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Review

The impact of Cesarean section on female fertility: a narrative review

Lorenz Hinterleitner[1], Herbert Kiss[2], Johannes Ott[1,*]

[1] Clinical Division of Gynecologic Endocrinology and Reproductive Medicine, Medical University of Vienna, 1090 Vienna, Austria

[2] Department of Obstetrics and Gynecology, Medical University of Vienna, 1090 Vienna, Austria

*Correspondence: johannes.ott@meduniwien.ac.at (Johannes Ott)

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Objective: The mode of giving birth has changed over the years. In 1990, approximately 10% of women delivered by Cesarean section (CS), whereas this procedure is performed daily in obstetrics today. When a surgical intervention performed, it is necessary to consider special risks and complications, including long-term effects. *Mechanism*: This review focuses on fertility after CS. Evidence suggests that many women who aim to have subsequent children have difficulties becoming pregnant after they have delivered by CS. *Findings*: There are several causes for subfertility/infertility after CS, including post-Cesarean niches, intraabdominal adhesions, and the preference for a smaller family size, among others. *Conclusion*: This review provides an overview of the available literature, which supports the conclusion that CS is associated with decreased odds of subsequent pregnancy and live birth.

Keywords

Cesarean section; Fertility; Infertility; Niche; Fallopian tubes; Adhesions

1. Introduction

Over the past several decades, the mode of birth has been the subject of global discussion. Cesarean section (CS) has established itself as one of the most common methods. When medically indicated, this procedure can be a live-saving act. There is a trend towards an increase in CS frequency that is expected to continue, not only for primiparous but also for multiparous women. Notably, CS is currently the mode of delivery for every fourth pregnancy in Europe, while this was the case in only approximately 11% of all pregnancies in 1990, indicating an increase of 3.4% per year and 13.8% in total [1]. Due to this trend, it is necessary to monitor the short-term and long-term consequences of CS [2]. Women who have undergone previous CS are at elevated risk for several outcomes, including the need for another CS in future pregnancies, mainly due to the risks of uterine rupture; the presence of an unusual placenta position (odds ratio [OR] for placenta previa, 1.74; 95% confidence interval [CI] 1.62–1.87) or invasive placentation (OR for placenta accreta, 2.95; 95% CI 1.32–6.60) [2]. Moreover, compared with vaginal delivery, previous CS is associated with a 23% increase in the risk of stillbirth. In addition, mothers have a 14% higher risk of a preterm delivery in their subsequent pregnancy (OR 1.14; 95% CI 1.12–1.16) [3]. Uterine rupture, an emergency complication, is also strongly linked with CS. Many of these situations may lead to the affected woman's inability to give birth to a living child in the future, either due to intrauterine fetal death, a previous hysterectomy, or other circumstances. After a CS, there are also higher chances of experiencing uterus rupture if a vaginal delivery is performed. This occurs in 5% of women who have undergone a CS [4]. However, in total numbers, these worst-case scenarios are still rare. When focusing on the ability to achieve a live birth after CS, the main concerns are about a possible negative impact of CS on future fertility, i.e., the chance to become pregnant or stay pregnant without miscarriage. Many studies investigating aspects of fertility after CS have been published and will be summarized in the next chapter.

2. (In-)Fertility after Cesarean section

Twelve months of regular unprotected sexual intercourse without the appearance of a clinical pregnancy is characterized as infertility [5]. Globally, 8–12% of all couples of reproductive age are affected [6]. Notably, infertility can be separated into two subgroups of primary and secondary infertility, depending on whether there was a previous clinically diagnosed pregnancy. If there was not, the infertility is defined as primary. Otherwise, the infertility has been established since the last clinical pregnancy and is called secondary [5]. The latter is a major reason for the unfulfilled wish to have children and affects 10.5% of all women globally [7]. This is reflected particularly in the developing world, where sexually transmitted pelvic infections are more common [8, 9]. Pelvic infections resulting from poor abortion handling and poor overall maternity care can also lead to secondary infertility [10]. Although the absolute number of infertile women is increasing due to population growth, a relative reduction in both primary (1.6% to 1.5%, posterior probability [pp] = 0.90) and secondary infertility (3.9% to 3.0%, pp >0.99) can be observed worldwide [7]. Notably, countries with a high sociodemographic index reveal an increas-

ing trend of secondary infertility in women, with an annual percentage change of approximately 0.8% [11]; this could be caused by the increasing age of childbearing in these countries.

