



## Research Paper

## Influence of previous laparoscopic surgical and pathological diagnosis of endometriosis on pregnancy outcomes in women with adenomyosis

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## ABSTRACT

**Objectives:** Previous studies demonstrated that endometriosis and adenomyosis are closely linked to lots of adverse pregnancy outcomes while the role of endometriosis in pregnant women with adenomyosis has not been explored yet. The present study aimed to evaluate the influence of previous laparoscopic surgical and pathological diagnosis of endometriosis on pregnancy outcomes in women with adenomyosis.

**Methods:** A total of 60 pregnant women who were diagnosed with adenomyosis before or during pregnancy were included in this study. Among them, 8 were also diagnosed with endometriosis by previous laparoscopic surgery. The demographic characteristics and pregnancy outcomes were compared between women with adenomyosis only and those with the surgical history of endometriosis.

**Results:** Compared with women with adenomyosis only, those concomitant with the surgical history of endometriosis had significantly higher age at delivery [37.5(36.25–39.75) vs. 35(33.25–37),  $P = 0.016$ ] and an increased risk of postpartum hemorrhage (PPH) (adjusted OR: 5.992, 95% CI: 1.03–34.857,  $P = 0.046$ ) while no significant differences were found in other adverse pregnancy outcomes between these two groups. Then we further detected the risk factor of PPH in women with adenomyosis and found that the surgical history of endometriosis (OR: 6.995, 95% CI: 1.16–42.171,  $P = 0.034$ ) and assisted reproductive technology (ART) (OR: 5.062, 95% CI: 1.494–17.146,  $P = 0.009$ ) were the parameters closely associated with the occurrence of PPH.

**Conclusions:** The history of previous laparoscopic surgical and pathological diagnosis of endometriosis in pregnant women with adenomyosis may increase the risk of PPH, which still needs to be verified by future studies with a large sample size. Besides, pregnancy through ART is also an increased risk factor for PPH in women with adenomyosis. Pregnant women with adenomyosis who conceived with the surgical history of endometriosis or by ART should be closely monitored for the reason of being at high risk of PPH.

## 1. Introduction

Endometriosis and adenomyosis are defined as the endometrial glands and stroma located outside the uterus and in the myometrial wall, respectively.<sup>1</sup> There is a strong link between endometriosis and adenomyosis, and the prevalence of adenomyosis in patients affected by endometriosis ranges from 20% to 50%.<sup>2,3</sup> Di Donato et al.<sup>4</sup> demonstrated that the correlations between endometriosis and adenomyosis

were closely related to age, parity, increased intensity of dysmenorrhea, and the presence of deep invasive endometriosis.

In the past decades, a large number of studies have reported that endometriosis is associated with various adverse pregnancy outcomes.<sup>5,6</sup> In our previous research, we detected that endometriosis significantly increases the risk of postpartum hemorrhage (PPH) and the tendency of other adverse pregnancy outcomes.<sup>7</sup> Women with adenomyosis were also at increased risk of various adverse pregnancy outcomes.<sup>8–10</sup> Scala

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et al.<sup>11</sup> explored the impact of adenomyosis on the adverse pregnancy outcomes in women with endometriosis and proved that the presence of diffuse adenomyosis is the independent risk factor for delivery of a small-for-gestational-age (SGA) infant. However, previous studies have paid little attention to the impact of endometriosis on the pregnancy outcomes of patients with adenomyosis. The purpose of this study is to evaluate the pregnancy outcomes of women with adenomyosis with or without the surgical history of endometriosis.

## 2. Materials and methods

### 2.1. Patients

We retrospectively investigated 60 women who had been diagnosed with adenomyosis in the Department of Obstetrics and Gynecology, Peking University People's Hospital, from 2015 to 2021. These pregnant women underwent regular check-ups throughout the whole pregnancy and give birth in the same hospital. All adenomyosis in this study is diagnosed by ultrasonography examination (USG) and the inclusion criteria for adenomyosis were the following features<sup>12</sup>: (i) myometrial anterior-posterior asymmetry; and/or (ii) thickening of the anterior and posterior myometrial walls, with either increased or decreased echogenicity. Among those included 60 women, 33 were diagnosed with adenomyosis before pregnancy, and the remaining 27 were diagnosed with adenomyosis during pregnancy. 8 cases of women also had endometriosis which was diagnosed by previous laparoscopic surgery and pathology. Women with severe fetal structural abnormalities, known autoimmune diseases or fetal aneuploidy, and women with multiple pregnancies were excluded. The present study aimed to evaluate the influence of the surgical history of endometriosis on adverse pregnancy outcomes in women with adenomyosis. Adverse pregnancy outcomes included cesarean section rate (CS), hypertensive disorders of pregnancy (HDCP), gestational diabetes mellitus (GDM), placenta previa, premature rupture of membranes (PROM), abortion, preterm birth, postpartum hemorrhage (PPH) (>500 ml), severe PPH (>1000 ml), SGA, macrosomia, low birth weight infant (LBW), very low birth weight infant (VLBW). This study was approved by the Institutional Review Board of the Peking University People's Hospital.

