Mode of delivery and subsequent fertility

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STUDY QUESTION: When compared with vaginal delivery, is Cesarean delivery associated with reduced childbearing, a prolonged inter-birth interval or infertility?

SUMMARY ANSWER: Women whose first delivery was by Cesarean section were not significantly different from those who delivered vaginally with respect to subsequent deliveries, inter-birth interval or infertility after delivery.

WHAT IS ALREADY KNOWN: Some studies have suggested that delivery by Cesarean section reduces subsequent fertility, while others have reported no association.

STUDY DESIGN, SIZE, DURATION: This was a planned secondary analysis of the Mothers’ Outcomes After Delivery study, a longitudinal cohort study. This analysis included 956 women with 1835 deliveries, who completed a study questionnaire at 6–11 years (median [interquartile range]: 8.1 [7.1, 9.8]) after their first delivery.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Exclusion criteria regarding the first birth were: maternal age < 15 or > 50 years, delivery at < 37 weeks gestation, placenta previa, multiple gestation, known fetal congenital abnormality, stillbirth, prior myomectomy and abruption. Of the 956 women included, the first delivery was by Cesarean section for 534 women and by vaginal birth for 422 women. Infertility was self-reported. To compare maternal characteristics by mode of first delivery, P-values were calculated using Fisher’s exact test or Pearson’s χ² test for categorical variables and a Kruskall–Wallis test for continuous variables. We also considered whether, across all deliveries to date, a prior Cesarean is associated with decreased fertility. In this analysis, self-reported infertility after each delivery (across all participants) was considered as a function of one or more prior Cesarean births, using generalized estimating equations to control for within-woman correlation.

MAIN RESULTS AND THE ROLE OF CHANCE: No differences were observed between the Cesarean and vaginal groups (for first delivery) with respect to infertility after their most recent delivery (7 versus 6%, P = 0.597), the interval between their first and second births (30.8 versus 30.6 months, P = 0.872), or multiparity (75 versus 76%, P = 0.650). Across all births, a history of Cesarean delivery was not significantly associated with infertility (odds ratio [OR], 0.90; 95% confidence interval [CI], 0.64–1.26). Women who reported infertility prior to their first delivery were significantly more likely to report infertility after each subsequent delivery (OR, 5.16; 95% CI, 3.60–7.39).

LIMITATIONS, REASONS FOR CAUTION: Due to the use of self-reported infertility, the fertility status of some participants may be misclassified. Also, the small sample size may result in insufficient power to detect small differences between groups. Finally, a relatively high proportion of our participants were over age 35 at the time of first delivery (26%) and highly educated (37% with graduate degrees), which may indicate that our population may not be generalizable.

WIDER IMPLICATIONS OF THE FINDINGS: While some prior studies have shown decreased family size among women who deliver by Cesarean, our results suggest that the rate of infertility is not different after Cesarean compared with vaginal birth. Our findings should be reassuring to women who deliver by Cesarean section.

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Key words: Cesarean section, fertility, reproduction, childbearing, inter-birth interval
Introduction

Several studies have found that Cesarean delivery is associated with reduced parity compared with vaginal birth (Hemminki et al., 2005; Molisson et al., 2005; Kjerulf et al., 2013). However, others have concluded that there is no association (Tower et al., 2000; Ejsink et al., 2008). Cesarean delivery might plausibly influence subsequent parity via subfertility, confounding factors or maternal choice. Subfertility after Cesarean delivery could result from infection at the wound site or pelvic adhesions (Murphy et al., 2002). It is also plausible that reduced fecundity after Cesarean versus vaginal delivery might be due to confounding factors, such as advanced maternal age (Smith et al., 2006).

Alternatively, differences in family size after Cesarean versus vaginal birth might reflect a difference in women’s reproductive choices (Porter et al., 2003; Oral and Elter, 2007; Tolland et al., 2007). One recent study of US women found that women who prefer small family size may be more likely to deliver by Cesarean (Kjerulf et al., 2013). Moreover, some researchers have speculated that a difficult or traumatic birth experience might alter a woman’s decision to pursue additional pregnancies (Bahl et al., 2004). Bhattacharya et al. (2006) reported worse birth experiences following emergency abdominal and vaginal operative deliveries, while Rowlands and Redshaw (2012) reported higher rates of post-traumatic stress symptoms among women who had forceps-assisted vaginal births when compared with other delivery modes.

