Cases of Retroverted Uterus Involving Placenta Previa and Low-Lying Placenta Previa Are Significantly Associated with Endometriosis

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Background: The purpose of this study was to determine whether cases of placenta previa and lowlying placenta previa in patients with retroverted uterus are significantly associated with endometriosis. **Methods:** Participants were patients who underwent cesarean section at our hospital with a diagnosis of placenta previa or low-lying placenta previa within a 7-year period from January 2015 to December 2022. Of these, patients with multiple pregnancies and those without a complete uterine image in the medical record at less than 12 weeks' gestation were excluded. Included patients were divided into two groups according to the presence or absence of endometriosis. The presence of endometriosis was determined based on intraoperative findings. A retrospective case-control study was conducted by examining the presence or absence of retroverted uterus during early pregnancy and the presence or absence of posterior placenta.

Results: A total of 110 patients were included, 32 in the group with endometriosis and 78 in the group without endometriosis. There were 15 (46.9%) cases of retroverted uterus in the group with endometriosis and 17 (21.8%) in the group without endometriosis, indicating significantly more cases in the group with endometriosis (P=0.01). There were 15 (46.9%) cases of retroverted uterus with posterior placenta in the group with endometriosis and 16 cases (20.5%) in the group without endometriosis, indicating significantly more cases in the group with endometriosis (P=0.009).

Conclusion: Placenta previa and low-lying placenta previa in cases of retroverted uterus are significantly associated with endometriosis. (J Nippon Med Sch 2025; 92: 22–28)

Key words: endometriosis, low-lying placenta previa, placenta previa, posterior extrauterine adhesions, retroverted uterus

Introduction

Many recent reports have shown a relationship between endometriosis and perinatal complications¹⁻⁵. Placenta previa is a notable endometriosis-related perinatal complication⁶⁷, but what mechanisms in endometriosis contribute to placenta previa remain unclear. Elucidating the causes of endometriosis resulting in placenta previa is therefore important. To explore this factor, we previously conducted a study comparing cases of placenta previa and low-lying placenta previa with cases of normal placenta previa. The results showed that the rate of endometriosis complication was higher in cases of placenta previa and low-lying placenta previa (odds ratio [OR]: 2.77; 95% confidence interval [CI]: 1.66-4.61; P<0.001), and endometriosis occurrence was more common in the posterior uterine wall (OR: 5.07; 95% CI: 2.79-9.45; P< 0.001). Endometriosis was also significantly associated with posterior uterine wall adhesions (OR: 17.8; 95% CI: 6.74-47.1; P<0.01; adjusted OR: 11.0; 95% CI: 5.08-23.8)⁸.

Endometriosis-related posterior extrauterine adhesions are also a problem in gynecology because they increase the difficulty of surgery. Consequently, there has been a

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focus on preoperative imaging to confirm the presence of endometriosis-related posterior extrauterine adhesions. One of the preoperative diagnoses of posterior uterine adhesions is uterine retroversion^{9,10}. Based on this, we added the hypothesis that a retroverted uterus in early pregnancy represents a risk factor for placenta previa and low-lying placenta previa.

On the other hand, we noted that while endometriosis is diagnosed comprehensively based on subjective symptoms, medical examinations, imaging tests, and laboratory findings, such as CA125 levels, no specific diagnostic criteria have been established. Previous studies that have shown the relationship between endometriosis and perinatal complications have also often lacked a clear diagnostic definition of endometriosis, and many of the cases reviewed were only postoperative cases of endometriosis¹¹⁻¹⁶. Similarly, the presence or absence of endometriosis at the time of conception has not been investigated.

Based on the above clinical questions, we divided patients who underwent cesarean section with a diagnosis of placenta previa or low-lying placenta previa into two groups: those who had endometriosis lesions at the time of cesarean section and those who did not. We evaluated 1) presence or absence of uterine retroversion during early pregnancy and 2) presence or absence of posterior placenta.

Materials and Methods

The study period was 7 years, from January 2015 to December 2022, and included patients who underwent cesarean section with a diagnosis of placenta previa or lowlying placenta previa at Nippon Medical School Musashi Kosugi Hospital. In our hospital, cases of low-lying placenta previa in which the placenta does not border the internal ostium but the path from the uterine internal ostium to the placental margin is less than 2 cm undergo cesarean section. As a result, we added low-lying placenta previa to placenta previa. Exclusions were cases with multiple pregnancies, and cases for which no full uterine image was recorded in early pregnancy. Included patients were divided into two groups: those with endometriosis lesions at the time of cesarean section (Endometriosis complicated group) and those without endometriosis lesions at the time of cesarean section (No endometriosis group). Intraoperative diagnosis of endometriosis was based on the revised-American Society for Reproductive Medicine (r-ASRM) classification, and the presence of ovarian chocolate cysts, deep endometriosis, or peritoneal lesions based on red (red, red-pink, and clear lesions), white (white, yellow-brown, and peritoneal defects), and black (black and blue lesions) coloration were defined as endometriosis lesions¹⁷. Histopathologic diagnosis was obtained by biopsy in some cases, but removal of endometriotic tissue during pregnancy tended to result in uncontrollable bleeding, and was not a requirement for pathologic diagnosis.

