

Obstetric Outcomes in Chinese Women with Endometriosis: A Retrospective Cohort Study

Hong Lin, Jin-Hua Leng, Jun-Tao Liu, Jing-He Lang

Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing 100730, China

Abstract

Background: The effect of endometriosis on obstetric outcomes is still ambiguous. The aim of our study was to determine the association between endometriosis and adverse obstetric outcomes in a cohort of Chinese women.

Methods: A retrospective cohort study was undertaken to compare obstetric outcomes between 249 women with endometriosis and 249 women without endometriosis. All women were nulliparous and achieved singleton pregnancies naturally. Women with endometriosis were diagnosed during surgery and confirmed histologically. Odds ratios (ORs) and 95% confidence intervals (CIs) of measures of obstetric outcomes were calculated.

Results: Women with endometriosis showed significantly increased risks of preterm labor (adjusted OR, 2.42; 95% CI, 1.05–5.57), placenta previa (adjusted OR, 4.51; 95% CI, 1.23–16.50), and cesarean section (adjusted OR, 1.93; 95% CI, 1.31–2.84). No significant differences were observed in the incidence of pregnancy-induced hypertension, fetal growth restriction, small for gestational age, placental abruption, or luteal support in the first trimester between the two groups.

Conclusions: Women with endometriosis are at a higher risk of preterm labor, placenta previa, and cesarean section during pregnancy and need additional care.

Key words: Endometriosis; Pregnancy Outcome; Premature Birth

INTRODUCTION

Endometriosis is characterized by the presence of endometrial glands and stroma outside the uterus. It is associated with many distressing symptoms, including dysmenorrhea, chronic pelvic pain, and infertility.^[1] The prevalence of endometriosis in women of reproductive age is estimated to be 6–10%.^[2,3]

Endometriosis is a chronic, estrogen-dependent inflammatory disorder that can lead to infertility through a series of mechanisms. However, the effect of endometriosis on obstetric outcomes is still ambiguous. Evidence for this issue is scanty and inconsistent. The aim of our study was to determine the association between endometriosis and adverse obstetric outcomes in a cohort of Chinese women.

METHODS

The study protocol was approved by the Institutional Review Board of Peking Union Medical College Hospital. Informed

consent was not required because of the retrospective and anonymous nature of this study.

This investigation was a 1:1 retrospective cohort study conducted in the Department of Obstetrics and Gynecology of Peking Union Medical College Hospital. During 1995–2013, 249 women with histologically proven pelvic endometriosis who attended a routine prenatal check-up and delivered in our hospital were enrolled as the study group. In addition, 249 women without endometriosis were selected as the unexposed group by means of stratified sampling based upon the year of delivery. Corresponding numbers of women were sampled randomly according to the proportions of the endometriosis group from: 1995–1999; 2000–2004; 2005–2009; 2010–2013. All women were nulliparous who achieved their singleton pregnancies without assisted reproduction techniques (ARTs). Data were available for all women. Social and demographic characteristics were obtained at the first prenatal check-up. Indicators measured were adverse obstetric outcomes (preterm labor, pregnancy-induced hypertension [PIH], placenta previa, placental abruption, fetal growth restriction [FGR], small for

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.151077

Address for correspondence:

Prof. Jin-Hua Leng,
Department of Obstetrics and Gynecology, Peking Union Medical
College Hospital, Chinese Academy of Medical Science and Peking
Union Medical College, Beijing 100730, China
E-Mail: lengjenny@vip.sina.com

gestational age [SGA], cesarean section), and luteal support in the first trimester.

Inclusion and exclusion criteria

The endometriosis group comprised of pregnant women with pelvic endometriosis confirmed histologically and visually at the surgical procedure. The unexposed group included women who did not have a previous clinical or surgical diagnosis of endometriosis, and who did not have any ultrasonographic sign of endometriosis. Women with factors known to influence pregnancy outcomes (e.g. multipara, multiple pregnancies, conception through ARTs) were excluded, as were women with malignancies, immune-system diseases, or cardiovascular diseases.

Definitions

Preterm labor refers to the delivery before 37 weeks of gestation. PIH includes gestational hypertension and preeclampsia. Gestational hypertension is defined as elevated blood pressure $\geq 140/90$ mmHg after 20 weeks of gestation in a formerly normotensive woman. Preeclampsia is gestational hypertension with proteinuria (≥ 300 mg/24 h). Placenta previa is the presence of placental tissue that reaches or extends over the internal cervical os. Placental abruption is bleeding at the decidual-placental interface that causes partial or total placental detachment before delivery of the fetus. FGR is defined as an estimated fetal weight below the tenth percentile for gestational age and sex based on sonography. SGA is a birth weight below the tenth percentile for gestational age and sex (for term infants, the standard is <2500 g.)

