Effect of Endometriosis on Obstetric Outcomes: A Tertiary Center Experience

¹⁰ Aytaj MAHMUDOVA^a, ¹⁰ Elifnur BİÇER^b, ¹⁰ Burçin KARAKUŞ^c, ¹⁰ Kutsiye Pelin ÖÇAL^b

^aClinic of Obstetrics and Gynecology, Yeni Yüzyıl University Gaziosmanpaşa Hospital, İstanbul, Türkiye ^bDepartment of Obstetrics and Gynecology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye ^cClinic of Obstetrics and Gynecology, Çamlıca Medipol University Hospital, İstanbul, Türkiye

ABSTRACT Objective: The aim of this study is to compare the course of pregnancy in women with and without endometriosis for obstetric complications. **Material and Methods:** Patients applied to İstanbul University-Cerrahpasa were included in the case group, 49 patients in the control group, and evaluated retrospectively. Early and late pregnancy complications were recorded. P<0.05 was considered statistically significant. **Results:** A decrease in the rate of spontaneous pregnancy and a significant increase in the IVF rate were observed in the endometriosis group (p<0.05). Gestational hypertension, placental abruption, placental adhesion anomalies, premature rupture of membranes, fetal growth restriction, threat of preterm birth and oligohydramnios there was no significant difference between the two groups (p>0.05). The rate of cesarean delivery was 55.1% in the control group and 61.0% in the endometriosis group (p>0.05). Postpartum uterine atony, bladder injury during cesarean section and requirement of postpartum blood transfusion seen in 6 (6.7%), 2(1.1%), and 1 (11.1%) patients respectively (p<0.05). Neonatal intensive care unit requirement was 39.0% and 24.4% in case and control group (p>0.05). **Conclusion:** Women with endometriosis greational diabetes mellitus in the second and third trimesters, postpartum uterine atony, blood transfusion requirement, and surgical complications during regnancy. The rates of miscarriage in the early gestational weeks, preeclampsia, placenta previa, gestational diabetes mellitus in the second and third trimesters, postpartum uterine atony, blood transfusion requirement, and surgical complications during regnancy.

Keywords: Endometriosis; placenta; previa; preeclampsia; complications

Endometriosis is a chronic inflammatory disease characterized by the presence of endometrial gland and stroma outside the uterine cavity.¹ The prevalence of endometriosis in reproductive women is approximately 10%.

Endometriosis is associated with pelvic pain in 60-80% of cases and infertility in 30-40%. Adhesions and anatomical disorders due to fibrosis, endocrine abnormalities and immunological factors are shown as the causes of infertility in women with endometriosis. Pregnancy rates increase with assisted reproductive techniques and treatments in endometriosis cases.²

Physical examination findings in women with endometriosis are variable and depend on the location and size of the implants.³ While the physical examination findings help the diagnosis, the examination may also be completely normal, the normal examination does not exclude the disease.⁴ Various biochemical markers, transabdominal and transvaginal sonography, magnetic resonance imaging, and computed tomography methods are various methods used for the diagnosis of endometriosis. However, the definitive diagnosis is made by histological evaluation of a lesion biopsied during surgery.⁵

Correspondence: Elifnur BİÇER
Department of Obstetrics and Gynecology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye
E-mail: drelifnurbicer@gmail.com
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It is thought that pregnancy positively affects endometriosis due to amenorrhea and anovulation.⁶ However, with the increase in the success rates in the treatment of endometriosis in recent years, the complication rates in pregnancies have also attracted attention. There are studies showing that endometriosis is associated with early pregnancy complications (ectopic pregnancy, abortion, abortus imminens), placental pathologies (placenta previa, placenta attachment anomalies), placental abruption, preterm birth threat and preterm delivery, fetal growth restriction, oligohydramnios, gestational diabetes, and hypertensive diseases of pregnancy.^{1,7,8} It has been reported that the risk of cesarean delivery, postpartum hemorrhage and neonatal complications is high in cases with endometriosis.9,10 Uterine rupture, intestinal perforation, spontaneous hemoperitoneum or uroperitoneum are also rare obstetric complications related to endometriosis.¹¹ It is not clear whether there is a relationship between the stage and type of the disease and the risk of developing neonatal and obstetric complications.12

The aim of this study is to examine the effects of endometriosis on pregnancy outcomes by comparing certain characteristics of women with and without endometriosis, and to determine and evaluate maternal complications because of pregnancy of endometrisis.

