The sensitivity estimate for the NDDG criteria is more stable. If the next abnormal glucose tolerance were correctly identified by the NDDG criteria, the sensitivity would rise from 18 to 24%. Any dichotomy of a continuous variable, such as glucose concentration, is arbitrary, and some complications of pregnancy that can perhaps be reduced by such screening do occur even with glucose concentration in the normal range during pregnancy (14,16, 19,27).

The WHO test was abnormal in a greater proportion of women with adverse outcomes than was the NDDG test. The WHO test is at least as good as the NDDG test in predicting adverse outcomes, is easier to administer, more acceptable to pregnant women, and has the added advantage of being directly comparable to the standard glucose tolerance test that will be administered to these women during follow-up after their pregnancies.

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