Given the previous conflicting results, we sought to further investigate fertility as a function of mode of delivery, using data from the Mothers’ Outcomes After Delivery (MOAD) study (Handa et al., 2011). Specifically, we compared infertility, parity and inter-birth interval among women who delivered by Cesarean versus those who delivered vaginally. We also considered the impact of emergency abdominal and vaginal operative deliveries on subsequent fertility. Finally, considering all deliveries reported to date (6–11 years from the first delivery), we investigated whether one or more Cesarean deliveries influence subsequent fertility.

Materials and Methods

Study population

This was a planned secondary analysis of the MOAD study. MOAD is a longitudinal cohort study, established to investigate pelvic floor disorders and other health outcomes in women after vaginal versus Cesarean child-birth (Handa et al., 2011). Recruitment into the study was initiated in 2008 and is ongoing. Study design and recruitment methods have been described previously (Handa et al., 2011). Participants were recruited from Greater Baltimore Medical Center (GBMC), a large, private hospital in suburban Maryland, USA. Potential participants were identified from obstetric hospital discharge records. To be eligible, women must have given birth to their first child 5–10 years prior to enrollment. Exclusion criteria for the MOAD study (applied only to the index birth) included: maternal age < 15 or > 50 years, delivery at < 37 weeks gestation, placenta previa, multiple gestation, known fetal congenital abnormality, stillbirth, prior myomectomy and abrupton. Due to the goals of the larger study, Cesarean delivery was over-represented in the study population, and the Cesarean and vaginal birth groups were matched for years since first birth and for maternal age at first delivery.

Study variables

Between 2008 and 2013, data were collected for this report via a questionnaire at study enrollment (e.g. 5–10 years after first delivery) and ~ 1 year later. The web-based questionnaire was self-administered. The primary outcome for this analysis was infertility after delivery. This was self-reported. Specifically, when reporting a delivery, participants were asked, ‘Did you have infertility (difficulty getting pregnant) before this pregnancy?’ Additionally, participants were asked, ‘Since your most recent pregnancy, have you had infertility (difficulty getting pregnant)?’ Women who reported menopause, hysterectomy or the removal of both ovaries were not asked about infertility subsequent to their most recent delivery.

Women were asked to list the date for each of their deliveries. These data were used to calculate secondary outcomes for this research, which included total parity and, for women who had at least two deliveries, the interval (in months) between the first and second delivery.

Exposures were also derived from the study questionnaires. The primary exposure was Cesarean versus vaginal birth. In most cases, the route of delivery was ascertained by review of the medical record. Specifically, trained abstractors reviewed the obstetrical record for the 95% of deliveries that occurred at GBMC; maternal recall was used to classify the remaining births. Chart review confirmed Cesarean or vaginal birth for each delivery and provided additional delivery data (including whether the Cesarean was performed during active labor and whether vaginal birth required operative intervention with forceps or vacuum).

Additional exposures of interest included obesity, race, smoking history and age. Each participant’s weight and height were measured at the study visit and body mass index (BMI) was calculated (as weight (kg)/(height (m))^2). Current obesity was defined as a BMI of 30 kg/m^2 or greater. Race was self-reported. Cigarette smoking was classified as ‘never’ or ‘ever’ based on whether the woman reported smoking at least 100 cigarettes in her lifetime. For time-varying exposures (gravidity, parity, obesity and cigarette smoking), we used the data reported at the assessment 1 year after enrollment (6–11 years after first delivery). Among women missing a BMI measurement at this follow-up (n = 79), the BMI from enrollment was used.

Statistical analysis

The first set of analyses compared fertility outcomes for women who delivered their first child by Cesarean with those who delivered their first child vaginally. Fertility outcomes for this analysis included the proportion with fertility (difficulty getting pregnant)? Women who reported menopause, hysterectomy or the removal of both ovaries were not asked about infertility subsequent to their most recent delivery.