MATERIAL AND METHODS

This study was conducted at İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, following the necessary approval of the ethics committee (date: March 3, 2021, no: E-83045809-604.01.02-43516). This study is conducted based on the principles of Helsinki Declaration. The information of the patients who applied to the obstetrics and of İstanbul Universitygynecology clinics Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Obstetrics and Gynecology between 2015-2020 were scanned retrospectively using the hospital electronic database system and patient archive files. The files of patients with endometriosis diagnosed before or during pregnancy were identified. Informed consent was obtained from each patient. For the case group, patients with clinical diagnosis of endometriosis with ultrasound imaging, and for the control group, nulliparous pregnant women without a history of chronic systemic disease were included in the study.

Patients under the age of 18 and over the age of 45, patients with a body mass index (BMI) below 18.5 kg/m² and above 35 kg/m², patients with chronic systemic diseases (chronic kidney diseases, autoimmune diseases, chronic hypertensive diseases, antiphospholipid antibody syndrome and other causes of thrombophilia), patients with autoimmune, genetic diseases, factor deficiencies, diabetes mellitus Type 1 and 2, multiparous patients, patients with a history of previous endometriosis surgery, uterine anomalies, and patients with a history of previous uterine surgery were not included in the study.

For statistical analysis, SPSS 27.0 (IBM, USA) program was used. The Kolmogorov-Smirnov test, independent sample t-test, the Mann-Whitney U test, chi-square test, the Fischer test were used. In statistical analysis, those with a significance level less p<0.05 were considered significant.

RESULTS

In our study, the results of 41 cases in the case group and 49 cases in the control group were examined. In Table 1, the case and control groups were examined about the demographic characteristics. The mean age was 27.5 ± 4.8 years in the control group and 29.4 ± 4.2 years in the case group. Mean BMI values were 27.2 ± 3.7 and 27.0 ± 3.1 in the control and case groups, respectively.

In the endometriosis group, 23 (56.1%) of 41 cases were diagnosed with ultrasonography and 18 (43.9%) were diagnosed surgically (histopathologically). Isolated ovarian endometrioma was seen in 34 (82.9%) cases, deep infiltrative endometriosis and ovarian endometrioma were observed in 6 (14.6%) cases, and adenomyosis was observed in 1 (2.4%) case with ovarian endometrioma with ultrasound imaging. The mean diameter in patients with ovarian endometrioma was 5.1 ± 1.7 cm.

Spontaneous pregnancy was observed in 46 (93.9%) of 49 patients in the control group, and pregnancy was achieved in 3 (6.1%) patients with in-

			Control group			Case group		
Demographic characteristics		n	X ±SD	%	n	X±SD	%	p value
Age			27.5±4.8			29.4±4.2		0.064ª
Body mass index			27.2±3.7			27.0±3.1		0.785 ^b
Smoking status		46		93.9	38		92.7	0.821°
		3		6.1	3		7.3	
Alcohol consumption		49		100.0	41		100.0	1.000°
		0		0.0	0		0.0	
Gravida	1	44		89.8	31		75.6	0.129°
	2	4		8.2	10		24.4	
	3	1		2.0	0		0.0	
Parity	0	49		100.0	41		100.0	1.000°
	1	0		0.0	0		0.0	
Abortus	0	44		89.8	31		75.6	0.129
	1	4		8.2	10		24.4	
	2	1		2.0	0		0.0	

aMann-Whitney U test; bt-test; Chi-squared test; SD: Standard deviation.

trauterine insemination (IUI) and in vitro fertilization (IVF). Of the pregnancies in the case group, 9 (22.0%) were IVF, 3 (7.3%) were IUI, and 29 (70.7%) were spontaneous pregnancies. When the two groups were statistically compared, it was found that the pregnancy rate obtained by IVF was significantly higher in the case group, and spontaneous pregnancies were lower (p<0.05) (Table 2).

Abortion was detected in 22% of patients with endometriosis which was significantly higher in endometriosis group than control group (p<0.05) (Table 3).

