Screening for Gestational Diabetes—Analysis by Screening Criteria

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A previously studied glucose screening test for gestational diabetes was evaluated by six screening test criteria for appropriateness and cost effectiveness as a widespread screening tool. The test consisted of a serum glucose level in a pregnant patient one hour after 50 g of a glucose solution was ingested. Determination was made of price per case detected and of the number of cases missed when using this test or the oral glucose tolerance test on all prenatal patients or on a selected subset of patients. Screening all pregnant patients aged over 25 years for gestational diabetes with the one-hour glucose screening test is recommended. The need for further evaluation of the sensitivity of this screening test is discussed.

Whether to screen patients for various diseases has become an issue of interest and importance both to the medical profession and to patients. The American Diabetes Association[1] has recommended screening of all pregnant women by the 28th week of gestation for gestational diabetes. One of the screening methods advocated is an abbreviated glucose tolerance test studied by O'Sullivan and colleagues.[2] This report will critically evaluate the use of this glucose screening test (GST) as a screening tool.

Frame and Carlson[3] have promoted the following criteria for a screening test:

1. The disease must have a significant effect on quality or quantity of life.
2. Acceptable methods of treatment must be available.
3. The disease must have an asymptomatic period during which detection and treatment significantly reduce morbidity or mortality.
4. Treatment in the asymptomatic phase must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.
5. Tests must be available at reasonable cost to detect the condition in the asymptomatic period.
6. The cost of screening must be justified by the incidence of the condition.

Several protocols for screening tests for gestational diabetes have been studied and advocated. O'Sullivan et al[2] studied a one-hour, 50-g glucose screening test in 752 patients. Both the screening test and a three-hour oral glucose tolerance test were performed on all patients. A sensitivity of 79 percent and a specificity of 87 percent were determined. Westman[4] supported a two-hour, 100-g

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glucose screening test, and Merkatz et al[5] studied a two-hour, 75-g screening test, but false-negative data were unavailable for these studies. Carpenter and Coustan[6] advocated lowering the threshold value for abnormality from the criteria of O'Sullivan et al to increase the sensitivity of the test, but again there is a lack of false-negative data. Subsequently, the screening test by O'Sullivan et al will be analyzed by these screening criteria.

The test consists of a serum glucose determination one hour after the patient has ingested 50 g of a glucose solution. No previous preparation is required. Serum glucose values greater than 150 mg/dL are considered abnormal, and patients with such values are then tested with a 3-hour oral glucose tolerance test (OGTT). The upper limits of normal values for the OGTT are 105 mg, 190 mg, 165 mg, and 145 mg/dL for the fasting, 1-hour, 2-hour, and 3-hour serum glucose values, respectively. Two values exceeding these OGTT limits are necessary for the diagnosis of gestational diabetes.

Analysis by Screening Criteria

Diabetes is present in approximately 2.8 percent of pregnancies.[7] Approximately 90 percent of these cases are gestational diabetes, defined as an abnormal glucose tolerance during pregnancy that remits after the conclusion of the pregnancy. Gestational diabetes has been convincingly associated with an elevated perinatal mortality and morbidity. Studies by Pedersen et al[8] and O'Sullivan et al[9] demonstrated a four- to fivefold increased incidence of mortality, macrosomatia, and pregnancy complications in such patients when compared with rates for the general pregnant population. The National Commission on Diabetes[7] estimated that in 1973 there were 4,500 infant deaths in the perinatal period associated with undiagnosed or untreated gestational diabetes, a figure comparable with the number of children dying of sudden infant death syndrome each year. Recent studies have shown long-term morbidity associated with gestational diabetes, both for the patient and for the offspring. O'Sullivan[10] evaluated women with gestational diabetes eight and 16 years after the diagnosis was made, finding nonpregnant glucose intolerance in 23 percent and 60 percent of these patients, respectively. This risk of subsequent diabetes was more marked in obese women with gestational diabetes than in women of normal weight.[11] A report on Pima Indian women with gestational diabetes indicated an association between this condition and subsequent obesity in the offspring of these women.[12] Criterion 1 for the screening test is therefore met: gestational diabetes does have a significant effect on the quality and quantity of life for women and their offspring.

The efficacy of acceptable forms of treatment has also been evaluated. Several authors have demonstrated that diagnosis and treatment of gestational diabetes have a significant effect on reducing morbidity and mortality. Gyves et al[13] demonstrated a statistically and clinically significant reduction in perinatal mortality following rigid control of serum glucose in gestational diabetic patients who had had previous perinatal loss (from 8.3 percent mortality to 0.0 percent mortality following treatment in pregnancies of 59 women). The study by Adashi et al[14] reveals a similarly improved outcome. These studies support criterion 2: acceptable treatment is available for this disease.

