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Labor induction and cesarean delivery: A prospective cohort study of first births in Pennsylvania, USA

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Abstract

Background: Mode of delivery at first childbirth largely determines mode of delivery at subsequent births, so it is particularly important to understand risk factors for cesarean delivery at first childbirth. In this study, we investigated risk factors for cesarean delivery among nulliparous women, with focus on the association between labor induction and cesarean delivery.

Methods: A prospective cohort study of 2851 nulliparous women with singleton pregnancies who attempted vaginal delivery at hospitals in Pennsylvania, 2009-2011, was conducted. We used nested logistic regression models and multiple mediational analyses to investigate the role of three groups of variables in explaining the association between labor induction and unplanned cesarean delivery—the confounders of maternal characteristics and indications for induction, and the mediating (intrapartum) factors—including cervical dilatation, labor augmentation, epidural analgesia, dysfunctional labor, dystocia, fetal intolerance of labor, and maternal request of cesarean during labor.

Results: More than a third of the women were induced (34.3%) and 24.8% underwent cesarean delivery. Induced women were more likely to deliver by cesarean (35.9%) than women in spontaneous labor (18.9%), unadjusted OR 2.35 (95% CI 1.97-2.79). The intrapartum factors significantly mediated the association between labor induction and cesarean delivery (explaining 76.7% of this association), particularly cervical dilatation <3 cm at hospital admission, fetal intolerance of labor, and dystocia. The indications for labor induction only explained 6.2%.

Conclusions: Increased risk of cesarean delivery after labor induction among nulliparous women is attributable mainly to lower cervical dilatation at hospital admission and higher rates of labor complications.

KEYWORDS
cervical dilatation, cesarean delivery, labor induction, nulliparous

1 | INTRODUCTION

In 2012 the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the American Congress of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine held a workshop to develop strategies to prevent the first cesarean delivery.[1] This workshop was prompted in part by the growing recognition

of the short- and long-term complications that result from cesarean delivery—such as higher rates of maternal and neonatal morbidity resulting from the index cesarean, and higher rates of complications in subsequent pregnancies—including abnormal placentation, uterine rupture, and stillbirth.[2-7] Because labor induction has been associated with increased risk of cesarean delivery, a particular focus of this workshop was on ways to reduce the rate of labor induction, which has more than doubled in the United States since 1990, when the induction rate was 9.6% to 23.3% in 2012.[8]

Numerous studies comparing women whose labor is induced to those who begin labor spontaneously have reported higher cesarean delivery rates among women who undergo labor induction, in most cases nearly double the risk of cesarean delivery.[9-15] In addition, nulliparous women who are induced are much more likely to have cesarean delivery than induced multiparous women who have had a previous vaginal delivery.[14,16,17] What remains unclear is the extent to which the increased risk of cesarean delivery among induced women is attributable to maternal characteristics and indications for labor induction that lead to the decision to induce labor, or to intrapartum factors that occur more commonly in association with or after labor induction. Recent advancements in mediation analysis provide new tools to investigate underlying mechanisms to explain treatment-outcome associations in observational studies[18-20] in this case, the labor induction-cesarean delivery association.

The purpose of mediation analysis is to disentangle the pathways that could explain the effect of a treatment on an outcome. Mediating variables occur temporally after the exposure or treatment, or occur more frequently as a consequence of the treatment.[19] Confounding variables are factors that are associated both with the treatment and outcome, but occur before the treatment. Several systematic reviews have noted that a limitation of previous studies of cesarean delivery which compared women who were induced with those who began labor spontaneously was a failure to control for confounding by indication for induction.[21,22] Maternal characteristics and pregnancy complications that can lead to labor induction overlap considerably with indications for cesarean delivery and thus it is reasonable to hypothesize that these indications for labor induction are the primary drivers of the increased risk of cesarean delivery among women who are induced in comparison to those who begin labor spontaneously.

This study set out to address a clinically important question—why nulliparous women who are induced are more likely to undergo cesarean delivery in comparison to nulliparous women who begin labor spontaneously. The association between labor induction and cesarean delivery was investigated by way of nested logistic regression models and mediation analysis[20] to explore the mechanisms by which labor induction increases women's risk of cesarean delivery at first childbirth.

2 | METHODS

Data in this paper are from the First Baby Study, a prospective, cohort study designed to investigate the association between mode of first delivery and subsequent childbearing.[23] The First Baby Study was approved by the Penn State College of Medicine ethics review board and the ethics review boards of the hospitals and other organizations which supported participant recruitment.

