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Cesarean delivery and subsequent fecundability

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Abstract

Introduction—Studies have shown that cesarean delivery is associated with fewer subsequent births relative to vaginal delivery, but it is unclear whether confounding by pregnancy intention or indication for surgery explained these results. We evaluated the association between cesarean delivery and subsequent fecundability among 910 primiparous women after singleton live birth.

Methods—In a cohort of Danish women planning pregnancy (2007–2012), obstetrical history was obtained via registry linkage; time-to-pregnancy and covariate data were collected via questionnaire. Fecundability ratios (FR) and 95% confidence intervals (CI) were adjusted for potential confounders.

Results—Relative to spontaneous vaginal delivery, emergency cesarean delivery with cephalic presentation showed little association with fecundability (FR=1.0, 95% CI: 0.83, 1.3, but cesarean delivery with breech presentation (FR=0.72, 95% CI: 0.53, 0.97) and planned cesarean delivery with cephalic presentation (FR=0.51, 95% CI: 0.25, 1.0) were associated with reduced fecundability.

Conclusions—The cesarean-fecundability association varied by previous fetal presentation and emergency status.

Keywords

Cesarean section; fertility; cohort studies; pregnancy complications; pregnancy

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Introduction

Some,¹⁻¹² but not all,¹³ studies have reported fewer subsequent births after cesarean delivery compared with vaginal delivery, but none of these studies was able to rule out plausible competing explanations.¹⁴ The extent to which the cesarean–parity association reflects a biological effect of cesarean delivery³ or confounding by medical factors indicating cesarean, history of infertility,¹⁵ or future pregnancy intention¹⁴ is unclear.

Among women with one previous singleton live birth, we assessed the association between fecundability (per-cycle probability of pregnancy) and mode of delivery (cesarean versus spontaneous vaginal delivery) in the prior pregnancy. We used data from a preconception cohort study of Danish women planning pregnancy in which questionnaire data were linked with national registry data. By adjusting for indications for cesarean delivery, history of infertility, and maternal body size and lifestyle factors, we aimed to separate the effects of these factors on fecundity from the effect of the cesarean procedure, among couples planning another pregnancy.

Methods

The Snart-Gravid Study enrolled 5,046 Danish women aged 18–40 years who were trying to conceive spontaneously during 2007–2012.¹⁶ Participants completed a baseline questionnaire at enrollment and follow-up questionnaires every two months for up to 12 months. The baseline questionnaire elicited information on weight, height, reproductive and medical history, and lifestyle.¹⁷ Reproductive history included number of pregnancies and history of infertility: “Have you ever tried for one year or more to become pregnant without becoming pregnant during that time?” Participants reported diagnoses of conditions that might affect fertility, e.g., uterine leiomyoma. We used the participant's Civil Personal Registration number to link questionnaire data with the Danish Medical Birth Registry,¹⁸ obtaining records of births that occurred before study enrollment. Using the International Classification of Diseases, 10th Revision (ICD-10) codes, we classified the birth as spontaneous vaginal delivery or cesarean delivery. Almost all infants in breech or shoulder presentation were delivered by cesarean, consistent with Danish standard of care.¹⁹ Because indications for emergency cesarean delivery differ from that of planned cesarean delivery,²⁰ we further categorized cesarean delivery according to emergency status if the infant was in cephalic presentation.

Data on maternal comorbidities and obstetric complications from the previous birth were collected via linkage with the Danish National Patient Register.²¹ We retrieved Danish ICD-10 codes corresponding to obstetric diagnoses,²² uterine leiomyoma, and Müllerian anomalies (Table 1). From the birth registry, we used birth weight in grams to define macrosomia (>4,000 g) and low birth weight (<2,500 g), and gestational age (days) to define preterm and post-term deliveries (<259 days and ≥294 days, respectively). Selected diagnoses from these registries have been validated against medical records.^{18, 23}

The study protocol was approved by the Boston University Medical Center Institutional Review Board and the Danish Data Protection Agency [J. no. 2013-41-1922], and all participants provided informed consent.

Exclusions

Among 1,406 women with a history of one singleton live birth at enrollment, we excluded 26 women whose previous birth was before 1997 (because of changes in registry coding); two women lacking data on mode of delivery; and 468 women who had attempted pregnancy for >6 menstrual cycles at enrollment, leaving 910 women for analysis.

Data analysis

Women contributed menstrual cycles at risk from enrollment until a reported pregnancy or censoring event (fertility treatment, withdrawal, or 12 cycles attempted without success). We estimated fecundability ratios (FR) and 95% confidence intervals (CI) using proportional probabilities models.²⁴ A FR <1.0 corresponds to lower fecundability (longer time-to-pregnancy) among the exposed relative to the unexposed (i.e., spontaneous vaginal delivery). All models adjusted for cycle number at risk (1-12), maternal age at first birth (<25, 25-29, 30-34, 35 years), and gestational age of first birth (<37, 37-41, 42 weeks). Final models for emergency cesarean delivery with cephalic presentation and instrumental vaginal delivery were further adjusted for body mass index (BMI, <20, 20-24, 25-29, 30 kg/m²) and fetopelvic disproportion, whereas the final model for cesarean delivery with breech presentation was further adjusted for smoking history (never, ever smoker:<5, 5-9, 10 pack-years) and predisposing factors for breech presentation (leiomyoma, Müllerian anomaly, polyhydramnios, and placenta previa).