### 2.2. Statistical analysis

The data were calculated and analyzed by SPSS 22.0 software. Categorical variables were compared by Chi-square test or Fisher's exact test. Continuous variables that conform to the normal distribution are presented as mean  $\pm$  standard deviation (SD) and are compared by Student's t-test. For continuous variables that do not conform to the normal distribution, the median (interquartile range) is used for statistical description, and the Mann-Whitney *U* test is used for comparison. Multinomial logistic regression was used to evaluate the association between exposure covariates and adverse pregnancy outcomes.

**Table 1**

Comparison of maternal characteristics in women with adenomyosis according to whether combined with endometriosis.

Characteristics	Adenomyosis and endometriosis (N = 8)	Adenomyosis only (N = 52)	Statistics	P values
Age(y), median(interquartile range)	37.5(36.25–39.75)	35(33.25–37.00)	-2.402 <sup>c</sup>	0.016
BMI(kg/m <sup>2</sup> ), mean $\pm$ standard deviation	24.83 $\pm$ 6.08	23.84 $\pm$ 3.25	0.447 <sup>a</sup>	0.667
Weight gain (kg), mean $\pm$ standard deviation	9.93 $\pm$ 4.78	11.98 $\pm$ 4.48	-1.123 <sup>a</sup>	0.267
Gravidity $\geq$ 2, n (%)	4	35	0.913 <sup>b</sup>	0.433
Multipara, n (%)	2	21	0.694 <sup>b</sup>	0.698
ART, n (%)	3	16	0.145 <sup>b</sup>	0.699

Note.

<sup>a</sup> t values.

<sup>b</sup>  $\chi^2$  values.

<sup>c</sup> Z values; (y): (year); BMI: body mass index; ART: assisted reproductive technology.

## 3. Results

Women included in the study were divided into two groups: those with adenomyosis only and those with adenomyosis and the surgical history of endometriosis. Compared with women with adenomyosis only, those with the surgical history of endometriosis had significantly higher age at delivery [37.5(36.25–39.75) vs. 35(33.25–37), *P* = 0.016]. No other statistically significant differences in demographic characteristics were found between these two groups (Table 1).

As shown in Table 2, pregnancy outcomes were analyzed between these two groups and incidences of PPH (6/8 vs. 17/52, *P* = 0.045) was significantly higher in those with the surgical history of endometriosis, as compared with those with adenomyosis only while no significant differences were found in other adverse pregnancy outcomes between these two groups. Multinomial logistic regression was applied by adjusting for age at delivery as shown in Table 3. It showed that women conceived with adenomyosis and the surgical history of endometriosis had a significantly increased risk of PPH (adjusted OR: 5.992, 95% CI: 1.03–34.857, *P* = 0.046). Then we conducted a logistic regression analysis to assess the risk factors of PPH in women with adenomyosis (Table 4 and Table 5) and found that the surgical history of endometriosis (OR: 6.995, 95% CI: 1.16–42.171, *P* = 0.034) and ART (OR: 5.062, 95% CI: 1.494–17.146, *P* = 0.009) were the parameters associated with the occurrence of PPH.

## 4. Discussion

The present study demonstrates that the surgical history of endometriosis in pregnant women with adenomyosis will increase the risk of PPH while may not have an obvious impact on the occurrence of other adverse pregnancy outcomes. Besides, pregnancy through ART is also an increased risk factor for PPH in women with adenomyosis. Pregnant women with adenomyosis who conceived with the surgical history of endometriosis or by ART should be treated as being at high risk of PPH, and need closer monitoring.

A large number of studies have shown that endometriosis is associated with lots of adverse pregnancy outcomes, among which the top 5 obstetric complications are preterm birth, SGA, placenta previa, preeclampsia, and PPH.<sup>13</sup> In our previous research,<sup>7</sup> we found that pregnant women with a previous surgical diagnosis of endometriosis have a higher risk of PPH, and women with endometriosis conceived by ART are at higher risk of PPH and premature delivery than those conceived naturally. In the present study, we found a very high rate of PPH in women concomitant with adenomyosis and endometriosis (75%, 6/8) which may need to be further verified due to the limitation of sample size and we also found that compared with women with adenomyosis only, those concomitant with the presence of endometriosis had a significantly higher risk of PPH (6/8 vs. 17/52, *P* = 0.045). Previous researchers have speculated that the endometrium is different in women with endometriosis from healthy women, which harms the receptivity of the endometrium and the subsequent placentation and then further leads to the

**Table 2**  
Comparison of pregnancy outcomes in women with adenomyosis according to whether combined with endometriosis.

