# Induction of Labor versus Cesarean Delivery in Twin Pregnancies

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## **Abstract**

**Objective** This study was aimed to compare maternal and neonatal outcomes between women with twin pregnancies who underwent induction of labor with those women who had planned Cesarean delivery (CD).

**Study Design** This is a retrospective cohort study of women with twin pregnancies  $\geq$  24 weeks with an indication for delivery but not in labor. Two groups were examined, women who underwent induction and women who underwent planned CD. Maternal and neonatal outcomes were compared between groups both for deliveries at qestational age  $\geq$  37 weeks and < 37 weeks.

**Results** A total of 453 patients were included. Overall, 212 (46.8%) women underwent induction and 241 (53.2%) underwent planned CD. Women who underwent induction of labor had a high rate of VD, both in the term and preterm groups (69.8 and 73.6%, respectively). Women who underwent induction of labor had reduced maternal length of stay, neonatal length of stay, and blood loss, without any increase in adverse outcomes. Neonatal ventilation of either twin delivered < 37 weeks was higher in the CD compared with induction group (27.5 vs. 9.4%, p < 0.01), but this was not significant on adjusted odds ratio analysis (aOR = 0.71, 95% CI: 0.19–2.66).

**Conclusion** Labor induction in twin gestations have improved maternal outcomes and similar neonatal outcomes compared with planned CD.

# Keywords

- ► twin delivery
- ► induction of labor
- elective cesarean

The prevalence of twin pregnancies has increased in the United States over the last two decades, currently representing approximately 3% of all deliveries. As many as 75% of these twins are delivered by Cesarean delivery (CD), attributed to rising rates of elective CD in this population. The optimal mode of delivery for twin births, however, continues to be debated. Many recent studies have focused on the maternal and neonatal outcomes of planned vaginal delivery (VD) compared with planned CD for twin pregnancies. These studies have generally supported American College of Obstetricians and Gynecologists' (ACOG) recommendation to offer a VD for patients with twin pregnancies and no contra-

indications to labor.<sup>6</sup> These studies, however, do not address the clinical scenario of a twin pregnancy who has an indication for delivery but is not in labor. For example, twins at 37 or 38 weeks of gestation are usually scheduled for delivery by induction or CD at this time<sup>6,7</sup>; also, many twins require delivery prior to 37 weeks for indications, such as hypertensive disorders of pregnancy, fetal growth restriction, and cholestasis of pregnancy.<sup>6,7</sup> In this situation, the only two options are induction of labor and CD. With the possibility of spontaneous labor removed, it is unclear if in this setting a planned VD (i.e., induction of labor) is associated with similar outcomes as a planned CD.

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Data regarding induction of labor in twin pregnancies are limited. One retrospective study showed no differences in rates of successful VD or length of labor in women with twin pregnancies undergoing induction of labor compared with those women with singleton pregnancies. The study concluded that these results should be reassuring to women who opt for an induction of labor; their chance of successful VD is high. There have been few studies, however, that have examined the maternal and neonatal outcomes of women undergoing induction of labor with twin pregnancies as compared with women who have a planned CD.

In this study, we sought to compare maternal and neonatal outcomes between women with twin pregnancies who underwent induction of labor and planned CD.

# **Materials and Methods**

This was a retrospective cohort study of all women who were delivered by a single maternal-fetal medicine practice between July 2005 (when our computerized medical record was created) and February 2018. We included all women who delivered live twins  $\geq 24$  weeks of gestational age (GA). We excluded women with intrauterine fetal death of either twin, major fetal anomalies discovered before or after birth of either twin, twin–twin transfusion syndrome, monochorionic-monoamniotic twins, women with placenta previa, vasa previa, and history of prior CD or myomectomy.

Decisions concerning mode of delivery, timing of delivery, and labor management were made clinically according to contemporary guidelines and best practices. Induction of labor was performed according to the labor induction protocol for twin pregnancies of our practice. For patients who required cervical ripening, we used a transcervical Foley's catheter with a 60-mL balloon which was applied to gentle traction. Once the cervix was dilated, amniotomy was performed, and intravenous oxytocin was administered toward a goal of contractions approximately every 3 minutes. For patients with a favorable cervical examination, amniotomy was performed with or without the administration of intravenous oxytocin as necessary.

Our protocol for twin delivery has been previously described. Briefly, women are considered candidates for VD if the first twin is in cephalic presentation with no other contraindications to vaginal birth. If the second twin is noncephalic, the estimated fetal weight for the second twin must be  $\geq 1,500~g$  and the estimated fetal weight discordancy must be <20% to be eligible for vaginal birth. There must be no other contraindications to labor. In our practice, we utilized active management of the second stage for twin deliveries which included breech extraction of the noncephalic second twin, as well as internal podalic version, and breech extraction of a cephalic but unengaged second twin.