In accordance with the abovementioned criteria for the infertility subtypes, infertility after a CS is, by definition, secondary. One major question is whether CS truly leads to a decline in fertility. A meta-analysis from 2013 revealed a significant decrease in the chance for a subsequent pregnancy after a previous CS of 9% (RR 0.91; 95% CI 0.87–0.95) and in the live birth rate of 11% (RR 0.89; 95% CI 0.87–0.92). This analysis included 18 cohort studies with 591,850 women fulfilling the inclusion criteria. The Newcastle Ottawa scale was used to determine the risk of bias [12]. These results have recently been reiterated by Kjerulff *et al.*, who demonstrated that the conception rates of couples with regular unprotected intercourse were lower after CS (413/599 [68.9%]) than after vaginal delivery (1090/1422 [76.7%]; adjusted hazard ratio 0.85; 95% CI 0.74–0.96).

Moreover, a history of previous CS is associated with a longer time to conceive. The risk of taking more than one year to conceive from the time of planning a pregnancy has been reported to be higher, with an OR of 1.53 (95% CI 1.09–2.14). This association was stronger for women of parity ≥ 2 (OR 2.97; 95% CI 1.72–5.10) [13]. In other words, women who delivered by CS were less likely to have another pregnancy overall.

The observed lower likelihood of pregnancy following CS may occur because women who deliver by CS prefer a smaller family size or because of an inability to become pregnant. Both causes may contribute. In a retrospective cohort study with matched pairs, Hemminki *et al.* used the cross-sectional interview data from the 1982 National Survey of Family Growth and found that the differences in fertility were based on the inability to become pregnant and not the lack of desire to have another child. A total of 4292 primiparous women were included in this questionnaire study, of whom 413 delivered by CS. In the CS group, 53% reported wanting a subsequent child, whereas 47% of the women in the control group stated their desire for further family growth ($p < 0.001$). However, there were considerable differences in fertility status between the groups. Of the control group, 71% were fecund, compared with only 55% of the women who had undergone CS. These differences suggest that not only the desire to have subsequent children but the initial physical situation after CS is responsible for the decrease in live births after CS. This finding has also been demonstrated in several other studies [12, 14, 15].

Notably, women of a higher maternal age are more likely to deliver by CS than younger mothers, which often makes a subsequent pregnancy impossible. Moreover, there are specific pregnancy- and childbirth-related complications associated with not having a subsequent live birth. In a retrospective case-control study involving 52,498 women who had already had a first singleton live birth, Kjerulff *et al.* included these potentially confounding complications (diabetes-related disorders, abnormalities of the pelvis, fetal abnormalities, premature or prolonged rupture of membranes, hypertensive disorders, amnionitis, fetal distress, and other maternal health problems) as well as the demographic confounders of maternal age, race, education, marital status, and health insurance coverage in their model. However, these adjustments had minimal effects, and CS was still associated with a significantly increased risk of not having a subsequent live birth (RR 1.15; 95% CI 1.11–1.19). In addition, these data show that not only conception rates but also live birth rates are lower after CS [15]. However, it should be taken into account that women who deliver by CS are often advised not to become pregnant again in the near future. Recommendations suggest that a short interpregnancy interval (i.e., the time between delivery and the following conception) of 18 to 24 months or less would increase the patient's risk for a uterine rupture in the subsequent pregnancy [16]. This advice could also alter the women's preferences.

In addition to the data suggesting a link to an inability to become pregnant, there is also evidence linking the experience of birth with the desire for a subsequent conception. Women who gave birth by CS were more likely to wish to avoid or delay a future pregnancy. In a questionnaire study, 32% of the interviewed women who underwent CS stated that the birth experience influenced their decision to prevent another pregnancy. In comparison, of women who delivered vaginally and were unwilling to have another child, only 18% said that the delivery experience influenced their decision. Woman who chose to deliver by CS in advance were also more likely to avoid future pregnancies than those who had CS performed in an emergency setting (83% versus 69%, respectively; $p = 0.009$) [17].

Finally, one could argue that CS would increase the odds for unfavorable pregnancy outcomes, which would be inconsistent with live birth in the same pregnancy. This would include extrauterine gravidity. Notably, a meta-analysis did not find an increased risk for subsequent ectopic pregnancy (pooled OR 1.05; 95% CI 0.51–2.15) [18].

Since the mode of delivery affects future fertility, it is also necessary to determine whether there is any change in hormone profiles. There appear to be no significant changes in levels of anti-Mullerian hormone and atrial follicle count after CS [19].

3. Anatomical reasons for secondary infertility after Cesarean section

After a surgical intervention like a CS, many follow-up issues may have a negative impact on future fertility. These include intraabdominal adhesions, Fallopian tube dysfunction, and uterine abnormalities caused by the Cesarean scar, which can lead to potential postsurgical dysfunctions.

