ANZJOG

DOI: 10.1111/ajo.13505

ORIGINAL ARTICLE

Maternal and neonatal outcomes of women with gestational diabetes and without specific medical conditions: an Australian population-based study comparing induction of labor with expectant management

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Conflict of Interest: The authors report no conflicts of interest.

Funding information
This project was funded by a Diabetes Australia Research Program Grant. GP was supported with funding from the National Health and Medical Research Council of Australia Project and Investigator Grants #1099655 and #1173991 and the Research Council of Norway through its Centres of Excellence funding scheme #262700. NN is supported by Financial Markets Foundation for Children. SLH is supported by Diabetes NSW and ACT.

Received: 4 June 2021;
Accepted: 3 February 2022

Abstract

Background/aims: To evaluate maternal birth and neonatal outcomes among women with gestational diabetes mellitus (GDM), but without specific medical conditions and eligible for vaginal birth who underwent induction of labour (IOL) at term compared with those who were expectantly managed.

Materials and methods: Population-based cohort study of women with GDM, but without medical conditions, who had a singleton, cephalic birth at 38–41 completed weeks gestation, in New South Wales, Australia between January 2010 and December 2016. Women who underwent IOL at 38, 39, 40 weeks gestation (38-, 39-, 40-induction groups) were compared with those who were managed expectantly and gave birth at and/or beyond the respective gestational age group (38-, 39-, 40-expectant groups). Multivariable logistic regression analysis was used to assess the association between IOL and adverse maternal birth and neonatal outcomes taking into account potential confounding by maternal age, country of birth, smoking, residential location, residential area of socioeconomic disadvantage and birth year.

Results: Of 676 762 women who gave birth during the study period, 66 606 (10%) had GDM; of these, 34799 met the inclusion criteria. Compared with expectant management, those in 38- (adjusted odds ratio (aOR) 1.11; 95% CI, 1.04–1.18), 39- (aOR 1.21; 95% CI, 1.14–1.28) and 40- (aOR 1.50; 95% CI, 1.40–1.60) induction groups had increased risk of caesarean section. Women in the 38-induction group also had an increased risk of composite neonatal morbidity (aOR 1.10; 95% CI, 1.01–1.21), which was not observed at 39- and 40-induction groups. We found no difference between groups in perinatal death or neonatal intensive care unit admission for births at any gestational age.

Conclusion: In women with GDM but without specific medical conditions and eligible for vaginal birth, IOL at 38, 39, 40 weeks gestation is associated with an increased risk of caesarean section.

KEYWORDS
gestational diabetes mellitus, labour induced, labour complications, birth, term, caesarean section

INTRODUCTION

Gestational diabetes mellitus (GDM, diabetes diagnosed in the second/third trimester of pregnancy that was not clearly overt diabetes prior to gestation),[1] is one of the most common complications of pregnancy. GDM is associated with an increased risk of adverse maternal and perinatal outcomes that include caesarean section (CS), macrosomia, large-for-gestational age (LGA) infants, shoulder dystocia, birth trauma and neonatal respiratory issues and hypoglycaemia.[2,3]

Induction of labour (IOL) is indicated when maternal/fetal risks associated with continuation of pregnancy outweigh the risks associated with earlier delivery. In the general population, IOL between 37–41 weeks gestation has been shown to have a number of benefits including decreasing macrosomia related complications, shoulder dystocia and stillbirth.[4,5] In low-risk pregnancies, IOL has been associated with a decreased risk of CS and neonatal morbidity compared with those expectantly managed.[4,6,7] However, the optimal timing and management of birth for GDM pregnancies remain controversial, with limited evidence to support either IOL or expectant management in this population. The lack of consensus in current international guidelines[8] has resulted in significant variation in clinical management of women with GDM. There are no Australian national consensus guidelines concerning the timing of delivery of pregnancies complicated by GDM and local guidelines differ in their recommendations.[9] While randomised controlled trials are limited,[10,11] findings from population-based cohort studies are conflicting with some reporting reduced,[12] no difference or increased[13] rates of CS following IOL compared with expectant management. Similarly, for neonatal outcomes, studies have reported either no difference,[10] or increased rates of neonatal intensive care unit (NICU) admissions[12,13] and reduced perinatal death[14] in women with GDM who underwent IOL. These differences in findings may be explained by different cohort selection.[11-14] Further, although seldom assessed, birth outcomes may have differed by women with different risk profiles.

Population-based data may help inform decisions on management of term GDM pregnancies and birth to balance the risk of known perinatal adverse outcomes associated with GDM, with the potential risk of iatrogenic adverse perinatal outcomes associated with (early/late) obstetric intervention. The aim of this study was to evaluate maternal birth and neonatal outcomes among women with GDM but without specific medical conditions and eligible for vaginal birth who underwent IOL at either 38, 39, 40 weeks gestation compared with those who had expectant management.

MATERIALS AND METHODS

Data sources

Data for this study were extracted from three sources: New South Wales (NSW) Perinatal Data Collection (PDC), a statutory population-based surveillance system covering maternal characteristics, pregnancy, labour, birth and neonatal outcomes for all livebirths and stillbirths in NSW of at least 20 weeks gestation or 400 g birth weight; NSW Admitted Patient Data Collection (APDC), which includes demographic and coded clinical data for all patients admitted to public or private hospitals in NSW; and NSW Registry of Births, Deaths and Marriages (RBDM). All births were identified from NSW PDC, corresponding maternal and infant conditions were obtained from APDC (hospital records) and deaths were obtained from RBDM, to identify infant deaths within the first three months of life. Ethics approval was obtained from the NSW Population and Health Services Research Ethics Committee (2019/ETH11532).