In a second set of analyses, to more fully explore the impact of delivery type on infertility and birth interval, the mode of first delivery was further subdivided into six groups (Friedman et al., 2012). Our hypothesis, based on the findings of Gottvall and Waldenstrom (2002), was that women might be less likely to have additional children or might have a longer inter-delivery interval after a negative first birth experience. Prior research (Blomquist et al., 2011) suggests that women find unplanned Cesarean birth or operative delivery more distressing than planned Cesarean or spontaneous vaginal delivery. Therefore, for this analysis, women who delivered their first child by Cesarean were subdivided into three groups: those who delivered by Cesarean prior to labor, those who delivered by Cesarean during active labor and those who delivered by Cesarean after complete cervical dilation. Women who delivered their first child vaginally were subdivided into three groups: those who had a spontaneous vaginal delivery, those who had a vacuum delivery and those who had a forceps delivery.
Our final objective was to consider whether, across all deliveries, a prior Cesarean is associated with decreased fertility. In this analysis, self-reported infertility after each delivery (across all participants) was considered as a function of one or more prior Cesarean births. Thus, for this analysis, the primary exposure was history of Cesarean delivery, but we also used multivariable analysis to control for the following potential confounders: self-reported infertility prior to first delivery, maternal age at the time of the delivery (<30 versus ≥35 to ≤35 versus >35), parity (first delivery (reference) versus one previous delivery versus two or more previous deliveries) and obesity. For this analysis, 252 (26%) women contributed one delivery to the analysis, 542 (57%) contributed two deliveries and 162 (17%) women contributed three or more deliveries to the analysis.

All analyses were performed using SAS 9.2™ statistical software. Statistical significance was defined at the α = 0.05 level. To compare maternal characteristics by mode of first delivery, P-values were calculated using Fisher’s exact test (Table I) or Pearson’s χ² test (Table II) for categorical variables and a Kruskall–Wallis test for continuous variables. To calculate the relative odds of infertility across all deliveries (Table III), generalized estimating equations with robust variance estimates were used to control for within-woman correlation.

Ethical approval
Institutional review board approval was obtained and all participants provided written, informed consent.

Results
At the time of this analysis, 982 women of the 1247 women (79%) who were due for the second survey (1 year after enrollment) had completed it. Completion of the questionnaire did not differ by first delivery type. These 982 women contributed 1883 deliveries. Of these women, 48 reported having experienced menopause, a hysterectomy or the removal of both ovaries subsequent to the most recent delivery. Because they were not asked about fertility problems since their first and only delivery. The 22 remaining multiparous women were retained in the analysis, but their final delivery record was dropped because of the lack of fertility data. These exclusions left 1835 deliveries from 956 women.

Of the 956 participants, 534 had Cesarean sections and 422 had vaginal births for their first delivery. As seen in Table I, no differences were observed between these two groups with respect to infertility after most recent delivery (7 versus 6%, P = 0.597), the interval between the first and second births (30.8 versus 30.6 months, P = 0.872), and multiparity (75 versus 76%, P = 0.650). The groups were also similar with regard to potential confounders, including infertility prior to first delivery, number of pregnancy losses or abortions, ever smoking and maternal age ≥35 years at first delivery. Women who delivered their first child by Cesarean had a higher prevalence of current obesity (P < 0.001). The two groups were similar regarding prior hysterectomy (2 versus 2%, P = 0.812) and intent to have more children (4 versus 5%, P = 0.878). Compared with women whose first delivery was vaginal, more women whose first delivery was Cesarean reported tubal ligation (20 versus 7%, P < 0.001) and fewer reported partners with vasectomy (16 versus 24%, P = 0.002). Additionally, the two groups were similar according to race (14 versus 11% African American; P = 0.280) and maternal education (P = 0.282).

Table II compares infertility across six groups based on obstetrical exposures at first delivery. No differences were found between groups regarding infertility prior to first delivery, infertility after first delivery or interval between first and second birth (among women with at least two births). The groups were also similar in their percentage of multiparous participants (P = 0.469).

