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MATERNAL-FETAL MEDICINE

Induction of labor versus expectant management for gestational diabetes mellitus at term

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Abstract

Purpose To evaluate whether induction of labor (IOL), as compared with expectant management, in gestational diabetes mellitus (GDM) mothers at term (between $37^{0/7}$ and $40^{6/7}$), decreases caesarean section (CS) rate and the rate of adverse composite neonatal outcomes.

Methods A retrospective cohort study, of all women with GDM and a singleton gestation who delivered at term in a single, tertiary, university-affiliated medical center (2007–2014). We compared outcomes of women who underwent IOL at each week of gestation between $37^{0/7}$ and $40^{6/7}$ weeks with women who were managed expectantly. The primary outcome was CS rate.

Results Overall, 2472 GDM patients included in the study, of which 880 women had IOL. CS rate was not found to be significantly different between the groups at any gestational age. IOL at 37 weeks was associated with adverse composite neonatal outcome (aOR 2.2, 95% CI 1.4–3.6) and NICU admission (aOR 2.5, 95% CI 1.4–4.4). At 38 weeks, with NICU admission (aOR 2.0, 95% CI 1.4–2.9), and at 39 weeks with fracture of the clavicle. In a sub-analysis of nulliparous women, IOL at 37 weeks had higher odds of NICU admission and adverse composite neonatal outcomes, at 38 weeks with CS and at 39 weeks with fracture of the clavicle.

Conclusions IOL in GDM mothers at term does not reduce CS rate and may be associated with increased CS rate among nulliparous women at 38 weeks. It is also associated with increased risk for adverse composite neonatal outcome or NICU admission when done prior to $39^{0/7}$ weeks.

Keywords Cesarean section · Gestational diabetes · Induction of labor · Maternal outcome · Neonatal outcome

Introduction

The prevalence of gestational diabetes mellitus (GDM) depends on ethnicity, maternal age, screening tool and diagnostic criteria [1]. It has been rising over time, probably due to increasing maternal age and weight, and now reaching 6–7% in the United states [2]. Several adverse outcomes have been associated with GDM including preeclampsia, macrosomia, shoulder dystocia, operative delivery, birth trauma, neonatal respiratory problems and metabolic complications [3, 4].

Induction of labor (IOL) is indicated when maternal or fetal risks associated with continuation of pregnancy outweigh the risks associated with early delivery [5]. Early-term IOL among women with GDM may potentially decrease GDM-associated complications, especially macrosomia-related [6, 7] and stillbirth [8]. However, it can also be associated with both neonatal morbidities such as respiratory distress syndrome, mechanical ventilation, hypoglycemia and more [9, 10], and maternal risks such as increased length of labor and hospital stay, hemorrhage and infection [11].

Several studies [12, 13] demonstrated decreased odds for cesarean section and neonatal morbidity in low-risk

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pregnancies undergoing IOL compared with those managed expectantly [12, 13]. However, in GDM patients, timing of delivery remains controversial. An older Cochrane review from 2000 [14] included only one RCT and a few observational studies, and concluded that there is very little evidence to support either IOL or expectant management in those patients. In a more recent Cochrane review [15] including only one RCT with 425 women [16], IOL at 38–39 weeks was not found to be associated with increased neonatal morbidity but the study was underpowered. Melamed et al. [7] also compared IOL of GDM mothers at 38 or 39 weeks to expectant management and showed lower rates of CS with higher neonatal intensive care unit (NICU) admission rate [7]. In their study, they obtained data from a province registry including one province with few medical centers using different protocols. With regards to national guidelines, there is no uniformity in the recommendations. While The Society of Obstetricians and Gynecologists of Canada (SOGC) [17] offer IOL at 38–40 weeks, others [18-20] recommend that delivery should not be executed before 39 weeks or even later. We think that the question weather to induce mothers with GDM or manage them expectantly remains unanswered.

The aim of our study was to evaluate whether IOL, as compared with expectant management at term stratified by gestational week (between $37^{0/7}$ and $40^{6/7}$), in GDM mothers, while using one uniformed protocol of diagnosis and management, decreases caesarean section rate and the rate of other adverse maternal and neonatal outcomes.

Materials and methods

This was a retrospective cohort study, of all women with GDM and a singleton gestation who delivered at term ($37^{0/7}$–$40^{6/7}$ weeks' gestational age) in a single, tertiary, university-affiliated medical center between August 1st, 2007 and December 31st, 2014. Indications for IOL were as follows: suspected macrosomia, non-reassuring fetal heart rate, premature rupture of membranes, and post-date.