To evaluate potential for selection bias, we stratified the analysis by cycles attempting pregnancy at enrollment (<3, 3). We also stratified analyses by primigravidity versus multigravidity at enrollment to address potential confounding by prior pregnancy loss.

We used multiple imputation across five datasets²⁵ to impute missing values for covariates reported on the baseline questionnaire using SAS/STAT® software.²⁶

Results

During 12 cycles of follow-up, 708 (78%) of the 910 participants conceived spontaneously, 48 (5%) initiated fertility treatment before completing follow-up, 111 (12%) withdrew, and 43 (5%) completed the study without conceiving. Relative to spontaneous vaginal delivery, cesarean delivery for breech presentation was positively associated with age at first birth and enrollment; preterm delivery and polyhydramnios at first birth; pack-years of smoking (mean 2.9 vs. 2.6 pack-years); and caffeine intake (mean 171 vs. 160 mg per day) (Table 1). Emergency cesarean delivery with cephalic presentation was positively associated with age at first birth, BMI (mean 26.2 vs. 24.5 kg/m²), and complications affecting the first pregnancy, labor, and delivery. The prevalence of cesarean delivery in our study (20.7%) was similar to the 2011 Danish national prevalence (20.6%).²⁷

Cesarean delivery had little association with fecundability among women who had an emergency cesarean delivery with cephalic presentation (adjusted FR=1.0, 95% CI: 0.83, 1.3), but it was inversely associated with fecundability when the fetal presentation was breech or shoulder (adjusted FR=0.72, 95% CI: 0.53, 0.97) (Table 2). Among the 15 women who had a planned cesarean delivery with cephalic presentation, seven became pregnant over follow-up (crude FR=0.51, 95% CI: 0.25, 1.0). Results were similar in analyses stratified by cycles attempting pregnancy at enrollment and by gravidity (eTable 1). Instrumental vaginal delivery was not associated with fecundability relative to spontaneous vaginal delivery (adjusted FR=1.0, 95% CI: 0.84, 1.2).

Discussion

Among Danish women planning a pregnancy following one live birth, emergency cesarean delivery with cephalic presentation—the most common type of cesarean delivery—was not appreciably associated with fecundability, but cesarean delivery with breech presentation and planned cesarean delivery with cephalic presentation were associated with reduced fecundability. Differences in association by fetal presentation and emergency status of the cesarean are either the result of chance, bias, or interaction between the procedure and its indication(s), but are not readily explained by an adverse effect of cesarean delivery per se.

Some,¹⁻¹² but not all,¹³ studies have found fewer subsequent live births associated with cesarean delivery relative to vaginal delivery, and with cesarean categorized by fetal presentation^{3, 5} and emergency status.^{2, 3, 5-7} However, one study found no appreciable association with emergency procedures.⁸ After accounting for maternal medical and lifestyle factors in our study, emergency cesarean delivery with cephalic presentation had a precise FR close to the null value, which did not support the hypothesis that cesarean delivery decreases fecundity. The most common indication for emergency cesarean delivery was fetal distress, consistent with prior studies,^{20, 28} and this was not associated with fecundability. In contrast, conditions that distort the uterine cavity²⁹—e.g., leiomyoma and Müllerian anomalies—may be a common cause of breech presentation and secondary infertility.³⁰

Previous studies have investigated other explanations for the cesarean–parity association. Although studies with limited control for confounding reported a somewhat increased risk of spontaneous abortion after cesarean delivery,^{2, 3, 9, 31-33} there was no increased risk in a large, registry-based study that adjusted for maternal and obstetric factors.³⁴ Also, lack of childbearing after cesarean delivery could be voluntary, although little association has been found between mode of delivery at first birth and desire for further childbearing.^{14,35}

If cesarean delivery is a marker of impaired fertility and highly fecund women were less likely to participate in our study because they were less likely to plan their pregnancies, associations may have been attenuated because fewer highly fecund women would be included in the spontaneous vaginal delivery category. Under-participation of highly fecund women may also explain the greater prevalence of breech presentation in our cohort (6.8%) compared with the general population (3-4%¹⁹). The bias, however, should be small because a high proportion of pregnancies are planned in Denmark.^{36, 37} By conditioning on pregnancy planning, we effectively excluded women with fertility-ending complications in

their first birth. However, mode of delivery is rarely the cause of emergency peripartum hysterectomy.³⁸

We could not distinguish between the effect of factors leading to breech birth and the effect of the cesarean procedure because all but one breech birth were by cesarean. The small number of planned cesarean deliveries with cephalic presentation and the various obstetric complications that were more prevalent among this group hindered analytical adjustment for confounding. Residual confounding is possible when certain obstetric complications that lead to both cesarean delivery and lower fecundity are under-recorded in registry data.^{18, 23, 39} The expected bias would be away from the null if the underascertainment is non-differential by cesarean delivery because the estimated effect of cesarean delivery would include the effect of certain comorbidities that lead to both cesarean delivery and lower fecundity.⁴⁰

