OBSTETRICS

# Induction of labor before 40 weeks is associated with lower rate of cesarean delivery in women with gestational diabetes mellitus

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**BACKGROUND:** In women with gestational diabetes mellitus, it is not clear whether routine induction of labor at <40 weeks of gestation is beneficial to mother and newborn infant.

**OBJECTIVE:** The purpose of this study was to compare outcomes among women with gestational diabetes mellitus who had induction of labor at either 38 or 39 weeks with those whose pregnancy was managed expectantly.

**STUDY DESIGN:** We included all women in Ontario, Canada, with diagnosed gestational diabetes mellitus who had a singleton hospital birth at ≥38 + 0 weeks of gestation between April 2012 and March 2014. Data were obtained from the Better Outcomes Registry & Network Ontario, which is a province-wide registry of all births in Ontario, Canada. Women who underwent induction of labor at 38 + 0 to 38 + 6 weeks of gestation (38-IOL; n = 1188) were compared with those who remained undelivered until 39 + 0 weeks of gestation (38-Expectant; n = 5229). Separately, those women who underwent induction of labor at 39 + 0 to 39 + 6 weeks of gestation (39-IOL; n = 1036) were compared with women who remained undelivered until 40 + 0 weeks of gestation (39-Expectant; n = 2162). Odds ratios and 95% confidence intervals were adjusted for maternal age, parity, insulin treatment, and prepregnancy body mass index.

**RESULTS:** Of 281,480 women who gave birth during the study period, 14,600 women (5.2%) had gestational diabetes mellitus; of these, 8392 women (57.5%) met all inclusion criteria. Compared with the 38-Expectant group, those women in the 38-IOL group had lower odds for cesarean delivery (adjusted odds ratio, 0.73; 95% confidence interval, 0.52—0.90), higher odds for neonatal intensive care unit admission (adjusted odds ratio, 1.36; 95% confidence interval, 1.09—1.69), and no difference in other maternal-newborn infant outcomes. Compared with the 39-Expectant group, women in the 39-IOL group likewise had lower odds for cesarean delivery (adjusted odds ratio, 0.73; 95% confidence interval, 0.58—0.93) but no difference in neonatal intensive care unit admission (adjusted odds ratio, 0.83; 95% confidence interval, 0.61—1.11).

**CONCLUSION:** In women with gestational diabetes mellitus, the routine induction of labor at 38 or 39 weeks is associated with a lower risk of cesarean delivery compared with expectant management but may increase the risk of neonatal intensive care unit admission when done at <39 weeks of gestation.

**Key words:** gestational diabetes mellitus, induction, expectant management, delivery

Gestational diabetes mellitus (GDM), which is 1 of the most common medical complications of pregnancy, affects >7% of pregnancies in the United States[1] and has been shown to be associated with adverse pregnancy outcome.[2,3]

One of the major controversies in the management of pregnancies that are complicated by GDM relates to the optimal timing of delivery. A policy of a routine induction of labor (IOL) at 38-39 weeks of gestation carries the potential benefit of decreasing macrosomia-related complications that include cesarean delivery, shoulder dystocia, anal sphincter injuries, and birth trauma.[4-8] Furthermore, in some cases, clinicians may choose to induce labor at 38-39 weeks to eliminate the risk of GDM-related stillbirth, although data regarding the association of GDM with stillbirth are conflicting.[9-12] However, such a policy of routine IOL might also be associated with certain risks that include increasing the risk of cesarean delivery because of induction failure, fetal distress because of uterine hyperstimulation, or neonatal morbidity that is related to early-term delivery (eg, respiratory morbidity, jaundice) when induction takes place at <39 weeks of gestation.[13-18]

Data regarding the benefits and risks of routine IOL in women with GDM are sparse. This question has been addressed by only a small number of studies that were limited by small sample size, lack of adequate control group, lack of adjustment for potential confounders (eg, type of treatment, body mass index [BMI]) and potential for selection bias.[19-22] Indeed, in a recent systematic review,[23] it was concluded that the substantial heterogeneity of these studies precludes the completion of a quantitative synthesis of the data or drawing definite conclusions about timing of delivery in women with GDM. However, recent evidence that IOL in low-risk pregnancies[4,24] and in pregnancies with large-for-date fetuses[25] does not increase the rate of cesarean delivery and may decrease the rate of shoulder dystocia[25] provides indirect support to the rationale underlying such a practice of routine IOL in women with GDM. Furthermore, in a recent large population-based study on the risk of stillbirth and infant death by gestational age in women with GDM, the authors concluded that expectant treatment at 39 and 40 weeks of gestation in women with GDM is associated with significantly greater risk of perinatal death (stillbirth and infant death) compared

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with delivery at these corresponding weeks.[9]

Our aim was to compare pregnancy outcomes among women with GDM who had IOL at either 38 or 39 weeks of gestation and those who were treated expectantly.