This study was approved by the local Institutional Review Board ('The Helsinki Committee', RMC-0421–014, September 9th, 2014). Due to the retrospective nature of the study, consent for participation was not required.

We excluded neonates with structural or chromosomal anomalies, as well as women with pregestational diabetes mellitus, multiple gestation, or women not deemed eligible for a trial of vaginal delivery (e.g., breech presentation, previous multiple CS, etc.). We also excluded women with chronic medical conditions that potentially could have an effect on a decision to induce labor, such as women with chronic hypertension or renal disease, cardiac or pulmonary disease, autoimmune conditions, or hematologic diseases.

We compared composite outcomes of women who underwent IOL at each week gestational age, between $37^{0/7}$ and $40^{6/7}$ weeks, with women who did not have induction of labor at that week (expected management). Gestational age at delivery was categorized as 37, 38, 39 and 40 completed weeks.

Data were retrieved from the computerized perinatal database of the birthing unit and was cross-tabulated using an individualized identification number per patient. Data from the neonatal unit and the neonatal intensive care unit (NICU) were integrated with the birthing unit database using a unique admission number assigned to each parturient and her offspring. Collected data included demographic and obstetrical parameters, labor and delivery data as well as short-term neonatal and maternal outcome (up to discharge).

Gestational age was based on last menstrual period and was affirmed by a first trimester sonogram, when available. Diagnosis of GDM was based on the American College of Obstetricians and Gynecologist (ACOG) from 2001 [21]. These guidelines recommend screening for GDM with a 50-g glucose challenge test (GCT) between 24 and 28 weeks' gestation; when the results were positive (>7.8 mmol/L or 140 mg/dL), a 100-g 3-h oral glucose tolerance test (OGTT) was followed (cutoff values: fasting, ≥ 5.3 mmol/L or 95 mg/dL; 1 h ≥ 10 mmol or 180 mg/dL; 2 h ≥ 8.6 mmol/L or 155 mg/dL; 3 h ≥ 7.8 mmol/L or 140 mg/dL) [21]. GDM was defined as ≥ 1 abnormal OGTT values or a GCT result of ≥ 10.3 mmol/L or 185 mg/dL based on previous reports [22] which showed that one abnormal value may be used to define GDM.

Prolonged first stage of labor was defined as women at or beyond 6 cm dilatation with ruptured membranes who fail to progress despite 4 h of adequate uterine activity, or at least 6 h of oxytocin administration with inadequate uterine activity and no cervical change [23].

Prolonged second stage was established after 3 h of full dilatation among nulliparous with regional analgesia (RA), 2 h among nulliparous with no RA or multiparous with RA, and 1 h among multiparous without RA. Fetal heart rate tracing was categorized using the National Institute of child health and human development (NICHD) criteria [24].

According to our departmental protocol, all women with GDM underwent a sonographic estimation of fetal weight at 36–37 weeks of gestation. IOL was recommended at 38–39 weeks of gestation to women carrying large-for-gestational age (LGA) fetuses, or to women with poor glycemic control. All others were followed until 40 weeks' gestation with twice weekly follow-up (NST and BPP). IOL was recommended for all women with GDM at $40^{0/7}$ weeks' gestation.

The primary outcome was defined as CS rate. Indications for CS were non-reassuring fetal heart rate (NRFHR), suspected macrosomia or arrested labor.

Secondary outcome was adverse composite neonatal outcome which was defined as one or more of the following: shoulder dystocia (defined as delivery that required additional obstetric maneuvers following failure of gentle downward traction on the fetal head to effect delivery of the shoulders, or head-to-shoulder delivery time exceeding 60 s [25]), 5-min Apgar score < 7, birth asphyxia (pH < 7 and base deficit ≥ 12 mmol/L at birth in a newborn exhibiting early signs of moderate or severe encephalopathy) [26], seizures, umbilical cord pH < 7.05, hypoglycemia, respiratory distress syndrome (RDS), mechanical ventilation, clavicular fracture, Erb's palsy and jaundice that requires phototherapy.

Statistical analysis was performed with the SPSS v25.0 package (IBM, Armonk, NY). Continuous variables were compared using Student's *T* test or Mann–Whitney *U* test. The Chi-square and Fisher's exact tests were used for the comparison of categorical variables, as appropriate. Logistic regression analysis was used to adjust outcomes for potential confounders. Differences were considered significant when *p* value was less than 0.05.