Gestational diabetes rarely presents with symptoms suggestive of the diagnosis. Polyuria and polydipsia are rarely seen. Glucosuria, although more common in pregnancy than in the nonpregnant state, is not a sensitive or specific indicator of gestational diabetes risk.[15,16] Therefore, gestational diabetes is usually asymptomatic.

The lack of symptoms suggestive of the disease has prompted a search for other criteria that might be used to recognize this group. In the study by O'Sullivan et al,[2] the rates of detection of diabetes in pregnancy were compared between those patients with a positive clinical history of traditional diabetes risk factors and those with no risk factors. The traditional risk factors studied were the birth of a baby weighing 9 lb or more; a history in two or more pregnancies of fetal death, neonatal death, congenital anomaly, prematurity, excessive weight gain, hypertension, or proteinuria; or a family history of diabetes. They found that the best predictor of a "high risk" population for gestational diabetes was a positive glucose screening test (13.8 percent had a positive OGTT). Patients with traditional risk factors, but a negative glucose screening, were less likely than the general population to have a positive OGTT. Twenty-seven

Table 1. Comparison of Glucose Screening Test Outcome and Presence of Gestational Diabetes[2]

Screening Blood Sugar	Number	Gestational Diabetes	
		Present	Absent
Positive	109	15	94
Negative	643	4	639

From O'Sullivan JB[2]

percent of those with OGTT-documented gestational diabetes had no traditional risk factors at all. Furthermore, this study indicated that patients aged 25 years or older were at a greater risk for gestational diabetes, and those with a positive GST in this age group, regardless of other factors, identified an increased percentage of gestational diabetics (14 to 50 percent).

Lavin et al[17] studied prenatal patients from 1978 to 1980 using the screening test described by O'Sullivan et al. They compared the yield of documented gestational diabetes in those with any of an expanded list of risk factors—both historical and clinical—and in those with none of these factors. In this study all patients were given a GST, and those with a positive result were then given a glucose tolerance test. Lavin and co-workers found no increased yield of gestational diabetics in the group with positive risk factors as opposed to the general prenatal population. In the studies by O'Sullivan et al and Lavin et al, the proportions of patients having positive risk factors were approximately 37 to 45 percent. Screening only those patients with positive risk factors would have missed greater than 50 percent of the cases of gestational diabetes in this population.

Whereas others have published data that clinical risk factors (such as past family and obstetrical history, obesity, and age) are associated with a higher risk group for gestational diabetes,[4] those without the risk factors still accounted for at least one half of the cases of gestational diabetes. This information indicates that if one does feel gestational diabetes should be detected during pregnancy, patients should be screened regardless of traditional risk factors.

Therefore, an asymptomatic period does exist; in fact, most gestational diabetics cannot be recognized by risk factors prior to delivery. Furthermore, the previous data suggest that treatment of these patients is beneficial. Subsequently, criteria 3 and 4 are met.

The preferable way to test for gestational diabetes depends on several factors. These include (1) efficacy of the test (both sensitivity and specificity), (2) side effects of the test, and (3) cost involved.

Efficacy of Screening Tests

Using data from the study by O'Sullivan et al (Table 1), the following parameters for their screening test (GST) can be obtained:

Percentage with a positive GST
= (15+94)/752 = 15 percent
Sensitivity = true positive GST ÷ total true positives
= 15/19 = 79 percent
Specificity = true negative GST ÷ total true negatives
= 639/733 = 87 percent
Percent of false negatives
= false negative GST ÷ total true positives
= 4/19 = 21 percent
Predictive value of a positive GST
= true positive GST ÷ total positive GSTs
= 15/(15+94) = 14 percent
Predictive value of a negative GST
= true negative GST ÷ total negative GSTs
= 639/(639+4) = 99 percent

These parameters indicate that if a patient has a negative glucose screening test, the chances are 99 percent that she does not have gestational diabetes, whereas if the screening test is positive, one in seven patients (14 percent) will have gestational diabetes as estimated by a subsequent glucose tolerance test. However, 21 percent of the cases with