In conclusion, after taking into account maternal medical history and childbearing intentions, the cesarean-fecundability association varied by previous fetal presentation and emergency status. Our results do not support a harmful biological effect of cesarean delivery on fecundability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Baseline characteristics according to mode of delivery and fetal presentation in 910 women with one prior live birth: Snart-Gravid Study, Denmark, 2007-2012^a

Table 1

	Vaginal delivery			Cesarean delivery		
	Spontaneous	Instrumental	Breech	Cephalic, Emergency	Cephalic, Planned	
Number of women, n	585	137	61	112	15	
Age at first birth 30 years (%)	27	34	34	36	27	
Age at enrollment, years (%)						
18-24	8	3	2	8	0	
25-29	37	42	35	35	39	
30-34	42	41	47	44	49	
35	13	15	16	13	13	
Time since last birth, ^b years (median)	2.2	2.1	2.0	3.7	2.0	
Attempt time at enrollment <3 cycles (%)	58	54	50	57	44	
Vocational training (%)						
None, basic, or <3 years	41	34	33	42	40	
<i>Obstetric complications</i>						
Birth weight <2,500 g (%)	2	1	3	11	0	
Birth weight 4,000 g (%)	13	13	12	27	16	
Prior miscarriage (%)	6	3	5	8	0	
Hypertensive disorder ^c (%)	7	11	7	15	8	
PPROM ^d (%)	2	1	6	3	0	
Preterm ^e (%)	6	3	11	11	0	
Post-term ^f (%)	7	8	6	18	0	
Placenta previa (%)	0	0	0	0	2	
Placental abruption (%)	1	0	2	2	0	
Polyhydramnios (%)	0	0	2	2	0	
Oligohydramnios (%)	1	0	0	4	5	
<i>Labor and delivery complications</i>						
Fetal distress (%)	17	57	3	46	13	

	Vaginal delivery			Cesarean delivery	
	Spontaneous	Instrumental	Breech	Cephalic, Emergency	Cephalic, Planned
Fetopelvic disproportion (%)	3	2	1	19	16
Caesarean section on maternal request (%)	0	0	1	4	32
<i>Reproductive and medical history</i>					
Infertility ^g (%)	17	16	16	18	16
Fibroids (%)	4	6	0	2	5
Müllerian anomaly (%)	0	0	3	0	5
Thyroid disorders (%)	4	5	5	0	0
Diabetes ^h (%)	4	4	1	4	13
Last contraceptive (%)					
Hormonal methods ⁱ	51	46	54	55	37
Barrier methods	39	44	40	34	54
Withdrawal, charting, other	11	10	6	11	11
Regular cycles (%)	78	79	79	88	63
Cycle length, days (mean)	30.1	29.8	29.3	29.1	29.5
Very heavy menstrual flow (%)	3	1	5	2	8
<i>Lifestyle habits</i>					
Frequency of intercourse:					
2 times/week (%)	57	56	50	55	57
Timing for fertile window (%)	50	58	59	58	39
7 Alcoholic drinks/wk (%)	7	7	7	7	0

^aWith the exception of age at first birth, statistics are standardized to the population distribution of age at first birth.

^bInterval from prior birth to start of the pregnancy attempt under study.

^cIncludes preeclampsia, eclampsia, pre-existing hypertension, pregnancy-induced hypertension without proteinuria, pregnancy-induced proteinuria without hypertension.

^dPPROM, preterm premature rupture of membranes.

^e<37 weeks gestation

^f42 weeks gestation

^gParticipant reported an episode before the pregnancy attempt under study when she attempted pregnancy for >12 months without success.

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Includes gestational and pre-existing diabetes.
 η_i
Includes oral contraceptive pills, injectable contraceptives, and patch contraceptives

Mode of delivery and fecundability in 773 women with one prior live birth: Smart-Gravid Study, Denmark, 2007-2012

Table 2

	Pregnancies	Cycles	Model 1 ^a		Model 2	
			FR	(95% CI)	FR	(95% CI)
Spontaneous vaginal delivery	463	2,013		1.00 ^b		1.00 ^b
Emergency cesarean, cephalic presentation ^c	87	419	0.92	(0.75, 1.1)	1.0	(0.83, 1.3)
Planned cesarean, cephalic presentation	7	67	0.51	(0.25, 1.0)	--	--
Cesarean, breech presentation ^d	40	259	0.70	(0.53, 0.95)	0.72	(0.53, 0.97)

^aModel 1 is adjusted for cycle number at risk.

^bReference category.

^cModel 2 is adjusted for age at first birth, gestational age of first birth, fetopelvic disproportion at first birth, and body mass index at enrollment.

^dThis category included emergency and planned procedures. Model 2 is adjusted for age at first birth, gestational age of first birth, pack-years of smoking at baseline, and history of the following diagnoses: uterine leiomyomata, Müllerian anomaly, polyhydramnios and placenta previa.