Oral Glucose Tolerance Test in Healthy Pregnant Nigerian Women

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Oral glucose tolerance tests (OGTTs) with 75 g glucose were performed in 20 healthy pregnant Nigerian women in each trimester of pregnancy and the puerperium; 34 nonpregnant control subjects matched for age and parity were also studied. The blood glucose levels from fasting to 60 min were lower in pregnant subjects, but the 90- and 120-min values were higher. The highest blood glucose values were observed in the first trimester with an apparent improvement in glucose tolerance in the second and third trimesters. This observation is strikingly different from the established pattern of OGTT in pregnant Caucasian women. With pooled data from OGTT results in the three trimesters for the 20 pregnant women (60 OGTTs), a statistically derived criterion (based on mean + 2SD approximated to the nearest 5) for the interpretation of OGTT in pregnant Nigerian women was devised. This criterion defines the upper limits of normal for venous whole-blood glucose in pregnant Nigerian women during an OGTT with a 75-g glucose load as follows: fasting, 90; 30 min, 135; 60 min, 150; 90 min, 145; and 120 min, 125 mg/dl. These values are lower than those recommended for pregnant women by the National Diabetes Data Group (O'Sullivan and Mahan criteria) and the World Health Organization. The results from this study underscore the need for caution regarding uncritical application of data from one racial or ethnic group to others. *Diabetes Care* 11:412–15, 1988

To diagnose diabetes mellitus in pregnant women who do not have overt symptoms or a clearly abnormal blood glucose level, the only tool available is still the oral glucose tolerance test (OGTT). There are at least two widely published sets of criteria for the performance and interpretation of the OGTT in pregnancy. The National Diabetes Data Group (NDDG; 1) recommended the criteria of O'Sullivan and Mahan (2), and this has been endorsed by both the Second International Workshop-Conference on Gestational Diabetes Mellitus (3) and the American Diabetes Association (4). The World Health Organization (WHO) Expert Committee on Diabetes has, on the other hand, suggested a different set of criteria, which is the same as that for adult men and nonpregnant women (5).

The O'Sullivan and Mahan criteria are widely used in the United States; however, investigators and practitioners in other parts of the world use either of the two criteria and sometimes others that are less well known (6–8). Note that these two sets of criteria were derived from data in Caucasian populations in North America and Europe. The lack of reliable data for both pregnant and nonpregnant subjects in other populations, especially those of the developing countries, has often been lamented. A plea for more studies on the pattern of carbohydrate tolerance in these populations has been made. Earlier studies in healthy Africans, for example, have noted lower blood glucose values during an OGTT compared with healthy Caucasians (9–11). In one of the few studies in pregnant African women, Fraser (12) observed an improvement in carbohydrate tolerance as pregnancy advanced instead of the deterioration often described in Caucasian women (6,13,14).

In this study, which was designed to determine the pattern of oral glucose response in healthy pregnant Ni-

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TABLE 1
Oral glucose tolerance test results for control and pregnant subjects

	Glucose values (mg/dl)				
		Pregnant subjects (n = 20)			
Time (min)	Control subjects (n = 34)	T1	T2	T3	PP
0	72.90 ± 13.11	70.75 ± 9.97	66.10 ± 12.61	66.80 ± 13.83	71.95 ± 7.50
30	100.97 ± 16.72	102.30 ± 21.97	93.30 ± 19.10	92.10 ± 18.35	94.25 ± 17.56
60	106.20 ± 22.59	108.10 ± 29.70	99.70 ± 19.29	98.80 ± 19.71	94.85 ± 14.20
90	93.20 ± 17.94	109.70 ± 23.65*	99.40 ± 22.15	96.00 ± 18.75	91.65 ± 14.23
120	79.94 ± 16.62	96.10 ± 21.70*	87.10 ± 16.97	85.70 ± 12.65	86.80 ± 13.57

Values are means ± SD. T1, first trimester; T2, second trimester; T3, third trimester; PP, puerperium.
*$P < .05$, Newman-Keuls test compared with other group means.

gerian women, we observed that there was no worsening of carbohydrate tolerance with advancing pregnancy. In addition, our results indicate that the criteria for defining abnormal glucose tolerance in pregnant Nigerian Africans may be different from those currently in use for Caucasians.

MATERIALS AND METHODS

Study subjects. Pregnant women attending the antenatal clinic of the University College Hospital, Ibadan, Nigeria, were studied. Women who were sure of their menstrual dates and who presented in the first trimester of pregnancy were eligible. Other criteria for inclusion in the study were as follows: Nigerian nationality and the granting of an informed consent; a normal physical examination; absence of known risk factors for diabetes in pregnancy, e.g., a strong family history of diabetes, previous history of large babies (birth wt ≥4 kg), history of unexplained intrauterine death or stillbirth, gross obesity (wt ≥90 kg), or glycosuria in the current pregnancy; absence of any other medical problems, e.g., anemia (packed cell vol <30%), hypertension in pregnancy (blood pressure ≥140/90 mmHg), heart disease, systemic infections, hepatitis, or hemoglobinopathy; and absence of obstetric complications, e.g., preeclampsia or eclampsia, hydramnios, or severe antepartum hemorrhage.