2.1 | Participants

The First Baby Study participants were recruited during pregnancy from a variety of settings throughout the State of Pennsylvania, including childbirth education classes, hospital tours, targeted mailings, and on-line and print advertisements. Inclusion criteria were as follows: (1) aged 18-35 (at the time of recruitment), (2) singleton pregnancy, (3) nulliparous, (4) English or Spanish speaking, and (5) planning to deliver in Pennsylvania. Exclusion criteria were: (1) planning to have a tubal ligation during the childbirth hospitalization, (2) planning for the infant to be adopted, (3) planning to deliver at home or in a birthing center not associated with a hospital, and (4) prior pregnancy of more than 20 weeks' gestation. Deliveries occurred at 78 hospitals (76 in Pennsylvania and 2 outside the state), from January 2009 to April 2011.

2.2 | Measurement

Participants were interviewed in their third trimester (between 30 and 42 weeks' gestation) and again at 1, 6, 12, 18, 24, 30, and 36 months postpartum. The birth certificate and hospital discharge data from the deliveries were also obtained. The survey questions that addressed labor and delivery in the 1-month interview were adapted from the Listening to Mothers Surveys.[24]

The primary independent variable in this study was labor induction and the primary outcome was cesarean delivery, among women attempting vaginal delivery. Women who underwent a scheduled cesarean (n=155) were not included in these analyses, leaving an analytic sample of 2851 women. As is common in the United States, women with a fetus in breech position at term underwent planned cesarean delivery and therefore were not included in this study. Women were asked if they were in labor when they went to the hospital to have their baby and "Did a doctor or nurse in the hospital try to cause your labor to BEGIN by the use of drugs or some other technique?" Women who answered "no" to the first question and "yes" to the second question were classified as undergoing labor induction. Participants who reported one or more cervical ripening procedures before hospital admission were also classified as having been induced.

The maternal characteristics investigated were age, race/ethnicity, education, insurance coverage, marital status, preconception body mass index in three categories (<25.0 kg/m^2, 25.0-29.9 kg/m^2, and ≥30.0 kg/m^2), and pregnancy weight gain based on Institute of Medicine guidelines in three categories (less than recommended, recommended, and more than recommended),[25] height, gestational age, and newborn birthweight. We included newborn birthweight with the maternal characteristics as a proxy for size of the fetus, which would likely play a role in the decision to induce, and the risk of cesarean delivery.

We examined seven categories of conditions that have been defined as "indications for induction of labor," based on the American Congress of Obstetricians and Gynecologists 2009 Practice Bulletin "Induction of Labor."[26] Women with one or more of these categories of conditions were identified by the use of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes noted in the hospital discharge, as follows: (1) *Hypertension (pregestational and gestational),* including preeclampsia and eclampsia (642.0-642.9, 401.0-405.9), (2) *Diabetes (pregestational and gestational) and abnormal glucose tolerance* (648.0, 648.8, 250.0-250.9), (3) *Other maternal medical conditions*—including renal disease, chronic pulmonary disease, liver disease, coagulation defects, and lupus (585.1-585.9, 646.21, 490.0-496.0, 518.89, 646.7, 573.0-573.9, 571.0-571.9, 286.0-286.7, 286.9, 710.0), (4) *Premature rupture of membranes and/or chorioamnionitis* (658.1-658.9), (5) *Fetal compromise,* including isoimmunization and fetal growth restriction (V072, 655.0-656.2, 656.5), (6) *Hydramnios or oligohydramnios* (657.0-658.0), and (7) *Late term and postterm pregnancy*. Women were categorized as late term and postterm if the gestational age of the newborn was at least 41 weeks, 0 days, as reported in the birth certificate data. If hypertension (pregestational and gestational) or diabetes (pregestational and gestational) were reported in the birth certificate data women were categorized as having these conditions as well.

If neither the hospital discharge data nor the birth certificate data identified any of the seven categories of induction indications, we investigated maternal self-report to determine if there were indications that the records had missed. In the 1-month postpartum interview, the participants were asked "Why did a doctor or nurse in the hospital try to make your labor begin?" If the mother reported that her water had broken, it was classified as prelabor or premature rupture of membranes. If the mother reported that the baby was not doing well and needed to be born soon, it was classified as fetal compromise. If the mother reported that she had too little or too much amniotic fluid (or variations along those lines), it was classified as hydramnios or oligohydramnios. Some of the women reported that they were induced because they had specific conditions, such as lupus—these were categorized as other maternal medical conditions.