Pregnancy outcomes	Adenomyosis and endometriosis (N = 8)	Adenomyosis only (N = 52)	Statistics	P values
Gestational age(w), median(interquartile range)	271(263.50–281)	272(257.50–275.75)	−0.479 <sup>f</sup>	0.632
Birth weight(g), mean ± standard deviation	3245.71 ± 212.50	3128.94 ± 620.27	0.965 <sup>a</sup>	0.343
CS, n (%)	5 (62.50)	27 (51.92)	0.312 <sup>b</sup>	0.712
HDCP, n (%)	1 (12.50)	10 (19.23)	0.21 <sup>b</sup>	1
GDM, n (%)	2 (25)	14 (26.92)	0.013 <sup>b</sup>	1
Placenta previa, n (%)	1 (12.50)	7 (13.46)	0.006 <sup>b</sup>	1
PROM, n (%)	1 (12.50)	10 (19.23)	0.21 <sup>b</sup>	1
Abortion, n (%)	0	4 (7.70)	0.659 <sup>b</sup>	1
Premature birth, n (%)	1 (12.50)	8 (15.38)	0.045 <sup>b</sup>	1
PPH, n (%)	6 (75)	17 (32.69)	5.25 <sup>b</sup>	0.045
Severe PPH, n (%)	4 (50)	12 (23.08)	2.57 <sup>b</sup>	0.192
SGA, n (%)	0	4 (7.70)	0.659 <sup>b</sup>	1
Macrosomia, n (%)	0	3 (5.80)	0.486 <sup>b</sup>	1
LBW, n (%)	0	6 (11.50)	1.026 <sup>b</sup>	0.585
VLBW, n (%)	0	3 (5.80)	0.486 <sup>b</sup>	1

CS: cesarean section; HDCP: hypertensive disorder complicating pregnancy; GDM: gestational diabetes mellitus; PROM: premature rupture of membrane; PPH: postpartum hemorrhage; SGA: small for gestational age; LBW: low birth weight infant; VLBW: very low birth weight infant.

<sup>a</sup> t values.

<sup>b</sup>  $\chi^2$  values.

<sup>c</sup> Z values.

**Table 3**  
Comparison of pregnancy outcomes in women with adenomyosis according to whether combined with endometriosis adjusted for age at delivery.

Pregnancy outcomes	Adenomyosis and endometriosis (N = 8)	Adenomyosis only (N = 52)	Adjusted OR (95% CI)	P values
Gestational age(w), median(interquartile range)	271(263.50–281)	272(257.50–275.75)	–	0.632
Birth weight(g), mean ± standard deviation	3245.71 ± 212.50	3128.94 ± 620.27	–	0.343
CS, n (%)	5 (62.50)	27 (51.92)	1.674(0.34–8.245)	0.526
HDCP, n (%)	1 (12.50)	10 (19.23)	0.508(0.052–4.953)	0.56
GDM, n (%)	2 (25)	14 (26.92)	0.855(0.144–5.078)	0.863
Placenta previa, n (%)	1 (12.50)	7 (13.46)	0.797(0.078–8.18)	0.848
PROM, n (%)	1 (12.50)	10 (19.23)	0.621(0.064–6.041)	0.682
Abortion, n (%)	0	4 (7.70)	–	–
Premature birth, n (%)	1 (12.50)	8 (15.38)	1.092(0.106–11.224)	0.941
PPH, n (%)	6 (75)	17 (32.69)	5.992(1.03–34.857)	0.046
Severe PPH, n (%)	4 (50)	12 (23.08)	2.913(0.588–14.439)	0.191
SGA, n (%)	0	4 (7.70)	–	–
Macrosomia, n (%)	0	3 (5.80)	–	–
LBW, n (%)	0	6 (11.50)	–	–
VLBW, n (%)	0	3 (5.80)	–	–

OR: Odd ratio; CI: Confidence interval; (w): (week); CS: cesarean section; HDCP: hypertensive disorder complicating pregnancy; GDM: gestational diabetes mellitus; PROM: premature rupture of membrane; PPH: postpartum hemorrhage; SGA: small for gestational age; LBW: low birth weight infant; VLBW: very low birth weight infant. \*t values; <sup>†</sup> $\chi^2$  values; <sup>‡</sup>Z values.

