

# Bowel complications of deep endometriosis during pregnancy or in vitro fertilization

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**Objective:** To review bowel complications caused by deep endometriosis during pregnancy or in vitro fertilization (IVF).

**Design:** Three case reports and a systematic review.

**Setting:** A tertiary referral center for deep endometriosis surgery.

**Patient(s):** Three case reports of bowel perforation or occlusion during pregnancy caused by deep endometriosis.

**Intervention(s):** A PubMed search was conducted to identify complications of deep endometriosis during pregnancy or IVF. The literature search identified 13 articles. According to these, 12 articles described 12 bowel complications caused by progression of deep endometriosis during pregnancy, and 1 article described six cases of bowel occlusion during IVF.

**Result(s):** In 12 of 15 women, complications occurred during the third trimester of pregnancy, whereas 3 of 15 women presented with complications in the postpartum period. All complications during IVF occurred during stimulation. No specific factors that could predict these complications were identified, leading to the conclusion that endometriosis complications that occur in pregnancy or in IVF patients are probably underreported.

**Conclusion(s):** Bowel complications during pregnancy or IVF stimulation may occur in women with deep endometriosis. This suggests that the endocrine environment of pregnancy does not prevent progression, at least in some women. These complications are rare, although probably underreported. (Fertil Steril® 2014;101:442–6. ©2014 by American Society for Reproductive Medicine.)

**Key Words:** Endometriosis, pregnancy, IVF, bowel perforation, bowel occlusion

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**E**ndometriosis is defined as the presence of glands and stroma outside the uterus. It is an enigmatic disease, and its pathophysiology, progression, and natural history are poorly understood. Even though it is believed to be a progressive disease, progression was not seen in some women followed for more than 1 year without surgery (1). The hormonal responsiveness of the lesions is believed to be comparable to that of the endome-

trium. Nevertheless, it is unclear whether the hormonal responsiveness of all deep endometriosis lesions follows a similar pattern. Indeed, it is still unclear whether the endometriotic cells are identical to the endometrium, as suggested by the Sampson theory of retrograde menstruation and implantation. If, however, deep endometriotic lesions are the consequence of a genomic incident (2), the hormonal responsiveness of each lesion might be different.

During pregnancy, superficial endometriosis lesions have been reported to decidualize, preventing progression. The use of pseudopregnancy or oral contraceptives as a medical treatment for endometriosis (3) is, indeed, based on this mechanism. For deep endometriosis, however, decidualization during pregnancy has, to the best of our knowledge, not yet been confirmed.

Three patients presenting recently to our center with deep endometriosis causing a spontaneous bowel perforation during pregnancy prompted us to review the literature.

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## MATERIALS AND METHODS

A systematic review was performed using the PRISMA (Paris Rome Italy States Mother Africa) guidelines. A

combination of the keywords “pregnancy,” “endometriosis,” “IVF,” “bowel perforation,” “intestinal perforation,” and “intestinal occlusion” was used to identify the maximum number of relevant citations in PubMed. Institutional review board approval was not required for such a literature review or the case reports.

## RESULTS

### Systematic Review

In the literature, 12 case reports of bowel perforation during pregnancy caused by endometriosis were found: 2 involved the small intestine, 1 the caecum, 3 the appendix, and 6 the rectosigmoid colon (4–15). Seven of twelve perforations occurred between the 26th to the 37th weeks of pregnancy (information not available in 2 cases) and the remaining three in the immediate postpartum period. All perforations presented as an acute abdomen, and the pathology reported deposits of endometriosis on the bowel. All patients underwent emergency surgery for acute diffuse peritonitis, and a Hartman operation and/or segmental resection was performed. Healthy babies were delivered in all seven cases; a cesarean section was performed in four of seven cases, whereas in three of seven cases the baby was delivered by vaginal birth. Surprisingly, only 3 of 12 women had a clear history of endometriosis, whereas in 4 of 12 such information was missing and the remaining 5 of 12 had no history.

