Single abnormal value on 3-hour oral glucose tolerance test during pregnancy is associated with adverse maternal and neonatal outcomes: a systematic review and metaanalysis

Jared T. Roeckner, MD; Luis Sanchez-Ramos, MD; Rubymel Jijon-Knupp, MD; Andrew M. Kaunitz, MD

Gestational diabetes mellitus (GDM), a carbohydrate metabolism disorder with onset or first recognition during pregnancy,[1] is linked to maternal and perinatal morbidity.[2-4] Although a 75-g oral glucose tolerance test (OGTT) is endorsed by the International Association of Diabetes in Pregnancy Study Group (IADPSG) and is used in many parts of the world, in the United States GDM usually is diagnosed with the use of a 2-step method with a 3-hour, 100-g OGTT reserved for women with an abnormal 1-hour, 50-g glucose challenge test (GCT). Abnormal values for the 1-hour, 50-g glucose screening test range from 130—140 mg/dL. Based on work done in the 1960s, GDM is diagnosed by 2 abnormal values on the OGTT with the use of either Carpenter and Coustan (CC) or National Diabetes Data Group (NDDG) cut-offs.[5-7]

Although the increased maternal-fetal morbidity with GDM is well established,[8-11] controversy remains regarding the risk of an isolated abnormal value on the OGTT. These patients fall into a

OBJECTIVE DATA: The purpose of this study was to determine whether women with 1 abnormal value on 3-hour 100-g oral glucose tolerance test are at an increased risk for adverse pregnancy outcomes.

STUDY: Gestational diabetes mellitus is diagnosed by a 2-step method, with a 3-hour, 100-g oral glucose tolerance test that is reserved for women with an abnormal 1-hour, 50-g glucose challenge test. Although the increased maternal-fetal morbidity with gestational diabetes mellitus is well established, controversy remains about the risk that is associated with an isolated abnormal value during a 3-hour, 100-g oral glucose tolerance test.

STUDY APPRAISAL AND SYNTHESIS METHODS: Prospective and retrospective studies that evaluated the maternal and perinatal impact of 1 abnormal glucose value during a 3-hour, 100-g oral glucose tolerance test were identified with the use of computerized databases. Data were extracted and quantitative analyses were performed.

RESULTS: Twenty-five studies (7 prospective and 18 retrospective) that met criteria for metaanalysis included 4466 women with 1 abnormal glucose value on oral glucose tolerance test. Patients with 1 abnormal glucose value had significantly worse pregnancy outcomes compared with women with zero abnormal values with the following pooled odds ratios: macrosomia, 1.59 (95% confidence interval, 1.16—2.19); large for gestational age, 1.38 (95% confidence interval, 1.09—1.76); increased mean birthweight, 44.5 g (95% confidence interval, 8.10—80.80 g); neonatal hypoglycemia, 1.88 (95% confidence interval, 1.05—3.38); total cesarean delivery, 1.69 (95% confidence interval, 1.40—2.05); pregnancy-induced hypertension, 1.55 (95% confidence interval, 1.31—1.83), and Apgar score of <7 at 5 minutes, 6.10 (95% confidence interval, 2.65—14.02). There was also an increase in neonatal intensive care unit admission and respiratory distress syndrome. Similar results were seen that compared 1 abnormal glucose value to a population with a normal 1-hour 50-g glucose challenge test (normal glucose screen). With the exception of birthweight, outcomes of patients with 1 abnormal glucose value were similar to outcomes of patients with gestational diabetes mellitus.
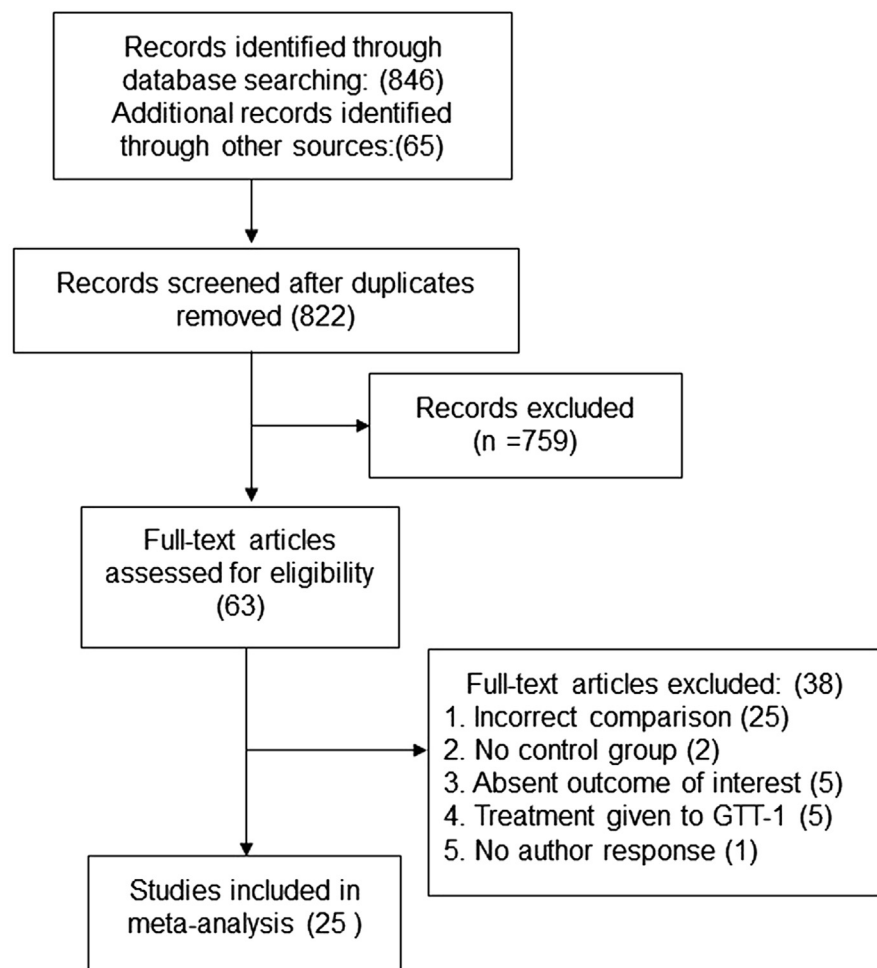
CONCLUSION: Women with 1 abnormal value on 3-hour, 100-g oral glucose tolerance test have a significantly increased risk for poor outcomes comparable with women who have gestational diabetes mellitus.