## Methods

### Study population

This was a retrospective cohort study of all women with GDM who had a singleton hospital birth at ≥38 + 0 weeks of gestation in Ontario, Canada, between April 2012 and March 2014. Data were obtained from the Better Outcomes Registry & Network (BORN) Ontario (https://www.bornontario.ca/en/about-born/) BORN Ontario is a province-wide registry of all births in Ontario, Canada. Whenever a woman is admitted to a hospital to give birth, data are collected by health care providers and hospital staff from charts, clinical forms, and patient interview then entered into the BORN Information System (either directly or by electronic upload from a hospital's electronic medical records system). The BORN Information System contains maternal demographics, health behaviors, reproductive history, and clinical information related to pregnancy, labor, and birth, fetal, and neonatal outcomes. An ongoing program of data verifications, quality checks, and formal training sessions for individuals who collect and enter data assures that a high level of data quality is maintained.

To create a "low-risk" GDM cohort, women with any of the following conditions were excluded from the study: gestational age at birth of ≥42 + 0 weeks, women who were not candidates for vaginal birth (eg, nonvertex presentation, placenta previa), previous cesarean delivery, major fetal anomalies, or chronic maternal medical conditions that potentially could influence a decision to induce labor at 38-39 weeks of gestation that include pre-GDM, chronic hypertension, chronic renal disease, cardiac disease (congenital or acquired), pulmonary disease (pulmonary hypertension, cystic fibrosis, pulmonary embolism), autoimmune conditions (systemic lupus erythematosus), or hematologic diseases (hemophilia, sickle cell disease; Figure).

Some of the previous observational studies on the effects of IOL are limited by the use of a control group of women who experience spontaneous onset of labor. However, in clinical practice, the real choice is not between IOL and spontaneous labor, but between IOL and expectant management; the latter option carries that risk of new onset of pregnancy complications and the potential for labor induction at a later stage of gestation. Thus, to simulate the decision faced by physicians in real-life, women who underwent IOL at 38 + 0 to 38 + 6 weeks of gestation in the current study (38-IOL group) were compared with those who were treated expectantly and remained undelivered until 39 + 0 weeks of gestation (ie, delivered anytime between 39 + 0 and 41 + 6 weeks of gestation; 38-Expectant group). A separate comparison was performed between women who underwent IOL at 39 + 0 to 39 + 6 weeks of gestation (39-IOL group) and those who were treated expectantly and remained undelivered until 40 + 0 weeks (ie, delivered anytime between 40 + 0 and 41 + 6 weeks of gestation; 39-Expectant group; Figure). Only women whose sole documented reason for IOL was GDM or macrosomia were included in the 38-IOL and 39-IOL groups (Figure).

### Outcomes

The primary outcome was the rate of cesarean delivery. Secondary outcomes included the rate of instrumental delivery, postpartum hemorrhage, intrapartum fever, anal sphincter injury (defined as a third- or fourth-degree perineal laceration), shoulder dystocia, and neonatal morbidity. *Neonatal respiratory morbidity* was defined as any of the following events: need for respiratory support in the form of continuous positive airway pressure or mechanical ventilation, a diagnosis of transient tachypnea of the newborn infant, or respiratory distress syndrome. *Composite neonatal morbidity* was defined as the presence of any of the following events: perinatal death, 5-minute Apgar score <7, admission to the neonatal intensive care unit (NICU), hypoglycemia, jaundice that required phototherapy, or neonatal respiratory morbidity.

### Diagnosis of GDM

This study spans 2 time periods with regards to criteria for the diagnosis of GDM in Ontario. Before April 2013, the criteria for diagnosis were according to 2008 Canadian Diabetes Associations guidelines.[26] These guidelines recommended screening for GDM with a 50 g glucose challenge test (GCT); when the results were positive (>7.8 mmol/L or 140 mg/dL), a 75g oral glucose tolerance test (OGTT) followed (cutoff values: fasting, ≥5.3 mmol/L or 96 mg/dL; 1 hour ≥10.6 mmol or 191 mg/dL; 2 hours ≥ 8.9 mmol/L or 160 mg/dL). *GDM* was defined as ≥2 abnormal OGTT values or a GCT result of ≥10.3 mmol/L or 185 mg/dL. The presence of a *single abnormal OGTT value* was defined as impaired glucose tolerance.

In April 2013 new Canadian Diabetes Associations criteria were published.[27] The new guidelines allowed two options for screening/testing for GDM. The "Preferred" option was essentially identical to the Canadian Diabetes Associations 2008 guidelines aside from increasing the diagnostic 50g-GCT value from 10.3 mmol (185 mg/dL) to ≥ 11.1 mmol (200 mg/dL), and the 2-hour 75g-OGTT threshold from 8.9 mmol/L (160 mg/dL) to 9.0 mmol/L (162 mg/dL). The distinction between impaired glucose tolerance and GDM was eliminated in these new guidelines.

### Data analysis

Multivariable logistic regression analysis was used to adjust for potential confounding variables that included maternal age (as a continuous variable), nulliparity, need for insulin treatment, prepregnancy BMI (as a continuous variable), and macrosomia (birthweight, >4000 g). This analysis was repeated within a subgroup of nulliparous women, because parity is a major determinant of the success of labor induction.[28] In addition, because we did not have data about the Bishop's cervix score (which is associated with the likelihood