Six case reports of bowel occlusion during IVF were reviewed. In all cases a rapid progression of a small sigmoid lesion was observed (16). All patients had been diagnosed with a stage IV endometriosis. Three patients had undergone excision of endometriotic lesions before ovarian stimulation.

### Case Reports

Written informed consent was obtained from the patients for the publication of these case reports.

**Case 1.** A 36-year-old Portuguese woman with one uneventful pregnancy was diagnosed with a 3-cm rectosigmoid endometriosis nodule by magnetic resonance imaging. Both the mother and sister also had deep endometriosis. Because of infertility, the patient underwent IVF treatment and became pregnant during the ninth cycle. During the 28th week of pregnancy she presented with acute and severe abdominal pain. Pyelonephritis was diagnosed, and *broad-spectrum antibiotics* were initiated, but her symptoms got worse and she became septic. An exploratory laparotomy confirmed the peritonitis with large quantities of purulent liquid. A bowel perforation, however, was not found, although cultures revealed *Escherichia coli*. With antibiotic treatment the patient gradually improved and was discharged 2 weeks later. At 37 weeks of pregnancy, a healthy baby was delivered by cesarean section.

The patient did not breast feed, and 2 months later she returned with complaints of dysmenorrhea, severe pelvic pain, catamenial diarrhea, rectorrhagia, and dyschesia.

At clinical examination a 4-cm rectovaginal nodule invading the vagina and a 2-cm bladder nodule were identified.

Colonoscopy revealed a third endometriotic nodule in the sigmoid causing severe stenosis (<2 cm lumen). Magnetic

resonance imaging diagnosed cystic ovarian endometriosis (a 3-cm and a 4-cm nodule on the right and left ovary, respectively) and bilateral hydrosalpinx.

The patient underwent total laparoscopic hysterectomy, adnexectomy, partial cystectomy, rectovaginal septum nodule excision, and segmental resection of the rectosigmoid colon by laparoscopy. Pathology confirmed the diagnosis of endometriosis.

Throughout the follow-up the patient was completely asymptomatic.

**Case 2.** A 35-year-old Portuguese woman with one uneventful pregnancy and without any relevant medical or family history presented with severe pain symptoms suggestive of deep endometriosis. She became spontaneously pregnant, and at the 35th week of pregnancy she experienced acute and severe abdominal pain for which a laparotomy was performed. A healthy baby was delivered by cesarean section, during which a concealed bowel perforation was detected and thus a rectosigmoid segmental resection with latero/lateral anastomoses as well as appendectomy was performed.

The pathology report revealed colonic, nodal, and appendicular endometriosis with pseudodecidualization of the stroma.

Six months later the patient presented with dyspareunia, and a 3-cm rectovaginal nodule with vaginal invasion was clinically detected. A vaginal ultrasound scan confirmed the presence of deep endometriosis involving the rectovaginal septum and the sigmoid infiltrating the muscularis of the rectum.

Because she was breast feeding without severe pain symptoms, expectant management with oral contraceptives was chosen. Colonoscopy performed 6 months after delivery revealed no residual disease. The patient's quality of life remained satisfactory throughout the 6-month follow-up.

**Case 3.** An asymptomatic 34-year-old Portuguese woman without symptoms suggesting endometriosis was admitted with severe abdominal pain and pollakisuria during the 16th week of a spontaneous pregnancy. A vaginal ultrasound scan detected a septated hemorrhagic cyst of 11 × 10 cm of the left ovary and free peritoneal fluid. A laparotomy was performed because torsion was suspected. During surgery, multiple pelvic abscesses were found involving the uterus, the left ovary, the sigmoid colon, and the small bowel. The capsule of the ovarian cyst was broken. After lavage the patient remained in intensive care and underwent multiple peritoneal rinsings until resolution of peritonitis. Abdominal wall closure was performed 6 days later.