Statistical analysis

Data analysis was carried out using SPSS 20.0 (IBM, Armonk, NY, USA). Continuous variables were compared using Student's *t*-test. Categorical variables were assessed using the Chi-square test. Fisher's exact test was applied if the minimal estimated expected value was <5 . Logistic regression analysis was used to evaluate the association between endometriosis and adverse obstetric outcomes. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated after adjustment for maternal age. $P < 0.05$ was considered statistically significant.

RESULTS

Maternal social and demographic characteristics are presented in Table 1. The two groups were comparable in terms of gravidity, body mass index, and smoking habits. A significant difference in maternal age was noted as women with endometriosis were older than those without endometriosis (32.8 ± 4.0 vs. 30.6 ± 3.5 years, respectively; $P < 0.001$).

Obstetric outcomes and luteal support in the first trimester are shown in Table 2. The number of instances of preterm labor in women with and without endometriosis were 20 (8.0%) and 9 (3.6%), respectively. Of the 20 cases in the endometriosis group, four cases were caused by spontaneous preterm labor, 13 by premature rupture of membrane (PROM), and three because of maternal or fetal indications. In the nonendometriosis group, three cases were caused by spontaneous preterm labor, four by PROM, and two because of maternal or fetal indications.

When controlling for maternal age, women with endometriosis experienced an increased risk of preterm

Table 1: Demographic characteristics of women with and without endometriosis

Characteristics	Endometriosis, <i>n</i> = 249	No endometriosis, <i>n</i> = 249	<i>P</i>
Maternal age (years), mean \pm SD	32.8 \pm 4.0	30.6 \pm 3.5	<0.001*
Gravidity, <i>n</i> (%)			
1	129 (51.8)	125 (50.2)	0.637
2	78 (31.3)	73 (29.3)	
3	30 (12.0)	40 (16.1)	
≥ 4	12 (4.8)	11 (4.4)	
BMI (kg/m ²), <i>n</i> (%)			
Underweight (<18.5)	33 (13.3)	24 (9.6)	0.641
Normal (18.5–23.9)	165 (66.3)	172 (69.1)	
Overweight (24–27.9)	49 (19.7)	51 (20.5)	
Obese (≥ 28)	2 (0.8)	2 (0.8)	
Smoking, <i>n</i> (%)			
Yes	0 (0)	1 (0.4)	1.000
No	249 (100.0)	248 (99.6)	

*Statistically significant. SD: Standard deviation; BMI: Body mass index.

Table 2: Adverse obstetric outcomes and luteal support in the first trimester in women with and without endometriosis

Items	Endometriosis, <i>n</i> = 249 (<i>n</i> (%))	No endometriosis, <i>n</i> = 249 (<i>n</i> (%))	Adjusted OR (95% CI)	<i>P</i>
Preterm labor	20 (8.0)	9 (3.6)	2.42 (1.05–5.57)	0.038*
PIH	9 (3.6)	11 (4.4)	0.78 (0.31–2.00)	0.608
Placenta previa	13 (5.2)	3 (1.2)	4.51 (1.23–16.50)	0.023*
Placental abruption	1 (0.4)	2 (0.8)	0.98 (0.71–1.34)	0.460
FGR	3 (1.2)	2 (0.8)	1.53 (0.24–9.99)	0.655
SGA	6 (2.4)	3 (1.2)	1.75 (0.41–7.49)	0.450
Cesarean section	174 (69.9)	121 (48.6)	1.93 (1.31–2.84)	0.001*
Luteal support	37 (14.9)	25 (10.0)	1.28 (0.72–2.25)	0.400

*Statistically significant. PIH: Pregnancy-induced hypertension; FGR: Fetal growth restriction; SGA: Small for gestational age; OR: Odds ratio; CI: Confidence interval.

labor, placenta previa, and cesarean section compared with women without endometriosis. The adjusted OR was 2.42 (95% CI, 1.05–5.57), 4.51 (95% CI, 1.23–16.50), and 1.93 (95% CI, 1.31–2.84), respectively. No significant differences were observed in the incidence of PIH, FGR, SGA, placental abruption, or luteal support in the first trimester between the two groups.

DISCUSSION

Our study showed that women with endometriosis are at a higher risk of preterm labor, placenta previa, and cesarean section compared with women without endometriosis. There was no significant difference in the other variables tested. However, there was an increased trend for women with endometriosis developing SGA (adjusted OR, 1.75; 95% CI, 0.41–7.49) and FGR (adjusted OR, 1.53; 95% CI, 0.24–9.99), but the risk was not significant. The relatively small sample size may have contributed to this result.

