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Epidemiology of endometriosis in female evacuated from the Eastern Ukrainian military conflict regions: results a multicenter study (2022-2024)

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ABSTRACT

Aim: To estimate the prevalence and risk factors associated with endometriosis in female evacuated from the Eastern Ukrainian military conflict regions. **Materials and Methods:** A prospective multicenter cohort study was based on surveillance data for endometriosis. 982 women undergoing pelvic surgery were compared to 264 patients unexposed to surgery. The study cohort included women, who underwent a diagnostic and/or therapeutic laparoscopy or laparotomy in 2022-2024. Endometriosis among women was diagnosed visually at laparoscopy/laparotomy or by pelvic magnetic resonance imaging. **Results:** The prospective multicenter study included 1,246 women. The overall prevalence of endometriosis was 31.5%. Prevalence of the three types of endometrioses included peritoneal/superficial endometriosis, ovarian endometriotic cyst/endometrioma and deep infiltrating endometriosis was 13.8%, 9.8%, and 4.8%, respectively. Three hundred sixty-one women 36,8% in the surgical group and thirty-one women 13.3% in the community treatment group (unexposed to surgery, population cohort) were diagnosed with incident endometriosis. The pelvic pain, infertility and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts. Data analysis showed that odds were decreased for gravidity, parity, and BMI. Factors that increased the odds of endometriosis diagnosis included dysmenorrhea, older age at first sex, pelvic pain as a surgical indication for laparoscopy, and higher education. **Conclusions:** Our study findings demonstrate the high prevalence of endometriosis among women in Ukraine. The pelvic pain, infertility and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts are of endometriosis among women in Ukraine. The pelvic pain, infertility and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts.

KEY WORDS: women evacuated from the military conflict regions, endometriosis, prevalence, risk factors, Ukraine

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INTRODUCTION

Endometriosis is a common benign gynecological disease in female of reproductive age, but the prevalence of these condition is not exactly known. According to the literature, prevalence of endometriosis affects up to 10% of females worldwide [1] and it most often occurs on or around reproductive organs in the pelvis, including Fallopian tubes, Ligaments around the uterus, Lining of the pelvic cavity, Ovaries, Outside surface of the uterus, Cervix, Vagina or vulva, Space between the uterus and the rectum or bladder.

Endometriosis significantly impacts women's reproductive health. This disease not only leads to reduced female fertility but may also be a risk factor for adverse pregnancy outcomes [2-5]. Moreover, endometriosis associated with depression, fatigue, and a reduction in work productivity, leading to a substantial economic burden [6]. According to the literature, endometriosis imposes a yearly cost of ~\$78 billion in the United States [7]. The health care costs for endometriosis were approximately \$4,000 per affected woman [8]. In Belgium annual total cost per woman with endometriosis was €9579 [7].

Endometriosis predominantly affects women in their reproductive years and characterized by lesions resembling the endometrium found outside the uterus (ectopic endometrium), primarily in the pelvic tissues and organs [9, 10]. In addition, ectopic endometrium can invade almost any part of the body, including the lungs and pleura, but most commonly the pelvic organs and parietal peritoneum [11]. The most common signs of endometriosis in female are painful periods, painful intercourse, chronic pelvic pain, ovarian cysts, and infertility [12]. However, these symptoms aren't exclusive to endometriosis, there may be other conditions. The varied symptomatology can also be attributed to other conditions [13]. The complex diagnostic challenge of endometriosis drives the delay in diagnosis. In addition, there are no effective biomarkers for the detection of endometriosis.

The pathogenesis of endometriosis is multifactorial and include retrograde menstruation, celomic metaplasia, embryologic rests, and lymphovascular spread [14]. Etiology and the association between the severity and location of endometriosis remains unclear [15]. Current surgical and medical approaches (including hormonal treatments) to endometriosis are ineffective for a sizable proportion of women. According to the literature, approximately 50% of women with endometriosis have recurrent symptoms over a period of 5 years, irrespective of the treatment approach [16]. An improved understanding of the pathogenesis of endometriosis is needed for the development of targeted medical approaches. However, no studies have been conducted on endometriosis in women living in the zone of the Ukrainian-Russian military conflict. Knowledge of endometriosis and risk factors in these regions are unknown.

AIM

The aim this study to estimate the prevalence and risk factors associated with endometriosis in female evacuated from the Eastern Ukrainian military conflict regions.

