No Relationship Between Pregnancy Complications and Variations in Blood Glucose Levels Among Nondiabetic Women

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Research using high-risk pregnant women suggests that postprandial blood glucose levels at the high end of normal are associated with greater risk of adverse pregnancy outcomes than low-normal levels. The objective of this study was to determine the relationships between pregnancy complications and glucose levels in low-risk pregnant women. Based on 2-hour postprandial glucose testing at 27 to 33 weeks, 337 women with normal reproductive histories were divided into three groups: group A, glucose < 5.6 mmol/L (100 mg/dL), group B, 5.6 to 6.6 mmol/L (100 to 119 mg/dL), and group C, 6.7 to 9.1 mmol/L (120 to 164 mg/dL). Women with glucose levels ≥ 9.2 mmol/L (165 mg/dL) were excluded. The groups were compared to detect differences in rates of various maternal outcomes (preeclampsia, cesarean delivery, forceps delivery) and neonatal outcomes (macrosomia, Apgar scores, prematurity, fetal death, infant death, congenital anomalies). No significant differences were found.

These data indicate that variations in maternal glucose tolerance (within the normal range) are not associated with adverse outcomes in normal pregnant women.

A pproximately 2.5% of women in the United States develop diabetes during pregnancy. These women are said to have gestational diabetes mellitus. An additional 0.3% of US pregnancies occur among women with established diabetes mellitus.[1,2] In total, approximately 90,000 women with gestational or established diabetes give birth each year in the United States.[2]

Numerous studies have demonstrated that the presence of maternal diabetes is associated with adverse pregnancy outcomes. Infants born to mothers with diabetes mellitus are at risk for numerous problems, including macrosomia, birth trauma resulting from difficult delivery, hypoglycemia, hypocalcemia, and hyperbilirubinemia. In addition, there is an increased incidence of fetal and neonatal mortality and congenital anomalies among infants of diabetic

mothers.[3–7] For each of these complications, the association with diabetes refers to women with clear-cut abnormalities of glucose tolerance (ie, women with definite gestational or established diabetes).[1,8,9]

Investigations have also been made into the significance of variations in glucose levels within the normal range. That is, in a population of women whose glucose tolerance test results fall within the traditionally accepted normal range,[10] are pregnancy outcomes among those with high-normal levels of blood glucose different from outcomes among those with low-normal levels?

There has been some limited information available which suggests that, in fact, women with high-normal blood glucose levels are at increased risk for pregnancy complications. Frisoli and colleagues[11] reported that women who initially had abnormal screening tests but subsequently had normal results on definitive tests for glucose tolerance were more apt to have macrosomic infants. The authors suggested that "diabetic tendencies" were present in women with borderline abnormalities of glucose tolerance.

In a more recent study, Tallarigo and associates[12] reviewed the pregnancy outcomes of 249 women who had

normal results on a 2-hour blood glucose test after a 100-g glucose load performed at 26 to 30 weeks' gestation. The women were divided into three groups based on test results: those with low-normal, mid-normal, and high-normal postprandial plasma glucose levels. The groups with higher postprandial glucose levels had a significantly increased incidence of macrosomia, congenital anomalies, preeclampsia, and requirement for cesarean section delivery. The authors concluded that mild degrees of maternal hyperglycemia, even at levels currently considered to be within the normal range, may affect the outcome of pregnancy.

Although the study by Tallarigo et al was the most extensive investigation to date on the relationship of normal blood glucose to pregnancy outcome, the methods used in that research have been subject to much criticism. Some of the criticism related to statistical methods used to demonstrate relationships between blood glucose levels and complication rates.[13,14] More significant, however, is the subject population used in the study, which had an extraordinarily abnormal reproductive history, including a 19.6% rate of premature delivery and a 17% rate of intrauterine or perinatal death. The infants were judged to be normal in only 59% of the subjects' previous pregnancies.[15]

Since the predictive value of laboratory tests is directly related to the underlying frequency of disease in the population to which the test is being applied, and Tallarigo et al utilized a nonnormative sample for their research, the results of their study cannot necessarily be applied to the general population of pregnant women.[16] Relationships between blood glucose and pregnancy outcomes may fail to exist in a population of nondiabetic prenatal patients who have normal, uncomplicated pregnancy histories.