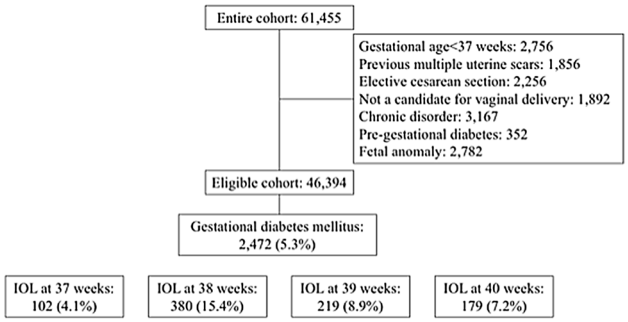

Fig. 1 Description of the study cohort. *IOL* induction of labor

Results

Characteristics of the study population

Overall, out of 61,455 women who gave birth during the study period, 2472 GDM patients met the inclusion criteria and were included in the study (Fig. 1). From all women included in the study, 102 women (4.1%) underwent IOL at $37^{0/7}$–$37^{6/7}$ weeks of gestation and were compared with 2370 women who were managed expectantly. Similarly, 380 (15.4%) women who had IOL at $38^{0/7}$–$38^{6/7}$ weeks of gestation were compared with 1759 women who were not induced at 38 weeks. 219 women (8.9%) underwent IOL at $39^{0/7}$–$39^{6/7}$ weeks of gestation and were compared with 1061 women who were managed expectantly, and 179 women (7.2%) who underwent IOL at $40^{0/7}$–$40^{6/7}$ weeks of gestation were compared with 395 women who delivered later. Overall, 880 women (32.9%) had an IOL (Table 1).

The characteristics of the induction and expectant groups are presented in Table 1. Gestational hypertension and preeclampsia without severe features were more prevalent in the induction group than in the expectant management group at 38 and 39 weeks of gestation, respectively. There were no other differences in characteristics between the groups.

Women who had induction at 38 weeks were more prone to have an epidural anesthesia and had lower rate of

Table 1 Characteristics of the induction and expectant management groups (2472)

Characteristics	37 weeks		38 weeks		39 weeks		40 weeks	
	Induction	Expectant	Induction	Expectant	Induction	Expectant	Induction	Expectant
N	102	2370	380	1759	219	1061	179	395
Mean maternal age (years)	33.1 ± 4.5	32.8 ± 4.8	33 ± 4.8	32.7 ± 4.8	32.8 ± 5.1	32.64 ± 4.7	33 ± 4.5	32.3 ± 4.9
Parity (*n*)	2.5 ± 1.8	2.3 ± 1.5	2.2 ± 1.4	2.3 ± 1.4	2.1 ± 1.3	2.3 ± 1.5	2.2 ± 1.3	2.3 ± 1.4
Gestational age at delivery (weeks)		38.7 ± 1$^{£££}$		39.1 ± 0.8$^{£££}$		39.6 ± 0.6$^{£££}$		40.2 ± 0.4$^{£££}$
Nulliparity	34 (33.3)	890 (37.6)	150 (39.5)	670 (38.1)	96 (43.8)	410 (38.6)	74 (41.3)	158 (40)
Previous single CS	5 (4.9)	169 (7.1)	24 (6.3)	122 (6.9)	13 (5.9)	78 (7.4)	13 (7.3)	30 (7.6)
Gestational hypertension	2 (2)	32 (1.4)	**10 (2.6)**	**21 (1.2)$^{£}$**	3 (1.4)	13 (1.2)	2 (1.1)	5 (1.3)
Preeclampsia without severe features	3 (2.9)	35 (1.5)	5 (1.3)	17 (1)	**6 (2.7)**	**3 (0.3)$^{£££}$**	1 (0.6)	1 (0.3)
Preeclampsia with severe features	1 (1)	14 (0.6)	3 (0.8)	6 (0.3)	0 (0)	4 (0.4)	0 (0)	1 (0.3)
Oligohydramnios	6 (5.9)	64 (2.7)	12 (3.2)	50 (2.8)	8 (3.7)	26 (2.5)	5 (2.8)	10 (2.5)
Polyhydramnios	4 (3.9)	110 (4.6)	17 (4.5)	77 (4.4)	6 (2.7)	38 (3.6)	8 (4.5)	14 (3.5)
Induction of labor at a later gestational age		**808 (34.1)$^{£££}$**		**428 (24.3)$^{£££}$**		**209 (19.7)$^{£££}$**		**30 (7.6)$^{£££}$**

Data are presented as mean ± SD or *n* (%)

CS cesarean section

$^{£}p < 0.05$, $^{££}p < 0.01$, $^{£££}p < 0.001$ for the difference between delivery and ongoing pregnancy groups. Appear in bold

meconium stained amniotic fluid during labor than those managed expectantly (Table 2). They also had less episiotomies and less minor tears compared to their counterparts (Table 2).

