Risk of Cesarean Delivery for Women with Obesity Using a Standardized Labor Induction Protocol

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Abstract

Objective We aimed to determine the risk of cesarean among women with obesity undergoing labor induction within a prospective trial that utilized a standardized labor protocol.

Study Design This was a secondary analysis of a randomized trial of induction methods. Term ($\geq$37 weeks) women with intact membranes undergoing induction with an unfavorable cervix (Bishop's score $\leq$6 and dilation $\leq$2 cm) were included. The trial utilized a labor protocol that standardized induction and active labor management, with recommendations for interventions at particular time points. Only women with a recorded body mass index (BMI) at prenatal care start were included in this analysis. The primary outcome was cesarean delivery compared between obese ($\geq$30 kg/m^2) and nonobese ($<$30 kg/m^2) women. Indication for cesarean was also evaluated.

Results A total of 465 women were included: 207 (44.5%) obese and 258 (55.5%) nonobese. Women with obesity had a higher risk of cesarean compared with women without obesity (33.3 vs. 23.3%, $p = 0.02$), even when adjusting for parity, weight change over pregnancy, and indication for induction (adjusted relative risk [aRR] $= 1.79$, 95% confidence interval [CI]: [1.34–2.39]). Compared with women without obesity, women with obesity had a higher risk of failed induction (47.8 vs. 26.7%, $p = 0.01$) without a difference in arrest of active phase ($p = 0.39$), arrest of descent ($p = 0.95$) or fetal indication ($p = 0.32$), despite adherence to a standardized labor protocol.

Conclusion Compared with women without obesity, women with obesity undergoing an induction are at increased risk of cesarean, in particular a failed induction, even within the context of standardized induction management. As standardized practices limit provider variation in labor management, this study may support physiologic differences in labor processes secondary to obesity.

Keywords
► obesity
► induction of labor
► cesarean delivery
► failed induction
► labor protocol

Key Points
- Even with a standardized induction protocol, women with obesity are at higher risk of cesarean.
- In particular, women with obesity are at increased risk of cesarean for failed induction.
- These findings support a possible biologic relationship between obesity and failed induction.

Obesity is a critical health issue in the reproductive population. In addition to antenatal complications, such as spontaneous abortion, recurrent miscarriage, gestational diabetes, preeclampsia, cardiac dysfunction, and stillbirth, multiple retrospective analyses have demonstrated that women with obesity are more likely to undergo cesarean delivery.[1–6] This finding is most pronounced among women with obesity undergoing labor induction. In a systematic review evaluating women undergoing labor induction, cesarean delivery was 80% more likely among women with obesity compared with women of normal weight.[7] This and other work have consistently demonstrated longer length of induction, higher prostaglandin, and oxytocin doses, as well as higher rates of cesareans for failed induction and arrest disorders.[7–9]

The basis for differences in labor induction outcomes among women with obesity is not entirely clear. Possible explanations include (1) physiologic differences and (2) care variation. One method to reduce care variation in medicine is to structure clear practice guidelines. In theory, such standardization of care would minimize differences in clinician management that contribute to disparate outcomes. There are minimal data surrounding the impact of variation in labor induction practices by body mass index (BMI) on mode of delivery and obstetric morbidity.

In this work, we aimed to compare cesarean delivery rates among women with and without obesity in a controlled environment, in the context of a randomized trial that utilized a strict labor induction protocol. We hypothesized that differences in cesarean delivery rate by BMI would remain despite minimizing variation in labor management, adding support to a physiologic relationship between obesity and failed labor induction.

Materials and Methods

We performed a secondary analysis of a randomized clinical trial that compared time to delivery among four different induction methods (misoprostol alone, the cervical Foley alone, misoprostol/the cervical Foley concurrently, and the cervical Foley/oxytocin concurrently).[10] This study was performed at the Hospital of the University of Pennsylvania from May 2013 to June 2015. This study was approved by the institutional review board at the University of Pennsylvania and all women provided written consent before participation in this study.

Women were included in the original randomized trial if they had labor induced for any indication and met the following inclusion criteria: full term (≥37 weeks), ≥18 years of age in cephalic presentation, with intact amniotic membranes, and an unfavorable cervical examination (Bishop's score ≤6 and cervical dilation ≤2 cm). Women were exclud-

ed from the study if they had a prior cesarean delivery, major fetal anomaly, or had HIV, HELLP (hemolysis elevated liver enzymes low platelets) syndrome, eclampsia, or severe fetal growth restriction with abnormal umbilical artery dopplers.[10] For the purpose of this secondary analysis, we also excluded women who did not have a BMI at the start of prenatal care recorded.

