ORIGINAL ARTICLE

CONTENTS

Obstetric and gynecological surgical procedures, and surgical site infections as risk for the development of endometriosis: a multicenter study

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ABSTRACT

Aim: Aim this study was to evaluate the incidence of endometriosis in women with a recent history of surgical site infections (SSIs), and obstetric and gynecological surgical procedures.

Materials and Methods: A retrospective multicenter cohort was conducted on patients who have had obstetric or gynecological surgical procedures performed from January 2022 to December 2024 in 16 hospitals from six Ukrainian regions. Definitions of SSIs were adapted from the Centers for Disease Control and Prevention's National Healthcare Safety Network. The criteria for endometriosis were adapted from the ESHRE endometriosis guideline.

Results: The study included 33,126 reproductive women with endometriosis who had 16,724 obstetric and 32,383 gynecologic surgical procedures. The incidence of endometriosis in women with history of obstetric and gynecologic surgical procedures, and SSIs was 25.5% [95% confidence interval (CI), 24.3-26.4], 33.3% (95% CI, 33.0-33.6), and 22,1% (20.8-24.2), respectively. Multivariate analysis identified SSIs, obstetric and gynecological surgical procedures as three factors positively associated with the risk of endometriosis. Factors that increased the odds of endometriosis was SSIs (adjusted odds ratio [AOR], 3.76; 95% CI, 2.29–6.20), and obstetric and gynecological surgical procedures (AOR, 7.91; 95% CI, 3.68–37.3). An SSIs and obstetric and gynecological surgery history increased the odds of an endometriosis >7-fold in the cohort (AOR, 7.96; 95% CI, 3.64–37.2).

Conclusions: Obstetric and gynecological surgical injury, and the inflammation resulting from SSIs may play a role in developing endometriosis.

KEY WORDS: endometriosis, obstetric and gynecological surgery, surgical site infections, risk factor, Ukraine

Wiad Lek. 2025;78(7):1291-1297. doi: 10.36740/WLek/208988 DOI

INTRODUCTION

Endometriosis is an estrogen-dependent and multifactorial, chronic inflammatory disease in women. Women with endometriosis are at elevated risk for serious adverse outcomes [1-4].

According to the literature, women with endometriosis had higher odds of gestational hypertension and/or pre-eclampsia, gestational diabetes, gestational cholestasis, placenta praevia, antepartum hemorrhage, antepartum hospital admissions, and malpresentation [5,6]. In addition, in women with endometriosis were also more likely to have preterm birth and neonatal death [7]. Among women who conceived with the use of assisted reproductive technology, endometriosis associated with preterm birth [8, 9].

Endometriosis disease is the cause of depression. This pathology leads to a loss of productivity at work. According to the literature, medical cost range of endometriosis from US$1459 to US$20,239 [10].

Currently, the pathophysiology and risk factors of the disease are not fully understood. Previous studies have shown that inflammation related to genital tract infection and surgical injury may cause endometriosis [11, 12]. According to the literature, in patients with a previous cesarean section presented a twofold increased risk of endometriosis. Also, it has been reported that dissemination of endometrial cells may occur during cesarean section after entry into the uterine cavity [13].

According to the literature, Inflammation in the pelvic cavity is one of the leading factors an important pathologic process of endometriosis. Both pathogens and physical injury of tissue may cause inflammation [11]. Several researchers have focused on revealing the relationship between inflammation and endometriosis. Researchers reported that intrauterine microbial colonization and bacterial endotoxin were associated with endometriosis [14]. Similar studies have not been conducted in Ukraine. A previous study has focused on the prevalence of endometriosis and adverse pregnancy outcomes associated with endometriosis [3, 4, 9].

AIM

The aim of this study was to evaluate the incidence of endometriosis in women with a recent history of SSIs and obstetric and gynecological surgical procedures.

MATERIALS AND METHODS

STUDY DESIGN, SETTING AND PATIENTS

A retrospective multicenter cohort study based on surveillance data for endometriosis was conducted on patients who have had obstetric or gynecological surgical procedures performed from January 2022 to December 2024 in 16 hospitals from six Ukrainian regions (Kharkiv, Odessa, Kyiv, Vinnytsya, Lviv, Lutsk). This study included patients after a clinical suspect of endometriosis confirmed by ultrasound or magnetic resonance imaging, and in case of laparoscopic diagnosis with histopathological confirmation of stage III or IV according to the r-ASRM (revised American Society for Reproductive Medicine) classification for endometriosis with ovarian localization. Patients were excluded: (a) in case of a history of surgeries for endometriosis, and (b) laparotomy, for staging or restaging of ovarian, tubal, or primary peritoneal malignancy (second look), with or without omentectomy, peritoneal washing, biopsy of abdominal and pelvic peritoneum, diaphragmatic assessment with pelvic and limited para-aortic lymphadenectomy. Ultrasound evidence of DIE was confirmed by magnetic resonance imaging.