Preeclampsia was observed in 1 (2%) patient in the control group and 6 (14.6%) in the endometriosis group (p<0.05). In other words, the risk of developing preeclampsia was significantly higher in patients with endometriosis. When evaluated in terms of obstetric complications such as gestational hypertension, abruption of placenta, premature rupture of membranes, growth restriction of fetus, threat of preterm birth, and oligohydramnios, no significant difference was found in the two groups (p>0.05). No case of placenta previa was observed in 49 patients in the control group. Placenta previa developed in 9.8% of the patient group with endometriosis, and the risk was higher than control group (p<0.05). Although the

TABLE 2: Pregnancy chara the case an				s exam	ined in
		ol group =49)		e group 1=41)	
Obstetric features	n	%	n	%	p value
Intrauterine insemination pregnancy	1	2	3	7.3	0.326
In vitro fertilization pregnancy	2	4.1	9	22	0.024
Spontaneous pregnancy	46	93.9	29	70.7	0.008
Single fetus	49	100	39	95.1	0.205
Twin fetuses	0	0	2	4.9	

rate of placenta previa was significantly higher in cases with endometriosis, no significant difference was found in terms of placenta attachment anomalies (p>0.05). Placental adhesion anomaly was detected in 1 patient in the control group and in 5 patients in the case group. Placenta accreta was observed in 1 patient in the control group, and 4 of the patients in the case group. Placenta percreta was observed in 1 case in the endometriosis group, and bladder injury was reported during cesarean delivery. 22.0% of the patients with endometriosis and 6.1% of the patients were diagnosed with gestational diabetes in the control group (p<0.05).

While the mean week of gestation at birth was 38.3 ± 2.1 in the control group, this value was 37.2 ± 2.2 in the endometriosis group. The median val-

	Control	group (n=49)	Case gr		
Complications	n	%	n	%	p value
Imminent abortion	49	100.00	32	78.00	0.000
	0	0.00	9	22.00	
Preeclampsia	48	98.00	35	85.40	0.032
	1	2.00	6	14.60	
Gestational hypertension	48	98.00	39	95.10	0.590
	1	2.00	2	4.90	
Placental abruption	48	98.00	41	100.00	1.000
	1	2.00	0	0.00	
Placenta previa	49	100.00	37	90.20	0.040
	0	0.00	4	9.80	
Placental adhesion anomalies	48	98.00	36	87.80	0.054
	1	2.00	5	12.20	
Early rupture of membranes	47	95.90	37	90.20	0.282
	2	4.10	4	9.80	
ntrauterine growth restriction	48	98.00	38	92.70	0.327
	1	2.00	3	7.30	
Threatened preterm labor	45	91.80	35	85.40	0.331
	4	8.20	6	14.60	
Oligohidramniosis	44	89.80	36	87.80	0.765
	5	10.20	5	12.20	

ues were 39.0 and 38.0, respectively (p=0.009) (Table 4).

While the mean birth weight of the babies of the patients was 3266.1 ± 618.4 grams in the control group, it was 3074.8 ± 552.8 grams in the case group (p>0.05).

Cesarean section rate was 55.1% in the control group, and 61.0% in endometriosis group (p>0.05). Due to the development of acute abdomen after endometriotic cyst rupture in 2 of the patients diagnosed with endometriosis, emergency cesarean delivery was decided (Table 4).

Complications developed during delivery in 8 (19.5%) patients in the case group, and all these patients delivered by cesarean section. Uterine atony was observed in 6 patients and bladder injury was observed in 2 patients. The risk of complications was significantly higher in patients with endometriosis than in the control group (p=0.001). There was no need for blood transfusion in the postpartum period in

49 patients in the control group. However, 10 patients in the endometriosis group received blood transfusion (p<0.05) (Table 5).

Neonatal intensive care unit (NICU) requirement was 39.0% and 24.4% in the case group and control group, respectively. Mostly, the reasons for NICU requirement were prematurity, neonatal transient tachypnea, and congenital malformations. Congenital malformation was observed in 6 (14.6%) newborns in the case group. Of these, 2 had cleft palate-lip, 2 had cardiac anomaly, 1 had omphalocele, and 1 had bilateral hydronephrosis. Congenital malformations were reported in 5 (10.2%)newborns in the control group. Of these, 1 had cleft palate-lip, 2 had cardiac anomaly, 1 had hydrops fetalis, and 1 had fetal vein of galena aneurysm. When the overall malformation rates in the case and control groups, as well as the malformation subgroups were compared, no significant statistical difference was found.

