

Obstetrical complications of endometriosis, particularly deep endometriosis

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Over the past few years, a new topic in the field of endometriosis has emerged: the potential impact of the disease on pregnancy outcomes. This review aims to summarize in detail the available evidence on the relationship between endometriosis, particularly deep endometriosis (DE), and obstetrical outcomes. Acute complications of DE, such as spontaneous hemoperitoneum, bowel perforation, and uterine rupture, may occur during pregnancy. Although these events represent life-threatening conditions, they are rare and unpredictable. Therefore, the current literature does not support any kind of prophylactic surgery before pregnancy to prevent such complications. Results on the impact of DE on obstetrical outcomes are debatable and characterized by several limitations, including small sample size, lack of adjustment for confounders, lack of adequate control subjects, and other methodologic flaws. For these reasons, it is not possible to draw conclusions on this topic. The strongest evidence shows that DE is associated with higher rates of placenta previa; for other obstetrical outcomes, such as miscarriage, intrauterine growth restriction, preterm birth and hypertensive disorders, results are controversial. Although it is unlikely that surgery of DE may modify the impact of the disease on the course of pregnancy, no study has yet investigated this issue. (*Fertil Steril*® 2017;108:895–912. ©2017 by American Society for Reproductive Medicine.)

Key Words: Complication, deep endometriosis, placenta previa, pregnancy, surgery

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Academically, endometriosis is distinguished in three different phenotypes: ovarian endometrioma, superficial peritoneal endometriosis, and deep endometriosis (DE) (1). DE affects ~1% of women of reproductive age and it is considered to be the most severe form of the disease (2). It may involve the rectovaginal septum and/or uterosacral ligaments as well as also other abdominal structures, such as bowel, ureters, and bladder (3).

It is traditionally thought that endometriosis and its related pain symptoms improve during pregnancy not only because of the blockage of

ovulation preventing bleeding of endometriotic tissue, but also owing to various metabolic, hormonal, immune, and angiogenesis changes related to pregnancy (4–7). However, in the past few years, several authors have investigated whether endometriosis may affect the regular development of pregnancy and delivery outcomes, showing controversial results (8, 9).

Therefore, the aim of this review is to offer the reader an exhaustive and updated overview on the available evidence on the impact of endometriosis, particularly DE, on obstetrical outcomes.

MATERIALS AND METHODS

We searched Pubmed for articles published in the English language since inception through August 2017 with the use of the following MeSH search terms: “endometriosis” combined with “bladder,” “bowel,” “deep,” “colorectal,” “complication,” “pregnancy,” rectovaginal endometriosis, “urinary tract,” “uterosacral,” “uterus,” “uterine rupture,” “abruptio placentae,” “adverse pregnancy outcome,” “anteartum haemorrhage,” “cesarean delivery,” “gestational diabetes mellitus,” “hypertension,” “intrauterine growth restriction,” “miscarriage,” “placenta previa,” “postpartum hemorrhage,” “preeclampsia,” “preterm labor,” “small for gestational age,” and “spontaneous hemoperitoneum in pregnancy.” Data were extracted independently by three authors (A.I., V.G., and U.L.R.M.), who also performed an initial screening of the title and abstract of all articles to exclude citations deemed by

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all of the observers to be irrelevant. A manual search of review articles and cross-references completed the search. Data presented exclusively as abstracts in national and international meetings were also excluded. No Institutional Review Board approval was required, because only published deidentified data were analyzed.

ENDOMETRIOSIS-RELATED COMPLICATIONS DURING PREGNANCY

Several authors reported cases of acute endometriosis-related complications occurring during pregnancy. More frequently, this kind of event happens in the second or third trimester of pregnancy and may represent life-threatening conditions for both the mother and the fetus (Table 1; Supplemental Table 1 [available online at www.fertstert.org]) (10–73). The literature search aimed to identify only cases of obstetrical complications reported in women affected by DE.