Key words: 1 abnormal value, birthweight, gestational diabetes mellitus, glucose tolerance, large for gestational age, macrosomia, neonatal hypoglycemia, oral glucose tolerance test

category of glucose intolerance that has been labeled as borderline GDM, impaired glucose tolerance, or mild gestational hyperglycemia.[12-14] Since the 1980s, the significance of 1 abnormal value on the 3-hour OGTT has been

investigated with mixed results.[13-30] Although some investigators have found that impaired glucose tolerance is associated with increased risk of large-for-gestational-age (LGA) infants, macrosomia,[26] cesarean delivery,

FIGURE 1
Flow diagram of study selection process

Metaanalysis of Observational Studies in Epidemiology[36] flow diagram for inclusion of studies that examine the relationship between 1 abnormal value during glucose tolerance test and maternal and neonatal outcomes.

GTT-1, 1 abnormal value.

Roeckner. Single abnormal glucose tolerance value and adverse outcomes. Am J Obstet Gynecol 2016.

to the Meta-analysis of Observational Studies in Epidemiology guidelines.[36] The protocol was registered in Prospero (CRD42015032462). Institutional Review Board approval was not needed. A thorough and extensive search of published literature from January 1966 to December 2015 was conducted with PubMed, Medline, Google Scholar, Cochrane, and clinicaltrials.gov. The key words "gestational diabetes" and "glucose tolerance test" were searched independently as well as in conjunction with the following keywords: "1 abnormal value," "large for gestational age," "cesarean delivery," "NICU admission," "hypoglycemia," and "macrosomia." Prospective and observational studies that evaluated the maternal and perinatal impact of 1 abnormal value during a 3-hour, 100-g GTT were identified and selected. Each study assessed ≥1 of the following maternal and perinatal outcomes: macrosomia (at least 4000 g at birth), LGA based on a birthweight at least in the 90th percentile for gestational age, neonatal hypoglycemia, cesarean delivery, neonatal intensive care unit (NICU) admission, abnormal Apgar scores, or preeclampsia or pregnancy-induced hypertension (PIH) based on American College of Obstetricians and Gynecologists' criteria. Randomized clinical control trials were included if data could be extracted from the noninterventional arm. Non–English-language studies were not excluded. Article references and syllabi from scientific meetings were screened for additional articles.

Because each report did not assess all outcomes of interest, specific outcome metaanalyses were performed based on a variable number of studies that were related to that outcome. Studies that used a 2-hour, 75-g OGTT were excluded. Studies were also excluded if they lacked a suitable comparison group (ie, combined patients with zero abnormal value [GTT-0] or 1 abnormal value [GTT-1] on OGTT), if they lacked sufficient quantitative data for extraction,[37-57] if they lacked a comparison group,[31,58] if they lacked assessment of neonatal outcomes of interest,[59-63] if the authors failed to provide a breakdown of

preeclampsia,[17] and increased risk of diabetes mellitus later in life[18]; other investigators have not found increased risk,[19,22] and trials of diet have found mixed results.[21,31,32] Screening, early prediction,[33,34] and treatment can result in unnecessary and costly intervention.[5,35]

The specific goal of this systematic review and metaanalysis is to determine whether women with 1 abnormal value on the 3-hour, 100-g OGTT are at an increased risk for poor pregnancy outcomes that include LGA, macrosomia,

increased birthweight, cesarean delivery, hypertensive disorders that are related to pregnancy, hypoglycemia, low Apgar scores, and respiratory distress when compared with (1) pregnant women with all normal values on OGTT, (2) women with a normal 1-hour 50-g screening test, and (3) women with GDM.

Materials and Methods

This systematic review and metaanalysis was preceded by a prospectively written protocol and was conducted according