In Table III, infertility was considered at the delivery level, among 956 women with 1835 deliveries using generalized estimating equations. Fertility problems were reported after 181 (10%) deliveries. There were 572 women (60%) who had at least one Cesarean birth and 384 (40%) women who had no Cesarean births. In this analysis, our primary exposure was history of Cesarean delivery, and we adjusted for fertility

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cesarean birth at first delivery (n = 534)</th>
<th>Vaginal birth at first delivery (n = 422)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility after most recent delivery (%)</td>
<td>7</td>
<td>6</td>
<td>0.597</td>
</tr>
<tr>
<td>Interval between first and second birth (months)</td>
<td>30.8 (23.4, 43.3)</td>
<td>30.6 (23.8, 41.6)</td>
<td>0.872</td>
</tr>
<tr>
<td>Current parity (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>25</td>
<td>24</td>
<td>0.650</td>
</tr>
<tr>
<td>Two or more</td>
<td>75</td>
<td>76</td>
<td>0.339</td>
</tr>
<tr>
<td>Infertility prior to first delivery (%)</td>
<td>22</td>
<td>20</td>
<td>0.597</td>
</tr>
<tr>
<td>Number of pregnancy losses and abortions (gravidity-parity) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero</td>
<td>51</td>
<td>49</td>
<td>0.250</td>
</tr>
<tr>
<td>One</td>
<td>28</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Two or more</td>
<td>22</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Smoker everd</td>
<td>33</td>
<td>31</td>
<td>0.486</td>
</tr>
<tr>
<td>Maternal age &gt;35 years at first delivery</td>
<td>26</td>
<td>27</td>
<td>0.883</td>
</tr>
<tr>
<td>BMI 30 kg/m² or higher</td>
<td>31</td>
<td>19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior sterilization (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>2</td>
<td>2</td>
<td>0.812</td>
</tr>
<tr>
<td>Tubal ligation</td>
<td>20</td>
<td>7</td>
<td>0.001</td>
</tr>
<tr>
<td>Vasectomy</td>
<td>16</td>
<td>24</td>
<td>0.002</td>
</tr>
<tr>
<td>Intent to have more children</td>
<td>4</td>
<td>5</td>
<td>0.878</td>
</tr>
<tr>
<td>African American race</td>
<td>14</td>
<td>11</td>
<td>0.280</td>
</tr>
<tr>
<td>Maternal education (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;College degree</td>
<td>20</td>
<td>18</td>
<td>0.282</td>
</tr>
<tr>
<td>College degree</td>
<td>45</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>≥Graduate degree</td>
<td>35</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

*Fisher’s exact test for categorical variables and Kruskall–Wallis test for continuous variables.
1Excludes women who reported prior hysterectomy.
2Natural menopause or removal of both ovaries (n = 22).
3Among 722 women with current parity ≥2; data are median (interquartile range).
4Smoker ever = smoked at least 100 cigarettes in entire life.

Table II compares infertility across six groups based on obstetrical exposures at first delivery. No differences were found between groups regarding infertility prior to first delivery, infertility after first delivery or interval between first and second birth (among women with at least two births). The groups were also similar in their percentage of multiparous participants (P = 0.469).
parity increased beyond two. We found no significant association between fertility problems and age at delivery or current obesity.

**Discussion**

Our findings suggest no association between mode of delivery and subsequent fertility. Women whose first delivery was by Cesarean were no more likely than those who delivered vaginally to experience fewer subsequent deliveries, a prolonged inter-birth interval or infertility after delivery. While some investigators have reported reduced childbearing following Cesarean delivery (Hemminki et al., 2005; Mollison et al., 2005; Kjerulf et al., 2013b), others have questioned whether the observed association is causal (Gurol et al., 2013). Studies of Cesarean section for breech presentation compared with unassisted vertex vaginal deliveries have shown comparable rates of subsequent birth (Smith et al., 2006; Eijink et al., 2008). To date, research on this topic has varied significantly in methodology and design, adding to the challenge of interpretation (Gurol et al., 2013; O’Neill et al., 2013).