Primary outcome

Cesarean section rate was not found to be significantly different between the groups at any gestational age, or were rates of spontaneous vaginal delivery (Table 2). At 37 weeks, women in the IOL group were less likely to have a vacuum-assisted delivery than women in the expectant management group, and all four assisted deliveries were indicated by NRFHR (Table 2).

At 37 weeks gestational age, IOL was associated with an increased rate of non-reassuring fetal heart rate leading to CS, while at 38- and 39-weeks gestational age, failure to progress at the first stage of labour was more common in the IOL group. Suspected fetal macrosomia was less likely to be an indication for a CS in the induction group at 38–40 weeks gestational age (Table 2).

Figure 2 depicts the contribution of each expectantly managed group to the deliveries at an index gestational age.

The *Y* axis represent a certain gestational age at delivery, while the *X* axis represent the rate of patients who were managed expectantly at each of the gestational weeks. For example, of all women who were managed expectantly at 39 weeks (i.e., did not have an IOL at 39 weeks), 45.9% delivered at 39 weeks, 33.9% delivered at 30 weeks and 9.2% delivered at > 41 weeks of gestation (Fig. 2).

Table 2 Pregnancy outcome of the induction and expectant management groups (2472)

Characteristics	37 weeks		38 weeks		39 weeks		40 weeks	
	Induction	Expectant	Induction	Expectant	Induction	Expectant	Induction	Expectant
N	102	2370	380	1759	219	1061	179	395
Epidural analgesia	75 (73.5)	1636 (69)	**286 (75.3)**	**1200 (68.2)**$^{££}$	160 (73.1)	724 (68.2)	120 (67)	270 (68.4)
Meconium	8 (7.8)	190 (8)	**9 (2.4)**	**169 (9.6)**$^{£££}$	21 (9.6)	123 (11.6)	20 (11.2)	55 (13.9)
Mode of delivery								
NVD	82 (80.4)	1793 (75.7)	286 (75.3)	1327 (75.4)	163 (74.4)	810 (76.3)	135 (75.4)	286 (72.4)
OVD	**4 (3.9)**	**239 (10.1)**$^{£}$	36 (9.5)	186 (10.6)	31 (14.2)	113 (10.7)	23 (12.8)	48 (12.2)
CS	16 (15.7)	338 (14.3)	58 (15.3)	246 (14)	25 (11.4)	138 (13)	21 (11.7)	61 (15.4)
TOLAC*	4 (3.9)	141 (5.9)	22 (5.8)	104 (5.9)	12 (5.5)	70 (6.6)	12 (6.7)	28 (7.1)
VBAC**	3 (2.9)	121 (5.1)	20 (5.3)	88 (5)	8 (3.7)	61 (5.7)	10 (5.6)	21 (5.3)
Indications for OVD								
NRFHM	4 (3.9)	76 (3.2)	11 (2.9)	63 (3.6)	13 (5.9)	42 (2)	11 (6.1)	17 (4.3)
PSS	**(0)**	**162 (6.8)**$^{££}$	25 (6.6)	122 (6.9)	17 (7.8)	71 (6.7)	12 (6.7)	31 (7.8)
Indications for CS								
NRFHR	**7 (6.9)**	**40 (1.7)**$^{£££}$	7 (1.8)	31 (1.8)	5 (2.3)	19 (1.8)	4 (2.2)	9 (2.3)
PFS	9 (8.8)	115 (4.9)	**39 (10.3)**	**73 (4.2)**$^{£££}$	**17 (7.8)**	**42 (4)**$^{£}$	11 (6.1)	17 (4.3)
PSS	0 (0)	27 (1.1)	5 (1.3)	20 (1.1)	1 (0.5)	14 (1.3)	3 (1.7)	4 (1)
Macrosomia	0 (0)	83 (3.5)	**3 (0.8)**	**72 (4.1)**$^{££}$	**1 (0.5)**	**39 (3.7)**$^{£}$	**0 (0)**	**18 (4.6)**$^{££}$
Episiotomy***	12 (11.8)	414 (17.5)	**49 (12.9)**	**336 (18.1)**$^{££}$	51 (23.3)	202 (19)	46 (25.7)	78 (19.7)
Minor perineal tear***	15 (14.7)	18.1)	**51 (13.4)**	**329 (18.7)**$^{£}$	33 (15.1)	208 (19.6)	23 (12.8)	74 (18.7)
Major perineal tear***	0 (0)	8 (0.3)	0 (0)	7 (0.4)	0 (0)	3 (0.3)	1 (0.6)	0 (0)
Shoulder dystocia***	1 (1)	8 (0.3)	1 (0.3)	7 (0.4)	2 (0.9)	5 (0.5)	1 (0.6)	2 (0.5)
PPH	3 (2.9)	50 (2.1)	11 (2.9)	33 (1.9)	2 (0.9)	25 (2.4)	5 (2.8)	13 (3.3)