DEFINITION

An SSI was defined as an infection arising >48 h after surgical procedures. The criteria for specific SSI site after obstetric or gynecological surgical procedures were adapted from the CDC/NHSN (Centers for Disease Control and Prevention's and National Healthcare Safety Network's) case definitions [15]. The postsurgical residual was defined as visible evidence of unresectable endometriotic lesions. Ovarian endometriosis was identified as an ovarian cyst with a regular wall containing thick-brown fluid. Peritoneal endometriosis was identified as superficial black, dark-brown, or bluish-puckered lesions, nodules, or small cysts containing old hemorrhage surrounded by fibrosis. Deeply infiltrative endometriosis (DIE) was identified as nodules infiltrating the pouch of Douglas, vagina, posterior vaginal fornices, lateral vaginal fornices, retrocervical area, uterosacral ligaments, rectovaginal septum, bladder, rectosigmoid junction, or rectum [16].

DATA COLLECTION

In this study, we analyzed the inpatient data medical records patients with endometriosis to identify and describe the type of surgical procedures and postoperative SSIs. Medical records and epidemiological data were used to find risk factors for endometriosis in patients with SSIs after obstetric and gynecological surgical procedures. The surgical procedures involved the abdominal hysterectomy (includes that by laparoscope), Cesarean section, Laparotomy, Vaginal hysterectomy, and Ovarian surgery. In this study, all participants were queried regarding history of SSIs after obstetric or gynecological surgical procedures, sociodemographic characteristics, reproductive and medical history.

ETHICS

The Zarifa Aliyeva International Center of Medical Science (Kyiv, Ukraine) approved this study. Patients agreed to participate in this study.

STATISTICAL ANALYSIS

All statistical analyses were performed using Microsoft® Excel (Microsoft Corporation, Redmond, WA, USA). The data are presented as numbers and percentages. Pearson's

Table 1. Incidence of surgical site infections (SSIs) after obstetrical and gynecological surgery procedures in Ukraine (2022-2024)