Forty subjects were recruited in the first trimester, but only 20 completed the study by being tested in every trimester and the puerperium. Their ages ranged from 19 to 38 yr with a mean of 26.2 yr, and their parity ranged from 0 to 5 with a mean of 2.1.

Nonpregnant nondiabetic women attending the gynecological clinic of the University College Hospital for minor problems such as menstrual irregularity or vulvovaginitis were matched with the pregnant subjects for age and parity. There were 34 control subjects, and their ages ranged from 20 to 40 yr with a mean of 28.6 yr. Their parity ranged from 0 to 6 with a mean of 1.7. None had any past history suggestive of diabetes mellitus.

Oral glucose tolerance testing. All study participants were instructed about the OGTT. All subjects had been on a typical Nigerian diet that comprised at least 60% carbohydrate so that no special dietary preparation was necessary. The test was performed in the morning after a 10- to 12-h overnight fast. With the subject sitting in a chair, a 19-gauge needle was inserted into an antecubital vein and was kept patent with a small volume of heparinized saline. After fasting blood had been drawn, 75 g of glucose powder dissolved in 400 ml H_2O was administered orally over 2–3 min. Thereafter, blood was drawn every 30 min for glucose over the next 120 min.

Glucose samples were analyzed within 3 h of collection with the glucose oxidase method. Venous whole-blood glucose was measured. Each pregnant woman

TABLE 2
Pooled glucose data for three trimesters in 20 healthy pregnant Nigerian women

	Blood glucose (mg/dl)				
	0 min	30 min	60 min	90 min	120 min
Control subjects (mean)	72.90	100.97	106.20	93.20	79.94
Pooled data (mean ± SD)	67.90 ± 12.20	95.92 ± 20.10	102.20 ± 23.40	101.70 ± 21.50	89.60 ± 17.80
95% confidence intervals	64.81–70.99	89.81–101.01	96.28–108.12	96.26–107.14	85.10–94.10
Mean + 2SD	92.30	136.10	148.70	144.70	125.30
Mean + 3SD	104.50	156.22	172.40	166.20	143.0

n = 60 OGTTs (20 pregnant women tested in the 3 trimesters).

had an OGTT performed in the first trimester (8–14 wk), second trimester (24–28 wk), third trimester (32–36 wk), and the puerperium (~2 wk after delivery). The control subjects were studied similarly, but only one OGTT was performed.

Statistical analysis. Data related to age, parity, and blood glucose are expressed as means ± SD. Analysis of variance (ANOVA) was used for comparison of multiple group means. When found to be significant, the Newman-Keuls test was used to compare individual group means (15).

RESULTS

Of the 40 pregnant women recruited in the first trimester, only 20 had OGTTs performed in all three trimesters and the puerperium. The data of only those who completed the study were analyzed. Thirty-four control subjects were studied.

The mean (±SD) weights of the pregnant subjects were 59.3 ± 5.4 kg in the first trimester, 60.1 ± 6.2 kg in the second trimester, and 64.3 ± 5.1 kg in the third trimester. The mean weight for the nonpregnant control subjects was 57.6 ± 9.4 kg. None of the study participants was obese.

Table 1 presents the mean glucose values during OGTT in the cases and control subjects. The mean fasting blood glucose levels in the three trimesters and the puerperium were lower than the corresponding results for nonpregnant control subjects but were not significantly different ($P > .10$).

Variance analysis at 0, 30, and 60 min showed that, with 4 and 107 df, there were no differences in the group mean values ($P > .1$). However, for the 90- and 120-min values, statistically significant differences at the 5% probability level were found. The difference occurred due to the first-trimester values being significantly higher than the other results ($P < .05$, Newman-Keuls test). Table 2 presents the pooled blood glucose data for the three trimesters in the pregnant women. The results again show that for the first 60 min of the OGTT, the values for the control subjects were higher but not to a level of significance ($P > .05$). At 90 and 120 min, however, the glucose levels in the pregnant women were significantly higher ($P < .05$). Table 2 also provides the mean + 2SD and the mean + 3SD for these pooled data. Theoretically, for a normal distribution these will embrace 95 and 99.7% of the population, respectively. Table 3 shows a composite of established criteria for interpretation of the OGTT in pregnancy and those derived from this study for possible application in Nigerian women.