Data are presented as mean ± SD or *n* (%)

NVD normal vaginal delivery, *OVD* operative vaginal delivery, *CS* cesarean section, *TOLAC* trial of labor after cesarean section, *VBAC* vaginal birth after cesarean section (successful TOLAC), *NRFHR* non-reassuring fetal heart rate, *PFS* prolonged first stage of labor, *PSS* prolonged second stage of labor, *Minor perineal tear* grade 1–2 perineal tear, *Major perineal tear* grade 3–4 perineal tear, *PPH* postpartum hemorrhage

$^{£}p < 0.05$, $^{££}p < 0.01$, $^{£££}p < 0.001$ for the difference between delivery and ongoing pregnancy groups. Appear in bold

*Percentage out of women with previous single cesarean delivery

**Percentage out of women with TOLAC

***Percentage out of NVD or OVD

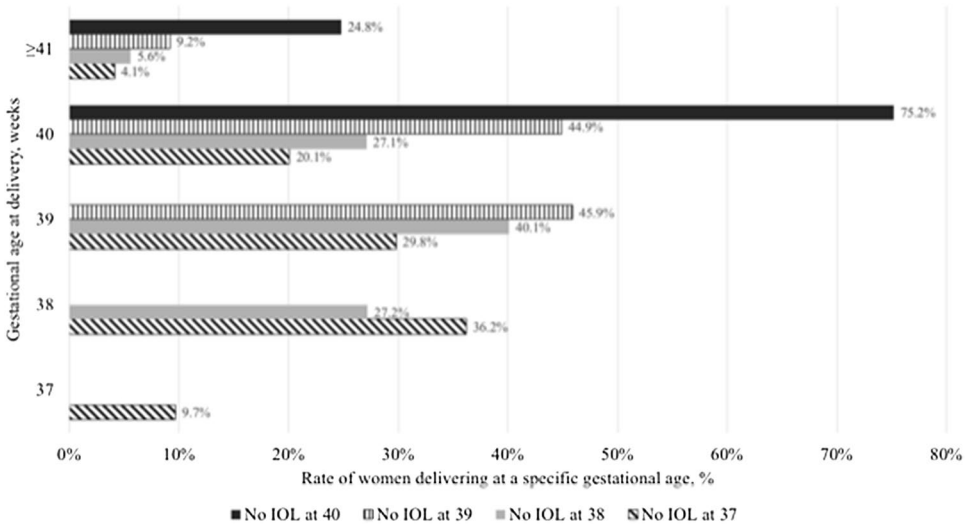

Fig. 2 Gestational age at delivery for patients who did not have an induction of labor at any given week. *IOL* induction of labor

Neonatal outcomes

Neonatal outcomes are presented in Table 3. Adverse composite neonatal outcome was significantly higher in the IOL group at 37 weeks' gestation (24.5% vs. 13.6%, $P < 0.01$). There was no significant difference in the composite outcome between the groups at all other gestational age groups (Table 3).

Mean birth weight in the IOL groups were lower at 37, 38 and 39 weeks of gestation, and the prevalence of birth weight > 4000 g was lower in the IOL groups at 38- and 40-weeks' gestation.

Neonates of mothers in the induction group at 37 and 38 weeks had a higher rate of admission to NICU and jaundice that required phototherapy (Table 3). Fracture of the clavicle was found to be more frequent in neonates in the IOL group at 39 and 40 weeks of gestation (Table 3).