Seven intrapartum factors were investigated: cervical dilation at hospital admission, labor augmentation, use of epidural analgesia, dysfunctional labor, dystocia, fetal intolerance of labor, and maternal request of cesarean during labor. To measure labor augmentation, participants were asked "During your labor and birth, did someone"…"Break your membranes to release amniotic fluid after labor began?" and "Give you Pitocin (pit) to strengthen labor or speed contractions after labor had begun?" Women who answered "yes" to either (or both) of these questions were categorized as having their labor augmented. Participants were also asked "How many centimeters was your cervix dilated when you were first examined after you were admitted to the hospital for delivery?" and to report at what point their contractions became regular and 5 min or less apart (before or after hospital admission). Those who reported that their contractions never did become regular and 5 min or less apart were classified as having dysfunctional labor. Women were also asked "At any point while you were in labor did you specifically request a cesarean delivery?" Dystocia was measured, using the ICD-9-CM diagnostic codes noted in the discharge summary data for obstructed labor (660.0-660.9, except 660.7), abnormality of forces of labor (661.0-661.9, except 661.3), prolonged labor (662.0-662.2), and failed induction (659.0-659.1). These ICD-9 codes have been used in previous studies,[27,28] based on evidence of good concordance with medical records.[27]

Because there has been concern in recent years as to the validity of measures of fetal intolerance of labor,[29,30] we compared fetal intolerance of labor codes noted in the hospital discharge data (ICD-9 codes of 656.3 ["fetal distress"] and 659.7 ["abnormality in fetal heart rate or rhythm"]) to the birth certificate measure of fetal intolerance of labor. Based on the ICD-9 codes, there were 653 newborns with a code for fetal intolerance of labor and 371 reported in the birth certificate data. While the fetal intolerance of labor measure in the birth certificate data was positively and significantly associated with assisted ventilation of the newborn, NICU admission, newborn hospital length of stay, maternal reported newborn complications, and unplanned cesarean delivery, the ICD-9 code measure exhibited little concordance with these variables, and in fact was slightly inversely associated with unplanned cesarean delivery. The birth certificate data measure of fetal intolerance of labor exhibited superior construct validity in comparison to the ICD-9 code measure. Therefore, we used the birth certificate measure of fetal intolerance of labor rather than the ICD-9 code measure.

2.3 | Analysis

Chi-square analyses were used to measure the bivariate associations between the maternal and newborn characteristics, indications for induction, and intrapartum factors in relation to labor induction and mode of delivery (vaginal or

cesarean). Instrumental deliveries were combined with spontaneous vaginal deliveries for these analyses because of small numbers of instrumental deliveries. Multivariable logistic regression was used to model the association between labor induction and cesarean delivery in four stages. We combined categories among the confounders wherever possible to eliminate small sample sizes in cells and to increase statistical power and model fit for the regression equations.

Mediation analyses were conducted, using the Karlson, Holm, and Breen method.[20,31] The Karlson, Holm, and Breen method can be used with multiple mediators, multiple confounders, and with categorical or dichotomous confounding and outcome variables. The coefficients produced are not affected by rescaling or attenuation bias. The Karlson, Holm, and Breen program conducts decomposition analysis to estimate the relative contribution of each of the confounding and mediating variables to the association between the independent and dependent variables,[20] in this case, labor induction and cesarean delivery. We used nested logistic regression models and mediation analysis to determine the extent to which the increased risk of cesarean delivery after labor induction could be explained by the confounding variables of maternal characteristics alone (model 2), and then maternal characteristics and the indications for labor induction (model 3), to model the incremental confounding effects of the labor induction indications. In model 4, we added the factors and events (the mediators) that occurred as a consequence of the decision to induce labor (such as low cervical dilatation) or after labor induction but after cesarean delivery, such as increased risk of dystocia.

We calculated the variance inflation factor for each predictor to assess multicollinearity. Sensitivity analyses were conducted to evaluate the effects of hospital clustering. We also conducted sensitivity analyses to measure the potential effect of year of delivery (2009, 2010, or 2011). The results of sensitivity analyses showed that control for hospital clustering and year of delivery had only minor and nonsignificant effects on the regression results. Therefore, these variables were not included in the regression models. Investigation of collinearity among the variables revealed variance inflation factor scores very close to 1.00, indicating little or no collinearity among the variables. All analyses were conducted using Stata Version 14 (StataCorp, College Station, TX, USA).

3 | RESULTS

Women who were induced were more likely to undergo cesarean delivery than those who began labor spontaneously, regardless of cervical dilation at hospital admission (Figure 1). Women who were induced were more likely to deliver by cesarean than women who presented in spontaneous labor overall and within each gestational age category. The risk of cesarean delivery increased from early term to postterm among women who were induced while the risk of cesarean delivery remained stable until postterm among women who began labor spontaneously (Figure 2). Insurance coverage and marital status were not associated with labor induction or cesarean delivery (Table 1), while higher levels of preconception body mass index, pregnancy weight gain, newborn birthweight, and gestational age were associated with increased likelihood of both labor induction and cesarean delivery.

