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# Good News About Endometriosis and Preterm Delivery

# Saavalainen, Liisu

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**Invited Commentary** | Obstetrics and Gynecology

## **Good News About Endometriosis and Preterm Delivery**

Liisu Saavalainen, MD. PhD: Oskari Heikinheimo, MD. PhD

Endometriosis is a common inflammatory disease of the female pelvis; typical symptoms include pelvic pain and subfertility. Endometriosis is often divided into subtypes of peritoneal, ovarian, and deep infiltrating endometriosis. Classically (ie, surgically) diagnosed endometriosis has been associated with increased risk for ovarian cancer, cardiovascular disease, and some autoimmune diseases<sup>1</sup>. In addition, endometriosis has emerged as a risk factor for various adverse pregnancy outcomes, such as cesarean delivery, placenta previa, and postpartum bleeding.<sup>2</sup>

Several studies have suggested that women with endometriosis have a slightly increased risk for preterm birth. The cause seems to be related to factors associated with pathogenesis of endometriosis, such as inflammation, reactive oxygen species, progesterone resistance, and alterations in the junctional zone of uterus leading to the shallow invasion of the placenta and to preterm birth. Other endometriosis-associated obstetric risks, such as hypertension and preeclampsia, placenta previa, intrauterine growth retardation, and gestational diabetes, might also relate to the increased risk for preterm birth. However, these studies were mostly retrospective, had differing processes for classification of endometriosis and selection of patients, and typically included predominantly women with subfertility. The possible concomitant adenomyosis is an important confounding factor for which these studies rarely adjusted. In addition, the follow-up and management of pregnancy and delivery varied nationally and regionally.

The heterogeneity of endometriosis complicates the issue further. The different subtypes of endometriosis might represent pathogenetically distinct diseases and deserve specific attention. Moreover, the strength and duration of the endometriosis exposure are impossible to measure because the activity and severity of the disease are not stable, and the phenotype might evolve during the follow-up. Thus, the risks of different outcomes might vary according to the duration and phenotype of endometriosis.

Data are scarce on the implications of specific phenotypes and their combinations for obstetric outcomes. According to previous studies, the risk for preterm birth is more pronounced in women with deep endometriosis than in women with ovarian endometriosis.<sup>3</sup> Little is known about the possible implications of previous endometriosis surgery for obstetric outcomes.

The prospective study by Marcellin et al  $^7$  adds important knowledge to the previous studies. The study assessed the risk for preterm delivery (ie, birth before 37 weeks' gestation) in women with endometriosis and those without endometriosis from several maternity centers in France. The women with endometriosis were classified according to the clinically judged severity of their disease, ranging from superficial (n = 48) to ovarian (n = 83) to deep (predominantly sacrouterine) (n = 339) endometriosis; the ovarian and deep phenotypes included combinations of endometriosis. The distribution of the diagnosis reflected the treatment in a tertiary care center rather than the disease spectrum itself.

In contrast to most of the previous studies, the study by Marcellin et al<sup>7</sup> reported no differences in the risk for preterm delivery between women with endometriosis (34 of 470 [7.2%]) and those without endometriosis (53 of 881 [6.0%]), even when adjusted for multiple factors. Moreover, no differences in the risk for preterm delivery were found among the different phenotypes of endometriosis or between the types of preterm birth (spontaneous or induced).<sup>7</sup>

By reporting no association between endometriosis and preterm delivery in women with endometriosis, the novel results by Marcellin et al<sup>7</sup> challenge the findings of most previous studies on

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this topic. These results are valuable and comforting. However, they are also likely to trigger new studies on the pregnancy risks associated with different types of endometriosis. That is good news.

#### **ARTICLE INFORMATION**

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**Corresponding Author:** Oskari Heikinheimo, MD, PhD, Department of Obstetrics and Gynecology, Helsinki University Hospital, PO Box 140, FI-00029 HUS, Helsinki, Finland (oskari.heikinheimo@helsinki.fi).

**Author Affiliations:** Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland.

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### **REFERENCES**

- 1. Kvaskoff M, Mu F, Terry KL, et al. Endometriosis: a high-risk population for major chronic diseases? *Hum Reprod Update*. 2015;21(4):500-516. doi:10.1093/humupd/dmv013
- 2. Horton J, Sterrenburg M, Lane S, Maheshwari A, Li TC, Cheong Y. Reproductive, obstetric, and perinatal outcomes of women with adenomyosis and endometriosis: a systematic review and meta-analysis. *Hum Reprod Update*. 2019;25(5):592-632. doi:10.1093/humupd/dmz012
- 3. Leone Roberti Maggiore U, Ferrero S, Mangili G, et al. A systematic review on endometriosis during pregnancy: diagnosis, misdiagnosis, complications and outcomes. *Hum Reprod Update*. 2016;22(1):70-103. doi:10.1093/humupd/dmvO45
- **4**. Vannuccini S, Clifton VL, Fraser IS, et al. Infertility and reproductive disorders: impact of hormonal and inflammatory mechanisms on pregnancy outcome. *Hum Reprod Update*. 2016;22(1):104-115. doi:10.1093/humupd/dmv044
- 5. Bruun MR, Arendt LH, Forman A, Ramlau-Hansen CH. Endometriosis and adenomyosis are associated with increased risk of preterm delivery and a small-for-gestational-age child: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2018;97(9):1073-1090. doi:10.1111/aogs.13364
- **6.** Gordts S, Koninckx P, Brosens I. Pathogenesis of deep endometriosis. *Fertil Steril*. 2017;108(6):872-885.e1. doi: 10.1016/j.fertnstert.2017.08.036
- 7. Marcellin L, Goffinet F, Azria E, et al. Association between endometriosis phenotype and preterm birth in France. *JAMA Netw Open*. 2022;5(2):e2147788. doi:10.1001/jamanetworkopen.2021.47788