3.1 Tubal abnormalities after Cesarean section

Concerning tubal abnormalities, no significant difference was observed between mothers who underwent CS and a

control group (16.3% and 15.8%, respectively) in a retrospective cohort of more than 1700 women undergoing infertility treatment. On the other hand, previous abdominal or gynecological surgeries were associated with a significant increase in tubal abnormalities (34.8% and 27%, respectively) [20]. These results are comparable to those of an even larger study in which women who suffered from secondary infertility caused by tubal factors (n = 220) were compared with two control groups: one group of women with diagnosed non-tubal secondary infertility (n = 1244) and a second group of fertile women who had their second delivery during the same period (n = 18,376). A total of 21.4% of the women who suffered from tubal infertility had a history of CS, whereas this was the case in 21.6% in the non-tubal infertility group. In the fertile control group, the association with CS was lower (14.5%). These findings suggest that there is no significant link between CS and tubal infertility, whereas other factors were found to be predictive of secondary tubal infertility. These include a history of intrauterine device use, pelvic inflammatory disease, ectopic pregnancy, endometriosis, and previous pelvic surgery [21].

3.2 Post-Cesarean niche

Performing a surgical intervention always leads to scarring and its accompanying consequences. In the case of CS, the sewing of the uterine tissue leaves a scar in the endometrium. Wang *et al.* examined 4250 women with a history of CS via transvaginal ultrasonography. A scar defect was diagnosed in 293 (6.9%) patients [22]. Scar insufficiencies can lead to a post-Cesarean niche (isthmocele), which is visible in ultrasound as a triangular hypoechoic area. This interruption of the endometrium is believed to be caused by an insufficient healing process [23].

Choosing the appropriate diagnostic tool for post-Cesarean niche is important for a better reproductive outcome. Two-dimensional sonohysterography is by far the most common method of detection, although three-dimensional sonohysterography is an increasingly popular method. These methods show high agreement concerning the detection of a CS niche. Three-dimensional sonohysterography gives the examiner a more detailed image of the niche with regard to base width and scar depth. More precise data leads to a better prediction of the outcome in future pregnancies and is important to guide follow-up niche management [24, 25].

Of note, it has been shown that multiple CS and retroflexed uteri are risk factors for larger Cesarean scar defects. The size of the defect is of clinical relevance as it is associated with postmenstrual spotting, dysmenorrhea, and chronic pelvic pain [22]. In addition, these scar insufficiencies are associated with secondary infertility [26]. It is suspected that this is due to the retention of menstrual blood in the uterine scar niche as well as bleeding from the scar itself, which then impairs implantation [27]. According to a CS follow-up study, 142 of 189 women (75.1%) had fluid pooling in the Cesarean scar area during the ovulatory phase [28].

Standard treatment options for isthmocele include hysteroscopy, vaginal surgery, or laparotomy. A recent study included 18 patients with CS niche who underwent surgical treatment. Of 10 women who were affected by secondary infertility, six achieved a pregnancy (60%). All patients who wanted to become pregnant and underwent hysteroscopy achieved a subsequent pregnancy. These results suggests that hysteroscopy might be the best treatment option in case of infertility [29]. A recent systematic review reiterated these findings by showing an absolute pregnancy rate of 58.71% (95% CI 59.03–82.48%) in women with uterine Cesarean niche who underwent hysteroscopic treatment. In total, the meta-analysis comprised 18 studies and 692 patients. Notably, only women who wanted to get pregnant and suffered from secondary infertility were included. Moreover, in addition to the fertility issue, there was an overall improvement rate of uterine scar defect symptoms (comprising pelvic pain and abnormal bleeding) of 78.83% (95% CI 72.46–85.76%) after a hysteroscopic treatment [30].

Laparoscopic intervention should be especially considered for larger defects (>3 mm) and when symptoms are present [31]. The advantage of this approach is the superior visualization of the defect as well as the restoration of myometrial tissue. Donnez *et al.* described the outcome of 38 women after a laparoscopic niche repair. Of 18 mothers who experienced secondary infertility, 44% became pregnant and gave birth to a child after the intervention was completed. In this case, the niche was closed by three layers, including a peritoneum running suture. In a three-month follow-up, an increasing mean myometrial thickness (from 1.43 ± 0.7 mm to 9.62 ± 1.8 mm) was observed [32].

These findings indicate hysteroscopy as the main recommended treatment for women with uterine Cesarean niche who suffer from secondary infertility. It appears to be superior compared to laparoscopic treatment because of the associated fertility outcomes as well as its minimally invasive practicability. For patients with large scar defects or a small myometrial thickness, laparoscopic treatment should be suggested.