The objective of this study, therefore, was to investigate the relationship between variations of blood glucose levels within the normal range and rates of pregnancy complications among a population of normal healthy women who, as a group, had an unremarkable reproductive history.

METHODS

Subjects

This was a retrospective study for which potential subjects included all women who presented for prenatal care to the Family Practice Clinic at the University of Arizona College of Medicine in Tucson between 1979 and 1987. The Family Practice Center is a large ambulatory care teaching facility that is visited by approximately 22,000 patients per year. Prenatal care and delivery are provided by family practice residents and faculty physicians.

A total of 909 women enrolled for prenatal care during the period under study. Subjects were eligible for inclusion in the study if they met the following criteria: (1) a 2-hour postprandial glucose screening test had been performed between 27 and 33 weeks of gestation, (2) the results of glucose screening were normal (< 9.2 mmol/L [$<$ 165 mg/dL]),[10] and (3) no high-risk factors warranting referral to an obstetrician were identified prior to blood glucose screening at 27 to 33 weeks. Subsequent to the time of screening, patients who developed pregnancy complications that necessitated referral to an obstetrician were routinely referred to the high-risk center at the University Medical Center in Tucson. Medical records of such patients were available for project staff to review, and these patients were included in the study if they met other eligibility criteria.

Subjects were excluded if they met any of the following criteria or had any of the following conditions: (1) systemic hypertension (diastolic blood pressure > 90 mmHg), (2) history of gestational diabetes in a previous pregnancy, (3) history of diabetes when not pregnant, (4) abnormal 2-hour glucose results (≥ 9.2 mmol/L [165 mg/dL]), (5) any condition warranting referral to a high-risk obstetrician prior to blood glucose testing, or (6) no record of delivery outcome (eg, patient moved away, left the university system).

Glucose Testing

Clinic protocol required that all patients undergo blood glucose screening at 28 to 32 weeks of gestation. Subjects were included in the study if testing was performed between 27 to 33 weeks to allow inclusion of patients who were tested just after or just before the usual time.

The testing procedure was as follows: Patients were asked to consume a large meal consisting of at least one serving of each of the four basic food groups. Meals were eaten in locations of the patients' choice, such as home, hospital cafeteria, restaurant, etc, and patients were not specifically monitored to assure that they consumed the proper food. Patients were instructed to exclude all food, drink (except water), or vigorous exercise from the time the meal was finished until the blood sample was measured. Patients were asked to return for venipuncture in time to have their blood drawn at exactly 2 hours after the conclusion of their meal. Blood samples were drawn and sent to the University Medical Center Clinical Laboratory, where blood glucose was assayed by standard glucose-oxidase techniques.

Data Collection

A trained research assistant reviewed the complete medical record of all eligible patients and their newborns to

obtain the following demographic and historical medical information: maternal age, gravidity, parity, family history of diabetes, and previous pregnancy outcomes including prior term deliveries, preterm deliveries, abortions, operative (cesarean section) delivery, perinatal infant deaths, intrauterine fetal deaths, or congenital anomalies in prior infants. In addition, the results of the 27- to 33-week 2-hour postprandial glucose screening test were recorded.

The research assistant also reviewed each case record for the presence of maternal and infant complications and outcomes during the pregnancy under study. The following recorded maternal outcomes were included: preeclampsia (blood pressure over 140 mmHg systolic or 90 mmHg diastolic with either edema or proteinuria), eclampsia (convulsive seizure occurring in a patient with preeclampsia), cesarean section delivery, and other outcomes that might result from having delivered a large infant (fourth-degree perineal tear, low-forceps delivery, and mid-forceps delivery).

Infant complications and outcomes that were recorded included macrosomia (birthweight 4000 g or more), prematurity (delivery prior to 37 weeks of gestation), Apgar scores, intrauterine fetal death, infant death during the period of observation in the hospital, infant requiring special care (other than routine care in normal nursery), and congenital anomalies.

Data Analysis

The independent variable in this study was the blood glucose level, measured in a 2-hour postprandial test at 27 to 33 weeks. For purposes of distinguishing whether glucose levels within the normal range influence the outcome of pregnancy, patients were divided into three groups on the basis of their 2-hour glucose level in a manner similar to that used by Tallarigo et al.[12] Group A consisted of women with blood glucose levels less than 5.6 mmol/L (100 mg/dL). Group B consisted of women whose glucose levels were 5.6 to 6.6 mmol/L (100 to 119 mg/dL). Group C patients had glucose levels from 6.7 to 9.1 mmol/L (120-164 mg/dL).