Type of procedure	Number of procedures, n	SSIs				Incidence of SSIs (95% CI)
		Yes		No		
		n	%	n	%	
Abdominal hysterotomy (e.g., for hydatidiform mole, abortion)	1,748	367	21.1	1381	79.0	20.0 – 22.0
Operative vaginal delivery	985	218	22.1	767	77.9	20,9 – 23.4
Cesarean delivery	2,431	618	25.4	1,823	74.6	24.5 – 26.4
Postpartum hemorrhage	2,017	362	17.9	1,655	82.1	17.1 – 18.8
Genital tract lacerations after vaginal delivery	987	211	21.4	776	78.6	20.1 – 22.7
Manual removal of the placenta (vaginal or cesarean delivery)	1,887	488	25.9	1,399	74.1	24.9 – 26.9
Multiple vaginal examinations after vaginal delivery	2,711	1,024	37.8	1,687	62.2	36.9 – 38.7
Induced abortion with cervical dilation and hysterotomy	1,812	659	36.4	1,153	63.6	35.3 – 37.5
Surgical curettage after vaginal delivery	2,146	817	38.1	1,329	61.9	37.1 – 39.2
Abdominal hysterectomy (corpus and cervix), with or without removal of tube(s) or ovary(s)	1,229	348	28.3	881	71.7	27.0 – 29.6
Supracervical abdominal hysterectomy, with or without removal of tube(s) or ovary(s)	816	117	14.3	699	85.7	13.1 – 15.5
Laparoscopy, surgical, supracervical hysterectomy, with removal of tube(s) and/or ovary(s)	1,533	336	21.9	1,197	78.1	20.8 – 23.0
Laparoscopy, surgical, supracervical hysterectomy, with removal of tube(s) and/or ovary(s)	2,118	301	14.2	1817	85.8	13.4 – 15.0
Laparoscopy, surgical, with vaginal hysterectomy, with removal of tubes(s) and /or ovary(s)	1,926	411	21.3	1,515	78.7	20.4 – 22.2
Laparoscopy, surgical, with lysis of adhesions (salpingolysis, ovariolysis) (separate procedure)	1,422	231	16.2	1,191	83.8	15.2 – 17.2
Laparoscopy, surgical; with removal of adnexal structures (oophorectomy or salpingectomy)	1,184	112	9.5	1,072	90.5	8.7 – 10.4
Laparoscopy, surgical, with excision of lesions of the ovary, pelvic viscera, or peritoneal surface	10,228	1,856	18.1	8,372	81.9	17.7 – 18.5
Salpingo-oophorectomy, complete or partial, unilateral or bilateral (separate procedure)	512	85	16.6	427	83.4	15.0 – 18.2
Lysis of adhesions (salpingolysis, ovariolysis)	1,046	123	11.8	923	88.2	10.8 – 12.8
Drainage of ovarian cyst(s), unilateral or bilateral (vaginal approach)	1,207	211	17.5	996	82.5	16.4 – 18.6
Drainage of ovarian cyst(s), unilateral or bilateral (abdominal approach)	1,127	109	9.7	1,018	90.3	8.8 – 10.6
Drainage of ovarian abscess (vaginal approach, open)	1,401	211	15.1	1,190	84.9	14.1 – 16.1
Drainage of ovarian abscess (abdominal approach)	1,126	211	18.7	915	81.3	17.5 – 19.9
Biopsy of ovary, unilateral or bilateral (separate procedure)	1,452	547	37.7	905	62.3	36.4 – 39.0
Ovarian cystectomy, unilateral or bilateral	1,283	427	33.3	856	66.7	32.0 – 34.6
Closure of vesicouterine fistula; with hysterectomy	1,024	257	25.1	767	74.9	23.8 – 26.5
Vaginal hysterectomy, with removal of tube(s), and/or ovary(s)	986	233	23.6	753	76.4	22.3 – 25.0
Vaginal hysterectomy, with or without endoscopic control	763	152	19.9	611	80.1	27.1 – 28.2
Total	**49,107**	**11,042**	**22,5**	**38,065**	**77,5**	**22.3 – 22.7**

SSIs, surgical site infections; CI, confidence interval

chi-square ($\chi 2$) test was performed to check the matching performance between the case and comparison groups and compare the differences between groups for categorical variables. The Cox model calculated the hazard ratio (HR) and 95% confidence interval (CI) of endometriosis in patients undergoing SSIs or obstetric and gynecological surgical procedures compared to the comparison group. Logistic regression estimated the adjusted odds ratios (AORs) and 95% confidence intervals for each cohort. The P value under 0.05 was considered significant.

RESULTS

The study included 33,126 reproductive women with endometriosis who had 16,724 obstetric and 32,383 gynecologic surgical procedures. Of all endometriosis cases, 18.7% (6,195/33,126) were peritoneal/superficial endometriosis, 67.4% (22,327/33,126) were ovarian endometriotic cyst/endometrioma and 13.9% (4,603/33,126) were deep infiltrating endometriosis.

The incidence of endometriosis in women with history of obstetric and gynecologic surgical procedures, and SSIs was 25.5% [95% confidence interval (CI), 24.3-26.4], 33.3% (95% CI, 33.0-33.6), and 22,1% (20.8-24.2), respectively. Most cases (28.6%, 95% CI, 27.2-29.3) of all endometriosis was diagnosed in women with history of operations on ovary and related structures. Endometriosis in women with history of vaginal hysterectomy, abdominal hysterectomy and obstetrical delivery by cesarean section was 9.3%, 5.3%, and 3.7%, respectively.

A total 33,126 women with endometriosis had 11,042 histories of SSIs. The highest number (>30%) of SSIs was

found after surgical curettage (38.1%, 95% CI, 37.1-39.2), multiple vaginal examinations after vaginal delivery (37.8%, 95% CI, 36.9- 38.7), biopsy of ovary (37.7%, 95% CI, 36.4-39.0), induced abortion with cervical dilation and hysterotomy (36.4%, 95% CI, 35.3-37.5), and ovarian cystectomy (33.3% 95% CI,32.0-34.6). The analysis of post-operative infections (SSIs) is presented in Table 1.