Ten days later the patient deteriorated, with symptoms of bowel occlusion and sepsis. A second laparotomy was performed, and several abscesses were detected. Forty-eight hours later a Hartman's procedure was performed for diffuse peritonitis caused by sigmoid perforation. Two more lavage revisions by laparotomy were necessary, and 20 days later the wall was closed. Bacteriologic tests reported *E. coli*, whereas the pathology report showed a “mucosal perforation due to decidualization of endometriotic lesion” in the resected bowel specimen.

The patient underwent an uneventful vaginal delivery at 39 weeks, but because she never returned for consultation, no follow-up is available.

TABLE 1

## Six cases of intestinal occlusion during IVF cycles (16).

First author (reference)	Year	Presenting complaint	History of endometriosis	Site of perforation	Surgical management	Histologic confirmation of endometriosis	Stage of endometriosis	Patient status	Onset of complaint (wk)	Delivery	No. of cases
Haufler (12)	1931	Acute abdominal pain	NA	Jejunum	NA	Yes	n.a	Pregnant	n.a.	n.a.	1
Clement (10)	1977	Left quadrant acute abdominal pain	Yes	Sigmoid colon	Hartman's procedure	Yes	n.a	Pregnant	37	Vaginal	1
Rud (9)	1979	n.a	NA	Sigmoid colon	NA	Yes	n.a	Pregnant	n.a	n.a.	1
Gini (8)	1981	Right and left quadrant abdominal pain	NA	Vermiform appendix	Appendectomy	Yes	n.a.	Pregnant	35	Cesarean section	1
Floberg (13)	1984	Acute abdominal pain	NA	Sigmoid colon	Segmental bowel resection	Yes	Ovarian and colon lesions	Postpartum	41	n.a.	1
Nakatani (7)	1987	Acute abdominal pain	No	Vermiform appendix	Appendectomy	Yes	n.a.	Pregnant	26	Vaginal	1
Loverro (14)	1999	Left quadrant acute abdominal pain	No	Sigmoid colon	Segmental bowel resection	Yes	n.a.	Pregnant	35	Cesarean section	1
Schweitzer (6)	2006	Acute abdominal pain	No	Sigmoid colon	Segmental bowel resection	Yes	n.a.	Postpartum	40	Cesarean section	1
Faucheron (11)	2008	Right quadrant acute abdominal pain	No	Vermiform appendix	Appendectomy	Yes	n.a.	Pregnant	27	n.a.	1
Anaf (16)	2000	Acute abdominal pain	Yes	Sigmoid colon	Segmental bowel resection	Yes	IV	Under IVF	–	–	6
Beamish (5)	2010	Acute abdominal pain	No	Caecum	Segmental bowel resection	Yes	n.a	Postpartum	37	Cesarean section	1
Pisanu (4)	2010	Acute abdominal pain	Yes	Rectum	Appendectomy and Hartman procedure	Yes	IV	Pregnancy	33	Vaginal	1
Nishikawa (15)	2013	Upper right quadrant acute abdominal pain	Yes	Ileum	Right hemicolectomy and segmental ileal resection	Yes	IV	Pregnancy	28	Cesarean section	1
Setúbal (present report)	2013	Acute abdominal pain	Yes, yes, no	Rectum and sigmoid colon	Segmental bowel resection	Yes	IV	Pregnancy	28, 35, 16	Cesarean section (cases 1 and 2), vaginal (case 3)	3
Total	1931–2013										21

Note: NA = information not available.

Setúbal. Deep endometriosis in pregnancy or IVF. *Fertil Steril* 2014.

## DISCUSSION

The systematic review together with our three case reports comprises 15 women with a bowel perforation caused by endometriosis during pregnancy or at the immediate postpartum period. One perforation occurred in the jejunum, one in the ileum, four perforations were found in the appendix/caecum, and nine in the rectosigmoid colon (4–15). In addition, six cases of intestinal occlusion were reported during IVF cycles (16) (Table 1).

No indication was present in any of the cases that could predict bowel complications.

The diagnosis of a bowel perforation can be difficult. Indeed, most women do not have antecedents suggesting endometriosis. Symptoms are nonspecific, and patients present with severe acute abdominal pain necessitating an exploratory laparotomy. In the majority of cases bowel perforation is not diagnosed during this laparotomy, and a repeat laparotomy is needed.