Record linkage

Maternal and infant birth, hospital and death data collections were linked by the NSW Centre for Health Record Linkage (CHeReL) using probabilistic record linkage methods, with a range of personal identifiers to cross-sectionally and longitudinally link individuals' records.[15]

Study population

Inclusion criteria

All women with GDM who had a singleton birth and gestational age at delivery between 38-41 completed weeks gestation inclusive, as determined by the best clinical estimate including early ultrasound and the first day of last menstrual period, in NSW, Australia, between January 2010 and December 2016.

Exclusion criteria

To identify a cohort of women who were suitable for vaginal birth and who were not candidates for early delivery due to the presence of maternal medical conditions, women with any of the following conditions were excluded: women not a candidate for vaginal birth (ie planned CS); major congenital anomalies, or chronic maternal medical conditions that could potentially influence a decision to induce labour at 38, 39 or 40 weeks gestation, including cardiac disease, chronic hypertension, chronic renal disease, autoimmune conditions, haematologic diseases, placenta praevia with or without haemorrhage, chronic obstructive pulmonary disease, psychiatric disorders, prelabour rupture of membranes at term, cholestasis of pregnancy, breech presentation, antepartum haemorrhage or abruption.[16,17] Definitions of these excluded conditions and their related data sources are presented in Supplementary Table S1 and were identified from the Perinatal Data Collection via a related checkbox or APDC where up to 51 clinical diagnoses for each admission are coded by clinical coders using the tenth revision of the International Classification of Diseases Australian Modification (ICD10-AM).

Comparison groups

To compare IOL (women having IOL at a particular gestational age) with expectant management (women giving birth at or beyond the particular gestational age of the IOL comparison group), three comparison groups were defined: (i) women who underwent IOL at 38 weeks gestation (38 + 0 to 38 + 6 weeks inclusive, '38-induction group') were compared with women giving birth anytime between 38–41 weeks gestation; (38 + 0 to 41 + 6 weeks inclusive, '38-expectant group'); (ii) women who underwent IOL at 39 weeks gestation (39 + 0 to 39 + 6 weeks inclusive, '39-induction group') were compared with women giving birth anytime between 39–41 weeks gestation; (39 + 0 to 41 + 6 weeks inclusive, '39-expectant group'); and (iii) women who underwent IOL at 40 weeks gestation (40 + 0 to 40 + 6 weeks inclusive, '40-induction group') were compared with women giving birth anytime between 40–41 weeks gestation; (40 + 0 to 41 + 6 weeks inclusive, '40-expectant group') (Figure 1).

Study outcomes

Maternal birth outcomes included mode of delivery, postpartum haemorrhage (>500 mL) and anal sphincter injury (third- or fourth-degree perineal laceration). We evaluated use of epidural as a possible potential confounder for instrumental birth and anal sphincter injury[18,19] with vaginal births as the denominator for these latter two outcomes.

Neonatal outcomes included low birthweight (<2500 g), small-for-gestational age (SGA; <10th percentile) and LGA age (>90th percentile),[20] admission and hours in intensive care unit, neonatal hypoglycaemia, respiratory morbidity, jaundice requiring phototherapy within 24 h of birth, birth trauma to the nervous system, bone fracture or any birth trauma, neonatal convulsions, five-minute Apgar score <7, shoulder dystocia, perinatal death (stillbirth at ≥20 weeks gestation or neonatal death up to 28 days postpartum) and composite neonatal morbidity (defined as any of the following events: perinatal death, five-minutes Apgar score <7, admission to the NICU, hypoglycaemia, jaundice that required phototherapy or neonatal respiratory morbidity).

Statistical analysis

Descriptive statistics with contingency tables were used to evaluate maternal characteristics (Table 1) of the three study groups with differences tested using χ^2 for categorical variables and *t*-test for continuous variables.

For maternal birth and neonatal outcomes, crude and multivariable logistic regression models with logit link were used to assess the association between IOL and study outcomes adjusting for potential confounders and generalised estimating equations with exchangeable correlation applied to account for the clustering effect of hospitals of birth. Potential confounding variables included maternal age, country of birth, smoking, residential location, residential area of socioeconomic disadvantage and birth year. The analysis was repeated excluding women with previous CS and hypertensive disorders of pregnancy as these may influence timing and method of delivery. Sub-group analysis was also conducted to assess results for specific groups of interest, including nulliparous and multiparous women, women using different treatments for GDM (diet-controlled and insulin) and women with LGA and non-LGA neonates. Analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Characteristics of the study population

During the study period, 676 762 women gave birth in NSW, Australia, with 66 606 (10%) diagnosed with GDM and 34 799 eligible for the study (Figure 1). Overall 5515 women underwent IOL at 38 weeks gestation, 6800 at 39 weeks and 3685 women at 40 weeks gestation. Women in the 38-, 39-, 40-induction groups were slightly older, a lower proportion had a previous CS, but a higher proportion required insulin treatment for GDM and had hypertensive complications compared to those in the 38-, 39-, 40-expectant groups (Table 1). A higher proportion of women in the 38-, 39-induction groups were smokers, with no difference between groups at 40 weeks. Although a lower proportion of women in the 38-induction group were nulliparous, they were more represented in 39-, 40-induction groups compared with respective expectant groups (Table 1).

Compared with women in the expectant groups, women in all induction groups had higher rates of CS, fewer anal sphincter injuries (except for 40-induction group) and greater use of epidural during labour and birth. Women in the 38-induction group had lower rates of instrumental birth, while those in the 39- and 40-induction groups had higher rates compared to those in the 38-, 39-, 40-expectant groups, respectively (Table 2).