It has been suggested that a negative first birth experience may result in fewer subsequent deliveries and longer interval to second birth (Gottvall and Waldenstrom, 2002). In one study, worse experiences during emergency abdominal and vaginal operative deliveries contributed to decisions by one-third of women to avoid future pregnancies (Bhatacharya et al., 2006). However, the results from the present study show no differences among six obstetric history groups in reported infertility after first delivery, interval between first and second birth (among women with at least two births) or multiparity. Similarly, Mollison et al. (2005) found no difference in subsequent deliveries after instrumental, when compared with spontaneous, vaginal deliveries.

A unique aspect of the present study is the opportunity to consider the effect of infertility prior to first delivery. Primary infertility was found to be a very strong predictor of later infertility: women who reported infertility prior to first delivery were five times more likely to report infertility after subsequent delivery, irrespective of mode of delivery. In our study, infertility before first delivery was similar across modes of delivery. However, other authors have observed that women who experience subfertility may be at greater risk of delivering by Cesarean (Pandian et al., 2001;
Murphy et al., 2002; Kjerulff et al., 2013a). Thus, primary infertility may be an important but unmeasured confounder in other datasets.

Strengths of this study include our ability to include information about self-reported infertility before and after each delivery, a more direct measure of fertility than parity or inter-pregnancy interval. Another strength of this study is that the Cesarean and vaginal groups were matched for age at first delivery. Also, for the first delivery, we excluded some conditions that might influence reproductive decisions, such as stillbirth, prematurity, multiple gestation and congenital anomalies. In other study populations, these conditions might be over-represented in the Cesarean group and might therefore contribute to lower parity after Cesarean. Finally, we were also able to consider the impact of obesity, which may be missing from studies utilizing administrative data or national health statistics.

Use of self-reported infertility poses a limitation; women in our study may define infertility differently from the scientific definition, and some may interpret the term differently from others. The accepted clinical definition of infertility is ‘the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse’ (Zegers-Hochschild et al., 2009). Our question addressing infertility did not specify a time period; thus, some participants may be misclassified as infertile if they were trying to conceive for less than the full 12 consecutive months; likewise, others may have tried to conceive for > 12 months and not considered this infertility. Dick et al. (2003) reported high specificity but relatively low sensitivity with their self-reported difficulty in conceiving question: ‘Have you or your partner had any problems in conceiving a child and seen a doctor about this?’ This question missed nearly one-third of women who would be classified as infertile based on the 12-month time frame and detailed reproductive histories, presumably because many infertile women do not seek medical care. Additionally, the question misclassified some women who had been trying to conceive for < 12 months but had already sought medical advice. Using the current duration approach, Thoma et al. (2013) estimated the prevalence of infertility in a nationally representative sample of US women, 15–44 years, at 24.3% among nulliparous women and 15.5% among women of all parity. In our study, 21% of women reported infertility prior to first delivery, while 16% reported infertility after first delivery.

If present, misclassification would tend to increase the likelihood of finding the null result. Recall bias could be present, but we do not suspect that maternal recall for infertility would be impacted by vaginal versus Cesarean birth.

Our study is restricted to a small sample size, which may result in insufficient power to detect differences between groups. As the differences between groups reported here are exceedingly small (7 versus 6% infertility after most recent delivery, 30.8 versus 30.6 months interval between first and second birth, 75 versus 76% multiparity), we do not anticipate that a larger sample size would be of merit; even if a statistical significance was detected, the differences identified here are not clinically meaningful.

We had limited information about contraception use across a lifetime, which may have influenced total parity. Furthermore, a relatively high proportion of our participants were over age 35 at the time of first delivery (26%) and highly educated (37% with graduate degrees), which may indicate that our population may not be generalizable.

In conclusion, this cohort study of US women with first deliveries between 1998 and 2006 provides a contrasting view to the findings of previous studies. In our cohort, women who delivered their first child by Cesarean were not less likely to have a subsequent birth, nor did they experience a longer time between births than women who delivered their first child vaginally. These findings should be reassuring to women who deliver by Cesarean section.

Authors’ roles

All authors have fulfilled all conditions required for authorship. E.C.E. assisted in data acquisition, interpretation and drafting of the article. K.C.M. performed the analyses and contributed to preparing the manuscript. J.L.B. and V.L.H. conceived the study design, contributed to data acquisition, analysis and interpretation, drafting and critical revisions of the article. All authors approved the final version.

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Conflict of interest

None declared.

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