We speculated that endometriosis may promote the occurrences of adverse obstetric outcomes in affected pregnant women. The eutopic endometrium and junctional zone have been reported to be abnormal at molecular and functional levels, which leads to impairment of endometrial growth, maturation and decidualization, endometrial receptivity, defective spiral artery remodeling, and defective deep placentation.^[4,5] Defective artery remodeling is a typical feature of preeclampsia and associated with a spectrum of pregnancy complications, including preterm labor and FGR.^[4,6] Abnormal placentation may result in an increased risk of placental complications. Endometriosis is also associated with a chronic pelvic inflammatory process, and increased levels of prostaglandins and cytokines have been documented in the peritoneal fluid of women with endometriosis.^[7,8] These increased levels of proinflammatory mediators may stimulate myometrial contractions and cervical ripening, leading to preterm labor.^[9,10] Moreover, the normal frequency and amplitude of uterine contractions are altered among women with endometriosis,^[11] which may affect the transportation and implantation of the embryo.^[12] Hence, uterine dysperistalsis could explain the increased risk of placenta previa.^[13] Increased obstetric complications may lead to an increased prevalence of cesarean section.

Clinical evidences are not fully consistent with our hypothesis, nevertheless. Several authors concur with our data and found that endometriosis negatively affect pregnancy outcomes to some extent.^[9,14,15] A nationwide study in Sweden involving more than 1.4 million singleton births demonstrated women with endometriosis carried higher risks of preterm labor, preeclampsia, placental complications, and cesarean section, but an association between SGA and endometriosis was not observed.^[9] One study in Italy showed a twofold risk of preterm labor in women with endometriosis.^[15] In contrast, other studies have failed to show an association between endometriosis and adverse obstetric outcomes. A retrospective cohort

study in Canada reported that women with endometriosis were not at an increased risk of preterm labor, PIH, SGA, or FGR.^[16] A study undertaken in Japan arrived at a similar conclusion.^[17] One study even reported that the risk of preeclampsia was decreased significantly in women with endometriosis;^[18] the author suggested that increased local expression of angiogenic factors and enhanced endometrial vascular perfusion may be the reasons. A further two studies reported the same trends, but they were not statistically significant.^[16,19]

In addition, some scholars have focused on certain types of endometriosis. Benaglia *et al.* compared pregnancy outcomes between 78 women with ovarian endometrioma and 156 cases without endometriosis. Significant differences were not observed in the incidence of preterm birth, preeclampsia, placental complications, SGA, or cesarean section.^[20] Fernando *et al.* suggested women with endometrioma were at an increased risk of preterm labor and SGA, but this risk was not present in women with other forms of endometriosis.^[14] Vercellini *et al.* assessed pregnancy outcomes among different types of endometriosis. A total of 419 cases was divided into four groups – rectovaginal endometriosis; ovarian endometrioma; ovarian endometrioma plus peritoneal implants; peritoneal endometriosis. They concluded that among the four groups, women with rectovaginal endometriosis were at a higher risk of placenta previa and women with only ovarian endometrioma were at a lower risk of preterm labor. The total incidence of placenta previa was increased by more than tenfold compared with the general population. The cesarean section rate was higher in women with ovarian endometrioma plus peritoneal implants and rectovaginal endometriosis.^[13] Notably, some of the studies mentioned above suffered from limitations such as insufficient sample sizes^[17-20] or lack of definitive histological diagnoses of endometriosis.^[9,14,18,20]

Our study is the first to show the effect of endometriosis on adverse obstetric outcomes in Chinese women. The main benefit of our study lies in the fact that women with endometriosis enrolled were confirmed histologically and visually at the surgical procedure, which reduced the risk of misclassification. Furthermore, we excluded parous women and those who conceived through ARTs, which are known to affect obstetric outcomes.

Some limitations have to be recognized. First, the sample size was relatively small but, nevertheless, some significant results were obtained. Second, an inherent bias is present in the data collection of retrospective studies; several evaluation indicators, such as spontaneous miscarriage and ectopic pregnancy, were not included in our study. Third, the women with endometriosis that we selected conceived spontaneously, which means most patients' condition was mild to moderate. Women with severe endometriosis usually cannot conceive naturally but can do this via ARTs, but we excluded women who conceived this way. Accordingly, there may have been a selection bias. Finally, our study is a single-center analysis.

The present study suggests that women with endometriosis are at a higher risk of developing preterm labor and placenta previa, as well as requiring cesarean section. Such patients may need additional care during pregnancy.