A higher proportion of infants of mothers in the 38-, 39-induction groups were LGA compared to expectant groups; with no difference between groups at 40 weeks. Infants born to women in the induction groups had higher rates of neonatal hypoglycaemia, admission to NICU, jaundice that required phototherapy and composite neonatal morbidity (all $P < 0.01$). There was no difference in perinatal deaths between induction and expectant groups (38 weeks, 0.31% vs 0.19%; 39 weeks, 0.21% vs 0.19%; 40-weeks, 0.22% vs 0.15%; all $P > 0.05$) (Table 2).

Association of IOL with adverse maternal and neonatal outcomes

After adjusting for confounders, IOL at 38, 39, 40 weeks gestation was associated with a 11% (adjusted odds ratio (aOR) 1.11; 95% CI, 1.04–1.18), 21% (1.21; 1.14–1.28) and 50% (1.50; 1.40–1.60) increased risk of CS. IOL at 38 weeks gestation was associated with a 10% (1.10; 1.01–1.21) increased risk of composite neonatal morbidity, with no association at 39 (1.06; 0.96–1.17) or 40 (1.00;

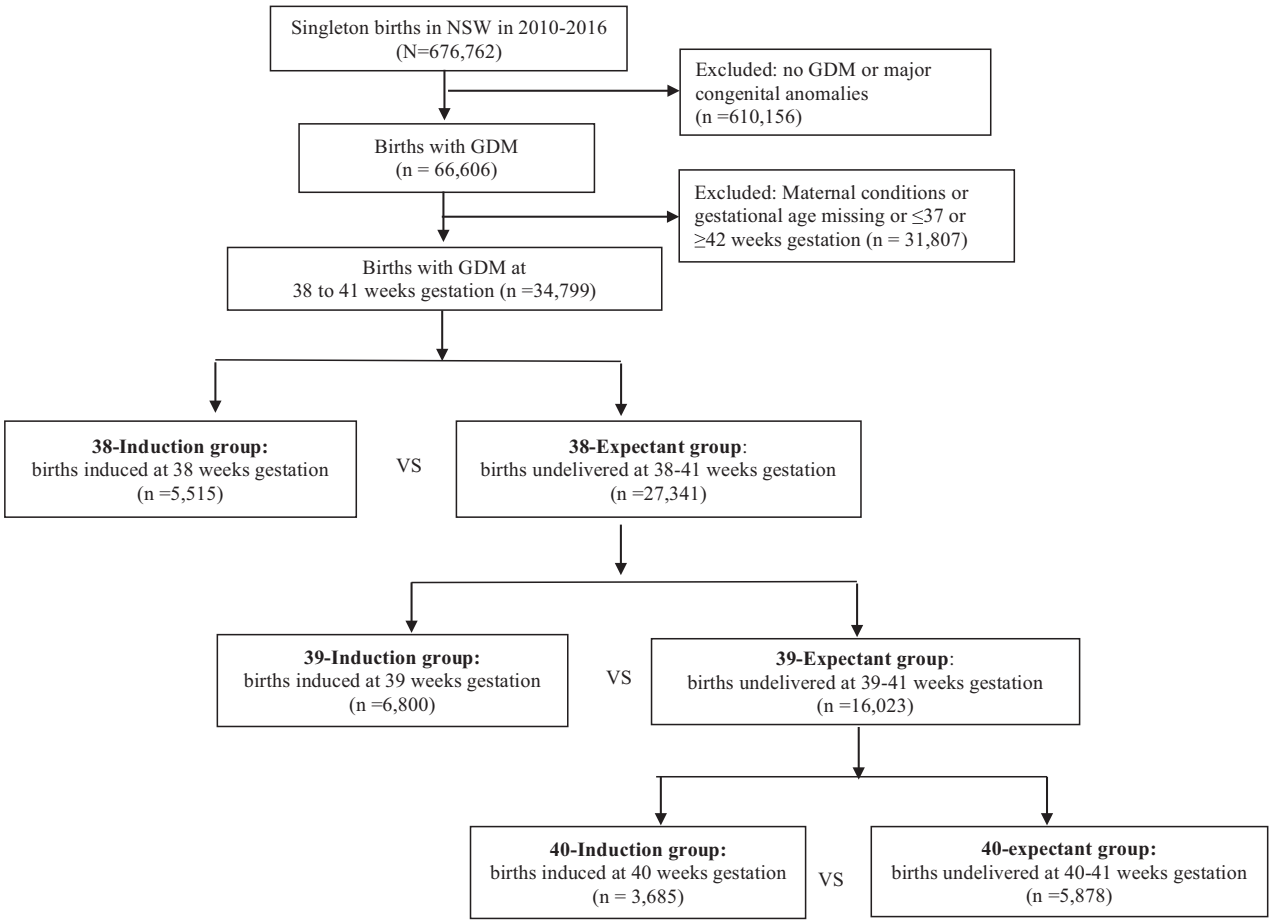

FIGURE 1 Selection of the induction and expectant management groups at 38, 39 and 40 weeks. GDM, gestational diabetes mellitus; NSW, New South Wales.

0.88–1.15) weeks gestation. IOL at 39 and 40 weeks gestation was associated with a 9% (1.09; 1.02–1.17) and 8% (1.08; 1.00–1.17) increased risk of instrumental birth, respectively, while IOL at 39 weeks gestation was associated with a 19% (0.81; 0.68–0.95) decreased risk of anal sphincter injury. There was no association between IOL at 38, 39 or 40 weeks gestation and NICU admission (Table 3). Results were similar when restricting to women without previous CS or hypertensive complications (Table 3).

Sub-group analysis revealed similar findings to the main analysis with increased risk of CS for women in the induction group at all gestations except at 38 weeks for multiparous women and those treated with insulin (Table 4). Neonatal morbidity was increased in the 38-week induction group except for the subgroups of women who were multipara, treated with insulin or with LGA infants. Results for increased odds of instrumental birth were attenuated and only remained among nulliparous women, those treated with diet-alone and had infants not LGA (Table 4).