			Control group			Case group		
Birth characteristics		n	⊼ ±SD	%	n	X ±SD	%	p valu
Gestational age at birth			38.3±2.1			37.2±2.2		0.009
Birth weight (g)			3266.1±618.4			3074.8±552.8		NS
Mode of delivery	Vaginal delivery	22		44.9	16		39.0	NS
	Caesarean section	27		55.1	25		61.0	
Caesarean section indicatios								
Severe preeclampsia		0		0.0	4		16.0	NS
Placental abruption		1		3.7	0		0.0	NS
Cephalopelvic disproportion		14		51.9	5		20.0	NS
Fetal distress		3		11.1	0		0.0	NS
Genital warts		2		7.4	0		0.0	NS
Twin pregnancy		0		0.0	2		8.0	NS
Failure to progress of delivery		1		3.7	4		16.0	NS
Ovarian cyst rupture		0		0.0	2		8.0	NS
Breech presentation		5		18.5	4		16.0	NS
Macrosomic fetus		1		3.7	1		4.0	NS
Plasenta previa		0		0.0	3		12.0	NS

NS: Not significant; SD: Standard deviation.

	Control group		Case group		
	n	%	n	%	p value
Birth complications (atonia, bladder injury)	49	100.00	33	80.50	0.001
	0 (none)	0.00	8	19.50	
Blood transfusion requirement	49	100.00	31	75.60	0.000
	0 (none)	0.00	10	24.40	
Neonatal intensive care unit requirement	39	79.60	25	61.00	0.052
	10	20.40	16	39.00	
Neonatal exitus	47	95.90	41	100.00	0.498
	2	4.10	0 (none)	0.00	
Congenital malformations	44	89.80	35	85.40	0.523
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DISCUSSION

Endometriosis is a chronic inflammatory disease that is usually associated with infertility and pelvic pain. Although the exact etiopathogenesis is not known, hormonal, immunological and inflammatory changes have been shown to be effective in the development and progression of the disease. It is also known that adhesions, fibrotic changes and anatomical distortions occur due to pelvic endometriosis. It is thought that all these biochemical and anatomical changes adversely affect fertility, obstetric and neonatal outcomes in women with endometriosis.¹ In our study, the obstetric and neonatal outcomes of patients with or without endometriosis who applied to the hospital between 2015 and 2020 were compared. In the cases examined in the endometriosis group, the pregnancy rate obtained by IVF was found to be high (22.0% in the endometriosis group, while 4.1% in the control group).

Miura et al. showed that, assisted reproductive technology (ART) pregnancies were found to be higher in cases with endometriosis (n=80) compared to the control group (n=2,689), like our study (p<0.01).¹³ It is known that this difference between the two groups is due to the relationship between en-

dometriosis and infertility. The prevalence of endometriosis in infertile women was found to be 25-50%.¹⁴

In our study, the abortion rate in the endometriosis group was 22.2%, and it was found to be higher than the control group (p<0.05). Similar results to our study were reported in a case-control study in which a total of 425 cases were examined. In this study by Porpora et al., the data of 145 patients with endometriosis in the case group and 280 patients in the control group were evaluated. Abortion rate was reported as 5% in the endometriosis group and 1% in the control group (p=0.036). Disruption of endometrial receptivity, remodeling of myometrial spiral vessels, abnormal decidualization, and impaired uterine contractility has been implicated as mechanisms for abortion.^{2,15}

In a meta-analysis of 39 studies conducted by Huang et al. in 2020, the effects of endometriosis and adenomyosis on the risk of miscarriage were evaluated, and it was shown that the risk of abortion increased in cases with endometriosis who conceived spontaneously. Similarly, it has been shown that the risk of miscarriage is high in cases with a diagnosis of endometriosis undergoing ART. In the spontaneously conceived group, the data could not be evaluated because the relevant data were missing. In subgroup analyzes of the same study, women with deep pelvic endometriosis and superficial peritoneal endometriosis have been shown to have a higher risk of miscarriage.¹⁶

In our study, the rate of preeclampsia was found to be higher in the endometriosis group. The rate of preeclampsia was 2% in the control group and 14.6% in the endometriosis group (p<0.05). Gestational hypertension rate was 4.9% in the endometriosis group and 2.0% in the control group (p>0.05). Wook Yi et al. mentioned that, the pregnancy processes of cases with and without endometriosis were compared, and like the results of our study, the rate of preeclampsia was found to be higher in the endometriosis group (p<0.0001). In the subgroup analysis of the same study, when only singleton pregnancies were evaluated, the rate of preeclampsia was found to be similar between the two groups. The high risk of preeclampsia detected in the general evaluation with these findings was attributed to the higher rate of multiple pregnancy in endometriosis group than the other group, rather than the presence of endometriosis (multiple pregnancy rate was 2.02% in the control group, and 6.23% in the case group).¹