We categorized patients by their GA at delivery ( $\geq$  37 weeks or < 37 weeks), as the indications for delivery would be different for these groups. For women with GA  $\geq$  37 weeks, indications for delivery would mostly be due to the GA of the pregnancy. For women with GA < 37 weeks,

indications for delivery would all be for a complication of pregnancy. In each GA group, women who underwent induction of labor were compared with women who underwent planned CD. We excluded women who went into spontaneous labor or had premature rupture of membranes for both groups. Women who were eligible for VD but elected to have a CD were classified in the group having a planned CD. Women who were not eligible for VD (such as breech presentation of the presenting twin) were also classified in the group having a planned CD. Among women who delivered < 37 weeks of GA, we also excluded women who were delivered for the indications of abruption, nonreassuring fetal status, and any pregnancy with fetal growth restriction that also had absent or reverse end-diastolic flow on the umbilical artery Dopplers.

Maternal baseline characteristics, delivery information, and hospitalization course were obtained by review of the outpatient and inpatient medical records. All patients were delivered at Mount Sinai Hospital which is a large tertiary academic medical center in New York City.

Maternal outcomes included mode of delivery, median maternal length of stay (LOS) after delivery, estimated blood loss (EBL), EBL  $\geq$  1,000, EBL  $\geq$  1,500, transfusion, third- or fourth-degree lacerations, endometritis (defined clinically as postpartum fever requiring antibiotics), wound complications (separation requiring packing or reclosure or infection requiring antibiotics), thrombosis, hysterectomy, bowel or bladder injury, intensive care unit (ICU) admission, maternal death and finally composite maternal morbidity (combining thrombosis, hysterectomy, bowel or bladder injury, ICU admission, and maternal death).

Neonatal outcomes included median LOS for each baby, neonatal intensive care unit (NICU) admission, ventilation, sepsis (confirmed with positive blood cultures), necrotizing enterocolitis, fracture, Erb's palsy, intraventricular hemorrhage (defined as a germinal matrix hemorrhage grade II or higher), intracranial hemorrhage, and neonatal death. For neonatal outcomes, we compared outcomes per mother; meaning, each outcome was considered present if either (or both) twin had the adverse outcome.

Comparisons between the two groups were performed using Chi-square and Student's t-test as appropriate (IBM SPSS for Windows 22.0, IBM Corp., Armonk, NY). Nonparametric testing (Mann-Whitney U-test) was performed for the variables EBL, maternal LOS, and neonatal LOS. A pvalue of  $\leq 0.05$  was considered statistically significant. Multiple regression analysis was performed for maternal and neonatal outcomes to control for differences in baseline characteristics between groups. Regression was first performed adjusting for all baseline differences between groups with a p-value of 0.05 or less. To remove the possibility of over-adjustment, regression was then repeated, controlling for a single characteristic that was thought to be the most important covariate. For the  $GA \ge 37$  weeks group, the variable was nulliparity; for the GA < 37 weeks group, the variable was GA at delivery.

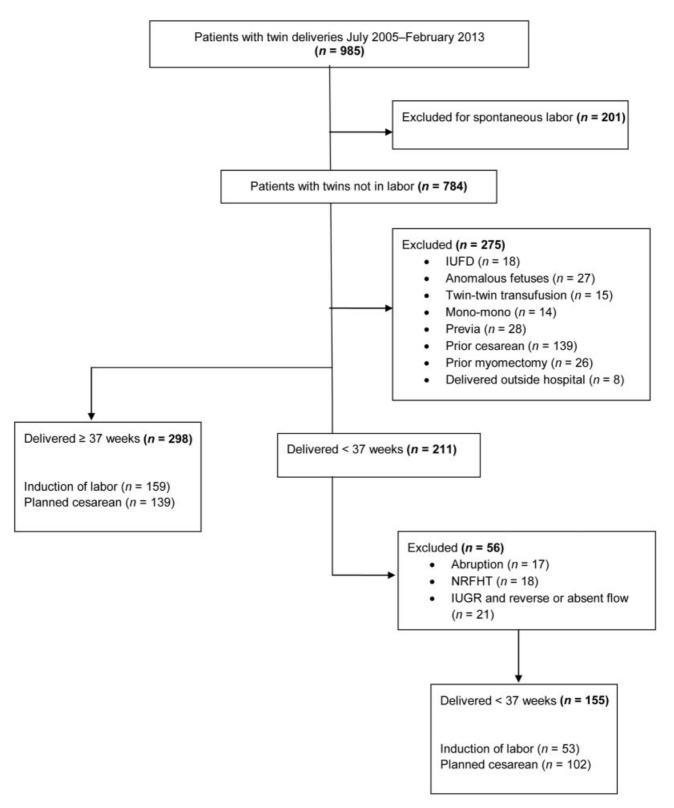
This project was approved by the Biomedical Research Alliance of New York Institutional Review Board.

### Results

Four hundred and fifty-three patients met inclusion criteria of whom 212 (46.8%) women underwent induction and 241 (53.2%) underwent planned CD. The patient flow diagram is shown in **Fig. 1**. Baseline characteristics of both groups are

shown in **Table 1**. Indications for induction included a GA beyond the indicated timing of delivery (53.8%), hypertensive disease (20.3%), intrauterine growth restriction with normal Doppler's (18.9%), and cholestasis (7.1%).