DISCUSSION

In this large population-based study women with GDM without specific medical conditions and eligible for vaginal birth who underwent IOL at 38, 39, 40 weeks gestation had an increased risk of CS compared to those managed expectantly at or above the respective gestation. This risk was numerically highest in women in the 40-induction group, which was observed irrespective of whether their infant was LGA. Nulliparity appeared to be a risk factor for CS after IOL compared to the expectantly managed group, irrespective of gestational age at the time of IOL. Women receiving pharmacotherapy with oral agents or insulin had a 1.5–3 times higher rate of induction across all gestational age groups compared with those managing GDM with diet. While there is no clear national consensus about timing of birth, women with GDM on insulin may be offered earlier IOL as such a practice can theoretically decrease the risk of LGA and macrosomia and the risk of CS because of dystocia. These data suggest that treatment modality for GDM is a clinical variable considered when determining whether a woman with GDM should be considered for IOL. Compared to those managed expectantly, women in the 38-induction group had increased risk of neonatal morbidity, which was not observed in the 39-, 40-induction groups. Importantly, we found no difference between the groups in perinatal death or NICU admission for birth at any gestational age.

A strength of this study is the large sample size that allowed us to adjust for several significant potential confounding variables. The comprehensiveness of the data allowed us to identify

TABLE 1 Characteristics of women in the induction and expectant management groups

	Weeks of gestation								
	38			39			40		
	Induction of labour (*N* = 5515), *n* (%)	**Expectant management (*N* = 27 341), *n* (%)**	***P*-value**	**Induction of labour (*N* = 6800), *n* (%)**	**Expectant management (*N* = 16 023), *n* (%)**	***P*-value**	**Induction of labour (*N* = 3685), *n* (%)**	**Expectant management (*N* = 5878), *n* (%)**	***P*-value**
Maternal age, years (mean ± *SD*)	31.8 ± 5.2	31.4 ± 5.2	<0.001	31.6 ± 5.2	31.3 ± 5.2	<0.001	31.4 ± 5.3	31.0 ± 5.1	<0.001
Maternal age categories, years			<0.001			<0.001			<0.001
<25	470 (8.5)	2563 (9.4)		587 (8.6)	1591 (9.9)		349 (9.5)	623 (10.6)	
25–34	3355 (60.8)	17 192 (62.9)		4230 (62.2)	10 162 (63.4)		2299 (62.4)	3790 (64.5)	
35–39	1273 (23.1)	5973 (21.8)		1524 (22.4)	3392 (21.2)		772 (20.9)	1194 (20.3)	
≥40	417 (7.6)	1613 (5.9)		459 (6.8)	878 (5.5)		265 (7.2)	271 (4.6)	
Marital status			<0.001			0.12			0.25
Married (including de facto) or widowed	4721 (85.6)	24 125 (88.2)		5940 (87.4)	14 168 (88.4)		3253 (88.3)	5137 (87.4)	
Never married	562 (10.2)	2472 (9.0)		666 (9.8)	1435 (9.0)		333 (9.0)	588 (10.0)	
Divorced or separated	169 (3.1)	544 (2.0)		134 (2.0)	314 (2.0)		68 (1.8)	119 (2.0)	
Country of birth			<0.001			<0.001			<0.001
Australia	3315 (60.1)	11 891 (43.5)		3482 (51.2)	6814 (42.5)		1808 (49.1)	2630 (44.7)	
New Zealand, Europe, Northern America, Central and South America and South Africa	451 (8.2)	2591 (9.5)		689 (10.1)	1520 (9.5)		396 (10.7)	557 (9.5)	
Middle East	167 (3.0)	1296 (4.7)		282 (4.1)	796 (5.0)		140 (3.8)	324 (5.5)	
South and North East Asia	574 (10.4)	5716 (20.9)		959 (14.1)	3495 (21.8)		593 (16.1)	1185 (20.2)	
Southern Asia	676 (12.3)	3868 (14.1)		959 (14.1)	2175 (13.6)		496 (13.5)	717 (12.2)	
Pacific Islands, Africa (excluding South Africa)	231 (4.2)	1283 (4.7)		274 (4.0)	794 (5.0)		162 (4.4)	311 (5.3)	
Residential location			<0.001			<0.001			0.99
Major cities	4484 (81.3)	22 842 (83.5)		5540 (81.5)	13 381 (83.5)		3009 (81.7)	4809 (81.8)	
Regional	760 (13.8)	2975 (10.9)		890 (13.1)	1,702 (10.6)		436 (11.8)	701 (11.9)	
Outer regional / remote	203 (3.7)	1001 (3.7)		268 (3.9)	598 (3.7)		156 (4.2)	246 (4.2)	

(Continues)

TABLE 1 (Continued)