Farland et al., in a cohort study, showed that the risk of preeclampsia and, in general, hypertensive disease in pregnancy was significantly higher. Although the etiology is not clear, it is thought that abnormal placentation, defective angiogenesis and local inflammation due to endometriosis may cause the development of hypertensive diseases during pregnancy in patients with endometriosis.¹⁷

Placenta previa was seen in 4 (9.8%) patients in the endometriosis group, and placenta previa was not observed in the control group cases (p=0.04). Placental adhesion anomalies were observed in 5 (12.2%) patients in the endometriosis group and in 1 patient (2.0%) in the control group (p=0.054). Ablatio placenta was observed in one case at 28 weeks of gestation (p=1.000) in the control group.

In a study by Chen et al., obstetric complications were evaluated in patients with surgically diagnosed endometriosis. In this study, the risk of placenta previa was shown to be twice as high in the endometriosis group, the rate of spontaneous abortion in the obstetric history of the endometriosis group was 30.13%, while it was 24.82% in control group (p=0.0076). The reason for the high rate of placenta previa in endometriosis group was thought to be spontaneous abortion and related endometrial traumas. However, the high rate of placenta previa in endometriosis group after correction for spontaneous or therapeutic abortion between the two groups showed that there are additional factors in the pathogenesis.¹⁸

In our study, the rate of premature rupture of membranes was found to be 9.8% in the endometriosis group and 4.1% in the control group (p=0.282). There was not any difference between the two groups for the threat of preterm birth (14.6% in the endometriosis group, 8.2% in control group; p=0.331). There wasn't any significant difference between the two groups in terms of oligohydramnios (p=0.765). Fetal growth restriction was observed in 3 patients in

the endometriosis group and in 1 patient in the control group (the rates were 7.30% and 2.00%, respectively; p=0.327).

In a meta-analysis study conducted by Zullo et al., including 24 studies, preterm birth and small for gestational age were found to be higher in endometriosis patients. In subgroup analysis of pregnancies obtained by ART with only endometriosis, the increase in preterm birth was found to be high, but the subgroup analysis of women with endometriosis who became pregnant spontaneously could not be performed with the available data.⁸ In our study, while the mean week of gestation at birth was 38.3±3.1 in the control group, this value was 37.2 ± 2.2 in the endometriosis group (p=0.009). A separate subgroup analysis could not be performed for deliveries <37 weeks due to the small number of cases examined. While the mean birth weight was 3266.1±618.4 grams in the control group, this value was 3074.8 ± 552.8 grams in the case group (p>0.05).

In a study by Porpora et al., similar to the results of our study, it was shown that risk of premature rupture of membranes, growth restriction of fetus and oligohydramnios development is not high in cases with endometriosis (p>0.05). Unlike our results, the risk of preterm labor and preterm delivery was found to be high in endometriosis cases examined in this study. While the rate of threat of preterm birth was found 9.6% for endometriosis group, it was reported to be 4.0% in the control group (p=0.014). The rate of preterm birth was 20.0% in the endometriosis group and 8.0% in the control group (p<0.001)² The increase in the expression of inflammatory cytokines, prostaglandins and metalloproteinase activation causes cervical maturation, disruption of collagen, uterine contractions, and inflammation of the membranes. In patients with endometriosis, these may explain the cause of preterm labor and premature rupture of membranes.19

Whether there is a relationship between endometriosis and gestational diabetes mellitus (GDM) is controversial. While the rate of GDM was 22.0% in the endometriosis group of our study, it was found to be 6.1% in the control group (p=0.028). In a review published in 2019 by Kobayashi et al., it was reported that the risk of GDM is high.²⁰ In a study conducted by Conti et al., in which the results of 216 primiparous cases with endometriosis were examined, increased GDM rates were found in the endometriosis group. The increased incidence of GDM is explained by chronic subclinical inflammation due to endometriosis.²¹

In our study, no significant difference was found between two groups in terms of cesarean and normal vaginal delivery rates, and cesarean section indications (p>0.05). The high rate of cesarean delivery in the control group is due to the fact that our clinic is a reference hospital. However, only nulliparous patients with endometriosis were included in our study. Therefore, placenta previa and placental adhesion anomalies were observed less frequently.