Among women delivered  $\geq$  37 weeks, 159 (53.4%) underwent induction and 139 (46.6%) underwent planned CD.



**Fig. 1** Flow chart of patients with twin deliveries from July 2005 to February 2013. IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction; NFHT, nonreassuring fetal heart tracing.

Table 1 Baseline characteristics of women with twin pregnancies undergoing induction of labor versus cesarean delivery

Baseline characteristics	Induction of labor	Cesarean delivery	<i>p</i> -Value
≥ 37 weeks of GA	(n = 159)	(n = 139)	
Maternal age (y)	33.4 ± 6.3	35.0 ± 5.7	0.03
White race (%)	134 (84.3)	120 (86.3)	0.62
Prepregnancy BMI (kg/m²)	23.3 ± 4.1	23.9 ± 4.6	0.23
In vitro fertilization (%)	83 (52.2)	85 (61.2)	0.12
Nulliparity (%)	96 (60.4)	104 (74.8)	0.008
Receiving anticoagulation (%)	4 (2.5)	7 (5.0)	0.21
Fibroids	7 (4.4)	9 (6.5)	0.30
Chorionicity			
Monochorionic diamniotic (%)	30 (18.9)	11 (7.9)	0.006
Dichorionic diamniotic (%)	129 (81.1)	128 (92.1)	
Gestational hypertension (%)	23 (14.5)	24 (17.3)	0.79
Preeclampsia (%)	12 (7.6)	13 (9.5)	0.57
Gestational diabetes (%)	16 (10.1)	16 (11.6)	0.67
GA at delivery (wk)	37.7 ± 0.9	37.7 ± 0.5	0.99
Mean birth weight smaller twin (g)	2,567.0	2,599.0	0.18
Mean birth weight larger twin (g)	2,847.0	2,896.0	0.16
Mean discordance in birth weight %	9.6%	10.0%	0.64
Discordance in birth weight > 20% (%)	13 (8.2)	18 (12.9)	0.18
Cervical dilation		-	-
0 cm (%)	20 (12.6)	-	-
1–2 cm (%)	66 (40.3)	-	-
3–4 cm (%)	62 (37.7)	-	-
≥ 5 cm (%)	7 (4.4)	-	-
Cervical effacement			
0-30%	36 (22.6%)	-	-
40–50%	40 (25.2%)	-	-
60-80%	66 (41.5%)	-	-
> 80%	8 (5.0%)	-	-
< 37 weeks of GA	(n = 53)	(n = 102)	
Maternal age (years)	33.4 ± 5.5	36.8 ± 6.7	0.002
White race (%)	43 (81.1)	77 (75.5)	0.43
Prepregnancy BMI (kg/m²)	22.9 ± 5.1	23.9 ± 4.5	0.21
In vitro fertilization (%)	24 (45.3)	65 (63.7)	0.03
Nulliparity (%)	34 (64.2)	90 (88.2)	< 0.001
Receiving anticoagulation (%)	0 (0.0)	4 (3.9)	0.21
Fibroids (%)	2 (3.8)	7 (6.9)	0.08
Chorionicity			
Monochorionic diamniotic (%)	17 (32.1)	16 (15.7)	0.02
Dichorionic diamniotic (%)	36 (67.9)	86 (84.3)	
Indications for delivery			
GHTN/preeclampsia (%)	19 (35.8)	65 (63.7)	< 0.001
Fetal growth restriction (%)	25 (47.2)	46 (45.1)	0.81

Table 1 (Continued)

Baseline characteristics	Induction of labor	Cesarean delivery	<i>p</i> -Value
≥ 37 weeks of GA	(n = 159)	(n = 139)	
Cholestasis	9 (17.0)	6 (5.9)	0.03
GA at delivery (wk)	35.9 ± 0.7	34.9 ± 1.9	< 0.001
< 32 wk (%)	1 (1.9)	6 (5.9)	0.42
32-36 <sup>6/7</sup> wk (%)	52 (98.1)	95 (94.1)	
Mean birth weight smaller twin (g)	2,053.4	1,981.2	0.48
Mean birthweight larger twin (g)	2,380.0	2,331.3	0.28
Mean discordance in birth weight (%)	13.4	15.3	0.23
Discordance in birth weight > 20% (%)	15 (28.3)	37 (36.3)	0.32
Cervical dilation in initial exam			
0 cm (%)	12 (22.6)	-	-
1–2 cm (%)	17 (32.1)	-	-
3–4 cm (%)	17 (32.1)	-	_
≥ 5 cm (%)	5 (9.4)	-	-
Cervical effacement in initial exam			
0-30%	14 (26.4%)	-	_
40-50%	17 (32.1%)	-	-
60-80%	15 (28.3%)	-	-
> 80%	5 (9.4%)	-	_

Abbreviations: BMI, body mass index; GA, gestational age; GHTN, gestational hypertension.