Intestinal Perforation and Other Bowel Complications

A total of 17 cases of bowel perforation during pregnancy related to the presence of endometriosis have been described among women with a mean (\pm SD) maternal age of 32.1 \pm 4.3 years (Table 1; Supplemental Table 1). Pregnancy was obtained with the use of assisted reproductive technology (ART) procedures in three cases (17.6%). Women did not have an earlier history of endometriosis in 9 out of 14 cases (64.3%) and did not undergo surgery for that indication before pregnancy in 10 out of 14 cases (71.4%; nonsurgical group). In the nonsurgical group, the most frequent location of perforations was the sigmoid colon or rectum (6/10; 60%). Surgery for endometriosis before pregnancy was performed in 4 out of 14 cases (28.6%) including one case of previous colorectal resection for the presence of a rectovaginal nodule (19) (surgical group). Among patients who underwent ovarian cystectomy before pregnancy, one had a diagnosis of a 3-cm rectosigmoid nodule and underwent in vitro fertilization (IVF) treatment; however, her perforation site was at the ileum (21). In the other surgical group cases, perforation occurred in the sigmoid colon ($n = 1$) or the rectum ($n = 2$). Among all of the patients, acute abdominal pain was the most common presenting symptom (16/17; 94.1%), with signs of peritonitis in 10 out of 16 patients (62.5%). All women underwent surgical interventions: segmental intestinal resection (11/17; 64.7%), repair of intestinal lesion (2/17; 11.8%), or appendectomy (4/17; 23.5%). In the case described by Setubal et al. (22), the patient underwent only an exploratory abdominal surgery during the 28th week of gestation and was treated with the use of antibiotics. Then, 2 months after a term delivery, total laparoscopic hysterectomy, adnexectomy, partial cystectomy, rectovaginal septum nodule excision, and segmental resection of the rectosigmoid were performed because severe symptoms had renewed. At histologic examination, decidualized endometriosis was demonstrated in all cases (14/14; 100%) for which specimens were obtained during pregnancy. All pregnancies ended in live births, with only 6 out of 16 (37.5%) preterm deliveries (<37 weeks of gestation).

One case of bowel-uterine fistula secondary to endometriosis was described during pregnancy. A 26-year-old woman, multigravida, developed acute abdomen, severe sepsis, and disseminated intravascular coagulation at 16 weeks of gestation. Because there was no response to broad-spectrum antibiotics, she underwent explorative abdominal surgery which showed a fistula between the cecum and uterus in a setting of purulent peritonitis. A subtotal hysterectomy with subsequent termination of pregnancy and intestinal resection were performed; the surgical specimen confirmed the presence of a colouterine fistula within extensive adenomyosis of the uterus and endometriosis of the cecum (25).

Appendicitis

Ten cases of acute appendicitis connected to appendiceal endometriosis during pregnancy have been reported (Table 1; Supplemental Table 1). Mean maternal age was 28.5 \pm 4.8 years. Surgical history of patients was not reported. Diagnosis was carried out more frequently in the second trimester (mean gestational age 21 \pm 8.1 weeks). During pregnancy, open appendectomy (8/10; 80%) or laparoscopic appendectomy (2/20; 20%) was performed in all cases, and on histologic examination, three cases (3/10; 30%) showed inflammation and decidualized endometriosis. One preterm labor with subsequent neonatal death and three live births delivered at term were reported.

Urinary System

Uroperitoneum during pregnancy owing to the presence of endometriosis has been described in two cases (47, 63). In the first case, the patient underwent operative laparoscopy for stage IV endometriosis without removing a deep nodule of the right uterosacral ligament. After 8 months, she conceived, and at 31 weeks of gestation she was hospitalized because of acute abdominal pain. A few hours later, hemorrhagic shock suddenly developed requiring volume resuscitation and abdominal surgery. Urohemoperitoneum detected during surgery was due to injury of both the right uterine artery and right ureter at the level of the homolateral broad ligament. Subsequent ligation of the vessel and ureteroneocystostomy were performed (47). In the second case, the diagnosis of uroperitoneum was performed 6 hours after a preterm delivery at 27+2 gestational weeks (63). One week earlier she had experienced severe abdominal pain and was hospitalized. Her clinical history was remarkable for intestinal and bladder endometriosis: She had undergone transurethral resection of a bladder nodule 2 years before conception. After postpartum bladder resection of endometriotic lesion, clinical resolution was obtained and the follow-up cystography was negative.

In two cases with no history of previous surgery for endometriosis, the disease caused ureteral stenosis with subsequent need of stent placement during pregnancy, without procedure-related complications (59, 62). In one case, pregnancy was uneventful, and in the other case intrauterine fetal death occurred at 16 weeks after

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