Association of induction with adverse outcome: multivariable analysis

To evaluate the independent contribution of IOL at each gestational week to adverse outcome, a multivariable logistic regression model was calculated. Included predictors were parity, gestational age at delivery, epidural and birth weights. IOL at 37 weeks was found to be a significant independent risk factor for NICU admission (aOR 2.5, 95% CI 1.4–4.4), jaundice requiring phototherapy (aOR 2.4, 95% CI 1.4–4.3) and composite neonatal outcome (aOR 2.2, 95% CI 1.4–3.6). At 38 weeks of gestation, IOL was associated with NICU admission (aOR 2.0, 95% CI 1.4–2.9). IOL at 39 weeks was found to be a significant independent risk factor for fracture of the clavicle in the newborn (aOR 3.3, 95% CI 1.2–9.5) and jaundice requiring phototherapy (aOR 1.8, 95% CI 1.1–3.2) (Table 4).

To better characterize the association of IOL with different outcomes, we further calculated a logistic regression model for nulliparous women only, using the same predictors. IOL at 37 weeks remained associated with NICU admission (aOR 4.0, 95% CI 1.7–9.0) and composite neonatal outcome (aOR 3.2, 95% CI 1.5–6.8, respectively; Table 5). At 38 weeks, IOL was found to be associated with increased odds ratio of cesarean section (aOR 1.8, 95% CI 1.1–2.7). Increased risk of clavicle fracture and composite neonatal outcome were also associated with IOL at 39 weeks (aOR 5.4, 95% CI 1.5–20.0, aOR 1.8, 95% CI 1.1–3.1, respectively; Table 5).

Discussion

In this study, we compared outcomes of induction of labor versus expectant management among mothers with GDM at term (from $37^{0/7}$ to $40^{6/7}$) stratified by gestational age. Our main findings were as follows: (1) induction of labor does not reduce the risk of cesarean section and among nulliparous at 38 weeks; it may be associated with increased risk of cesarean section; (2) induction of labor at 37 was associated with adverse composite neonatal outcome and NICU admission, and at 38 weeks with NICU admission; and (3) at 39 weeks, IOL was associated with a fracture of the clavicle.

In our cohort, we found no difference in the rate of cesarean section, regardless of gestational age. However, among the sub-population of nulliparous women, IOL at 38 weeks was found to be associated with an increased risk of CS. Our similar CS rates between the induction and non-induction groups correlate with other studies [27, 28] along with a recent RCT by Alberico et al. [16]. The latter randomized

Table 3 Neonatal outcomes in the induction and expectant management groups (2472)