Women who underwent induction of labor ≥ 37 weeks of GA were more likely to be younger and parous with monochorionic-diamniotic placentation than women who underwent planned CD. Of the women who underwent induction of labor, 20 (12.6%) women had a closed cervix on initial exam.

Among women who underwent delivery < 37 weeks, 53 (34.2%) underwent induction and 102 (65.8%) underwent planned CD. Women who underwent induction of labor < 37 weeks were more likely to be younger, non-IVF (in vitro fertilization), parous, have a monochorionic-diamniotic placentation, have GHTN/preeclampsia, have cholestasis, and deliver at a later GA than women who underwent planned CD. Of the women who underwent induction of labor, 12 (22.6%) women had a closed cervix on initial exam.

Maternal and neonatal outcomes for deliveries  $\geq 37$  weeks of GA are shown in **Fable 2**. Among women who underwent induction of labor, the rate of VD is quite high, with 111 (69.8%) successful VD of both. Women who underwent induction had a significantly shorter postpartum LOS than women who had a planned CD (2 vs. 4 days, p < 0.001). Women who underwent induction had a significantly lower median EBL and EBL  $\geq 1,000$  mL; however, this did not translate to a lower rate of blood transfusion (6.3 vs. 4.3%, p = 0.44). Five women who underwent induction of labor had an event captured by the composite maternal morbidity, but this was not significantly different between groups (3.1

vs. 0.0%, p=0.06). All other maternal outcomes including EBL  $\geq$  1,500 mL, endometritis, thrombosis, wound complications, hysterectomy, bowel/bladder injury, ICU admission, and maternal death were rare and not significantly different between groups.

Similarly, mothers who underwent induction of labor  $\geq$  37 weeks of GA had neonates with a shorter LOS compared with women who had planned CD (maximum LOS: 2 vs. 4 days, p < 0.001). More neonates in the induction group were admitted to the NICU but this was not significant (10.1 vs. 4.3%, p = 0.06). All other neonatal outcomes including ventilation, sepsis, necrotizing enterocolitis, fracture, Erb's palsy, intraventricular hemorrhage, intracranial hemorrhage, and neonatal death were rare and not significantly different between groups.

We performed a regression analysis to estimate the association between intended mode of delivery and maternal and neonatal outcomes at  $\geq$  37 weeks of GA, adjusting for variables found to be different in the univariable analysis (**\vdashTable 3**). After adjusting for differences in all baseline characteristics, maternal and neonatal LOS remained shorter and EBL lower among women who underwent induction. We performed a second analysis only adjusting for parity and we found a similar result.

Maternal and neonatal outcomes for deliveries < 37 weeks of GA are shown in ►**Table 4**. Again, among women who underwent induction of labor, the rate of VD is quite high, with 39 (73.6%) successfully delivering both twins vaginally.

**Table 2** Maternal and neonatal outcomes of women having twin deliveries by induction of labor versus cesarean delivery  $\geq$  37 weeks of GA<sup>a</sup>

Outcomes	Induction of labor $(n = 159)$	Cesarean delivery (n = 139)	<i>p</i> -Value
Maternal Outcomes			< 0.001
Mode of delivery (%)			
VD	111 (69.8)	0 (0.0)	
VD-CD	1 (0.6)	0 (0.0)	
CD	47 (29.6)	139 (100.0)	
Length of stay postpartum (d) <sup>b</sup>	2 (2, 3)	4 (3, 4)	< 0.001
EBL (mL) <sup>b</sup>	500 (500, 800)	800 (800, 1,000)	< 0.001
EBL ≥ 1,000 mL (%)	31 (19.6)	61 (43.9)	< 0.001
EBL ≥ 1,500 mL (%)	11 (7.0)	7 (5.0)	0.49
Transfusion	10 (6.3)	6 (4.3)	0.44
Third/fourth degree laceration (%)	1 (0.6)	0 (0.0)	0.35
Endometritis (%)	3 (1.9)	1 (0.7)	0.63
Wound complications (%)	1 (0.6)	0 (0.0)	0.99
Composite maternal morbidity (%)	5 (3.1)	0 (0.0)	0.06
Thrombosis (%)	2 (1.3)	0 (0.0)	0.51
Hysterectomy (%)	2 (1.3)	0 (0.0)	0.51
Bowel/bladder injury (%)	0 (0.0)	0 (0.0)	0.99
ICU admission (%)	2 (1.3)	0 (0.0)	0.51
Maternal death (%)	0 (0.0)	0 (0.0)	0.99
Neonatal outcomes			
Neonatal LOS (days) for the twin discharged second <sup>b</sup>	2 (2, 4)	4 (3, 4)	< 0.001
Neonatal LOS (days) for the twin discharged first <sup>b</sup>	2 (2, 3)	4 (3, 4)	< 0.001
NICU admission (either twin; %)	16 (10.1)	6 (4.3)	0.06
Ventilation (either twin; %)	2 (1.3)	1 (0.7)	0.99
Sepsis (either twin; %)	0 (0.0)	0 (0.0)	0.99
Necrotizing enterocolitis (either twin; %)	0 (0.0)	0 (0.0)	0.99
Fracture or Erb's palsy (either twin; %)	3 (1.9)	0 (0.0)	0.25
Intraventricular hemorrhage (either twin; %)	0 (0.0)	0 (0.0)	0.99
Intracranial hemorrhage (either twin; %)	0 (0.0)	0 (0.0)	0.99
Neonatal death (either twin; %)	0 (0.0)	0 (0.0)	0.99