**Table 4**  
Univariate Logistic regression analysis for prediction of postpartum hemorrhage in women with adenomyosis.

Variable	OR	95% CI	P values
Age (y)	1.062	0.91–1.24	0.451
BMI (kg/m <sup>2</sup> )	0.997	0.86–1.16	0.966
Multipara	0.415	0.13–1.29	0.128
ART	4.675	1.47–14.92	0.009
CS	0.698	0.25–1.99	0.501
HDCP	2.259	0.60–8.50	0.228
GDM	1.361	0.43–4.4	0.603
Macrosomia	3.429	0.29–40.13	0.326
Endometriosis	6.176	1.13–33.88	0.036

OR: Odd ratio; CI: Confidence interval; (y): (year); BMI: body mass index; ART: assisted reproductive technology; CS: cesarean section; HDCP: hypertensive disorder complicating pregnancy; GDM: gestational diabetes mellitus.

occurrence of complications such as PPH and premature delivery.<sup>14,15</sup> In addition, the history of previous laparoscopic surgery may be another cause of postpartum hemorrhage for the reasons of pelvic inflammation and adhesions.

Previous studies have shown that ART will increase the prevalence of adverse pregnancy outcomes,<sup>16,17</sup> and one recently meta-analyses<sup>18</sup>

**Table 5**  
Multinomial Logistic regression analysis for prediction of postpartum hemorrhage in women with adenomyosis.

Variable	OR	95% CI	P values
ART	5.062	1.49–17.15	0.009
Endometriosis	6.995	1.16–42.17	0.034

OR: Odd ratio; CI: Confidence interval; ART: assisted reproductive technology.

showed that women with endometriosis who conceived by ART are more significantly associated with a higher risk of preterm birth, PPH, placenta previa, and SGA. Shin et al.<sup>19</sup> detected the risk of preterm births in pregnant women with adenomyosis and demonstrated that the increased risk of premature birth and LBW infants was related to those women who conceived by ART. In the present study, we demonstrated that pregnancy through ART is more likely to have PPH compared with natural pregnancy (OR: 5.062, 95% CI: 1.494–17.146, P = 0.009) in women with adenomyosis. There are several speculations about the increasing risk of PPH in women conceived by ART. First of all, ART may interfere with the formation of the maternal-fetal interface in the early stage of embryo implantation and may cause structural abnormalities of the placenta which may play a role in the early separation of the placenta, and further

lead to uterine weakness and PPH.<sup>20–22</sup> Besides, studies have also shown that reduced levels of human chorionic gonadotropin during the luteal phase may be associated with an increased risk of PPH in ART pregnancy.<sup>23</sup>

The presented study has also some important limitations. Firstly, adenomyosis in this study was diagnosed by USG which may increase the risk of selection bias and endometriosis diagnosis was unable to be definite in cases without a previous surgical history. Secondly, this study is a retrospective study with a very small sample size conducted in a single-center, which inevitably reduces the credibility of the conclusions. Thirdly, though we adjusted for confounding factor (age at delivery), some other confounding factors such as the life history and socioeconomic status was not eliminated. Lastly, we did not include a normal control group in this study by which it will provide much more useful information as data from a normal control group lays ground for further analysis.

## 5. Conclusion

In conclusion, the present study demonstrated that the history of previous laparoscopic surgical and pathological diagnosis of endometriosis in pregnant women with adenomyosis may increase the risk of PPH, which still needs to be verified by future studies with a large sample size. Besides, pregnancy through ART is also an increased risk factor for PPH in women with adenomyosis. Pregnant women with adenomyosis who conceived with the surgical history of endometriosis or by ART should be closely monitored for the reason of being at high risk of PPH.

## Author contributions

Zhao Tian contributed to the study conception and drafted the article. Yi Li, Yue Wang, and Xiao-Hong Chang contributed to the discussion, reviewed and edited the manuscript. Hong-Lan Zhu and Heng Cui directed the project. Hong-Lan Zhu as the corresponding author had full access to all the information in the study and had final responsibility for the decision to submit for publication.

## Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Peking University People's Hospital Ethics Committee.

## Consent to participate

This study is a retrospective study and informed consent had been waived by Ethics Committee of Peking University People's Hospital.

## Consent for publication (all authors)

The Authors agree to publication in the Gynecology and Obstetrics Clinical Medicine.

## Conflict of interest statement

The authors declare that they have no conflicts of interest.

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