Maternal age at delivery, parity, pre-pregnancy body mass index (BMI), use of assisted reproductive technology (ART), and r-ASRM score were examined as maternal characteristics, and blood loss during cesarean section and neonatal birth weight were examined as outcomes. Medical records were used to determine the presence or absence of: 1) uterine retroversion on transvaginal ultrasound tomograms at <12 weeks 0 days of gestation; and 2) posterior placenta on transabdominal ultrasound tomograms after mid-term pregnancy. These characteristics were compared between the Endometriosis complicated group and No endometriosis group.

Based on the fact that ultrasound tomograms can diagnose uterine retroversion as well as MRI scans¹⁸, the presence or absence of uterine retroversion was determined by the following method using a transvaginal ultrasound tomogram that depicted the entire uterus at <12 weeks 0 days of gestation. The transvaginal ultrasound tomogram was taken with the bladder side on the left side of the screen and the Douglas fossa side on the right. As shown in Figure 1, the line connecting the inner uterine ostium and the uterine fundus was defined as the uterine body axis, and the line connecting the inner uterine ostium and outer uterine ostium as the cervical axis. The angle between the cervical axis and the uterine body axis was measured with a protractor in a counterclockwise direction as depicted in Figure 2, with an angle >180° defining uterine retroversion.

The study design was approved by the institutional review board of Nippon Medical School Musashi Kosugi Hospital (approval no. 687-4-52), and the need for informed consent was waived. By publishing the research notification via an opt-out method, we obtained tacit approval to conduct this research without obtaining consent from each of the participants. Statistical analyses were performed using IBM[®] SPSS[®] Statistics version 25 software (IBM, New York, USA). The t-test or Mann-Whitney U-test was used to compare characteristics between the Endometriosis complicated group and No endometriosis group and the χ^2 test or Fisher's exact test was used to compare the presence of retroverted uterus and posterior



Fig. 1 Uterine flexion

The line connecting the inner uterine ostium and uterine fundus is defined as the uterine body axis. The line connecting the inner uterine ostium and outer uterine ostium is defined as the cervical axis. The angle between the cervical axis and uterine body axis is measured using a protractor in a counterclockwise direction.

 \blacksquare : inner uterine ostium \blacktriangle : uterine fundus \blacksquare : outer uterine ostium

solid line: the uterine body axis, dotted line: the cervical axis

 \bigcirc : angle between cervical axis and uterine body axis (uterine flexion)

placenta. The level of statistical significance was set at p < 0.05.

Results

There were 225 patients who underwent cesarean section with a diagnosis of placenta previa or low-lying placenta previa at our hospital during the study period, of which 110 cases were included after omitting patients that met the exclusion criteria. Of these, 32 patients were in the Endometriosis complicated group and 78 patients were in the No endometriosis group. **Figure 3** shows the patient allocations. Maternal characteristics are shown in **Table 1**, and outcomes are described in **Table 2**. There were more ART cases and more blood loss at delivery in the Endometriosis complicated group. The data regarding presence or absence of uterine retroversion and posterior placenta for the two groups are shown in **Table 3**.

There were 15 (46.9%) cases of retroverted uterus in the Endometriosis complicated group and 17 (21.8%) cases in the No endometriosis group, indicating significantly more cases in the Endometriosis complicated group (P=0.01). There were 31 (96.9%) cases of posterior placenta in the Endometriosis complicated group and 69 (88.5%) cases in the No endometriosis group, showing no significant difference (P=0.26). There were 15 (46.9%) cases of retroverted uterus with posterior placenta in the Endometriosis complicated group and 16 cases (20.5%) in the No endometriosis group, indicating significantly



Fig. 2 Example of retroverted uterus An angle of uterine flexion >180° is diagnosed as retroverted uterus.

more cases in the Endometriosis complicated group (P= 0.009).

Discussion

By comparing the two cases of abnormal placental position with and without endometriosis, we found the following. Patients with placenta previa and low-lying placenta previa accompanied by endometriosis required significantly more ART and had significantly more blood loss at delivery than those without endometriosis. Placenta previa and low-lying placenta previa with retroverted uterus were significantly associated with endometriosis. Placenta previa and low-lying placenta previa of posterior placenta with retroverted uterus were also significantly associated with endometriosis.

Reports have suggested that endometriosis with only ovarian or peritoneal lesions does not increase the frequency of perinatal complications, but a high rate of placenta previa is seen in cases with deep endometriosis lesions^{19,20}. Another study indicated that endometriosis lesions infiltrating the posterior uterine wall, particularly the sacral uterine ligament, can cause fibrosis of the ligament, resulting in uterine retroversion²¹. From these reports, it may be suggested that endometriosis that results in uterine retroversion may be a factor in causing abnormal placental positioning. Nagase et al.22 reported that placenta previa with posterior extrauterine adhesions showed a posterior placenta more frequently than placenta previa without posterior extrauterine adhesions. Our results are consistent with those of that study and suggest that a retroverted uterus with endometriosis and posterior placenta may contribute to placenta previa and low-lying placenta previa. These causes may include abnormal implantation sites due to abnormal endometrial peristalsis²³, abnormal placentation due to changes in the