REFERENCES

1. Farquhar C. Endometriosis. *BMJ* 2007;334:249-53.
2. Giudice LC, Kao LC. Endometriosis. *Lancet* 2004;364:1789-99.
3. Buck Louis GM, Hediger ML, Peterson CM, Croughan M, Sundaram R, Stanford J, *et al*. Incidence of endometriosis by study population and diagnostic method: The ENDO study. *Fertil Steril* 2011;96:360-5.
4. Brosens I, Brosens JJ, Fusi L, Al-Sabbagh M, Kuroda K, Benagiano G. Risks of adverse pregnancy outcome in endometriosis. *Fertil Steril* 2012;98:30-5.
5. Brosens I, Pijnenborg R, Benagiano G. Defective myometrial spiral artery remodelling as a cause of major obstetrical syndromes in endometriosis and adenomyosis. *Placenta* 2013;34:100-5.
6. Brosens I, Pijnenborg R, Vercruyse L, Romero R. The “great obstetrical syndromes” are associated with disorders of deep placentation. *Am J Obstet Gynecol* 2011;204:193-201.
7. Pizzo A, Salmeri FM, Ardita FV, Sofò V, Tripepi M, Marsico S. Behaviour of cytokine levels in serum and peritoneal fluid of women with endometriosis. *Gynecol Obstet Invest* 2002;54:82-7.
8. Rakhila H, Carli C, Daris M, Lemyre M, Leboeuf M, Akoum A. Identification of multiple and distinct defects in prostaglandin biosynthetic pathways in eutopic and ectopic endometrium of women with endometriosis. *Fertil Steril* 2013;100:1650-9.e1.
9. Stephansson O, Kieler H, Granath F, Falconer H. Endometriosis, assisted reproduction technology, and risk of adverse pregnancy outcome. *Hum Reprod* 2009;24:2341-7.
10. Petraglia F, Arcuri F, de Ziegler D, Chapron C. Inflammation: A link between endometriosis and preterm birth. *Fertil Steril* 2012;98:36-40.
11. Kunz G, Beil D, Huppert P, Leyendecker G. Structural abnormalities of the uterine wall in women with endometriosis and infertility visualized by vaginal sonography and magnetic resonance imaging. *Hum Reprod* 2000;15:76-82.
12. Aguilar HN, Mitchell BF. Physiological pathways and molecular mechanisms regulating uterine contractility. *Hum Reprod Update* 2010;16:725-44.
13. Vercellini P, Parazzini F, Pietropaolo G, Cipriani S, Frattaruolo MP, Fedele L. Pregnancy outcome in women with peritoneal, ovarian and rectovaginal endometriosis: A retrospective cohort study. *BJOG* 2012;119:1538-43.
14. Fernando S, Breheny S, Jaques AM, Halliday JL, Baker G, Healy D. Preterm birth, ovarian endometriomata, and assisted reproduction technologies. *Fertil Steril* 2009;91:325-30.
15. Conti N, Cevenini G, Vannuccini S, Orlandini C, Valensise H, Gervasi MT, *et al*. Women with endometriosis at first pregnancy have an increased risk of adverse obstetric outcome. *J Matern Fetal Neonatal Med* 2014; <http://dx.doi.org/10.3109/14767058.2014.968843>.
16. Aris A. A 12-year cohort study on adverse pregnancy outcomes in Eastern Townships of Canada: Impact of endometriosis. *Gynecol Endocrinol* 2014;30:34-7.
17. Mekaru K, Masamoto H, Sugiyama H, Asato K, Heshiki C, Kinjyo T, *et al*. Endometriosis and pregnancy outcome: Are pregnancies complicated by endometriosis a high-risk group? *Eur J Obstet Gynecol Reprod Biol* 2014;172:36-9.
18. Brosens IA, De Sutter P, Hamerlynck T, Imeraj L, Yao Z, Cloke B, *et al*. Endometriosis is associated with a decreased risk of pre-eclampsia. *Hum Reprod* 2007;22:1725-9.
19. Kortelahti M, Anttila MA, Hippeläinen MI, Heinonen ST. Obstetric outcome in women with endometriosis – a matched case-control study. *Gynecol Obstet Invest* 2003;56:207-12.
20. Benaglia L, Bermejo A, Somigliana E, Scarduelli C, Ragni G, Fedele L, *et al*. Pregnancy outcome in women with endometriomas achieving pregnancy through IVF. *Hum Reprod* 2012;27:1663-7.

Received: 07-12-2014 **Edited by:** Li-Min Chen

How to cite this article: Lin H, Leng JH, Liu JT, Lang JH. Obstetric Outcomes in Chinese Women with Endometriosis: A Retrospective Cohort Study. *Chin Med J* 2015;128:455-8.

Source of Support: Nil. **Conflict of Interest:** None declared.