The induction indications of hypertension, diabetes, other maternal medical conditions, and hydramnios or oligohydramnios were associated both with induction and cesarean delivery

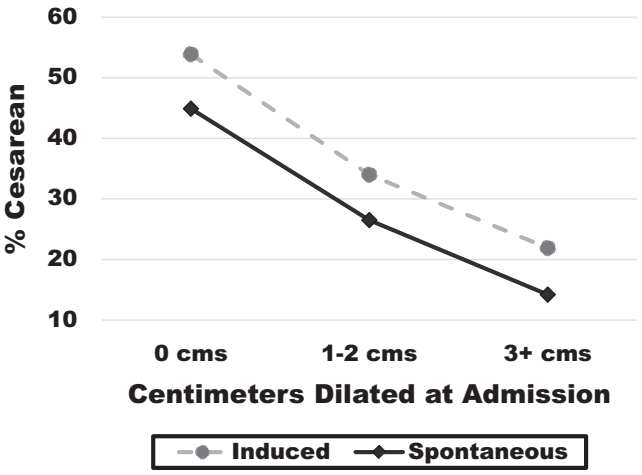

FIGURE 1 Rate of cesarean delivery by centimeters dilated at hospital admission among women whose labor was induced versus those who began labor spontaneously, Pennsylvania, United States, 2009-2011

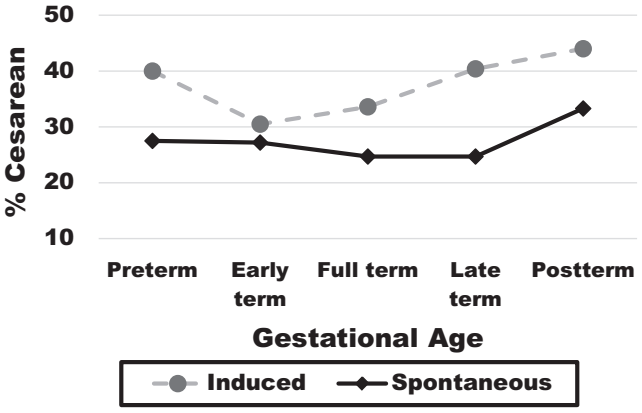

FIGURE 2 Rate of cesarean delivery by gestational age at delivery among women whose labor was induced versus those who began labor spontaneously, Pennsylvania, United States, 2009-2011
Preterm (34 weeks, 0 days to 36 weeks, 6 days)
Early term (37 weeks, 0 days to 38 weeks, 6 days)
Full term (39 weeks, 0 days to 40 weeks, 6 days)
Late term (41 weeks, 0 days to 41 weeks, 6 days)
Postterm (42 weeks or later)

TABLE 1 Maternal characteristics by labor induction and cesarean delivery, Pennsylvania, United States, 2009-2011

	Overall[b] No. (%)	Induced[c] No. (%)	Cesarean[d] No. (%)
	2851	977 (34.3)	708 (24.8)
Maternal age (years)			
18-24	792 (27.8)	274 (34.6)	162 (20.5)***
25-29	1130 (39.6)	388 (34.3)	277 (24.5)
30-36	929 (32.6)	315 (33.9)	269 (29.0)
Race/ethnicity			
White	2363 (82.9)	825 (34.9)	569 (24.1)
Black	213 (7.5)	67 (31.5)	62 (29.1)
Hispanic	160 (5.6)	58 (36.2)	44 (27.5)
Other	114 (4.0)	27 (23.7)	33 (28.9)
Education			
High school degree or less	484 (17.0)	187 (38.6)	118 (24.4)
Some college or technical school	767 (26.9)	265 (34.6)	183 (23.9)
College grad or higher	1600 (56.1)	525 (32.8)	407 (25.4)
Health insurance			
Private	2178 (76.4)	738 (33.9)	550 (25.3)
Public	671 (23.6)	238 (35.5)	156 (23.4)
Marital status			
Married	1987 (69.7)	674 (33.9)	490 (24.7)
Not married	864 (30.3)	303 (35.1)	218 (25.3)
Preconception body mass index category (kg/m^2)			
Normal/under (<25.0)	1643 (57.7)	459 (27.9)***	322 (19.6)***
Overweight (25.0-29.9)	640 (22.5)	246 (38.4)	180 (28.1)
Obese (≥30.0)	566 (19.9)	272 (48.1)	206 (36.4)
Pregnancy weight gain[a]			
Less than recommended	321 (11.3)	102 (31.8)***	59 (18.4)***
Recommended	1001 (35.2)	287 (28.7)	194 (19.4)
More than recommended	1521 (53.5)	584 (38.4)	453 (29.8)
Maternal height (inches)			
53-62	584 (20.5)	207 (35.4)	195 (33.4)***
63-65	1124 (39.4)	376 (33.5)	286 (25.5)
66-67	689 (24.2)	239 (34.7)	141 (20.5)
68-74	453 (15.9)	155 (34.2)	86 (19.0)
Gestational age (weeks)			
Preterm (34 0/7-36 6/7)	113 (4.0)	40 (35.4)***	31 (27.4)***
Early term (37 0/7-38 6/7)	544 (19.1)	199 (36.6)	132 (24.3)
Full term (39 0/7-40 6/7)	1703 (59.7)	444 (26.1)	379 (22.3)
Late term (41 0/7-41 6/7)	458 (16.1)	269 (58.7)	153 (33.4)
Postterm (42 +)	33 (1.2)	25 (75.8)	13 (39.4)
Newborn birthweight (g)			
<2500 (underweight)	86 (3.0)	40 (46.5)***	25 (29.1)***
2500-4000 (normal)	2469 (87.3)	800 (32.4)	558 (22.6)
>4000 (macrosomic)	274 (9.7)	128 (51.8)	117 (42.7)