	Weeks of gestation								
	38			39			40		
	Induction of labour (*N* = 5515), *n* (%)	Expectant management (*N* = 27 341), *n* (%)	*P*-value	Induction of labour (*N* = 6800), *n* (%)	Expectant management (*N* = 16 023), *n* (%)	*P*-value	Induction of labour (*N* = 3685), *n* (%)	Expectant management (*N* = 5878), *n* (%)	*P*-value
Residential area of socioeconomic disadvantage			<0.001			<0.001			<0.001
Most disadvantaged	1319 (23.9)	7917 (29)		1807 (26.6)	4678 (29.2)		897 (24.3)	1781 (30.3)	
Least disadvantaged	882 (16)	4494 (16.4)		1137 (16.7)	2670 (16.7)		679 (18.4)	922 (15.7)	
Nulliparity	2333 (42.3)	12 670 (46.3)	<0.001	3414 (50.2)	7649 (47.7)	<0.001	2152 (58.4)	2938 (50)	<0.001
Previous caesarean section	162 (2.9)	1757 (6.4)	<0.001	188 (2.8)	1024 (6.4)	<0.001	115 (3.1)	305 (5.2)	<0.001
Smoking during pregnancy	514 (9.3)	1926 (7)	<0.001	565 (8.3)	1040 (6.5)	<0.001	229 (6.2)	408 (6.9)	0.38
Treatment for gestational diabetes mellitus			<0.001			<0.001			<0.001
Diet	1698 (30.8)	18 164 (66.4)		2721 (40)	12 417 (77.5)		2515 (68.2)	5039 (85.7)	
Insulin	3282 (59.5)	6737 (24.6)		3457 (50.8)	2171 (13.5)		777 (21.1)	341 (5.8)	
Oral glucose-lowering medication	306 (5.5)	1014 (3.7)		294 (4.3)	541 (3.4)		175 (4.7)	144 (2.4)	
Unspecified	229 (4.2)	1426 (5.2)		328 (4.8)	894 (5.6)		218 (5.9)	354 (6.0)	
Hypertensive complications									
Pre-eclampsia	285 (5.2)	396 (1.4)	<0.001	194 (2.9)	161 (1.0)	<0.001	73 (2.0)	40 (0.7)	<0.001
Gestational hypertension	501 (9.1)	1130 (4.1)	<0.001	440 (6.5)	560 (3.5)	<0.001	227 (6.2)	160 (2.7)	<0.001
Male newborn infant	2807 (50.9)	13 852 (50.7)	0.75	3497 (51.4)	7938 (49.5)	<0.01	1828 (49.6)	2876 (48.9)	0.52
Birth year of baby			<0.001			<0.001			<0.001
2010	411 (7.5)	2695 (9.9)		652 (9.6)	1617 (10.1)		385 (10.4)	616 (10.5)	
2011	590 (10.7)	2966 (10.8)		727 (10.7)	1758 (11.0)		406 (11.0)	656 (11.2)	
2012	693 (12.6)	3575 (13.1)		885 (13.0)	2137 (13.3)		545 (14.8)	799 (13.6)	
2013	823 (14.9)	3709 (13.6)		857 (12.6)	2234 (13.9)		465 (12.6)	869 (14.8)	
2014	965 (17.5)	4080 (14.9)		951 (14.0)	2361 (14.7)		433 (11.8)	865 (14.7)	
2015	988 (17.9)	4486 (16.4)		1098 (16.1)	2528 (15.8)		516 (14.0)	862 (14.7)	
2016	1045 (18.9)	5830 (21.3)		1630 (24.0)	3388 (21.1)		935 (25.4)	1211 (20.6)	

Numbers may not add up to totals due to missing data.

TABLE 2 Maternal birth and neonatal outcomes in the induction and expectant management groups

	Weeks of gestation								
	38			39			40		
	Induction of labour (*N* = 5515), *n* (%)	**Expectant management (*N* = 27 341), *n* (%)**	***P*-value**	**Induction of labour (*N* = 6800), *n* (%)**	**Expectant management (*N* = 16 023), *n* (%)**	***P*-value**	**Induction of labour (*N* = 3685), *n* (%)**	**Expectant management (*N* = 5878), *n* (%)**	***P*-value**
Maternal birth outcomes									
Labour induction			<0.001			<0.001			<0.001
Spontaneous	-	15 636 (57.2)		-	11 118 (69.4)		-	4658 (79.2)	
Induced	5515 (100.0)	11 705 (42.8)		6800 (100)	4905 (30.6)		3685 (100)	1220 (20.8)	
Mode of delivery			<0.001			<0.001			<0.001
Normal vaginal	3667 (66.5)	18 508 (67.7)		4244 (62.4)	10 904 (68.1)		2086 (56.6)	3974 (67.6)	
Caesarean section	1132 (20.5)	4768 (17.4)		1479 (21.8)	2635 (16.4)		954 (25.9)	923 (15.7)	
Instrumental	716 (13.0)	4065 (14.9)		1077 (15.8)	2484 (15.5)		645 (17.5)	981 (16.7)	
Use of epidural	2501 (45.3)	9050 (33.1)	<0.001	3116 (45.8)	5007 (31.2)	<0.001	1723 (46.8)	1761 (30.0)	<0.001
Postpartum haemorrhage	618 (11.2)	3068 (11.2)	0.97	800 (11.8)	1883 (11.8)	0.98	519 (14.1)	735 (12.5)	0.03
Anal sphincter injury	132 (2.4)	828 (3.0)	<0.05	171 (2.5)	538 (3.4)	<0.01	124 (3.4)	197 (3.4)	0.97
Neonatal outcomes									
Birthweight, g (mean ± *SD*)	3311 ± 458	3405 ± 431	<0.001	3403 ± 434	3454 ± 421	*<0.001*	3503 ± 421	3529 ± 420	<0.001
Large-for-gestational-age infant	627 (11.4)	2064 (7.5)	<0.001	620 (9.1)	1093 (6.8)	<0.001	278 (7.5)	398 (6.8)	0.15
Small-for-gestational-age infant	544 (9.9)	3079 (11.3)	<0.05	735 (10.8)	1863 (11.6)	0.08	444 (12.0)	709 (12.1)	0.98
Birthweight >4000 g	361 (6.5)	2298 (8.4)	<0.001	559 (8.2)	1547 (9.7)	<0.001	432 (11.7)	745 (12.7)	0.17
Birthweight >4500 g	53 (1.0)	292 (1.1)	0.48	68 (1.0)	200 (1.2)	0.11	56 (1.5)	97 (1.7)	0.62
NICU admissions									
NICU admission	295 (5.3)	1055 (3.9)	<0.001	354 (5.2)	511 (3.2)	<0.001	152 (4.1)	155 (2.6)	<0.001
Hours in NICU (median (quartile range))	24.0 (24.0)	24.0 (30.0)	0.04	24 (34.0)	24.0 (29.0)	0.02	24.0 (30.0)	25.0 (42.0)	0.52
Neonatal hypoglycaemia	63 (1.1)	206 (0.8)	<0.01	63 (0.9)	102 (0.6)	<0.05	26 (0.7)	36 (0.6)	0.58
Respiratory morbidity	203 (3.7)	902 (3.3)	0.15	218 (3.2)	555 (3.5)	0.32	118 (3.2)	229 (3.9)	0.08
Jaundice requiring phototherapy at birth	285 (5.2)	892 (3.3)	<0.001	282 (4.1)	432 (2.7)	<0.001	108 (2.9)	138 (2.3)	0.08
Birth trauma									
Nervous system	21 (0.4)	84 (0.3)	0.38	27 (0.4)	44 (0.3)	0.13	7 (0.2)	17 (0.3)	0.35
Bone / fracture	9 (0.2)	46 (0.2)	0.93	17 (0.3)	24 (0.1)	0.10	7 (0.2)	8 (0.1)	0.52
Any birth trauma	231 (4.2)	1018 (3.7)	0.10	274 (4)	620 (3.9)	0.57	176 (4.8)	244 (4.2)	0.15

