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Relationship Between Normal Oral Glucose Tolerance Test in Women at Risk for Gestational Diabetes and Large For Gestational Age Infants

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Objective: To determine whether the glycemic status of pregnant women with a normal 3-h 100-g oral glucose tolerance test (OGTT) is related to outcome with respect to large for gestational age (LGA) infants. Research Design and Methods: A prospective study of 2631 women was conducted. One hundred seventy-six women had an OGTT based either on a 1-h 50-g OGTT (n = 105) or clinical risk factors (n = 71). Thirty-three women were diagnosed as having gestational diabetes mellitus. Results: Negligible discriminatory capacity for the variables with respect to prediction of LGA infants was indicated by the areas under the receiver operating characteristic (ROC) curves for fasting blood glucose, 2-h OGTT blood glucose, and the OGTT response curve area for women with a normal OGTT (n = 143). However, a statistically significant increased incidence of LGA infants was established for both the OGTT-positive and normal OGTT groups ($P < 0.0001$). Multiparity, a maternal weight ≥70 kg, and birth of a male infant were other factors associated with a significantly increased frequency of LGA infants. Conclusions: The results may be interpreted as either indicating a role for confounding variables, i.e., maternal weight, multiparity, and birth of a male infant, or the imprecision of the OGTT in assessing physiologically important changes in maternal hyperglycemia. ***Diabetes Care* 14:1092–94, 1991**

Gestational diabetes mellitus is associated with a significant incidence of large for gestational age (LGA) and macrosomatic infants. However, the definitive diagnostic procedure for gestational diabetes, the oral glucose tolerance test (OGTT), has many inherent limitations, including the designation of threshold levels unrelated to immediate adverse maternal-fetal outcome and poor reproducibility (1,2). Under this dichotomous strategy, there will arise a high proportion of misclassification not only because of test irreproducibility but also because a woman's glycemic status may be equivocal. It the degree of glucose intolerance is an important determinant of excess fetal weight gain, then a predictive relationship should exist between maternal glycemic status, as estimated by the OGTT, and the incidence of LGA infants. This hypoth-

esis may be most readily tested in women who have been selected initially by criteria suggestive of glucose intolerance but who subsequently have a normal OGTT. The same type of study in women with a positive OGTT is not possible, because the primary objective of clinical intervention is to limit fetal macrosomia.

RESEARCH DESIGN AND METHODS

This prospective study was restricted to women (n = 2631) who completed singleton pregnancies of ≥32 wk gestation at The Queen Elizabeth Hospital during 1988 and 1989; 176 of these women had OGTTs based either on a 1-h 50-g OGTT screen (blood glucose ≥6.8 mM, n = 105) or clinical risk factors (glycosuria, family history, or LGA infant; n = 71), and 33 (18.7%) women tested positive for gestational diabetes. Glucose intolerance was diagnosed according to the criteria specified by the National Diabetes Data Group (3). LGA was defined as a birth weight ≥90th percentile for the respective gestational length.

Blood glucose levels were measured with a YSI 23AM glucose analyzer (Yellow Springs, OH). The OGTT response curve area was estimated with the 3/8 formula (4). Receiver operating characteristic (ROC) curves and the respective area under the curve were determined as described previously (5).

RESULTS

The observed difference in the incidence of LGA infants between women with one abnormal OGTT value (n = 29) and those with none (n = 114) was not statistically significant (χ^2 = 1.08, P = 0.30). However, the small sample size precluded acceptance of the null hypothesis. The respective odds ratio (OR) was 1.95 (95% confidence interval [CI] 0.7–5.3).

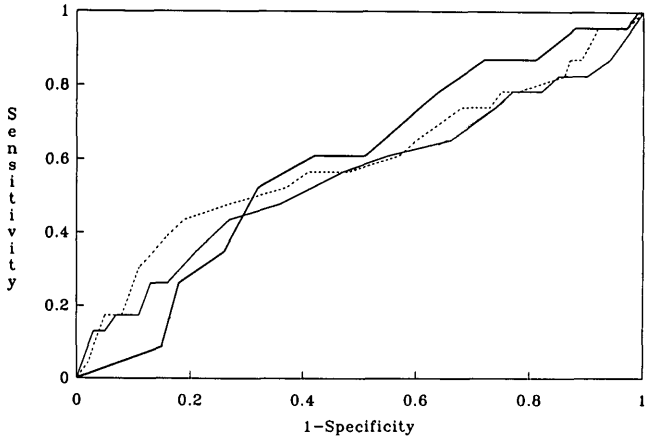

FIG. 1. Receiver operating characteristic curves for fasting blood glucose (*bold solid line*), 2-h oral glucose tolerance test (OGTT) blood glucose (*dashed line*), and OGTT response curve area (*solid line*) calculated from data for 143 pregnant women with normal OGTTs.