[a]Based on 2009 Institute of Medicine guidelines.[25]

[b]Column percents (sums to 100% in each category), denominator = 2851, except where there is missing data.

[c]Row percents (the percent of women who were induced in each row), denominator = 977.

[d]Row percents (the percent of women who had cesarean delivery in each row), denominator = 708.

***P<.001, **P<.01, *P<.05.

(Table 2). Among the women undergoing labor induction, there were 124 (12.7%) who had none of the 7 indications for labor induction. Among these 124 women, 72 reported that they were induced because the baby was overdue (0-6 days overdue), 33 said there were concerns about the size of the baby (although none of these 33 women delivered macrosomic newborns), 8 said they wanted to get the pregnancy over with or to control the timing of the delivery, 5 reported maternal discomfort, 3 reported placental problems, and 3 reported no reason (not shown in a table). Among the 1542 women who were found to have at least one of the 7 indications for induction, slightly more than half were induced (55.32%) (not shown in a table).

All of the intrapartum factors seen in Table 3 were associated with both labor induction and cesarean delivery. Women who underwent labor induction, with or without oxytocin, were more likely to deliver by cesarean than women who began labor spontaneously. In addition, women who were induced with oxytocin were more likely to be augmented with oxytocin (76.9%) than women who were induced without oxytocin (19.2%) and women who presented in spontaneous labor (50.5%) (not shown in a table). Overall, 69.0% of women who were induced were also augmented with oxytocin in comparison to 50.5% of the women who were not induced (not shown in a table). Women who were induced were more likely to receive epidural analgesia (92.3%) than those who began labor

TABLE 2 Indications for labor induction by labor induction and cesarean delivery, Pennsylvania, United States, 2009-2011

	Overall[a] No. (%)	Induced[b] No. (%)	Cesarean[c] No. (%)
	2851	977 (34.3)	708 (24.8)
Hypertension (chronic and gestational)			
Yes	386 (13.5)	245 (63.5)***	137 (35.5)***
No	2465 (86.5)	732 (29.7)	571 (23.2)
Diabetes (chronic and gestational)			
Yes	167 (5.9)	94 (56.3)***	57 (34.1)**
No	2684 (94.1)	883 (32.9)	651 (24.3)
Other maternal medical conditions (renal disease, liver disease, coagulation defects)			
Yes	53 (1.9)	39 (73.6)***	22 (41.5)***
No	2798 (98.1)	938 (33.5)	686 (24.5)
Premature rupture of membranes and/or chorioamnionitis			
Yes	482 (16.9)	200 (41.5)***	130 (27.0)
No	2369 (83.1)	777 (32.8)	578 (24.4)
Fetal compromise (including isoimmunization and fetal growth restriction)			
Yes	192 (6.7)	108 (56.2)***	57 (29.7)
No	2659 (93.3)	869 (32.7)	651 (24.5)
Hydramnios or oligohydramnios			
Yes	135 (4.7)	103 (76.3)***	50 (37.0)***
No	2716 (95.3)	874 (32.2)	658 (24.2)
Late term and postterm (41 0/7 weeks/days or later)			
Yes	491 (17.2)	294 (59.9)***	166 (33.8)***
No	2360 (82.8)	683 (28.9)	542 (23.0)
Number of above indications for labor induction			
0	1309 (45.9)	124 (9.5)***	227 (17.3)***
1	1216 (42.7)	649 (53.4)	359 (29.5)
2	293 (10.3)	182 (62.1)	109 (37.2)
3-4	33 (1.2)	22 (66.7)	13 (39.4)