Abbreviations: CD, Cesarean delivery; EBL, estimated blood loss; GA, gestational age; ICU, intensive care unit; LOS, length of stay; NICU, neonatal intensive care unit; VD, vaginal delivery.

Women who underwent induction had a significantly shorter postpartum LOS than women who had a planned CD (2 vs. 4 days, p=0.03). Women who underwent induction had a significantly lower median EBL and EBL  $\geq$  1,000 mL; however, this did not translate to a lower rate of blood transfusion (13.2 vs. 6.9%, p=0.19). No women in either group had an event captured by the composite maternal morbidity. All other maternal outcomes were rare and not significantly different between groups. We performed an analysis excluding the

seven patients delivered < 32 weeks and found no difference in the results (data not shown).

Neonatal LOS at GA < 37 weeks was also shorter for the induction group than planned CD (maximum 4 vs. 8 days, p=0.001). Fewer neonates were admitted to the NICU in the induction of labor group than planned CD, but this was not significant (54.7 vs 64.7%, p=0.23). Neonates in the induction group were significantly less likely to require ventilation (9.4 vs. 27.5%, p=0.01) and less likely to have sepsis (0.0 vs.

<sup>&</sup>lt;sup>a</sup>Parametric testing was performed for all analyses except estimated blood loss, maternal length of stay, and neonatal length of stay which were nonparametric.

<sup>&</sup>lt;sup>b</sup>Reported as a median (interquartile range).

**Table 3** Odds of maternal and neonatal morbidity by induction of labor vs. cesarean delivery  $\geq$  37 weeks of GA<sup>a</sup>

Outcomes	OR/correlation coefficient	aOR/correlation coefficient <sup>b</sup>	Adjusted for parity only
Maternal outcomes			
Length of stay postpartum (days)	-1.22 (-1.44, to -0.99)	-1.17 (-1.39 to -0.94)	-1.19 (-1.41 to -0.97)
EBL (mL)	-203.9 (-287.0 to -120.9)	-181.2 (-265.2 to -97.2)	-184.1 (-267.1 to -101.0)
EBL ≥ 1,000 mL	0.32 (0.19-0.54)	0.35 (0.21-0.59)	0.34 (0.20-0.57)
EBL ≥ 1,500 mL	1.41 (0.53–3.75)	1.63 (0.59–4.46)	1.59 (0.59–4.26)
Transfusion	1.81 (0.60-5.43)	1.63 (0.56–4.70)	1.91 (0.63–5.78)
Endometritis	2.65 (0.27–25.81)	2.79 (0.28–27.40)	2.41 (0.24–23.95)
Neonatal Outcomes			
Neonatal LOS (days) for the twin discharged second	-0.96 (-1.47 to -0.46)	-0.92 (-1.44 to -0.39)	-0.90 (-1.41 to -0.38)
Neonatal LOS (days) for the twin discharged first	-1.21 (-1.43 to -0.99)	-1.17 (-1.39 to -0.94)	-1.18 (-1.40 to -0.96)
NICU admission (either twin)	2.31 (0.87–6.13)	2.49 (0.92–6.70)	2.61 (0.98–6.94)
Ventilation (either twin)	1.76 (0.16–19.60)	1.92 (0.16–22.63)	2.17 (0.19–24.34)

Abbreviations: aOR, adjusted odds ratio; EBL, estimated blood loss; GA, gestational age; LOS, length of stay; NICU, neonatal intensive care unit. a Continuous variables (EBL, LOS) are reported as correlation coefficients while categorical variables (transfusion, endometritis, NICU admission, and ventilation) are reported as odds ratios.

6.9%, p = 0.05). All other neonatal outcomes were not significantly different between groups.

We performed a regression analysis to estimate the association between intended mode of delivery and maternal and neonatal outcomes at < 37 weeks of GA, adjusting for variables found to be different in the univariable analysis (>Table 5). After adjusting for differences in all baseline characteristics, maternal LOS remained shorter and EBL remained lower among women who underwent induction. Neonatal LOS and ventilation, however, were no longer significant after adjustment. After adjustment for GA at delivery, neonatal LOS was no longer significantly different between groups; after adjustment for differences in baseline characteristics, ventilation of either twin was no longer significantly different between groups. This suggests that differences between groups and the earlier GA at delivery in the planned CD group accounts for the observed differences in neonatal outcomes on univariate analysis.