TABLE 3
Possible criteria for interpretation of oral glucose tolerance test in pregnant Nigerian women

Study	Time					
	0	30	60	90	120	180
This study*	90	135	150	145	125	
This study†	105	155	170	165	145	
O'Sullivan and Mahan (1964)	90		170		145	125
WHO (1985)						
Definite diabetes	120				180	
Impaired glucose tolerance	<120				120–180	

All values are for venous whole-blood glucose in mg/dl. Glucose load for this study and WHO criteria, 75 g; for O'Sullivan and Mahan, 100 g.
*Mean + 2SD approximated to the nearest 5.
†Mean + 3SD approximated to the nearest 5.

DISCUSSION

There have been few published studies on oral glucose tolerance patterns in pregnant women from the developing countries of Africa, and the need for such data for comparison with other populations has been emphasized. In this study, 20 healthy nonobese pregnant Nigerian women were studied in each of the three trimesters of pregnancy and the puerperium. A control group of nonpregnant women was also investigated. The results have confirmed the previously noted observations that, although the fasting blood glucose is usually lower in pregnant women than in nonpregnant women (6,7), blood glucose levels tend to rise higher and to be more sustained in pregnant women (6,7,13).

One striking observation from this study was that the highest blood glucose levels were obtained during the first trimester in the pregnant women. Lower levels of blood glucose were achieved during OGTT in the second and third trimesters. Such apparent improvement in glucose tolerance was previously noted by Fraser (12) among Kenyan women, and it contrasts with the experience in Caucasian women, in whom the OGTT pattern in pregnancy has been reported to remain unchanged (16,17) or to worsen (6,13,14) as pregnancy progressed. We do not have an explanation for this trend in OGTT during pregnancy in our patients. There is very little to indicate any qualitative change in their diet during pregnancy, although a change in quantity cannot be ruled out. In addition, an increase in level of physical activity must be considered, because some Nigerian pregnant women are known to do more work as pregnancy advances. If studies establish this as a pattern in African women, it would mean that in these populations, OGTT for the diagnosis of gestational diabetes mellitus (GDM) may not need to be delayed or repeated in the third trimester, as is currently the practice. However, whether Nigerian women who are at high risk for GDM have a pattern of glucose tolerance in pregnancy similar to their healthy counterparts is not yet established. Until this is known, it would be wise to restudy pregnant women as the pregnancy advances when the circumstances so dictate.

With regard to the interpretation of the OGTT in pregnant women for diagnosis of GDM, the two criteria most commonly used are those of O'Sullivan and Mahan (2) and WHO (5). For many years, at the University College Hospital in Ibadan, we have used the criteria of O'Sullivan and Mahan, although not without reservation. These particular criteria are used because not only are they based on a large-scale study of an unselected group of pregnant women but their value in predicting future diabetes mellitus has been established through the long-term follow-up of a selected cohort (18). These factors were responsible for the adoption of these criteria by the NDDG (1) and their endorsement by the Second International Workshop-Conference on GDM (3) and the American Diabetes Association (4). The criteria, based on the mean + 2SD, were derived from OGTT results in pregnant women with pooled data from all the trimesters (2).

This study, although involving few subjects, followed the same group of women throughout pregnancy and thus minimized potential biases due to interindividual variability. The adjusted mean + 3SD of the pooled data yielded criteria that, except for the fasting values, are practically identical to that of O'Sullivan and Mahan (Table 3). If the adjusted mean + 2SD is used as was done by O'Sullivan and Mahan, it becomes clear that the upper limits of normal for the interpretation of the OGTT in pregnant Nigerian women are lower than those for North American women at 60 and 120 min, although the glucose loads were different. However, in a related study in another group of pregnant Nigerian women, we observed that the blood glucose values during OGTT were not higher with a 100-g load than with a 75-g load (R.A.A., O.O.F., B.O.A., unpublished observations). Our results also indicate that the WHO criteria will grossly underdiagnose GDM in Nigerian women. Because the prevalence of GDM in any population is a function of the criteria for diagnosis, the relevance of these observations should be clear.

A recent report suggests that even the limited degrees of maternal hyperglycemia now considered to be within the normal range may adversely affect the outcome of pregnancy (19). It was suggested that the criteria for GDM may need to be redefined and that closer attention must be paid in particular to women with 2-h postglucose load levels between 85 and 120 mg/dl (venous whole blood). O'Sullivan and Mahan (2) recommended an upper limit of normal for 2-h venous whole-blood glucose of 145 mg/dl, and WHO suggested 180 mg/dl (5). We suggest 125 mg/dl at 2 h for Nigerian women.

The criteria for Nigerian women still need to be validated by studying more healthy subjects, by applying the criteria to women at high risk of developing GDM, and by following up on a long-term basis those who test abnormally by use of these criteria to determine how many become diabetic. This study has nevertheless underscored the need to continue research into interpopulation differences in the pattern of OGTT in pregnancy.

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