[a]Column percents (sums to 100% in each category), denominator = 2851, except where there is missing data.
[b]Row percents (the percent of women who were induced in each row), denominator = 977.
[c]Row percents (the percent of women who had cesarean delivery in each row), denominator = 708.
***P<.001, **P<.01, *P<.05.

spontaneously (84.1%), and women who received epidural analgesia were more likely to undergo cesarean delivery than those who did not have epidural analgesia. Among those who were 0 centimeters dilated at hospital admission, 78.3% had been admitted for labor induction. More than half of the women who were 0 centimeters dilated at hospital admission had cesarean delivery (52.1%), as seen in Table 3, and more than half of the 188 women who were induced at 0 centimeters dilation delivered by cesarean (n=101, 53.7%) (not shown in a table). Among the women presenting for labor induction, 20.4% (n=198) were dilated ≥3 centimeters at hospital admission in comparison to 67.3% of the women in spontaneous labor (not shown in a table). Women who reported that their contractions never did become regular and 5 min or less apart (dysfunctional labor) were more likely to have been induced and to have cesarean delivery. Women who were induced were more likely to request cesarean during labor (7.1%) than those not induced, 3.4% ($P < .0001$) (not shown in a table), and those who requested cesarean during labor were more likely to undergo cesarean delivery (45.1%) than those who did not request cesarean during labor (23.8%) ($P < .0001$).

In model 2 (Table 4), the maternal characteristics most strongly associated with increased likelihood of cesarean delivery were short maternal stature, macrosomic fetus (>4000 g at birth), prepregnancy obesity, aged 30 or older, and weight gain beyond recommended Institute of Medicine guidelines.[25] In model 3, 4 of the 7 induction indications were significantly associated with increased risk of cesarean delivery—hypertension, other maternal medical conditions, hydramnios or oligohydramnios, and late term and postterm pregnancy. In model 4, all 7 intrapartum factors remained significantly associated with increased risk of cesarean delivery after controlling for the maternal characteristics, induction indications, and the other intrapartum factors. The most significant intrapartum factors were dystocia, cervical dilatation, and fetal intolerance of labor. In model 4, the women who were augmented were significantly less likely to deliver by cesarean than women not augmented. Both use of epidural analgesia and maternal request of cesarean delivery during labor remained significantly associated with increased likelihood of cesarean delivery, even after controlling for the maternal characteristics, indications for induction, and intrapartum factors. The unadjusted odds ratio for the association of labor induction with cesarean delivery was 2.35 (95% CI 1.97-2.79), model 1, that is, women who underwent labor induction had more than double the odds of subsequently having an unplanned cesarean delivery in comparison to women who began labor spontaneously. Adjusting for the maternal characteristics reduced the OR to 2.06 (95% CI 1.72-2.48), model 2, and further adjustment for the indications for labor induction reduced it to 1.74 (95% CI 1.42-2.14), model 3—reflecting the total effect (effect of the confounders). Analyses to measure the indirect effect (effect of just the mediators, without adjustment for the confounders) yielded an OR of 1.25 (95% CI, 0.98-1.60) (not shown in a table). After adjustment for both the confounding and the mediating variables (direct effect), the association between labor induction and cesarean delivery was 1.07 (95% CI 0.82-1.41), as seen in model 4.

TABLE 3 Mediating (intrapartum) factors by labor induction and cesarean delivery, Pennsylvania, United States, 2009-2011

	Overall[a] No. (%)	Induced[b] No. (%)	Cesarean[c] No. (%)
	2851	977 (34.3)	708 (24.8)
Method of labor induction			
Induced by way of oxytocin (with or without other methods)	857 (30.1)	-	305 (35.6)***
Induced without oxytocin	117 (4.1)	-	44 (37.6)
Not induced	1877 (65.8)	-	359 (19.1)
Labor augmentation			
Augmented with oxytocin (with or without other methods)	1634 (57.3)	674 (41.2)***	479 (29.3)***
Augmented without oxytocin	528 (18.5)	94 (17.8)	73 (13.8)
Not augmented	689 (24.2)	209 (30.3)	156 (22.6)
Epidural analgesia used			
Yes	2478 (86.9)	902 (36.4)***	673 (27.2)***
No	373 (13.1)	75 (20.1)	35 (9.4)
Centimeters dilated at hospital admission			
0	240 (8.5)	188 (78.3)***	125 (52.1)***
1-2	1139 (40.3)	584 (51.3)	347 (30.5)
3+	1450 (51.3)	198 (13.7)	222 (15.3)
Dysfunctional labor			
Yes	339 (11.9)	153 (45.1)***	142 (41.9)***
No	2512 (88.1)	824 (32.8)	566 (22.5)
Dystocia			
Yes	678 (23.8)	304 (44.8)***	443 (65.3)***
No	2173 (76.2)	673 (31.0)	265 (12.2)
Fetal intolerance of labor			
Yes	371 (13.0)	164 (44.2)***	185 (49.9)***
No	2480 (87.0)	813 (32.8)	523 (21.1)
Maternal request of cesarean during labor			
Yes	133 (4.7)	69 (51.9)***	60 (45.1)***
No	2717 (95.3)	908 (33.4)	647 (23.8)