Finally, we performed an exploratory subanalysis comparing women who underwent induction of labor with an unfavorable, closed cervix to all women undergoing planned CD. The rates of VD for these women were still quite high, with a VD rate of 65.0% among women who underwent induction at  $\geq$  37 weeks and 66.7% among women who underwent induction of labor < 37 weeks. The maternal and neonatal LOS was shorter and median EBL lower for women who underwent induction of labor with a closed cervix compared with planned CD both for term and preterm deliveries. For twins delivered at  $\geq$  37 weeks, there were no significant differences in all other maternal outcomes be-

tween women who were induced with a closed cervix and those who underwent planned CD, including transfusion (5.0 vs. 4.3%, p=0.44) and composite maternal morbidity (0.0 vs. 0.0%, p=0.99). There were also no significant differences in neonatal outcomes including NICU admission (10.0 vs. 4.3%, p=0.26) and ventilation (0.0 vs. 0.7%, p=0.99). This also held true for maternal and neonatal outcomes of twins delivered <37 weeks.

#### Comment

Our data suggest that there are improved maternal outcomes and no significant differences in neonatal outcomes for women with twin pregnancies between those who underwent induction of labor or planned CD. Women who underwent induction of labor both at  $\geq$  37 and < 37 weeks had a shorter LOS and lower blood loss compared with women underwent planned CD. Neonates delivered  $\geq$  37 weeks of GA, additionally had a shorter LOS after induction compared with planned CD. Serious maternal and neonatal morbidity were rare in this cohort. Among women who delivered ≥ 37 weeks, the rate of composite morbidity and NICU admission were higher in women who underwent induction of labor compared with planned CD, with the rate of these outcomes between groups approaching significance. While it is possible that with larger numbers these results may reach statistical significance, the absolute rates of these complications are so low among women who underwent induction of labor that they may still not be a clinically meaningful difference.

<sup>&</sup>lt;sup>b</sup>Adjusted for differences in baseline maternal age, nulliparity and chorionicity.

**Table 4** Maternal and neonatal outcomes of women having twin deliveries by induction of labor versus Cesarean delivery < 37 weeks of GA<sup>a</sup>

Outcomes	Induction of labor (n = 53)	Cesarean delivery (n = 102)	<i>p</i> -Value
Maternal outcomes			
Mode of delivery			
VD (%)	39 (73.6)	0 (0.0)	< 0.001
VD-CD (%)	0 (0.0)	0 (0.0)	
CD (%)	14 (26.4)	102 (100.0)	
Length of stay postpartum (days; %) <sup>b</sup>	2 (2, 3)	4 (4, 4)	0.03
EBL (mL) <sup>b</sup>	500 (450, 800)	800 (800, 1,000)	< 0.001
EBL ≥ 1,000 mL (%)	8 (15.7)	40 (39.2)	0.003
EBL ≥ 1,500 mL (%)	4 (7.8)	7 (6.9)	0.83
Transfusion (%)	7 (13.2)	7 (6.9)	0.19
Third/fourth degree laceration (%)	0 (0.0)	0 (0.0)	0.99
Endometritis (%)	1 (1.9)	6 (5.9)	0.42
Wound complications (%)	2 (3.8)	1 (1.0)	0.27
Composite maternal morbidity (%)	0 (0.0)	0 (0.0)	0.99
Thrombosis (%)	0 (0.0)	0 (0.0)	0.99
Hysterectomy (%)	0 (0.0)	0 (0.0)	0.99
Bowel/bladder injury (%)	0 (0.0)	0 (0.0)	0.99
ICU admission (%)	0 (0.0)	0 (0.0)	0.99
Maternal death (%)	0 (0.0)	0 (0.0)	0.99
Neonatal outcomes			
Neonatal LOS (days) for the twin discharged second <sup>b</sup> (%)	4 (2, 9)	8 (4, 22)	0.001
Neonatal LOS (days) for the twin discharged first <sup>b</sup> (%)	3 (2, 6)	4 (4, 17)	0.05
NICU admission (either twin; %)	29 (54.7)	66 (64.7)	0.23
Ventilation (either twin; %)	5 (9.4)	28 (27.5)	0.01
Sepsis (either twin; %)	0 (0.0)	7 (6.9)	0.05
Necrotizing enterocolitis (either twin; %)	0 (0.0)	3 (2.9)	0.55
Fracture or Erb's palsy (either twin; %)	0 (0.0)	0 (0.0)	0.99
Intraventricular hemorrhage (either twin; %)	0 (0.0)	2 (2.0)	0.55
Intracranial hemorrhage (either twin; %)	0 (0.0)	0 (0.0)	0.99
Neonatal death (either twin; %)	0 (0.0)	0 (0.0)	0.99

Abbreviations: CD, Cesarean delivery; EBL, estimated blood loss; GA, gestational age; ICU, intensive care unit; LOS, length of stay; NICU, neonatal intensive care unit; VD, vaginal delivery.