Most cases of very rare diseases are underreported. Therefore, this small number of reported cases is probably an important underestimation. Moreover, in some patients diagnosis could be missed if medical therapy spontaneously resolves severe abdominal pain in pregnant women, or because the perforation is sealed by the omentum. Most importantly, because in the majority of women the diagnosis is missed at first laparotomy, a publication bias is likely, because of medico-legal reasons. Finally, the diagnosis of endometriosis can easily be missed because it is unexpected during pregnancy and because during the “reproductive years” (17, 18) diagnosis of endometriosis often is not made given the diagnostic delay of some 7 years (19).

Bowel endometriosis is believed to have an incidence of approximately 3.3%–5.4% (20), whereas bowel involvement seems to be up to 71.8% in patients with clinical pelvic endometriosis (21, 22).

In women with infertility, treatment is initiated without prior diagnosis of severe deep endometriosis, because this is often missed. Deep endometriosis may often remain undiagnosed because symptoms can be nonspecific, and a diagnostic laparoscopy is not performed during infertility exploration. In addition, smaller deep lesions, especially at the level of the sigmoid, often remain undiagnosed even during laparoscopy. Finally, an endometriosis complication during pregnancy is unexpected because it is believed that endometriosis will regress during pregnancy. Because most of us only recognize what we know, the diagnosis of this rare complication tends to be missed (16). We therefore believe that perforations are underreported and underdiagnosed.

The pathophysiology of deep endometriosis complications involving the bowel during pregnancy is more difficult to explain. Sampson wrote, “the effect of pregnancy on those implants [...] lessens their incidence and the subsequent involutory changes may possibly retard the future development or even cause the retrogression of ANY implants present” (23). This concept of decidualization leads to the treatment with pseudopregnancy. Pain relief during treatment (24) seems to confirm this. Although this is probably true in most women with deep endometriosis, the complica-

tions described during pregnancy demonstrate that at least some lesions may grow and/or cause complications. Today, we can only speculate that extensive decidualization might weaken the bowel wall and that the associated adhesions might cause traumas during uterine growth. Additionally, assumptions have been made for the existence of a specific entity of deep endometriosis reacting differently to the hormonal environment of a pregnancy. If true, we suspect that during pregnancy the same could happen to other types described to be severely affected by endometriosis, including the bladder, ureter, small bowel, diaphragm, and the lungs.

Because this is a rare but severe complication, we strongly recommend an international database to collect cases. This will hopefully lead to better understanding and prevention.

In conclusion, the present study reports that we should be aware of the existence of severe bowel complications during the third semester of pregnancy in women with deep endometriosis. The prevalence of this complication is unknown because it is probably underreported. It is unclear whether this complication warrants specific investigations in infertile women before starting ovulation induction or IVF. The necessity for surgical treatment of deep endometriosis as well as the best possible surgical approach (discoid excision vs. segmental bowel resection) in women with infertility is beyond the scope of this article, as is the indication and method of treatment of the hydrosalpinx in the second case report.