The dependent variables were the frequencies of the various maternal and newborn outcomes noted above, including preeclampsia, eclampsia, cesarean section, fourth-degree tear, forceps delivery, macrosomia, Apgar scores, prematurity, intrauterine or infant death, congenital anomalies, or infants requiring special care.

A test for linear trends in proportions and the Mann-Whitney test were used to evaluate changes in the rate of complications of pregnancy over the range of glucose concentrations. One-way analysis of variance and the chi-square test were also used, as appropriate, to compare the differences in the incidence of fetal and maternal complications between groups. P values of less than .05 were considered significant.

It was determined that a subject population of at least 250 subjects would be needed to achieve statistical power equivalent to that found in the similarly designed study by Tallarigo et al (their study involved 249 subjects). If, as expected, the ratio of the current study's subjects classified into the low-, medium-, and high-glucose groups was similar to that found in the Tallarigo et al study population, 250 subjects would provide the present study with a power of .80 (at a significance level of $P = .05$) to detect pregnancy outcome differences between study groups of a magnitude similar to those found in the Tallarigo et al study.[12] Tallarigo et al found maternal complications in 40% of the high-glucose group compared with 19.9% of the low-glucose group. Macrosomia occurred 27.5% of the time in the high-glucose group and 9.9% in the low-glucose group, while the comparable percentages were 5.0% and 0.7% for congenital anomalies.

RESULTS

Subject Characteristics

Three hundred thirty-seven subjects met all eligibility criteria and were included in the study. The remaining 572 potential subjects were excluded because they were not tested at the approximate time during pregnancy (473 subjects), because they developed risk factors necessitating referral to a high-risk obstetrician prior to blood glucose testing (18 subjects), because the results of testing were abnormal (5 subjects), or because they were lost to follow-up (76 subjects).

Table 1 shows demographic characteristics of the 337 eligible subjects compared with those of the 473 patients who were excluded because they were not tested at the appropriate time during pregnancy. No significant differences were noted for any of these characteristics except for payer status. Excluded subjects were more likely to be self-insured or to have standard third-party health insurance ($P = .015$). There were, however, no statistically significant differences in any of the pregnancy outcomes measured in this research between the 337 subjects included in the study and the 473 excluded subjects.

For the 337 subjects included in the study, the mean age was 26.5 ($\pm$ standard deviation 5.5) years, with a range of from 16 to 46 years old. Other demographic characteristics of these subjects are shown in Table 1. Ten of the subjects (2.9%) had a family history of diabetes in a sibling; 45 (13.4%) reported having a parent with diabetes.

The mean gravidity of the 337 subjects was 2.4 ($\pm$ standard deviation 1.52). One hundred fifteen of the subjects were primigravidas. Therefore, only 222 subjects had a

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF SUBJECTS AND EXCLUDED PATIENTS

	Included Subjects (n = 377) No. (%)	Excluded Subjects (n = 473) No. (%)
Marital status		
Single	154 (45.7)	207 (43.8)
Married	133 (39.5)	189 (39.9)
Separated or divorced	37 (10.9)	45 (9.5)
Widowed	0 (0.0)	1 (0.2)
Data not available	13 (3.9)	31 (6.6)
Race		
Hispanic	139 (41.2)	150 (31.7)
White	107 (31.8)	176 (37.2)
Black	23 (6.8)	32 (6.8)
Oriental	8 (2.4)	6 (1.3)
Native American	2 (0.6)	8 (1.7)
Data not available	58 (17.2)	96 (20.3)
Educational level		
Less than high school	117 (34.7)	137 (29.0)
Completed high school	119 (35.3)	150 (31.7)
Some college	54 (16.0)	70 (14.8)
Completed 4 years of college	14 (4.2)	18 (3.8)
More than 4 years of college	2 (0.6)	4 (0.8)
Data not available	31 (9.2)	94 (19.9)
Payer status		
Medicaid*	268 (79.5)	331 (70.0)
Nongovernmental/third-party insurance	38 (11.3)	61 (12.9)
No insurance	15 (4.5)	43 (9.1)
Data not available	16 (4.7)	38 (8.0)