Analysis of the structure of SSIs showed that post-operative infections have different localizations of the pathological process. The most common types of SSI were endometritis after induced abortion (15,4%, 95% CI, 4.5-16.3), endometritis after multiple vaginal examinations (12,5%, 95% CI, 11,6-13.4), endometritis after cesarean delivery (12%, 95% CI, 11.1-12.9), oophoritis (9,3% 95% CI, 8.4-10.2), and tubo-ovarian abscess (8,7%, 95% CI, 7.8-9.6), followed by salpingitis (7.5%, 95% CI, 6.6-8.4), episiotomy infections (7.2%, 95% CI, 6.3-8.1), and vaginal cuff infections (6.6%, 95% CI, 5.7-7.5). Other types of infections accounted for less than 5% (Table 2).

We analysed the history of any surgical procedures grouped by laparotomy, laparoscopy, gynecologically and obstetric related procedures. Multivariate analysis identified SSIs, obstetric and gynecological surgical procedures as three factors positively associated with the risk of endometriosis. Factors that increased the odds of endometriosis was SSIs (adjusted odds ratio [AOR], 3.76; 95% CI, 2.29–6.20), and obstetric and gynecological surgical procedures (AOR, 7.91; 95% CI, 3.68–37.3). An SSIs and obstetric and gynecological surgery history increased the odds of an endometriosis >7-fold in the cohort (AOR, 7.96; 95% CI, 3.64–37.2) (Table 3).

DISCUSSION

This study is the first to report an increased risk of endometriosis in women with a recent history of obstetric and gynecological surgical procedures and post-operative healthcare-associated infections data. We investigated the incidence of endometriosis in women with a recent history of SSIs, obstetric and gynecological surgical procedures, or both. Inflammation is one of the leading factors and an important pathologic process of endometriosis. Inflammation related to post-operative infection and surgical injury may cause endometriosis. Therefore, we investigated the incidence of endometriosis in women with a recent history of SSIs, pelvic surgery, or both. This study was undertaken to test the hypothesis that obstetric and gynecological surgical procedures and SSIs increases the risk of endometriosis. We recruited patients with endometriosis and retrieved information on the history of any surgical procedures, grouped by obstetrical delivery by cesarean section (CSES), abdominal hysterectomy (includes that by laparoscope), operations on ovary and related structures, and vaginal hysterectomy (excludes the use of laparoscope) and cases of SSIs after these procedures. We then evaluated the association, if any, between endometriosis and history of surgical procedures and SSIs. This study showed that a history of obstetric and gynecological surgical procedures and SSIs increases the future incidence of endometriosis.

Endometriosis is an estrogen-dependent and multifactorial, chronic inflammatory disease in women, characterized by the presence of endometrial tissue outside the uterine cavity. Endometriosis most commonly affects peritoneal surfaces, ovaries and uterine ligaments and even may affect the vulva, vagina [17]. Endometriosis usually occurs in the pelvis. According to the literature, endometriosis usually develops in a previous surgical scar [18] However, few publications have focused on obstetric and gynecological surgical procedure as risk factor for endometriosis. According to the literature, cesarean scar endometriosis is the most common type of abdominal wall endometriosis [19]. Gunes M, et al. [20] reported 11 cases of incisional endometriosis after CSES, perineal episiotomy incision or the vaginal cuff after hysterectomy, and other gynecologic procedures. In addition, Díaz-Barreiro G, et al. reported a case of external endometriosis, pelvi-genital (vagina) and extrapelvic (on episiotomy scar) presentation [21]. Maillard C, et al. [22] reported that 95.3% presenting with vulvo-perineal endometriosis have undergone either episiotomy, perineal trauma or vaginal injury or surgery. Only 4.7% developed vulvo-vaginal endometriosis spontaneously. The examination which confirmed the diagnosis of endometriosis. Andolf et al. [23] and Liu et al. [24] reported that patients who underwent a previous CS presented a high risk for endometriosis compared with patients with vaginal deliveries only. Those studies focused on the surgical history before endometriosis diagnosis.

According to the literature, the presence of ectopic endometrial tissue embedded in the subcutaneous adipose layer and the muscles of the abdominal wall association with a previous surgical procedure [25]. Zhang P, et al. suggested that during CD (cesarean delivery), the endometrial tissue is inoculated directly in the cesarean incision [19].