(Continues)

TABLE 2 (Continued)

	Weeks of gestation								
	38			39			40		
	Induction of labour (*N* = 5515), *n* (%)	Expectant management (*N* = 27 341), *n* (%)	*P*-value	Induction of labour (*N* = 6800), *n* (%)	Expectant management (*N* = 16 023), *n* (%)	*P*-value	Induction of labour (*N* = 3685), *n* (%)	Expectant management (*N* = 5878), *n* (%)	*P*-value
Neonatal convulsions	8 (0.1)	39 (0.1)	0.97	11 (0.2)	22 (0.1)	0.66	2 (0.1)	12 (0.2)	0.06
5-min Apgar score <7	198 (3.6)	774 (2.8)	<0.01	212 (3.1)	452 (2.8)	0.22	107 (2.9)	164 (2.8)	0.74
Shoulder dystocia	113 (2.0)	452 (1.7)	0.04	136 (2.0)	276 (1.7)	0.15	79 (2.1)	108 (1.8)	0.29
Perinatal death	17 (0.3)	53 (0.2)	0.09	14 (0.2)	30 (0.2)	0.77	8 (0.2)	9 (0.2)	0.47
Composite neonatal morbidity	859 (15.6)	3081 (11.3)	<0.001	930 (13.7)	1634 (10.2)	<0.001	406 (11.0)	567 (9.6)	<0.05

Numbers may not add up to totals due to missing data.
Abbreviation: NICU, neonatal intensive care unit.

a 'low-risk' population.[4,6,12] However, there were some limitations. Lack of information collected on indication for induction may explain the elevated risk of CS rather than the induction per se. This is minimised by use of multiple data sources which contain various measures of pregnancy and birth outcomes, and longitudinal data linkage that enables ascertainment of pre-existing medical conditions. As this is observational data, clinical indicators may have influenced the decision to proceed to IOL, resulting in heterogeneity in maternal risk factors between induction and expectant groups. The study was insufficiently powered to assess rare outcomes such as perinatal mortality. Based on our findings, a randomised trial of over 100 000 and 500 000 low-risk women with GDM at 38 and 39 weeks gestation, respectively, would be required to demonstrate a difference in perinatal mortality between IOL and expectant management. Further, due to lack of data, we were unable to account for all potential confounding factors, including maternal weight/body mass index, which is not routinely collected in the NSW PDC, and may be associated with higher rates of complications. Variation in practice over time may have also influenced our findings but was overcome by adjustment for year of birth.

Our finding of increased risk of CS following IOL is similar to that seen among nulliparous women with GDM in Israel.[13] Other studies have also shown no increase[11] or reduced[12] risk of CS following IOL compared with expectant management in women with GDM. These differences in results from our study may be due to definition of the expectant management comparator groups in each of these studies. While some studies[13] compared women in the IOL group with women expectantly managed at that same week together with those who delivered at some future gestational age, others[12,14] compared women who were delivered at some future gestational age.

Induction has become a common intervention in obstetrics and there has been a considerable rise in women having inductions over recent decades in high income countries.[21,22] IOL was relatively high in our study. In Australia, rates of induction have increased from 25% in 2006 to 31% in 2016.[23] While nearly three-quarters of the observed rate of induction can be explained by socio-demographic (eg age, ethnicity), clinical characteristics of women, co-morbidities, or hospital factors, there remains widespread variation in the incidence of IOL between hospitals, ranging from 9.7% to 41.2%.[22,24] This has been attributed to variability in clinical guidelines in relation to indication and timing of IOL. In relation to GDM, current clinical guidelines present inconsistent recommendations with little consensus on validity and/or timing of induction, particularly in relation to GDM with no maternal/fetal complications.[9] These inconsistencies underline the variability in practice, making it hard for clinicians to provide consistent care and difficult for women to know what is likely to be best for them.