Arizona's Medicaid-equivalent indigent health care program

TABLE 2. PREVIOUS PREGNANCY OUTCOMES AMONG SUBJECTS

Outcome	Individual Subjects Who Experienced This Outcome in Any Prior Pregnancy (n = 222)† No. (%)	Outcomes of All Prior Pregnancies Among the Entire Subject Population (n = 491)* No. (%)
Overall outcome		
Term deliveries	179 (80.6)	319 (65.0)
Spontaneous abortion	55 (24.7)	75 (15.3)
Induced abortion	48 (21.6)	63 (12.8)
Preterm delivery	20 (9.0)	31 (6.3)
Fetal death	3 (1.4)	3 (0.6)
Maternal complication		
Preeclampsia	6 (2.7)	
Cesarean section	18 (8.1)	
Infant outcome		
Congenital anomalies‡	2 (0.9)	
Macrosomia (4000 g)	22 (9.9)	
Infant death	6 (2.7)	

Excludes the 115 primigravid subjects
†Totals exceed 100% because individual subjects may have experienced more than one outcome if they had more than one prior pregnancy
‡One infant had transposition of the great vessels, another had a club foot

prior pregnancy. As a group, these 222 patients had a total of 491 prior pregnancies (parity ranged from 1 to 6; mean parity 1.02). Outcomes of these 491 pregnancies, plus reproductive histories of the 222 individual subjects, are displayed in Table 2.

Tables 1 and 2 indicate that although the subject population included a large percentage of low-income, poorly educated, minority group patients, their prior reproductive histories were relatively uncomplicated. Only 8.1% had undergone cesarean section in a previous pregnancy, considerably fewer than would be expected based on national experience.[18] Similarly, the rates of congenital anomaly, fetal death, preeclampsia, and other complications were quite low.

Relationship Between Glucose Levels and Complication Rates

Of the 337 subjects, 255 (75.7%) had a 2-hour postprandial blood glucose level below 5.6 mmol/L (100 mg/dL), 59 (17.5%) had values between 5.6 mmol/L and 6.6 mmol/L (100 and 119 mg/dL), and 23 (6.8%) had blood glucose levels of 6.7 mmol/L to 9.1 mmol/L (120 to 164 mg/dL).

No relationship was demonstrated between 2-hour postprandial glucose levels and pregnancy outcomes (Table 3). No relationship was noted between glucose levels and macrosomia, congenital anomalies, preeclampsia, and cesarean section delivery. In addition, no relationship was found between 2-hour blood glucose levels and any of the other pregnancy outcomes used as dependent variables for this study.

DISCUSSION

Among the subjects in this study, all of whom were healthy women with normal reproductive histories, no relationship was found between the rates of various adverse pregnancy outcomes and the blood glucose level measured in a 2-hour postprandial test at 27 to 33 weeks. Women with high-normal blood glucose levels were no more likely to have adverse outcomes than were women who had low-normal glucose levels. Thus, the findings of this study differ from results of research that suggest such a relationship exists.[10,11]

The difference between the results of this study and those of prior investigations is best explained by differences in the subject populations used. As noted previously, the study population used in the research by Tallarigo et al

TABLE 3. FREQUENCY OF PREGNANCY OUTCOMES, ACCORDING TO 2-HOUR BLOOD GLUCOSE LEVELS AT 27 TO 33 WEEKS

Outcome	Group A < 5.6 mmol/L (< 100 mg/dL) (n = 255) No. (%)	Group B 5.6–6.6 mmol/L (100–119 mg/dL) (n = 59) No. (%)	Group C 6.7–9.1 mmol/L (120–164 mg/dL) (n = 23) No. (%)	P Value*
Fatal outcome				
Macrosomia (4000 g)	24 (9.4)	10 (16.9)	1 (4.3)	.14
Prematurity (37 wk)	15 (5.9)	2 (3.4)	1 (4.3)	.73
Intrauterine fetal death	2 (0.8)	2 (3.4)	0 (0.0)	.22
Infant death	1 (0.4)	1 (1.7)	0 (0.0)	.47
Not normal nursery	11 (4.3)	5 (8.5)	1 (4.3)	.42
Congenital anomaly	1 (0.4)	0 (0.0)	0 (0.0)	.85
Apgar score 1 minute (mean ± SD)	7.74 ± 1.5	7.39 ± 2.1	7.74 ± 2.3	.35†
Apgar score 5 minutes (mean ± SD)	8.83 ± 1.2	8.41 ± 2.0	8.65 ± 1.6	.11†
Maternal outcome				
Preeclampsia	6 (2.4)	1 (1.7)	0 (0.0)	.73
Eclampsia	0 (0.0)	0 (0.0)	0 (0.0)	—
Cesarean section	12 (4.7)	4 (6.8)	3 (13.0)	.23
Low-forceps delivery	6 (2.4)	2 (3.4)	0 (0.0)	.66
Midforceps delivery	10 (3.9)	1 (1.7)	1 (4.3)	.69
Fourth-degree tear	12 (4.7)	1 (1.7)	0 (0.0)	.34