Among women who underwent planned CD at < 37 weeks, neonates were more likely to require ventilation and have confirmed sepsis than the induction of labor group. After controlling for differences in baseline characteristics, the association between ventilation and CD was no longer significant. While we could not perform a regression for sepsis, the higher rate of sepsis in the CD group is likely related to the earlier GA at delivery for CDs compared with labor inductions. About 70% of women who underwent induction of labor had a successful VD both in the term

and preterm groups. When we restricted the analysis to women with a closed cervix at the time of induction initiation, the VD rate was still > 60% without any significant differences in maternal or neonatal morbidity. Since we excluded women with a prior CD, women with preterm nonreassuring fetal status, and absent or the reversed umbilical artery Doppler's, our results would not apply to pregnancies with any of these characteristics.

Previous studies have compared maternal and neonatal outcomes among women with twin pregnancies who intend

<sup>&</sup>lt;sup>a</sup>Parametric testing was performed for all analyses except estimated blood loss, maternal length of stay, and neonatal length of stay which were nonparametric.

<sup>&</sup>lt;sup>b</sup>Reported as a median (interquartile range).

Table 5 Odds of maternal and neonatal morbidity by induction of labor versus Cesarean delivery < 37 weeks of GA<sup>a</sup>

Outcomes	OR/correlation coefficient	Adjusted OR/correlation coefficient <sup>b</sup>	Adjusted for GA at delivery only
Maternal outcomes			
Length of stay postpartum (days)	-1.4 (-1.70 to -1.08)	-0.98 (-1.33 to -0.62)	-1.27 (-1.61 to -0.93)
EBL (mL)	-284.5 (-395.0 to -174.1)	-205.4 (-332.1 to -78.7)	-270.6 (-390.2 to -151.1)
EBL ≥ 1,000 mL	0.29 (0.13-0.64)	0.29 (0.11–0.78)	0.27 (0.11–0.64)
EBL ≥ 1,500 mL	1.05 (0.29–3.72)	2.30 (0.50–10.53)	1.27 (0.33-4.87)
Transfusion	2.02 (0.65-6.30)	2.61 (0.71–9.56)	1.55 (0.50-4.79)
Endometritis	0.40 (0.04-3.64)	0.14 (0.01–1.62)	0.26 (0.03-2.26)
Wound complications	3.33 (0.30–37.55)	14.93 (0.62–360.97	4.45 (0.31–63.53)
Neonatal outcomes			
Neonatal LOS (days) for the twin discharged second	-2.1 (-10.6 to 6.4)	-1.0 (-3.86 to 1.84)	0.10 (-2.68 to 2.86)
Neonatal LOS (days) for the twin discharged first	1.5 (-1.36 to 2.57)	0.03 (-2.43 to 2.49)	0.42 (-1.89to 2.69)
NICU admission (either twin)	0.86 (0.46–1.64)	1.94 (0.73–5.18)	1.35 (0.61–2.98)
Ventilation (either twin)	0.39 (0.16-0.96)	0.71 (0.19–2.66)	0.79 (0.25-0.55)

Abbreviations: EBL, estimated blood loss; GA, gestational age; LOS, length of stay; NICU, neonatal intensive care unit.

to labor to those women who do not intend to labor. These studies had shown that planned CD did not reduce the risk of short-term or long-term neonatal morbidity compared with VD.<sup>3,5</sup> Studies examining maternal outcomes by mode of delivery in twin pregnancies had shown variable results, with some indicating no differences and others indicating increased maternal morbidity among women who intended to labor.<sup>3,10</sup> A secondary analysis of the twin births study, a large randomized controlled trial of planned VD versus planned CD for twins, found that among women who underwent induction in the planned VD group, the method of induction had no effect on the rate of CD or on maternal and neonatal outcomes.<sup>11–14</sup>

A paucity of publications had evaluated labor induction in advanced twin gestations when compared with controls. We could identify only a single paper in the literature, which compared a retrospective cohort of induced nulliparous twin gestations to elective Cesarean sections  $\geq$  35 weeks. <sup>15</sup> The authors used misoprostol and oxytocin as their primary induction agents. They found that among 69 patients in whom labor was induced, 53 (76.8%) had a vaginal birth, three (4.3%) had a combined VD-CD, and 13 (18.8%) had a CD. They found no differences in fetal outcomes except a reduction in neonatal hospitalization in the induction group. Maternal outcomes were not reported but the authors noted that there were no cases of uterine rupture, and one case of postpartum hemorrhage in the elective CD group. Additionally, one case of a failed induction required a reoperation for an incisional hematoma. 15

Other studies examining induction of labor in twin pregnancies have compared induction to spontaneous labor. These studies did not find any differences in maternal or neonatal outcomes among women who had induction of labor compared with spontaneous labor. 16,17 These data are reassuring that induction is safe in twins; however, clinically, this does not help providers to answer the pragmatic question about management of delivery for twins who are not in labor but have an indication for delivery. Furthermore, these studies had higher rates of CD among women who underwent induction of labor, with one study reporting a CD rate of 60.6%<sup>17</sup> and another 40.5%.<sup>18</sup> In contrast, we found a low rate of CD among women who underwent induction, with a CD rate of 30.2% among women who underwent induction ≥ 37 weeks and 26.4% among women who underwent induction < 37 weeks, similar to Simões et al. 15