In terms of neonatal outcomes, our study showed no increased risk of NICU admission in the 38-, 39- or 40-induction groups compared with the expectant management groups, but an increased risk of composite neonatal morbidity in the 38-induction group. While some studies reported no increased risk of adverse neonatal outcomes,[10,13] others have shown an increased risk of

TABLE 3 Association between labour induction (vs expectant management) and adverse maternal and neonatal outcome: multivariable logistic regression analysis

	Induction vs expectant management, Odds ratio (95% confidence interval)		
Maternal and neonatal outcomes	**38-week gestation**	**39-week gestation**	**40-week gestation**
Caesarean section*,†			
Crude	1.10 (1.03–1.17)	1.26 (1.18–1.34)	1.62 (1.49–1.77)
Adjusted	1.11 (1.04–1.18)	1.21 (1.14–1.28)	1.50 (1.40–1.60)
No previous caesarean section	1.15 (1.07–1.23)	1.23 (1.15–1.31)	1.53 (1.42–1.64)
No hypertensive complications‡	1.11 (1.03–1.19)	1.21 (1.14–1.29)	1.47 (1.36–1.59)
Instrumental birth*,§,||			
Crude	0.85 (0.77–0.94)	1.05 (0.97–1.14)	1.11 (1.00–1.24)
Adjusted	0.98 (0.91–1.06)	1.09 (1.02–1.17)	1.08 (1.00–1.17)
No previous caesarean section	0.99 (0.92–1.07)	1.11 (1.03–1.18)	1.08 (1.00–1.17)
No hypertensive complications‡	0.97 (0.90–1.06)	1.10 (1.03–1.18)	1.09 (1.01–1.19)
Anal sphincter injury*,§,¶			
Crude	0.81 (0.67–0.99)	0.80 (0.66–0.96)	1.12 (0.87–1.45)
Adjusted	0.93 (0.75–1.15)	0.81 (0.68–0.95)	1.06 (0.81–1.39)
No previous caesarean section	0.95 (0.77–1.18)	0.81 (0.68–0.97)	1.07 (0.83–1.40)
No hypertensive complications‡	0.90 (0.72–1.14)	0.8 (0.68–0.93)	1.10 (0.84–1.45)
NICU admission*			
Crude	1.34 (1.00–1.81)	1.44 (1.07–1.93)	1.51 (1.27–1.78)
Adjusted	1.00 (0.82–1.20)	0.98 (0.80–1.19)	1.12 (0.92–1.36)
No previous caesarean section	1.02 (0.85–1.22)	0.99 (0.8–1.23)	1.14 (0.92–1.41)
No hypertensive complications‡	0.99 (0.82–1.21)	0.96 (0.77–1.2)	1.10 (0.87–1.38)
Composite neonatal morbidity#			
Crude	1.34 (1.20–1.49)	1.30 (1.16–1.45)	1.14 (0.99–1.32)
Adjusted	1.10 (1.00–1.21)	1.06 (0.96–1.17)	1.00 (0.88–1.15)
No previous caesarean section	1.11 (1.01–1.22)	1.05 (0.95–1.17)	1.01 (0.88–1.15)
No hypertensive complications‡	1.11 (1.00–1.22)	1.04 (0.93–1.16)	0.98 (0.86–1.12)

NICU, neonatal intensive care unit.
*Adjustments were made for the following potential confounders: maternal age categories, smoking, birth year of baby, nulliparity, previous caesarean section, pre-eclampsia, gestational hypertension, treatment for GDM, maternal country of birth, residential location, residential area of socioeconomic disadvantage and large for gestational age.
†Caesarean section was compared with any vaginal births (i.e. normal vaginal birth or instrumental birth).
‡Hypertensive complications refer to pre-eclampsia or gestational hypertension.
§Instrumental birth and anal sphincter injury were additional adjusted for: epidural in labor.
||Instrumental birth was compared with normal vaginal births.
¶Anal sphincter injury was restricted to any vaginal births (i.e. normal vaginal birth or instrumental birth).
#Adjustments were made for the following potential confounders: maternal age categories, previous caesarean section, pre-eclampsia, gestational hypertension, treatment for GDM, residential location, and large for gestational age.

NICU admissions when induced prior to 39 weeks gestation.[12,13] This is also consistent with other studies that have suggested the prevalence of neonatal morbidity is higher at early-term gestational age.[25,26]

Our data regarding neonatal outcomes suggest that 'lower-risk' women with GDM can be expectantly managed. Specifically, we showed that perinatal mortality was no different between IOL and expectant management at 38, 39, 40 weeks gestation. This is in contrast to some studies that reported an increase in perinatal morbidity and mortality with increasing weeks of gestation beyond 38-39 weeks.[5] However, these studies included all women with GDM, while our study included only women with GDM without specific medical conditions and eligible for vaginal birth, that is, a cohort of 'lower-risk' women with GDM. While stillbirth accounted for approximately 75-90% of perinatal deaths, due to the nature of our data we are unable to identify if these were intrapartum or antepartum stillbirths. Concerns about late-term stillbirth in women with GDM may lead clinicians to decide to induce at an earlier gestational age, rather than continue the pregnancy and expectantly manage. Such concerns may explain the observation that women

TABLE 4 Association between labour induction (vs expectant management) and adverse maternal and neonatal outcomes, stratified by parity, gestational diabetes mellitus treatment and large-for-gestational-age