ROC curves were used to evaluate the performance of fasting blood glucose, 2-h OGTT blood glucose level, and the area under the OGTT response curve as prognostic markers for the birth of an LGA infant. The calculated mean ± SE area under the ROC curve was 0.584 ± 0.061, 0.584 ± 0.073, and 0.552 ± .073, respectively (Fig. 1). All latter ROC curve areas were not statistically different from 0.5, the area under the diagonal that represents a test with no discrimination.

The OR associated with the birth of an LGA infant for women who had a positive OGTT versus all women without gestational diabetes was 5.8 (95% CI 2.8–12.1). A significantly increased OR of 2.3 (95% CI 1.4–3.6) was also found for women with a normal OGTT compared with those not tested. Other factors determined as significantly increasing the likelihood of an LGA infant included multiparity, maternal weight ≥70 kg at time of testing, and birth of a male; the respective OR were 2.5 (95% CI 1.7–3.6), 3.3 (95% CI 1.9–5.7), and 2.0 (95% CI 1.5–2.6).

CONCLUSIONS

Previous studies cited an increased risk for delivering macrosomic infants either for one abnormal OGTT value (6,7) or for all women selected for an OGTT (8–10). In contrast, Wiener (11) could not establish a relationship in nondiabetic women between the 2-h OGTT glucose level and various outcomes including LGA and macrosomia. This investigation reaffirmed that women selected for an OGTT on criteria suggestive of glucose intolerance but who subsequently have a normal OGTT are at an increased risk of delivering an LGA infant compared with women not considered at risk. However, no predictive relationship could be established between the OGTT results and the respective likelihood of an LGA infant. This was despite the use of the OGTT response curve area as a potentially more sensitive index of the blood glucose profile after an oral glucose load. The association of marked glucose intolerance with LGA infants is emphasized by the high incidence of LGA infants born to women with a positive OGTT, despite clinical management. Equally important is the fact that multiparity, maternal weight ≥70 kg, and the birth of a male infant are also risk factors for LGA infants (12).

Unlike prior dichotomous analyses (6–11), this study used ROC curve analysis to assess the performance of three glycemic variables, fasting blood glucose, 2-h OGTT blood glucose, and area under the OGTT response curve, as predictors of LGA infants. That the latter individual indices have no discriminating ability in the detection of LGA infants, even though the incidence is significantly elevated within the group, implies either the presence of confounding variables or a

marked diagnostic imprecision associated with nonreplicated OGTT determinations (13).

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New Semiquantitative Dipstick Test for Microalbuminuria

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Objective: We compared a new semiquantitative dipstick test for microalbuminuria (Micral-Test) with a quantitative immunoturbidimetric method. Research Design and Methods: This correlation study was performed at a pediatric and medical outpatient clinic at a university hospital. Overnight urine samples containing <200 mg/L albumin from 186 diabetic patients were analyzed. Results: The correlation coefficient between the new semiquantitative method and the immunoturbidimetric reference method was 0.82. Elevated albumin concentration was defined as >20 mg/L albumin in overnight urine, and the prevalence of samples with values above this level was 28%. By this definition, the Micral-Test assay level ≥20 mg/L had a sensitivity of 92.3% and a specificity of 82.1%. Of the diabetic subjects, 84.9% were correctly classified as having elevated urinary albumin concentration or not. Conclusions: The Micral-Test is useful for in-clinic screening for elevated urinary albumin concentration and monitoring the development of urinary albumin excretion in the low microalbuminuric range. ***Diabetes Care*** **14:1094–97, 1991**

Microalbuminuria is a predictor for later clinical diabetic nephropathy in both insulin-dependent diabetes mellitus (IDDM; 1–3) and non-insulin-dependent diabetes mellitus (NIDDM; 4) and for increased cardiovascular mortality (5). Elevated urinary albumin excretion is potentially reversible when near normoglycemia (6,7) or lowering of blood presure (8) is obtained and is therefore an important parameter of clinical care of patients with IDDM or NIDDM. The awareness of the importance of bringing tests closer to patients and the advantage of getting the result before the patient leaves the outpatient clinic have led to the demand for a simple, semiquantitative side-