Inflammation is an important factor pathologic process of endometriosis, and several researchers have focused on revealing the relationship between inflammation and endometriosis. According to the literature, both pathogens and surgical injury of tissue may cause inflammation. Khan et al. proposed a new concept. They reported that intrauterine microbial colonization and bacterial endotoxin were associated

Table 2. Distribution of surgical site infections (n=11,042) after obstetric and gynecological surgical procedures by localization of the pathological process in Ukraine (2022-2024)

Type of infection	SSI		95% CI
	n	%	
Endometritis after induced abortion	1695	15,4	14.5 – 16.3
Endometritis after multiple vaginal examinations	1382	12,5	11,6 – 13.4
Endometritis after cesarean delivery	1322	12	11.1 – 12.9
Oophoritis	1022	9,3	8.4 – 10.2
Tubo-ovarian abscess	964	8,7	7.8 – 9.6
Salpingitis	823	7,5	6.6 – 8.4
Episiotomy infections	786	7,2	6.3 – 8.1
Vaginal cuff infections	697	6,6	5.7 – 7.5
Endometritis after manual removal of the placenta	649	5,9	5.0 – 6.8
Pelvic abscess or cellulitis	489	4,4	3.5 – 5.3
Cervicitis	417	4,1	3.1 – 5.1
Adnexa utery	412	3,7	2.8 – 4.6
Parametritis	229	2,1	1.2 – 3.1
Other	155	0,7	0.5 – 0.9

SSIs, surgical site infections; CI, confidence interval.

Table 3. Logistic multivariate regression analyses of the factors associated with endometriosis in the study participants (2022-2024)

Risk factor	P value	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)
Sociodemographic		Ref		Ref
History of SSI	<0.001	3.78 (2.36–6.05)	<0.001	3.76 (2.29–6.20)
History of obstetric and gynecological surgery	<0.001	4.44 (2.42–8.16)	<0.001	4.47 (2.39–8.38)
History of SSI and obstetric and gynecological surgery	<0.001	7.13 (1.72–29.6)	<0.001	7.91 (1.69–37.2)

with endometriosis [26]. Our previous study showed that post-operative infection (Pelvic abscess or cellulitis, Salpingitis, and Oophoritis) after gynecologic surgical procedures had more risk for endometriosis [27]. In the present study pot-operative infections after obstetric and gynecological surgical procedures were associated with endometriosis. Although many studies have shown the relationship between endometriosis and SSIs after obstetric and gynecological surgical procedures, their causal relationship is unclear.

STRENGTHS AND LIMITATION

Our study is the first to report an increased risk of endometriosis in women with a recent history of post-operative healthcare-associated infections after obstetric and gynecological surgical procedures. The strengths of the present study lay in having included a highly selected population of patients who had obstetric and gynecological surgical procedures, and SSIs history to study the association with endometriosis. However, the retrospective nature of the study may have limited this analysis for the reduced possibility of evaluating the effect of unavailable confounding factors, which could increase the risk of having both a surgical procedures and endometriosis. These findings should be supported by other cohort studies.

CONCLUSIONS

The results of this study showed that obstetric and gynecological surgical procedures and post-operative SSI was associated with an increased risk of endometriosis. Endometriosis seems to be common in women who have had a cesarean section, although it does occur after other obstetric and gynecological surgical procedures. Surgical procedure and adverse outcome history as SSIs seem to represent crucial factors in endometriosis pathogenesis through multiple mechanisms. Endometriotic lesions may arise from minimal residual lesions undetected and unremoved from surgery or by de novo implants in the area traumatized during surgery or from spillage and dissemination of endometrial cells during the surgical procedures. Therefore, a different approach to follow up may be necessary for those patients, with closer or more targeted evaluations and wider use of medical therapy

after surgical procedures. Obstetric and gynecological surgical procedures and SSIs could increase the risk of endometriosis through two mechanisms: (a) surgery procedures it may promote the intraabdominal spread of endometrial cells after entering the uterine cavity, and (b) it could act through the previously described inflammatory and immunity-related mechanisms. The inflammation resulting from SSIs after obstetric and gynecological surgical procedures and surgical injury may play a role in developing endometriosis. Prevention of SSIs and careful surgical procedures to minimize tissue injury may reduce the incidence of endometriosis.

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The authors wish to acknowledge all the study subjects who provided us with the information required for conducting this study. The findings and conclusions in this study are those of the authors.

CONFLICT OF INTEREST
The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 11.01.2025
ACCEPTED: 27.06.2025