3.3 Intrauterine adhesions

Adhesions in the uterine cavity can occur after a trauma in the endometrial tissue. They appear most frequently after curettage in an incomplete abortion (33.3%) or postpartum hemorrhage (37.5%), but can also occur after a CS (2.0–2.8%) [33]. In the context of CS, adhesions are more likely to occur because of peri-interventional infections, postpartum curettage, or compression sutures [34]. Asherman syndrome is defined by intrauterine adhesions and, often, endometrial trauma as well. It may be the cause of hypomenorrhea or even amenorrhea. Notably, CS is considered a less common etiologic factor for intrauterine adhesion formation and Asherman syndrome. However, it has been stated that Asherman syndrome should be considered in patients with history of a CS presenting and amenorrhea/hypomenorrhea and infertility. In addition to the relevance of the endometrial

trauma itself leading to an impaired ability for implantation, the synechia can also lead to tubal occlusion and thus to infertility [35].

3.4 Intraabdominal adhesions

It has been speculated that pelvic adhesions following CS might predispose women to infertility. By the 1980s, it had been hypothesized that the added consequences of CS, which could include peritubal adhesions, could push women with non-surgical infertility over a certain threshold [36]. In literature, relevant adhesions after CS have been reported, in addition to several related problems. The latter include chronic pelvic pain, diarrhea, constipation, and irritable bowel syndrome [37–40]. In addition, post-CS adhesions can also affect the reproductive tract and can cause secondary infertility by attaching organs away from their normal site and/or disturbing the motility of the Fallopian tubes [12, 15, 17, 41–44]. In terms of fertility, it has been suggested that affected women would benefit from laparoscopic adhesiolysis [45]. In a recent randomized controlled trial, 184 women with secondary infertility diagnosed with periadnexal and pelvic adhesions were randomly assigned to either undergo laparoscopic adhesiolysis or be treated with controlled ovarian stimulation and intrauterine insemination (up to three trials). In the latter group, the overall one-year pregnancy rate was approximately 12% compared to 54% in the laparoscopy group ($p < 0.05$). Concerning the findings in women with the surgical intervention, only eight patients were inoperable (9.8%), and the majority revealed mild adhesions (n = 43, 52.4%). Notably, the one-year pregnancy rates in women with mild, moderate, and severe adhesions were 77%, 62%, and 20%, respectively.

In addition, the previous number of CS has a considerable impact on the development of intraabdominal adhesions. As in other surgical interventions, the rate of repeated surgical interventions increases the risk for adhesions. Tulandi *et al.* examined 203 women who delivered by CS for the first time as well as 1283 women with repeated delivery by CS. In primary CS patients, no intraabdominal adhesions were found. On the other hand, women with several previous surgical deliveries had an increased likelihood of intraabdominal adhesions, depending on their CS frequency. In detail, 24.4% of the women who had delivered by CS two times and 42.8% of those who delivered three times by CS were affected [46].

Overall, it can be concluded that laparoscopic adhesiolysis is the method of choice to deal with mild to moderate periadnexal adhesions following CS [41, 46].

3.5 The consequences of uterine rupture

Uterine rupture is an acute life-threatening situation for both mother and child and can lead to subsequent secondary infertility [47]. Fortunately, emergency peripartum hysterectomy is only rarely needed. In a prospective observational cohort study which included more than 30,000 women, serious maternal morbidity increased progressively with increasing number of previous deliveries via CS. This also held true for peripartum hysterectomy [48]. Accordingly, if a subsequent pregnancy occurs after a CS delivery, there are increasing chances of a perinatal uterine rupture. In detail, one in 200 women experiences a uterine rupture after CS [4]. Without a doubt, uterine rupture already presents a dangerous situation. However, the chances of a follow-up pregnancy are good if the uterus can be preserved. This is underlined by a series of 69,452 analyzed deliveries, where 27 women suffered from a uterine rupture and only two of these developed a secondary infertility [49].

4. Conclusions

CS is associated with decreased odds of subsequent pregnancy and live birth. This appears to be due to both a decreased desire for further family growth and somatic consequences of CS. The latter mainly include post-Cesarean niches and intraabdominal pelvic adhesions.

Author contributions

All Authors were part of planning, conducting, and reporting the work described in this article. LH and JO performed the major research for this review. They also contributed to editorial changes. HK worked as advisor for detailed improvements and as assistance for conducting this article. The final manuscript was read and approved by all authors.

Ethics approval and consent to participate

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Conflict of interest

The authors declare no conflict of interest. JO is the Editorial board member of this journal, given his role as Editorial board member, JO had no involvement in the peer-review of this article and has no access to information regarding its peer-review.

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