*Test for linear trend, except where indicated
†Analysis of variance

was clearly abnormal in that subjects had an extraordinarily high rate of prior pregnancy complications.[12]

Similarly, in the Frisoli et al study,[11] in which subjects with initially abnormal screening tests had an increased rate of macrosomic infants, the subject population was also abnormal. Their subjects included only women who were judged to be at increased risk for diabetes because of historical or clinical risk factors such as previous birth of a macrosomic infant, previous unexplained congenital anomaly, previous pregnancy wastage (habitual abortion, unexplained stillbirth, neonatal death), polyhydramnios, and so on. Thus, the subject population of both prior studies were "abnormal" and not comparable to patients found in an unselected primary care population.

The subject population in the current study, on the other hand, consisted of women whose pregnancy risks were low and whose pregnancy outcomes were generally uncomplicated. As noted, their cesarean section delivery rate was lower than the national average. In addition, the overall incidence of congenital anomalies was also low; only one of the 337 pregnancies (0.3%) resulted in an infant with a congenital anomaly, compared with an approximately 3% incidence of congenital anomalies in the general population.

Thus, the subject population in this study was an extremely low-risk group. Although atypical of the patients cared for by many obstetricians, the subjects in this study were typical of the low-risk pregnant women commonly managed by family physicians. In this low-risk population, higher levels of postprandial blood glucose within the normal range were not associated with increased risk of adverse pregnancy outcome.

Several factors may have affected the validity of this study's results, the most important of which is the lack of standardization of 2-hour postprandial glucose testing. This study was conducted over many years and relied upon the history of a meal consumed 2 hours prior to a blood test. Since meals were not monitored or supervised, the investigators could not be certain that each patient ate her meal exactly 2 hours prior to blood testing, or that each subject consumed the same amount of carbohydrate. In fact, it is likely that some patients, believing that high blood glucose levels are undesirable, may have eaten less in an attempt to achieve a lower postprandial glucose result. For these reasons, postprandial blood glucose testing, as used in this study, is not directly comparable to the standardized oral glucose challenge utilized in the study by Tallarigo et al, and the lack of standardized postprandial blood glucose testing may have affected the validity of this study's results.

It should be noted that the lack of standardization of 2-hour postprandial blood glucose testing has led the Centers for Disease Control, the American Diabetes Association, and the American College of Obstetricians and Gyne-

cologists to recommend that 2-hour postprandial blood glucose testing during pregnancy be replaced with a more standardized single 1-hour glucose measurement.[7] It is now recommended that a glucose measurement be obtained 1 hour after the ingestion of 50 g of a standard glucose solution. The solution is to be ingested over a 10-minute period without regard to time of day or last meal. If the 1-hour plasma glucose level exceeds 7.8 mmol/L (140 mg/dL), it is recommended that the patient undergo more definitive evaluation with a complete 3-hour glucose tolerance test with a 100-g oral glucose challenge following an overnight fast.

A second factor that may have affected interpretation of the study's results is that only 337 (37.1%) of 909 potential subjects were included. The majority (473, or 82.7%) of the 572 excluded subjects were excluded because they did not undergo blood glucose testing during the 27th to 33rd gestational week as required by study protocol. In almost all of these cases (97.1%) these patients were not tested because they presented for prenatal care after the 33rd week. A comparison of demographic characteristics and past pregnancy outcomes of the 473 excluded vs the 337 included subjects (Table 1) revealed no important differences between the two groups. The high rate of untested patients probably reflected only the overall low socioeducational status of patients cared for in the practice and their tendency to present for prenatal care late in pregnancy. Nonetheless, it remains possible that untested (excluded) subjects were somehow fundamentally different from the test group and that this factor introduced selection bias, which may have influenced the results of this research.