Characteristics	37 weeks		38 weeks		39 weeks		40 weeks	
	Induction	Expectant	Induction	Expectant	Induction	Expectant	Induction	Expectant
N	102	2370	380	1759	219	1061	179	395
Birth weight, g	**3062 ± 493**	**3319 ± 427**$^{£££}$	**3244 ± 389**	**3354 ± 419**$^{£££}$	**3324 ± 386**	**3387 ± 403**$^{£}$	**3393 ± 367**	3444 ± 400
Birth weight percentile (%)	62.3 ± 30	62.4 ± 26.5	63.1 ± 25.7	61.6 ± 26.5	59.1 ± 26.6	60.5 ± 26	59 ± 25	61 ± 26
APD	0 (0)	2 (0.1)	0 (0)	1 (0.1)	0 (0)	1 (0.1)	1 (0.6)	0 (0)
IPD	0 (0)	1 (0)	0 (0)	1 (0.1)	**1 (0.5)**	**0 (0)**$^{£}$	0 (0)	0 (0)
LGA	20 (19.6)	414 (17.5)	60 (15.8)	297 (16.9)	29 (13.2)	164 (15.5)	22 (12.3)	67 (17)
BW > 4000 g	2 (2)	141 (5.9)	**9 (2.4)**	**119 (6.8)**$^{££}$	10 (4.6)	77 (7.3)	**9 (5)**	**41 (10.4)**$^{£}$
BW > 4250 g	1 (1)	38 (1.6)	3 (0.8)	30 (1.7)	1 (0.5)	21 (2)	2 (1.1)	11 (2.8)
BW > 4500 g	0 (0)	9 (0.4)	0 (0)	6 (0.3)	0 (0)	4 (0.4)	0 (0)	3 (0.8)
Male neonate	55 (53.9)	1245 (52.5)	215 (56.6)	909 (51.7)	119 (54.3)	545 (51.4)	94 (52.5)	201 (50.9)
5-min Apgar score < 7	0 (0)	9 (0.4)	0 (0)	5 (0.3)	1 (0.5)	4 (0.4)	1 (0.6)	2 (0.5)
pH < 7.05	**2 (2)**	**11 (0.5)**$^{£}$	2 (0.5)	8 (0.5)	1 (0.5)	6 (0.6)	2 (1.1)	3 (0.8)
Clavicular fracture*	1 (1)	28 (1.2)	2 (0.5)	23 (1.3)	**6 (2.7)**	**10 (0.9)**$^{£}$	**3 (1.7)**	**0 (0)**$^{£}$
Erb's palsy*	0 (0)	3 (0.1)	1 (0.3)	2 (0.1)	1 (0.5)	1 (0.1)	0 (0)	1 (0.3)
NICU	**16 (15.7)**	**170 (7.2)**$^{££}$	**41 (10.8)**	**103 (5.9)**$^{£££}$	18 (8.3)	61 (5.8)	9 (5)	31 (7.9)
Asphyxia	1 (1)	20 (0.8)	4 (1.1)	10 (0.6)	2 (0.9)	8 (0.8)	2 (1.1)	5 (1.3)
Seizures	0 (0)	12 (0.5)	2 (0.5)	10 (0.6)	2 (0.9)	5 (0.5)	0 (0)	1 (1.3)
HIE	0 (0)	8 (0.3)	0 (0)	7 (0.4)	**4 (1.8)**	**2 (0.2)**$^{££}$	1 (0.6)	0 (0)
Hypoglycemia	3 (2.9)	46 (1.9)	4 (1.1)	29 (1.6)	4 (1.8)	13 (1.2)	1 (0.6)	7 (1.8)
RDS	0 (0)	2 (0.1)	1 (0.3)	1 (0.1)	**1 (0.5)**	**0 (0)**$^{£}$	0 (0)	0 (0)
Sepsis	4 (3.9)	79 (3.3)	9 (2.4)	52 (3)	6 (2.7)	33 (3.1)	4 (2.2)	19 (4.8)
Mechanical ventilation	0 (0)	9 (0.4)	1 (0.3)	5 (0.3)	1 (0.5)	3 (0.3)	1 (0.6)	1 (0.3)
Meconium aspiration	0 (0)	2 (0.1)	0 (0)	1 (0.1)	0 (0)	1 (0.1)	0 (0)	1 (0.3)
Jaundice	**19 (18.6)**	**238 (10)**$^{££}$	**48 (12.6)**	**148 (8.4)**$^{£}$	17 (7.8)	72 (6.8)	10 (5.6)	24 (6.1)
Phototherapy	**15 (14.7)**	**165 (7)**$^{££}$	**34 (8.9)**	**106 (6)**$^{£}$	**18 (8.2)**	**49 (4.6)**$^{£}$	10 (5.6)	11 (2.8)
NND	0 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Composite neonatal outcome**	**25 (24.5)**	**322 (13.6)**$^{££}$	53 (13.9)	216 (12.3)	33 (15.1)	118 (11.1)	21 (11.7)	43 (10.9)

Data are presented as mean ± SD or *n* (%)

APD antepartum fetal death, *IPD* intrapartum fetal death, *LGA* large for gestational age neonate (birth weight ≥ 90 percentile), *NICU* neonatal intensive care unit admission, *HIE* hemorrhagic ischemic encephalopathy, *RDS* respiratory distress syndrome, *NND* neonatal death

*Percentage out of NVD or OVD

**Composite neonatal outcome (≥ 1 of the following): shoulder dystocia, 5-min Apgar score < 7, asphyxia, seizures, HIE, pH < 7.05, hypoglycemia, RDS, sepsis, mechanical ventilation, phototherapy, clavicular fracture, Erb's palsy

$^{£}p < 0.05$, $^{££}p < 0.01$, $^{£££}p < 0.001$ for the difference between delivery and ongoing pregnancy groups. Appear in bold

Table 4 Association of labor induction (vs. expectant management) with adverse maternal and neonatal outcome: multivariable analysis

Variable/week	37 weeks	38 weeks	39 weeks	40 weeks
Cesarean section	1.7 (1.0–3.0)	1.2 (0.9–1.7)	0.8 (0.5–1.3)	0.6 (0.4–1.1)
Clavicle fracture	1.2 (0.2–9.1)	0.5 (0.1–2.0)	**3.3 (1.2–9.5)**	0
NICU admission	**2.5 (1.4–4.4)**	**2.0 (1.4–2.9)**	1.5 (0.9–2.6)	0.6 (0.3–1.3)
Jaundice requiring phototherapy	**2.4 (1.4–4.3)**	**1.5 (1.0–2.3)**	**1.8 (1.1–3.2)**	2.1 (0.9–5.0)
Composite neonatal outcome[a]	**2.2 (1.4–3.6)**	1.2 (0.9–1.6)	1.4 (0.9–2.1)	1.1 (0.6–1.9)