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## REFERENCES

1. Koninckx P, Ussia A, Adamyan L, Wattiez A, Donnez J. Deep endometriosis: definition, diagnosis, and treatment. *Fertil Steril* 2012;98:564–71.
2. Lobo RA. Endometriosis: etiology, pathology, diagnosis, management. In: Lentz GM, Lobo RA, Gershenson DM, Katz VL, editors. *Comprehensive gynecology*. 6th ed. New York: Elsevier; 2012:433–52.
3. Gompel C, Silverberg SG. The female peritoneum. In: Gompel C, Silverberg SG, editors. *Pathology in gynecology and obstetrics*. 4th ed. Philadelphia: Lippincott; 1994:425–31.
4. Pisanu A, Deplano D, Angioni S, Ambu R, Uccheddu. A rectal perforation from endometriosis in pregnancy. *World J Gastroenterol* 2010;16:648–51.
5. Beamish R, Aslam R, Gilbert JM. Postpartum caecal perforation due to endometriosis. *JRSM Short Rep* 2010;1:61.
6. Schweitzer KJ, van Bekkum E, de Groot CJ. Endometriosis with intestinal perforation in term pregnancy. *Int J Gynaecol Obstet* 2006;93:152–3.
7. Nakatani Y, Hara M, Misugi K, Korehisa H. Appendiceal endometriosis in pregnancy. Report of a case with perforation and review of the literature. *Acta Pathol Jpn* 1987;37:1685–90.
8. Gini PC, Chukudebelu WO, Onuigbo WI. Perforation of the appendix during pregnancy: a rare complication of endometriosis. Case report. *Br J Obstet Gynaecol* 1981;88:456–8.
9. Rud B. Colonic endometriosis with perforation during pregnancy. *Ugeskr Laeger* 1979;141:2831–2.
10. Clement PB. Perforation of the sigmoid colon during pregnancy: a rare complication of endometriosis. Case report. *Br J Obstet Gynaecol* 1977;84:548–50.
11. Faucheron J, Pasquier D, Voirin D. Endometriosis of the vermiform appendix as an exceptional cause of acute perforated appendicitis during pregnancy. *Colorectal Dis* 2008;10:518–9.

12. Hauffer F. Unusual complication of pregnancy due to heterotopic endometriosis in the small intestine. *Virchows Arch* 1931;280:822–8.
13. Floberg J, Bäckdahl M, Silferswärd C, Thomassen PA. Postpartum perforation of the colon due to endometriosis. *Acta Obstet Gynaecol Scand* 1984;63:183–4.
14. Loverro G, Cormio G, Greco P, Altomare D, Putignano G, Selvagi L. Perforation of the sigmoid colon during pregnancy: a rare complication of endometriosis. *J Gynecol Surg* 1999;15:155–7.
15. Nishikawa A, Kondoh E, Hamanishi J, Yamaguchi K, Ueda A, Sato Y, et al. Ileal perforation and massive intestinal haemorrhage from endometriosis in pregnancy: case report and literature review. *Eur J Obstet Gynecol Reprod Biol* 2013;170:20–4.
16. Anaf V, Nakadi I, Simon P, Englert Y, Peny M, Fayt I, et al. Sigmoid endometriosis and ovarian stimulation. *Humanit Rep* 2000;15:790–4.
17. Leibson CL, Good AE, Hass SL, Ransom J, Yawn BP, O'Fallon WM, et al. Incidence and characterization of diagnosed endometriosis in a geographically defined population. *Fertil Steril* 2004;82:314–21.
18. Rogers PA, D'Hooghe TM, Fazleabas A, Gargett CE, Montgomery GW, Rombauts L, et al. Priorities for endometriosis research: recommendations from an international consensus workshop. *Reprod Sci* 2009;16:335–46.
19. Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, et al. World Endometriosis Research Foundation Global Study of Women's Health consortium. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 2011;96:366–73.
20. Macafee CHG, Greer HLH. Intestinal endometriosis: a report of 29 cases: a survey of the literature. *J Obstet Gynaecol Br Emp* 1960;67:539–55.
21. Prystowsky JB, Stryker SJ, Ujiki GT, Poticha SM. Gastrointestinal endometriosis—incidence and indications for resection. *Arch Surg* 1988;123:855–8.
22. Faccioli N, Manfredi R, Mainardi P, Dalla Chiara E, Spoto E, Minelli L, et al. Barium enema evaluation of colonic involvement in endometriosis. *AJR Am J Roentgenol* 2008;190:1050–4.
23. McArthur JW, Ulfelder H. The effect of pregnancy upon endometriosis. *Obstet Gynecol Surv* 1965;20:709–33.
24. Coccia ME, Rizzello F, Palagiano A, Scarselli G. The effect of the hormonal milieu of pregnancy on deep infiltrating endometriosis: serial ultrasound assessment of changes in size and pattern of deep endometriotic lesions. *Eur J Obstet Gynecol Reprod Biol* 2012;160:35–9.