	Induction vs expectant management, adjusted odds ratio (95% confidence interval)		
Maternal and neonatal outcomes	**38-week gestation**	**39-week gestation**	**40-week gestation**
Nulliparous			
Caesarean section*,†	1.16 (1.08–1.24)	1.21 (1.14–1.29)	1.57 (1.43–1.71)
Instrumental birth*,§,||	0.97 (0.88–1.06)	1.09 (1.02–1.17)	1.07 (0.98–1.16)
Anal sphincter injury*,§,¶	0.97 (0.75–1.25)	0.74 (0.6–0.9)	1.22 (0.89–1.69)
NICU admission*	1.02 (0.84–1.25)	1.07 (0.83–1.38)	1.08 (0.82–1.44)
Composite neonatal morbidity#	1.12 (1.00–1.26)	1.14 (1.01–1.29)	1.07 (0.91–1.26)
Multiparous			
Caesarean section*,†	0.98 (0.86–1.12)	1.22 (1.08–1.39)	1.28 (1.05–1.57)
Instrumental birth*,§,||	1.06 (0.89–1.27)	1.10 (0.95–1.28)	1.22 (0.92–1.63)
Anal sphincter injury*,§,¶	0.80 (0.51–1.26)	1.04 (0.74–1.48)	N/A
NICU admission*	0.97 (0.76–1.24)	0.88 (0.70–1.10)	N/A
Composite neonatal morbidity#	1.10 (0.95–1.27)	0.95 (0.82–1.09)	0.90 (0.71–1.14)
Treatment for GDM with diet			
Caesarean section*,†	1.24 (1.13–1.37)	1.29 (1.19–1.41)	1.59 (1.47–1.72)
Instrumental birth*,§,||	1.08 (0.95–1.22)	1.13 (1.02–1.25)	1.10 (1.00–1.20)
Anal sphincter injury*,§,¶	0.76 (0.56–1.05)	0.84 (0.64–1.1)	1.00 (0.76–1.33)
NICU admission*	0.99 (0.67–1.45)	1.10 (0.85–1.42)	N/A
Composite neonatal morbidity#	1.20 (1.01–1.45)	1.11 (0.99–1.25)	0.97 (0.82–1.14)
Treatment for GDM with insulin			
Caesarean section*,†	1.07 (0.98–1.17)	1.12 (1.01–1.23)	1.37 (1.08–1.74)
Instrumental birth*,§,||	0.93 (0.84–1.03)	1.03 (0.89–1.18)	0.95 (0.78–1.15)
Anal sphincter injury*,§,¶	1.00 (0.79–1.27)	0.76 (0.62–0.94)	N/A
NICU admission*	0.97 (0.78–1.19)	0.96 (0.82–1.12)	N/A
Composite neonatal morbidity#	1.03 (0.93–1.16)	1.02 (0.90–1.16)	1.04 (0.75–1.45)
Large for gestational age			
Caesarean section*,†	1.19 (1.01–1.42)	1.28 (1.10–1.50)	1.31 (1.02–1.67)
Instrumental birth*,§,||	0.97 (0.70–1.35)	1.11 (0.86–1.43)	1.21 (0.9–1.64)
Anal sphincter injury*,§,¶	0.68 (0.40–1.17)	1.01 (0.62–1.65)	N/A
NICU admission*	0.84 (0.58–1.20)	1.19 (0.83–1.7)	N/A
Composite neonatal morbidity#	1.10 (0.90–1.35)	1.21 (0.97–1.5)	N/A
Not large for gestational age			
Caesarean section*,†	1.10 (1.04–1.17)	1.20 (1.13–1.27)	1.52 (1.41–1.63)
Instrumental birth*,§,||	0.99 (0.91–1.08)	1.10 (1.03–1.18)	1.08 (1.00–1.17)
Anal sphincter injury*,§,¶	0.97 (0.77–1.21)	0.79 (0.66–0.94)	1.03 (0.76–1.40)
NICU admission*	1.02 (0.85–1.23)	0.96 (0.77–1.20)	1.14 (0.93–1.40)
Composite neonatal morbidity#	1.11 (1.01–1.22)	1.04 (0.93–1.16)	1.03 (0.89–1.19)

N/A, not available: due to the small sample size we were unable to calculate adjusted odds ratio (95% confidence interval); NICU, neonatal intensive care unit.

*Adjustments were made for the following potential confounders: maternal age categories, smoking, birth year of baby, nulliparity, previous caesarean section, pre-eclampsia, gestational hypertension, treatment for GDM, maternal country of birth, residential location, residential area of socioeconomic disadvantage and large for gestational age. For the outcome of interest, this variable was not included as a confounder. For example, for the outcome nulliparous, nulliparity was not included as a confounder.

†Caesarean section was compared with any vaginal births (i.e. normal vaginal birth or instrumental birth).

§Instrumental birth and anal sphincter injury were additional adjusted for: epidural in labor.

||Instrumental birth was compared with normal vaginal births.

¶Anal sphincter injury was restricted to any vaginal births (i.e. normal vaginal birth or instrumental birth).

#Adjustment were made for the following potential confounders: maternal age categories, previous caesarean section, pre-eclampsia, gestational hypertension, treatment for GDM, residential location, and large for gestational age.

in 38-, 39-induction groups had more risk factors for adverse pregnancy outcomes including treatment with insulin, a higher prevalence of hypertensive disorders and more LGA infants.

In conclusion, among women with GDM but without specific medical conditions and eligible for vaginal birth, IOL at 38, 39, 40 weeks gestation was associated with an increased risk of CS, particularly at 40 weeks gestation, an increased risk of composite neonatal morbidity at 38 weeks gestation, which was not observed in the 39-, 40-induction groups and no difference in NICU admission or perinatal death. Although results should be confirmed in future randomised controlled trials, findings provide support that the optimal timing of IOL is at 39 weeks gestation and evidence for women and clinicians to make informed decisions regarding timing of birth and expectant management for women with GDM but without specific medical conditions and eligible for vaginal birth at term.

AUTHOR CONTRIBUTIONS

SLH, SKMS and NN developed the research question and designed the study. RVS, NN, FJS and GP did the data analysis. All authors contributed to the data interpretation. AM, GPR, ANS, SKMS and SLH provided clinical insight. RVS drafted the manuscript. All authors contributed to revision of the manuscript and approved the final version to be published.

ACKNOWLEDGEMENTS

Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Total number and definition of excluded conditions among women with gestational diabetes.