Table 2. Cost Analysis of Screening Tests

Screening Method	Cost per 1,000 patients	Cases Detected No.	Cost per Case Detected	Cases Missed (False Negative) No. (%)
1. GST* all patients If positive, OGTT**	$13,688 (1,000 GSTs, 145 OGTTs)	20	$684.40	5 (20)
2. GST only patients with risk factors. If positive, OGTT (assume 50 percent with risk factors)	$ 6,832 (500 GSTs, 72 OGTTs)	10	$683.18	15 (60)
3. OGTT all patients with risk factors	$12,200 (500 OGTTs)	13	$938.46	12 (48)
4. OGTT all patients	$24,400	25	$976.00	0 (0)
5. GST all patients > 25 years of age	$ 7,336 (480 GSTs, 101 OGTTs)	19	$386.11	6† (24)

*GST = Glucose screening test (glucose level one hour after ingesting 50 g glucose solution)
**OGTT = Oral glucose tolerance test (100 g glucose solution after overnight fast; glucose levels at 1/2, 1, 2, and 3 hours)
†Three cases were missed in those screened, three were missed in those not screened (< 25 years of age)

a positive OGTT were missed by the screening test in this study. In contrast, the OGTT is currently the standard for diagnosing diabetes. When performed correctly, its sensitivity and specificity are 100 percent.

Side Effects of Screening

Side effects vary between the two tests in question. The three-hour OGTT is associated with greater nausea, patient discomfort, and time requirements than is the glucose screening test.

Costs of Screening

The costs of five different protocols can be described (Table 2) using data from O'Sullivan et al[2] and assuming the following: (1) cost per glucose screening test is $10.15* (local hospital charges); (2) cost per OGTT is $24.40 (local hospital charges); (3) incidence of gestational diabetes from the general population is 2.5 percent; (4) incidence of prenatal patients with one or more risk factors for diabetes mellitus is 50 percent; (5) percentage of the pregnant population aged over 25 years is 48 percent but accounts for 85 percent of the gestational diabetes mellitus; (6) false-negative rate of the GST is 21 percent.** Performing an OGTT on all prenatal patients (item 4) is most costly per case detected, but misses no cases. Performing a GST on only those patients aged more than 25 years (item 5) was least costly per case detected, but missed approximately 24 percent of the cases. One could make an argument for either of these choices, depending on the resources available for testing and the perceived cost (morbidity or mortality) of missed cases. Table 2 also demonstrates that using traditional risk factors to determine who should be tested for diabetes (2 and 3) not only is costly per case detected, but misses at least one half of the cases. If future evaluation of the office glucometer as used in gestational diabetes screen-

*$9.00 for serum glucose determination; $1.15 for 50 g of Glucola

**Ninety-nine percent confidence limits = 2.7 to 39.4 percent

ing supports its usefulness, this will substantially reduce these costs on an absolute basis. The relative costs would remain.

The false-negative rate is a crucial factor in this analysis. If the outcome of the GST is considered a simple binomial distribution, the 95 percent confidence limits of the false-negative rate are 2.7 to 39.4 percent. If the actual false-negative rate approaches the lower limit (2.7 percent), the screening test rivals the efficacy of the glucose tolerance test (less than one case missed in example 1). If the actual false-negative rate is nearer the larger value (39.4 percent), the number of cases missed increases in all the screened groups (1,2,5). A large, controlled study will be necessary to clarify the false-negative rate.

These data estimate the cost of screening using current information. Whether the costs justify promoting widespread screening (criteria 5 and 6) must be decided by physicians, third-party payers, and society as a whole.

Summary

Gestational diabetes is a disease of pregnant women that can lead to significant morbidity and mortality if untreated, but which can be treated effectively.

An asymptomatic period exists in gestational diabetes during which a screening test can identify a high-risk population, and treatment can reduce morbidity and mortality.

Screening only those patients with classical historical or clinical risk factors for gestational diabetes is not cost effective and misses many cases.

The costs per case detected can be figured for various screening protocols. Whether this cost is reasonable depends on many factors including subsequent cost of treatment, rate of patient compliance with treatment, and values attached to perinatal and long-term mortality and morbidity.

Performing an oral glucose tolerance test on all pregnant patients is the most accurate means of detecting gestational diabetes, but is also costly per case detected.

According to the data of O'Sullivan et al,[2] performing a glucose screening test on all prenatal patients aged greater than 25 years will detect approximately 79 percent of the cases (99 percent confidence limits, 60.6 to 97.3 percent) at the lowest cost per case detected.

Based on the data now available, screening for gestational diabetes is sensitive and cost effective. Future analysis of the office screening with a glucometer may allow costs to be reduced even further. Screening all pregnant women aged over 25 years for gestational diabetes with a one-hour, 50-g glucose test is recommended.

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