In many studies, it has been shown that the rate of cesarean delivery is higher in patients with endometriosis.^{1,2,9,22} Leone Roberti Maggiore et al. showed in a study that endometriosis was associated with high cesarean section rates and the indications for cesarean section in the endometriosis group were fetal distress, breech presentation and disproportion, respectively.¹⁵ Other researchers explained the high rate of cesarean section in patients with endometriosis by the high rate of placental complications (placenta previa, placental abruption, placental attachment anomalies) and premature birth rates.² In addition, it is thought that patients with endometriosis prefer cesarean section to psychologically avoid pelvic pain in vaginal delivery.7

In our study, complications occurred at birth in 8 (19.5%) patients in the endometriosis group, and all patients delivered by cesarean section. Uterine atony was observed in 6 patients and bladder injury was observed in 2 patients. Complication risk was higher in patients with endometriosis (p=0.001). Postpartum blood transfusion was given to 10 patients in the endometriosis group, and no transfusion was required in the control group (p<0.05). Spontaneous hemoperitoneum developed due to cyst rupture in 2 patients in the endometriosis group.

In a case control study, Miura et al. showed that the risk of postpartum hemorrhage is high in cases with endometriosis, similar to the results of our study (p=0.04). When multivariate analysis is performed according to factors that increase the risk of postpartum hemorrhage, such as pre-pregnancy maternal weight (BMI \geq 25 kg/m²), maternal age (\geq 35 years), ART, gravida number, placenta previa, and macrosomia (>4,000 g), endometriosis is determined for postpartum hemorrhage. It was found that there was no independent risk factor (p=0.64).¹³ In our study, placental pathology was observed in 40% of the cases requiring blood transfusion.

In the review of Lier et al. in 2017, 44 articles were examined and a total of 59 spontaneous hemoperitoneum cases were reported. It was reported that surgery was performed in 39 cases due to maternal reasons (hemorrhagic shock, acute abdomen), fetal distress in 2 cases, and both of the above-mentioned maternal-fetal complications. No major complications developed in two cases, one patient died, and in this case, the diagnosis of hemoperitoneum due to endometriosis was confirmed at autopsy. The bleeding focus is from endometriotic implants (11/51 cases; 21.6%), decidualized hemorrhagic nodules (1/51 cases; 2.0%), ruptured utero-ovarian vessels (29/51 cases; 56.8%), or a combination (10/51 cases; 19.6%). Hysterectomy had to be performed in 4/59 cases (6.8%). There was no correlation between the severity of bleeding and the stage of endometriosis (p=0.43).²³ In our study, hemoperitoneum developed in 1 patient at 39th gestational week and in 1 patient at 33rd gestational week due to ovarian endometrioma rupture. Due to the development of acute abdomen in both cases, emergency cesarean delivery and cystectomy were performed.

When neonatal outcomes (neonatal exitus, congenital malformation, NICU requirement) were compared in our study, no significant difference was found between two groups (p>0.05). Porpora et al. reported that in their case-control study, similar to our results, no correlation was found between neonatal outcomes and endometriosis.² Lalani et al. reported in a systematic review and meta-analysis that in patients with endometriosis, NICU requirement, stillbirth, and neonatal exitus rates were found to be significantly higher. The reason for this has been shown to be the high rate of preterm birth due to obstetric complications such as placental anomalies and preeclampsia in patients with endometriosis.²²

CONCLUSION

Pregnancy carries a higher risk of obstetric complications in cases with endometriosis. Surgical complication rates such as the threat of miscarriage in early pregnancy weeks, preeclampsia, placenta previa, risk of GDM development in the second and third trimesters, postpartum uterine atony, need for blood transfusion and bladder injury in cesarean delivery are higher in women with endometriosis.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Aytaj Mahmudova, Elifnur Biçer; Design: Burçin Karakuş, Kutsiye Pelin Öçal; Control/Supervision: Aytaj Mahmudova; Data Collection and/or Processing: Elifnur Biçer; Analysis and/or Interpretation: Burçin Karakuş; Literature Review: Aytaj Mahmudova; Writing the Article: Aytaj Mahmudova; Critical Review: Kutsiye Pelin Öçal; References and Fundings: Kutsiye Pelin Öçal; Materials: Elifnur Biçer.

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