[a]Column percents (sums to 100% in each category), denominator = 2851, except where there is missing data.
[b]Row percents (the percent of women who were induced in each row), denominator = 977.
[c]Row percents (the percent of women who had cesarean delivery in each row), denominator = 708.
***P<.001, **P<.01, *P<.05.

The overall pseudo R^2 in model 4 was 0.33. The maternal characteristics, indications for induction, and intrapartum factors together explained 94.5% of the unadjusted OR. The maternal characteristics contributed 11.6%; the induction indications, 6.2%; and the intrapartum (mediating) factors, 76.7%. The intrapartum factors with the most explanatory power were <3 centimeters of cervical dilation at hospital admission (which contributed 34.4%), dystocia (23.8%), and fetal intolerance of labor (6.0%) (results in this paragraph not shown in a table). Thus, <3 centimeters cervical dilation at hospital admission was the single most powerful mediator of the association between labor induction and subsequent cesarean delivery.

4 | DISCUSSION

Women in this study who underwent labor induction had a higher risk of unplanned cesarean delivery in comparison to those who began labor spontaneously, consistent with findings from similar studies.[9–15] This study added the important finding that indications for labor induction played only a small role in the increased risk of cesarean delivery after labor induction. Rather most of the increase (more than three-quarters) was because of intrapartum factors, including the lower cervical dilatation at hospital admission among women

TABLE 4 Odds ratios and 95% confidence intervals of labor induction by cesarean delivery from logistic regression analyses, unadjusted and three sequential nested models of adjustment, Pennsylvania, United States, 2009-2011

	Unadjusted	Model 2	Model 3	Model 4
Labor induction (induced vs spontaneous)	2.35 (1.97-2.79)***	2.06 (1.72-2.48)***	1.74 (1.42-2.14)***	1.07 (0.82-1.41)
Maternal characteristics				
Age (years)				
18-24		Reference	Reference	Reference
25-29		1.29 (1.02-0.62)*	1.30 (1.03-1.65)*	1.46 (1.09-1.94)*
30-36		1.77 (1.40-2.24)***	1.77 (1.40-2.25)***	1.81 (1.34-2.43)***
Preconception body mass index category (kg/m$^{2)}$				
Normal/under (<25.0)		Reference	Reference	Reference
Overweight (25.0-29.9)		1.24 (0.98-1.56)	1.23 (0.98-1.55)	1.32 (1.00-1.75)
Obese (≥30.0)		1.89 (1.51-2.37)***	1.85 (1.46-2.33)***	1.66 (1.24-2.22)**
Gained more than recommended[a]		1.50 (1.23-1.82)***	1.48 (1.22-1.80)***	1.32 (1.04-1.68)*
Maternal height (inches)				
53-62		2.39 (1.88-3.04)***	2.40 (1.88-3.06)***	1.90 (1.41-2.55)***
63-65		1.45 (1.18-1.79)***	1.48 (1.20-1.82)***	1.25 (0.97-1.62)
66+		Reference	Reference	Reference
Macrosomic fetus		2.43 (1.85-3.20)***	2.38 (1.80-3.15)***	1.89 (1.33-2.69)***
Indications for labor induction				
Hypertension			1.35 (1.03-1.76)*	1.08 (0.77-1.50)
Diabetes			1.00 (0.70-1.43)	0.89 (0.57-1.37)
Other maternal medical conditions			1.91 (1.06-3.44)*	1.56 (0.73-3.34)
Premature or prolonged rupture of membranes and/or chorioamnionitis			1.12 (0.88-1.42)	0.80 (0.59-1.08)
Fetal compromise			1.22 (0.86-1.72)	1.54 (1.02-2.34)*
Hydramnios or oligohydramnios			1.52 (1.03-2.25)*	1.22 (0.75-1.98)
Late term and postterm			1.29 (1.01-1.66)*	1.09 (0.80-1.49)
Mediating (intrapartum) factors				
Centimeters dilated				
0				3.94 (2.62-5.91)***
1-2				1.81 (1.39-2.35)***
3+				Reference
Labor augmentation				
Augmented with oxytocin				0.74 (0.55-0.98)*
Augmented without oxytocin				0.57 (0.38-0.83)**
Not augmented				Reference
Epidural analgesia				1.96 (1.23-3.04)**
Dysfunctional labor				2.22 (1.63-3.04)***
Dystocia				12.91(10.22-16.33)***
Fetal intolerance of labor				3.13 (2.35-4.16)***
Maternal request of cesarean during labor				1.70 (1.06-2.74)*