A third factor that may have affected the study's results is that pregnancy outcome measurements used in this study were obtained by retrospective chart review and, as such, relied heavily on physicians' notes and discharge summaries that may have underreported adverse pregnancy outcomes such as minor congenital anomalies. In addition, delivering physicians were not blinded to the results of prenatal blood glucose testing results. It is possible, therefore, that underreporting of adverse pregnancy outcomes may have influenced study findings. For underreporting to have affected study results, however, there would have had to have been a systematic underreporting of abnormal outcomes in the high-glucose group. In fact, however, if physicians were aware of prenatal blood glucose results, it is more probable that they would have more fastidiously detected and recorded abnormal outcomes in the high-glucose group; this increase in abnormal outcomes did not occur. In addition, the likelihood that such underreporting occurred is also low because all intrapartum and postpartum events at the University Medical Center are routinely recorded by nursing staff on standardized data collection forms; these forms were available to and reviewed by study personnel.

Finally, the validity of this study may have been affected by sample size. Even though the sample size in the present study (337 subjects) was larger than the study population of 249 subjects used by Tallarigo et al, the proportion of subjects in the high-glucose group was smaller in this study (23 of 337 subjects, 6.8%) than it was in the Tallarigo et al study (40 of 259, 15.4%). This smaller number in the high-glucose group may have lessened the comparative statistical power of the present study to detect differences between groups.

Depending on the outcome variable being tested and the size of the intergroup difference being measured, the power of this study to detect significant differences ranged from as low as 0.10 to detect small (10%) differences to as high as 0.99 for detection of larger (40%) differences between groups for continuous variables such as birthweight, Apgar scores, and so on.[19] The power to detect differences in the frequency of discrete occurrences (eg, presence or absence of preeclampsia or cesarean section) was only 0.51 to 0.57 for differences between the high-normal and low-normal groups of magnitude similar to that found in the Tallarigo et al study. Thus, despite the larger sample size in the present study, the smaller number of subjects in the high-normal group of the current study limited the statistical power to detect intergroup differences.

CONCLUSIONS

The predictive value of a laboratory test in detecting a particular disorder will vary depending on the prevalence of the disorder in the population being tested. In prior studies of the relationship of glucose tolerance to pregnancy outcomes, adverse reproductive outcomes were very frequent. In these studies, borderline high blood glucose levels were statistically correlated with abnormal pregnancy outcomes. In the research reported here, however, the subjects had a very low rate of abnormal pregnancy outcomes, and borderline high blood glucose levels had no relationship to complications of pregnancy.

The present research is limited, however, by its retrospective design. In addition, each of the factors discussed above may have affected the validity of the study results and should be considered when interpreting the results.

Nonetheless, in the present study, which utilized a population of healthy low-risk pregnant women, no relationship was found between high-normal glucose levels and adverse pregnancy outcomes. The implication of this finding, which contrasts to findings of research using women at higher risk of abnormal pregnancy, is that the results of research reported in the medical literature can be applied only to populations similar to that on which the research was conducted. Failure to adhere to this principle may

result in inappropriate application and utilization of laboratory tests and other medical interventions.

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Commentary

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Standards of care for the diagnosis and management of gestational diabetes mellitus (GDM) have been widely discussed.[1–3] Yet areas of controversy remain. Weiss and his co-authors in the preceding article[4] address one such controversial question: What is the sensitivity and specificity of a particular screening method used to identify GDM? This question is graphically portrayed in Figure 1. Subjects under curve A have no GDM, while subjects under curve B do in fact have GDM. To detect all patients with GDM, the threshold for an abnormal screening test must be set low, in these curves, at 6.7 mmol/L (120 mg/dL). If the threshold is low, all cases of GDM will be detected; but the vast majority of individuals with "abnormal" screening tests will be found, after considerable expense and discomfort, to in fact not have GDM (false-positives).

In an effort to be more parsimonious of scarce resources, and to reduce the discomfort and expense associated with so many false-positives, we may elect to raise the threshold for the screening test to 8.9 mmol/L (160 mg/dL). What

happens then? A larger proportion of cases of GDM are missed by the screening test, while virtually no false-positives are identified.