Previous studies in singleton pregnancies had also investigated the optimal management of labor in women with indications for delivery < 37 weeks. One large retrospective cohort study found that there were no differences in maternal and neonatal outcomes among patients with singleton pregnancies who underwent induction of labor compared with planned CD. <sup>19</sup> Our data confirmed these findings in twins; women with twin pregnancies who was indicated preterm births and underwent induction had no worse maternal and neonatal outcomes compared with women underwent planned CD. This study in singleton pregnancies by Kuper et al, however, did not consider the outcomes maternal and neonatal length of stay. <sup>19</sup> We found that

<sup>&</sup>lt;sup>a</sup>Continuous variables (EBL, LOS) are reported as correlation coefficients while categorical variables (transfusion, endometritis, NICU admission, and ventilation) are reported as odds ratios.

<sup>&</sup>lt;sup>b</sup>Adjusted for differences in baseline maternal age, in vitro fertilization, nulliparity, chorionicity, gestational hypertension/preeclampsia, cholestasis, and gestational age at delivery.

women who underwent induction of labor of twins had a significantly shorter hospital stay, on average discharged 2 days sooner both for inductions  $\geq$  37 weeks and < 37 weeks than women who underwent planned CD. Neonates delivered at term in the induction of labor group were, like their mothers, discharged 2 days sooner than the planned CD group. This is an important outcome to consider, as an elective CD coupled with a longer maternal and neonatal hospital stay places added cost and burden on the health care system. <sup>20</sup> Longer hospitalization also increases the risk of hospital-acquired infections, although we did not find higher rates of postpartum endometritis or wound infection in the planned CD group. <sup>21</sup>

Our study is limited by its retrospective design. As with many studies similar to ours, this study was likely underpowered to find differences in rarer maternal and neonatal outcomes. While a randomized controlled trial to study maternal and neonatal outcomes in this cohort is possible, such a study would require a very large sample size. Since most women with twin pregnancies do, in fact, go into spontaneous labor, this population would be particularly difficult to study prospectively. Almost all patients in our study were delivered above 32 weeks, so it would be particularly difficult to draw conclusions from this paper for twins < 32 weeks. Additionally, our study may be limited by the homogeneous population. Our study included women from a single maternal-fetal medicine practice which has both strengths and drawbacks. We believe it increases the reliability of the data, as all maternal outpatient and hospital medical records were available for review. Also, since the deliveries were all by one practice, there is minimal variation in regards to pregnancy and labor management. Conversely, our findings may not be generalizable to other populations, and specifically in practices that do not routinely perform internal podalic version and breech extraction. This is highlighted by our lack of second twin CD after successful birth of the first vaginally in our cohort. We acknowledge that twin vaginal deliveries require a dedicated obstetrical team with close observation and management and our data may not be generalizable. Rare events, such as uterine rupture in the setting of labor induction of an overdistended uterus, cannot be evaluated in our cohort well and would need larger analysis to evaluate this endpoint. Finally, we found a lower EBL for women undergoing induction of labor compared with CD but no significant difference in rate of transfusion. This likely reflects the fact that providers are more likely to give a higher EBL for CD compared with VD. Instead, transfusion is likely the most accurate outcome and clinically the most important for providers and patients.

Finally, it is important to consider the differences in CD rates between women who underwent induction and those who had a planned CD. Previous studies have suggested that induction of labor in twin pregnancies increases the risk of CD; however, we found that among women who underwent induction of labor, only 30% had a CD.<sup>22</sup> This indicates that many women with twin pregnancies who undergo induction of labor are able to avoid a major abdominal surgery both when delivering  $\geq$  37 and < 37 weeks. Although CD is not

typically considered an outcome measure in twin deliveries, undergoing CD itself is an outcome worth considering.<sup>23</sup> Additionally, we found that induction of labor decreases the LOS for both the mother and the neonate. While it is true that all women undergoing CD will have a longer LOS by nature of the surgery, LOS is a measurable outcome which has real financial implications. Longer hospital stays place a burden on the health care system<sup>24</sup> and LOS could be reduced with induction of labor. This should be considered when making decisions concerning mode of delivery for twin pregnancies for women who are not in labor; women should be counseled that they have a low risk of CD and are more likely to have a shorter hospital recovery if undergoing induction.

#### **Conclusion**

In conclusion, among patients with twin pregnancies, women who underwent induction of labor had improved maternal outcomes and similar neonatal outcomes compared with women who underwent planned CD. Women who underwent induction are likely to have a successful VD, less blood loss, and had a shorter hospital stay, both when delivering  $\geq 37$  and < 37 weeks. Providers and patients can be reassured that if women with twin pregnancies are indicated for delivery but do not go into spontaneous labor, induction of labor is a safe option both for the mothers and their neonates.

Conflict of Interest None declared.

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