[a]More than recommended vs recommended or less than recommended by Institute of Medicine guidelines.[25]

Model 2 includes labor induction and all maternal characteristics seen in Table 4.

Model 3 includes labor induction, all maternal characteristics seen in Table 4, and all indications for labor induction seen in Table 4.

Model 4 includes labor induction, all maternal characteristics seen in Table 4, all indications for labor induction seen in Table 4, and all mediating factors seen in Table 4.

***P<.001, **P<.01, *P<.05.

whose labor was induced, and the events that followed labor induction—including higher rates of dystocia, use of epidural analgesia, fetal intolerance of labor, and maternal request of cesarean during labor among women undergoing labor induction. These findings are concordant with previous studies comparing labor induction to spontaneous labor, and explain why these studies generally report similar cesarean rates among induced women with and without medical indications.[9,13]

In our study, about a fifth of the women presenting for labor induction (20.27%) reported that they were ≥3 centimeters dilated at hospital admission. Previous studies have reported rates of cervical dilatation of ≥3 centimeters among nulliparous women presenting for labor induction ranging from 7.8% to 50.0%,[12,32–34] and found, as we did, that women undergoing labor induction with an "unfavorable cervix" were at increased risk for cesarean delivery.

Another key finding is that a large portion of the women with one or more indications for labor induction (44.7%) were not induced. Even among the women with two or more indications for labor induction only 65.0% were induced. If all of the women with a medical indication for labor induction had been induced, 70.3% of the 2851 women would have been induced, rather than the actual rate of 34.3%. One potential explanation is variation in provider willingness to recommend labor induction. Previous studies have found large variation in rates of labor induction across providers and hospitals, even after controlling for labor induction risk factors.[35-37] Although it is likely that variation in labor induction rates reflect differences in hospital policies, condition severity, fear of malpractice, provider training, and patient preference, it also likely reflects provider uncertainty as to when it is appropriate to recommend labor induction[38] or variation in clincal judgement as to the necessity of labor induction in specific circumstances. The guidelines published by the American Congress of Obstetricians and Gynecologists on induction of labor [26] describe the labor induction indications as "not absolute" and suggest that the provider take into account other factors, such as maternal and fetal conditions, gestational age, and cervical status.

4.1 | Strengths and limitations of the study

The major strength of this study is the use of mediation analysis to investigate the labor induction–cesarean delivery association. Mediation methodology provides a mechanism to measure the effects of multiple mediators individually and combined, and to determine which factors are most influential in terms of the difference between the unadjusted and adjusted odds ratios, by way of decomposition analysis.[20] Several limitations must also be considered. First, the study participants were more educated, more likely to be married, more likely to be white, and more likely to have private insurance than women aged 18-35 delivering their first child in the state of Pennsylvania as a whole, although they were not significantly different in mode of delivery.[23] Second, the First Baby Study did not include women over the age of 35 at the time of study recruitment because the primary goal of the study was to investigate the association between cesarean delivery and subsequent fertility. Third, there were likely differences between the women who were induced and those who began labor spontaneously, despite controlling for most known confounding factors. We were not able to abstract the medical records and therefore were not able to obtain data on Bishop score, length of time in labor after hospital admission, cervical dilatation at the beginning of epidural administration, maternal reported pain scores during labor, and other factors that might have served as additional intrapartum factors. Several of our key intrapartum variables were self-reported and subject to recall bias, including cervical dilatation at hospital admission. Nonetheless, these variables were strongly predictive of cesarean delivery and explained a relatively large portion of the association between labor induction and cesarean delivery, indicating that self-report of these variables was likely reasonably accurate.

5 | CONCLUSIONS

This prospective, cohort interview study adds to a growing body of evidence that nulliparous women who are induced are more likely to undergo unplanned cesarean delivery, in comparison to women who begin labor spontaneously. The increased risk of cesarean delivery is primarily explained by lower cervical dilatation among women who present for labor induction and secondarily by higher rates of intrapartum complications—including dysfunctional labor, fetal intolerance of labor, dystocia, and maternal request of cesarean during labor.

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