The choice of the optimal threshold point for such a screening test depends entirely upon the balance between the clinical significance of a missed case and the cost society is willing to pay to identify a case, as has been previously discussed in articles and commentaries published in the Journal[5,6] and elsewhere.[2]

The present study[4] concludes that for the 2-hour postprandial glucose test done at 27 to 33 weeks of gestation, a cutoff point of 9.2 mmol/L (165 mg/dL) is indeed appropriate. The authors acknowledge the many methodologic limitations of their study, such as selection bias, a sizable number of eligible subjects who did not have the test of interest, and missing information on many birth outcomes. Furthermore, the test they have evaluated has been replaced, because of its relative inaccuracy and lack of standardization, with a 50-g oral glucose ingestion followed by a 1-hour plasma glucose value with a screening threshold
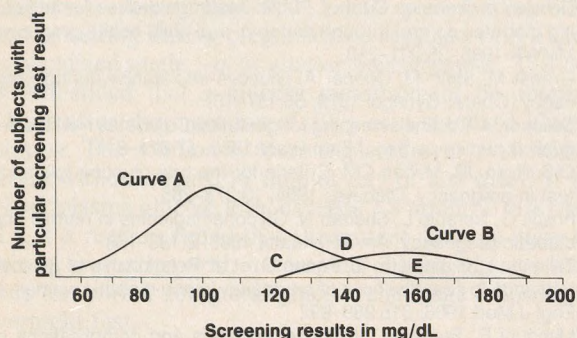
Figure 1. Theoretical distribution of screening test results of a population of pregnant women being screened for gestational diabetes mellitus (GDM). The test illustrated is the 50-g oral glucose load, 1-hour plasma glucose test done between 24 and 28 weeks of gestation, which is the currently recommended screening test for gestational diabetes mellitus. Subjects under curve A do not in fact have GDM. Point C represents the screening threshold needed to detect all cases of GDM, at the cost of many false-positive tests. Point D represents the screening threshold currently recommended, which detects about 90% of GDM and has many fewer false-positive results. Point E represents a screening threshold that avoids nearly all false-positive tests but also misses many subjects who actually have GDM.

currently set at 7.8 mmol/L (140 mg/dL) by most authorities.[7,8] But even for the newer test, discussion continues as to what the most effective screening threshold should be. It is possible that the use of the test should be tailored to particular populations of patients, as the predictive value of a positive tests will vary with the prevalence of GDM in different populations, and the costs of screening and confirmatory tests vary in different types of health care systems.[2,5]

Although the present study describes an obsolete test, the method used is appropriate to evaluate newer tests that have been proposed for screening for GDM. Such evaluation can be done by performing both the screening test of interest and a confirmatory test, such as the 3-hour 100-g glucose tolerance test (GTT), on all women presenting for prenatal care in order to calculate the sensitivity and specificity of the screening test as compared with the confirmatory test. Already there is some evidence that a 3-hour GTT that has one abnormal value (two abnormal values are required for an abnormal GTT) may be associated with increased risk of macrosomia.[9,10] Should an infant marker of GDM be identified that does not vary significantly with treatment of GDM, both the screening test and the confirmatory test could be compared with such a true "gold

standard." Traditional infant measures of GDM, however, as well as such measures as cord blood insulin levels, amniotic fluid insulin levels, and placental changes, may reflect only poor control of GDM. These changes may be minimal or absent when GDM is present but well controlled.

A further area ripe for study is whether a clinical set of risk factors can adequately identify a subset of gravid women who are at such low risk of GDM that they need not be screened. For example, women younger than 25 years of age with no family history of diabetes and no gross obesity are at very low risk for GDM. Current standards of care disagree on the appropriateness of universal screening.[1,3] More information on the psychological impact of being identified falsely as abnormal on such screening tests is also needed. Do such false-positive test results cause women to suffer significant psychological stress? Is their relationship with their physician or midwife, or their faith in the medical care system altered? Do such women tend more quickly to adopt sick-role behaviors? Qualitative research on the impact of false-positive test results could provide a much needed contribution to the ongoing debate on who and how to screen for GDM.

Many family physicians and nearly all family practice residency programs provide obstetric care to their patients. It is good to see that research interest in GDM is alive and well among family physicians, for many important research issues lend themselves well to integrated qualitative and quantitative research approaches with which family physicians are particularly conversant.

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