Women enrolled in the original trial had their induction and labor managed with a standardized protocol specific to the cervical ripening method. The protocol was derived by two of the investigators (L.D.L. and S.K.S.) and approved by an institutional obstetrical committee prior to initiation of the randomized trial. It was modeled after prior studies that utilized an active management protocol.[11–15] The protocol was used for induction management, as well as latent (defined as the stage of labor prior to 6-cm dilation) and active labor (defined as the stage of labor at ≥6 cm). The cervical ripening method was the only variable that differed among women. The protocol had multiple components include the following:

- Regular cervical examinations to assess for labor progress: every 3 hours in latent labor if cervical ripening agent being used remains in place, every 2 to 4 hours in latent labor if oxytocin was being utilized, and every 1 to 2 hours in active labor.
- Interventions if labor was not progressing which included, for example, initiation of oxytocin, amniotomy, and use of intrauterine pressure catheter.
- If the woman had not yet had membranes ruptured and cervix was ≥4-cm dilated, it was recommended that an amniotomy be performed at this time, if clinically feasible.
- Once cervical dilation was ≥5 cm, the four individual cervical ripening protocols converged and providers were instructed to proceed with the "active labor protocol," although active labor itself was defined as cervical dilation ≥6 cm for the purposes of defining arrest disorders. The cervical ripening method was the only thing that could differ among women and each protocol was tailored for the specific cervical ripening method chosen.[10] Lastly, within the labor protocol group, determination of the need for a cesarean for failed induction or arrest disorders was based off of the 2012 NICHD (National Institute of Child Health and Human Development) guidelines.[16] Failed induction was defined as "failure to generate regular (e.g., every 3 minutes) contractions and cervical change after at least 24 hours of oxytocin administration, with artificial membrane rupture if feasible."[16]

For the purposes of this analysis, women were grouped by BMI. The Institute of Medicine (IOM) definitions were used for obesity: women with obesity (≥30 kg/m^2) versus

without obesity ($<30\,kg/m^2$). BMI was determined by direct measurement at initial prenatal visit, regardless of gestational age. The primary outcome was cesarean delivery for any indication. Secondary outcomes included indication for cesarean, time to cesarean, total length of labor, and composite maternal morbidity (defined as ≥ 1 of the following during labor, delivery, or in the 4 weeks postpartum: third/fourth-degree perineal laceration, blood transfusion, endometritis, wound separation–infection [defined by the need for additional wound closure or the need for antibiotics], venous thromboembolism, hysterectomy, intensive care unit admission, or death). Time to cesarean was calculated as time from placement of first induction agent to time at cesarean start in hours. Total length of labor was calculated as time from placement of first induction agent to delivery time.

Bivariate comparisons of demographic and baseline clinical characteristics, as well as labor and delivery outcomes, were performed with Fisher's exact tests and Chi-square tests for categorical variables, and t-tests or Wilcoxon's rank-sum tests for continuous variables, where appropriate. Poisson's regression with robust variance was utilized to adjust for confounders; results are presented as relative risks (RRs). We limited covariates in the model to those demonstrated to be statistical confounders: demographic and clinical characteristics that were associated on bivariate tests ($p < 0.10$) with both the group/exposure variable (BMI category) and the outcome variable (cesarean delivery). Thus, parity, race, chronic hypertension, weight change over pregnancy, indication for induction, and birth weight were assessed as possible confounders. Study group, although not associated with BMI category, was evaluated but found not to be significant in multivariable modeling. Backward stepwise elimination of covariates (with $p > 0.10$ for removal) was performed to determine which covariates would be retained in the final model. Statistical analyses were performed with Stata 15 (StataCorp, College Station, TX). This study was performed with a fixed sample size determined by those who enrolled in the original trial. Based on the fixed sample size of 491 and a baseline cesarean rate of 25%, we had more than 80% power to detect a 1.5-fold difference in cesarean delivery.

Results

Of the 491 women included in the original randomized controlled trial, 465 had a recorded BMI at the start of prenatal care and were included in this analysis. Of those, 207 (44.5%) were classified as obese (BMI $\geq 30\,kg/m^2$) and 258 (55.5%) were classified as nonobese (BMI $< 30\,kg/m^2$).

Demographic and clinical characteristics among women with and without obesity are shown in ►Table 1. Women with obesity were more likely to be Black, have gestational diabetes, and have chronic hypertension. In addition, while women with obesity continued to have a higher BMI at delivery than women without obesity, women with obesity gained less weight over the course of their pregnancy. Finally, women with obesity were more likely to be induced for

maternal indications, while women without obesity were more likely to be induced for fetal indications.

Women with obesity had a higher rate of cesarean delivery than women without obesity (33.3 vs. 23.3%, $p = 0.02$; ►Table 2). This difference remained significant when controlling for parity, weight change over pregnancy, and indication for induction (adjusted RR [aRR] = 1.79, 95% confidence interval [CI]: [1.34–2.39]).