Data are presented as adjusted odds ratio (95% confidence interval). Values reflect the results of a multivariable logistic regression analysis and are adjusted for maternal age, gestational age at delivery, parity, epidural and birth weight

NICU neonatal intensive care unit

[a]Composite neonatal outcome (≥ 1 of the following): shoulder dystocia, 5-min Apgar score < 7, asphyxia, seizures, HIE, pH < 7.05, hypoglycemia, RDS, sepsis, mechanical ventilation, phototherapy, clavicular fracture, Erb's palsy

Table 5 Association of labor induction (vs. expectant management) with adverse maternal and neonatal outcome in a subgroup of nulliparous women: multivariable analysis

Variable/week	37 weeks	38 weeks	39 weeks	40 weeks
CS	1.7 (0.7–4.0)	**1.8 (1.1–2.7)**	0.7 (0.4–1.4)	0.6 (0.3–1.3)
Clavicle fracture	5.5 (0.6–47.8)	0.5 (0.1–3.7)	**5.4 (1.5–20.0)**	0
NICU admission	**4.0 (1.7–9.0)**	1.6 (0.9–2.8)	1.4 (0.7–3.0)	0.3 (0.1–1.1)
Composite neonatal outcome[a]	**3.2 (1.5–6.8)**	1.1 (0.7–1.8)	**1.8 (1.1–3.1)**	1.0 (0.5–2.0)

Data are presented as adjusted OR (95% CI). Values reflect the results of a multivariable logistic regression analysis and are adjusted for maternal age, gestational age at delivery, epidural and birth weight

OR odds ratio, *CI* confidence interval, *CS* cesarean section, *NICU* neonatal intensive care unit

[a]Composite neonatal outcome (≥ 1 of the following): shoulder dystocia, 5-min Apgar score < 7, asphyxia, seizures, HIE, pH < 7.05, hypoglycemia, RDS, sepsis, mechanical ventilation, phototherapy, clavicular fracture, Erb's palsy

425 women with GDM to either IOL or expectant management at 38 weeks' gestation and found no difference in CS rate. Nonetheless, others have found different results, such as Melamed et al. [7]. In their study, they evaluated induction of labor before 40 weeks and its association with CS rate in women with gestational diabetes mellitus. They have found a decrease in CS rate at 38- and 39-weeks' gestation in the IOL group. This decreased rate of CS was still present in a sub analyses of nulliparous women who were induced at 39 weeks of gestation [7]. Their results differ from ours, and the explanation to that might lie in different methodology and inclusion criteria of the studies. Their data were based on a province registry from one province in Canada including many medical centers which may use different management protocols. At out facility, we used a uniform protocol for diagnosis and management of all GDM mothers.

Some studies [6, 16] report no difference in neonatal outcome between IOL and expectant management groups while others [7, 29], including ours, report an increase in NICU admission for the induction group when women were induced < 39 weeks. In accordance with the later, the prevalence of NICU admission is expected to be higher in the early-term gestational age [9, 10] and especially in mothers with GDM who were induced due to a poor glycemic control.

We presented in our study that induction of labor at 39 weeks was associated with clavicular fracture. Nonetheless, the overall prevalence of clavicular fracture in our cohort was approximately 1%, and we did not find concurrent increase in shoulder dystocia, so this finding needs to be interpreted with caution, and we believe it is the result of chance rather than a finding with actual clinical consequences.

Given the retrospective design, some of the information, such as the maternal BMI, actual glycemic control, specific indication for induction of labor and modality of treatment in GDM (nutrition versus oral hypoglycemics or insulin) were not available. Thus, residual confounding cannot be ruled out. In addition, this study is powered insufficiently to assess rare outcomes. Nonetheless, our study included a relatively large cohort of women with GDM undergoing induction of labor versus an expectant management at a single center with uniform guidelines.

In conclusion, compared with expectant management, induction of labor in GDM mothers between 37 and 40 weeks of gestation did not reduce CS rate, and among nulliparous women at 38 weeks, CS rate was even higher. Additionally, IOL prior to 39 weeks of gestation was associated with adverse composite neonatal outcome and/or NICU admission. Therefore, while the recent literature recommends IOL versus expectant management in different populations, we think that women with GDM should be induced when they are presented with additional risk factor for adverse maternal or neonatal outcome, and not due to DGM alone.

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Compliance with ethical standards

Conflict of interest All the authors declare no conflict of interests. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. IRB was approved on September 9th, 2014. Number of approval was RMC-0421–14.

Informed consent Due to the retrospective nature of the study, there was no need for informed consent.

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