Placenta Previa and Endometriosis



Fig. 3 Study flowchart and patient allocations

Table 1	Maternal characteristics	in the Endometriosis co	omplicated and	No endometriosis	groups
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Maternal characteristics	Endometriosis complicated ($n = 32$)	No endometriosis (n = 78)	p value
Age (years) ^a	36.4±3.6	36.5±4.9	0.88
Parity ^b	0 (0-1)	1 (0-1)	0.72
Pre-pregnancy BMI (kg/m²) ^b	20.5 (18.6-23.5)	20.7 (19.0-22.4)	0.76
ART ^c	13 (40.6%)	15 (19.2%)	0.02
r-ASRM score ^b	4.0 (4.0-8.0)		

^a Data are presented as mean±standard deviation

^b Data are presented as median (interquartile range)

^c Data are presented as n (%)

ART: assisted reproductive technology, BMI: body mass index

r-ASRM: The revised American Society for Reproductive Medicine

intrauterine myometrium caused by impaired spiral artery remodeling^{24,25}, abnormal implantation due to chronic inflammation caused by endometriosis²⁶, and implantation in the cervix and placental dysplasia due to progesterone resistance in the endometrium and decreased levels of microRNA-200a in the cervix^{25,27,28}.

Placenta previa and low-lying placenta previa accompanied by endometriosis required significantly more ART. Endometriosis has also been identified as a cause of infertility²⁹⁻³¹, and with advances in in vitro fertilization, the number of pregnancies complicated by endometriosis is expected to increase in the future^{32,33}.

Therefore, it is desirable to conceive before endometriosis has progressed to the point of causing retroverted uterus. Dissemination of knowledge regarding endometriosis among the general population is thus important so that patients are aware of the different aspects regarding pregnancy and treatment for endometriosis. If a

Table 2 Outcomes in the Endometriosis complicated and No endometriosis groups

Outcomes	Endometriosis complicated ($n = 32$)	No endometriosis (n = 78)	<i>p</i> value
Blood loss (mL)	1,750.0 (1,012.5–2,167.5)	1,110.0 (844.0–1,517.5)	< 0.01
Birth weight (g)	2,892.0 (2,654.3–3,169.0)	2,699.0 (2,510.5–2,929.5)	0.02

Data are presented as median (interquartile range)

 Table 3
 Patients with or without retroverted uterus and posterior wall attachment placenta in the Endometriosis complicated and No endometriosis groups

	Endometriosis complicated ($n = 32$)	No endometriosis (n = 78)	P value
Retroverted uterus	15 (46.9%)	17 (21.8%)	0.01
Posterior wall attachment placenta	31 (96.9%)	69 (88.5%)	0.28
Retroverted uterus + posterior wall attachment placenta	15 (46.9%)	16 (20.5%)	0.009

Data are presented as n (%)

patient is suspected of having clinical endometriosis, early pregnancy should be recommended or hormone therapy should be administered to prevent the progression of endometriosis until pregnancy is desired. In cases of advanced endometriosis, surgery before conception should be considered. However, a previous study showed significantly more placenta previa in cases where deep infiltrating endometriosis was removed prior to conception than in cases without endometriosis, and there are still no clear guidelines as to which cases should undergo surgery before conception³⁴. In cases with suspected complications of endometriosis, such as strong menstrual cramps before pregnancy and retroverted uterus on ultrasound tomogram in the early stages of pregnancy, early risk management may be possible by keeping in mind the development of placenta previa and by examining perinatal risks³⁵.

Our study has several limitations. First, the sample size was small because this was a single-center study, many of the patients were referred from other hospitals after the second trimester of pregnancy, and we had to exclude many cases in which images of the entire uterus in early pregnancy were not available. Second, endometriosis lesions may have resolved during pregnancy in some cases. Endometriotic cysts were reported to be unchanged in 33% of pregnancies, increased in 8%, decreased in 13%, and undetectable in 46%³⁶. Third, the diagnosis of endometriosis was based on intraoperative findings at the time of cesarean section, and cases with endometriosis who had a vaginal delivery have not been studied. However, we believe the strength of this study lies in the selection of cases in which endometriosis lesions were reliably identified at the time of delivery.

This study also did not consider posterior uterine adhesions, but in recent years, the presence of deep infiltrative endometriosis has been predicted based on the presence or absence of a sliding sign on the ultrasound tomogram^{37,38}, and the presence of posterior extrauterine adhesions during pregnancy has been evaluated by magnetic resonance imaging³⁹. These applications are expected to facilitate examination of the relationship between the presence of posterior uterine adhesions and abnormal placental position in the future.

Conclusions

Significant associations with endometriosis were shown for placenta previa and low-lying placenta previa in retroverted uterus, and also posterior placenta previa and posterior low-lying placenta previa in retroverted uterus. It is important to control the progression of endometriosis prior to conception and pregnancy before the disease becomes severe. If a patient with endometriosis presents with retroverted uterus, the possibility of placenta previa should be kept in mind.

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Conflict of Interest: The authors declare no conflicts of interest.

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