Differences between women with and without obesity in indication for cesarean are also shown in ►Table 2. Women with obesity were significantly more likely to undergo a cesarean for failed induction of labor compared with women without obesity (47.8 vs. 26.7%, $p = 0.01$). This difference also remained significant when controlling for parity, weight change over pregnancy, and indication for induction (aRR = 1.78 95% CI: [1.09–2.92]). Other indications for cesarean, such as arrest of active phase, arrest of descent, and nonreassuring fetal status, were no different between BMI groups.

There was no significant difference in median time to cesarean between women with and without obesity. There was also no significant difference between women with and without obesity in median time to delivery overall or composite maternal morbidity.

Discussion

This study demonstrates that, even in the context of a standardized labor induction protocol, women with obesity are at higher risk of cesarean delivery. In particular, women with obesity are at increased risk of cesarean for failed induction. The use of a standardized protocol minimizes the effect of care variation related to BMI on labor management. Thus, the continued association between obesity and cesarean, despite standardization, may provide support to a physiologic explanation for the increased risk of cesarean in women with obesity undergoing labor induction.

Many studies have sought to evaluate the physiology of labor in women with obesity by linking obesity with abnormal labor from the perspective of basic science. One study comparing the contractility of myometrium collected during elective cesarean section by maternal BMI demonstrated a significant reduction in the amplitude and frequency of contractions among women with obesity when compared with women with normal weight.[17] This decrease in contractility is likely secondary to hormonal differences. For example, maternal obesity and high cholesterol are closely related.[18] Studies have shown that cholesterol and low-density lipoprotein (LDL) inhibit spontaneous contractions.[19] Further, adipokines, such as leptin, visfatin, adiponectin, resistin, and apelin, have also been implicated in the mechanism of decreased uterine contractility.[20–24]

Our findings are consistent with prior work evaluating the relationship between obesity and cesarean delivery. Wolfe et al performed an Ohio birth certificate–based cohort study encompassing 80,887 deliveries comparing rates of failed labor induction by prepregnancy obesity class. In this work, induction failure rates were 13% in normal-weight women

Table 1 Demographics and clinical characteristics among women with and without obesity undergoing labor induction using a standardized labor induction protocol

		With obesity ($n = 207$) n (%)	Without obesity ($n = 258$) n (%)	p-Value
Demographics				
BMI at initial prenatal visit (kg/m^2)[a]		36.5 [32.6–41.1]	24.9 [22.1–27.1]	<0.001
Maternal age (year)[a]		28 [23–32]	26 [22–32]	0.12
Race	Black	180 (87.0)	178 (69.0)	<0.001
	White	20 (9.7)	55 (21.3)	
	Asian	1 (0.5)	9 (3.5)	
	Other	6 (2.9)	16 (6.3)	
Ethnicity	Hispanic	3 (1.4)	10 (3.9)	0.16
Insurance	Private	61 (29.5)	99 (38.4)	0.05
	Medicaid/Medicare/uninsured	146 (70.5)	159 (61.6)	
Nulliparity		112 (54.1)	163 (63.2)	0.05
LEEP or CONE		7 (3.4)	9 (3.5)	0.95
Tobacco use during pregnancy		22 (10.6)	16 (6.2)	0.17
Gestational diabetes		21 (10.1)	10 (3.9)	0.007
Pregestational diabetes		8 (3.9)	3 (1.2)	0.07
Asthma		55 (26.6)	56 (21.7)	0.22
Chronic hypertension		24 (11.6)	14 (5.4)	0.02
History of venous thromboembolism		5 (2.4)	2 (0.8)	0.25
Renal dysfunction		2 (1.0)	4 (1.6)	0.70
Systemic lupus erythematous		1 (0.5)	2 (0.8)	1.00
Weight change over pregnancy (lbs)[a]		19 [9–27]	27 [17–36.5]	<0.001
Maternal BMI at delivery (mg/kg^2)[a]		39.3 [36.5–43.1]	29.0 [26.9–31.5]	<0.001
Clinical characteristics at admission				
Indication for induction	Postdates	27 (13.0)	33 (12.8)	<0.001
	Maternal Indications[b]	82 (39.6)	55 (21.3)	
	Fetal Indications[c]	75 (36.2)	141 (54.7)	
	Elective/other[d]	23 (11.1)	29 (11.2)	
Scheduled induction		92 (44.4)	118 (45.7)	0.78
Gestational age[a]		39 [38–40]	39 [38–40]	0.70
Cervical dilation at induction start	<1 cm	43 (20.8)	46 (17.8)	0.51
	1–2 cm	153 (73.9)	202 (78.3)	
	>2 cm	11 (5.3)	10 (3.9)	
Modified Bishop's score[a]		3 [2–4]	3 [2–4]	0.11

Abbreviations: BMI, body mass index; LEEP, loop electrical excision procedure.
[a]Median[interquartile range].
[b]Examples include: chronic hypertension, gestational hypertension, preeclampsia, diabetes, renal disease, history of venous thromboembolism, cardiac disease or other chronic medical condition where induction was recommended.
[c]Examples include: oligohydramnios, intrauterine growth restriction, and abnormality on fetal testing.
[d]Examples of "other" include history of an intrauterine fetal demise, vaginal bleeding at term, and cholestasis.

compared with 29% in class-III obesity.[9] Hermann et al evaluated 12,297 deliveries from the French National Perinatal Survey, comparing cesarean rates by prepregnancy BMI. Here, both obese primiparous and multiparous women with no previous cesarean delivery had increased adjusted RRs for intrapartum cesarean delivery (RR = 1.64; 95% CI: [1.36–1.98]; and RR = 1.66; 95% CI: [1.15–2.39], respectively).[25] While our study is comprised of a smaller sample than prior works, our data provide important support to those analyses. Furthermore, our data substantially add to the

Table 2 Outcomes among women with and without obesity undergoing labor induction using a standardized labor induction protocol

	With obesity (n = 207) n (%)	Without obesity (n = 258) n (%)	p-Value	aRR[a]
Cesarean delivery	69 (33.3)	60 (23.3)	0.02	1.79 [1.34–2.39]
Indication for cesarean[b]				
Failed induction	33 (47.8)	16 (26.7)	0.01	1.78 [1.09–2.92]
Arrest of active phase	15 (21.7)	17 (28.3)	0.39	0.73 [0.40–1.33]
Arrest of descent	6 (8.7)	7 (11.7)	0.58	0.85 [0.30–2.37]
Nonreassuring fetal status	33 (47.8)	34 (56.7)	0.32	0.90 [0.65–1.26]
Elective/other[c]	8 (11.6)	8 (13.3)	0.77	0.66 [0.24–1.82]
Dilation of amniotomy (cm)[d]	4 (4.5)	4 (4.5)	0.81	–
Time to amniotomy (h)[d]	6.9 [4.0–11.3]	6.7 [3.6–10.9]	0.80	–
Time to cesarean (h)[d]	21.6 [17.3–30.0]	19.8 [15.6–26.5]	0.34	–
Time to delivery (h)[d]	16.2 [10.6–23.2]	15.4 [10.3–20.8]	0.13	–
Composite maternal morbidity[e]	17 (8.2)	15 (5.8)	0.31	–

Abbreviation: aRR, adjusted relative risk.
[a]Adjusted for parity, weight change over pregnancy, and indication for induction.
[b]If listed as primary or secondary indication.
[c]Examples of "other" include malpresentation diagnosed during induction and worsening preeclampsia remote from delivery.
[d]Median [interquartile range].
[e]≥1 of the following during labor, delivery, or in the 4 weeks postpartum: third/fourth-degree perineal laceration, blood transfusion, endometritis, wound separation–infection (defined by the need for additional wound closure or the need for antibiotics), venous thromboembolism, hysterectomy, intensive care unit admission, or death.

current body of literature by demonstrating that differences in rates of cesarean delivery and failed induction remain for women with obesity despite standardized labor management.

Strengths and Limitations

This study has several strengths. Our work was performed as a secondary analysis of randomized trial which allowed for a highly controlled environment in which to evaluate outcomes in labor induction. We were able to assess the impact of multiple factors thought to mediate the relationship between obesity and cesarean, such as indication for induction and weight change over pregnancy. We were also able to specifically examine which indications for cesarean were increased among women with obesity. In addition, this study utilized directly measured weight to calculate BMI, limiting classification bias.

However, while the standardized protocol utilized here minimizes provider variation in management, this study is limited in that such practice differences can likely never be eliminated completely. Thus, results might differ if we were truly able to control every aspect of decision-making throughout a labor induction. In addition, protocol adherence was not assessed as a part of this work, thus we were unable to evaluate if clinicians were more likely to deviate from the protocol in women with obesity due to presumptions about vaginal birth success. Furthermore, this work was performed at one, urban, academic center with a fixed

sample size, which may limit generalizability. Due to sample size constraints, we were also unable to evaluate obesity with further granularity, such as by IOM class I (BMI = 30–34.9 kg/m²), II (BMI = 35–39.9 kg/m²), and III (BMI ≥40 kg/m²).

Conclusion

While we are beginning to understand the unique physiology of labor and induction in women with obesity from a basic science perspective, the results of this study support the need for additional research. Translational work to develop interventions that target differences in physiology for women with obesity may be beneficial. In addition, future work should evaluate whether we should alter the definitions of arrest disorders for women with obesity, thereby allowing for additional time in labor. Finally, an evaluation should be performed to assess whether standardization of labor induction impacts care variation that occurs due to demographics other than obesity, such as race, where disparate outcomes are less likely physiologic.

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