MATERIALS AND METHODS

STUDY DESIGN AND POPULATIONS

A prospective multicenter cohort study was based on surveillance data for endometriosis. The study cohort

comprised 1,246 women, aged 18-49 years, who were evacuated from the Eastern Ukrainian military conflict regions. Participants in this study were admitted to gynecologic departments at hospitals located in the Kyiv (4 hospitals), Vinnytsia (2 hospitals), Lviv (2 hospitals), Kharkiv (2 hospitals) and Odesa (2 hospitals) sites. In this study, 982 women undergoing pelvic surgery (exposed to surgery, operative cohort) were compared to population cohort of 264 women (unexposed to surgery, population cohort). The cohort included currently menstruating women, who underwent a diagnostic and/or therapeutic laparoscopy or laparotomy at 1 of 4 participating hospitals in June 1st, 2022 through December 31st, 2024. In this study, any surgical indication was acceptable and included pelvic pain, pelvic mass, menstrual irregularities, fibroids, tubal ligation, and infertility. Endometriosis among women was diagnosed visually at laparoscopy/laparotomy or by pelvic magnetic resonance imaging (MRI) in the operative and population cohorts, respectively.

Exclusion criteria: previous laparoscopic diagnosis of endometriosis; currently breast-feeding; history of cancer other than nonmelanoma skin cancer; currently hormonal therapy; women with urinary tract infection and gastrointestinal infections; women who refused to sign the informed consent form.

DEFINITION

In the present study, endometriosis is defined as a disease characterized by the presence of endometrium-like epithelium and/or stroma outside the endometrium and myometrium, usually with an associated inflammatory process [16]

DATA COLLECTION

In this study, we analyzed the inpatient data medical records to identify and describe the epidemiology of endometriosis. Medical records and epidemiological data were used to find risk factors for endometriosis. A standard data collection form was created to extract demographic and clinical data. The standardized data collection protocol included interview administered at baseline, an anthropometric assessment including body mass index (BMI). All participants were queried regarding sociodemographic characteristics, medical and reproductive history, pain, and life-style. The protocol was administered for the operative cohort and population cohort (patients unexposed to surgery). In addition, for operative cohort completed a standardized report immediately following surgery to capture gynecologic pathology and endometriosis

Table 1. Characteristics b	y female evacuated from the Eastern Ukrainian militar	y conflict regions and endometriosis dia	gnosis, 2022-2024 (n=1,246)
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	Endometriosis							
	Operative cohort (n = 982)			Population cohort (n = 264)				
	Endometriosis (n = 361)		No endometriosis (n = 621)		Endometriosis (n = 31)		No endometriosis (n = 233)	
	n	%	n	%	n	%	n	%
Age, y								
<20	9	2.6	15	2.4	0	0	9	3.9
20–24	42	11.6	57	9.2	8	25.8	43	18.5
25–29	91	25.2	121	19.5	2	6.5	46	19.7
30–34	84	23.3	129	20.8	6	19.4	36	15.5
≥35	135	37.4	299	48.1	15	48.4	99	42.5
Marital status								
Married	304	84.2	481	77.5	28	90.3	185	79.4
Other	57	15.8	140	22.5	3	9.7	48	20.6
Education								
Less than College grad	114	31.6	201	32.4	17	54.8	104	44.6
College grad or higher	247	68.4	420	67.6	14	45.2	129	55.4
Alcohol consumer								
Never	84	23.3	138	22.2	7	22.6	66	28.3
Past	116	32.1	207	33.3	13	41.9	82	35.2
Present	161	44.6	276	44.4	11	35.5	85	36.5
Age at first consenting sex								
≤17	174	48.2	345	55.6	8	25.8	114	48.9
18–20	95	26.3	147	23.7	14	45.2	78	33.5
≥21	92	25.5	129	20.8	9	29.0	41	17.6
Ever use oral contraceptives								
No	40	11.1	98	15.8	3	9.7	36	15.5
Yes	321	88.9	523	84.2	28	90.3	197	84.5
Gravidity								
Nulligravid (0)	154	42.7	163	26.2	11	35.5	95	40.8
Gravid (≥1)	207	57.3	458	73.8	20	64.4	138	59.2
Parity (no. of live births)								
Nulliparous	71	19.7	76	12.2	4	12.9	36	15.5
Parous	290	80.3	545	87.8	27	87.1	197	84.5
Age at first pregnancy, y								
<20	143	39.6	221	35.6	1	3.2	48	20.6
20–24	134	37.1	202	32.5	12	38.7	94	40.3
25–29	66	18.3	109	17.6	9	29.0	68	29.2
30–34	13	3.6	71	11.4	5	16.1	15	6.4
35–39	5	1.4	14	2.3	1	3.2	4	1.7
≥40	0	0	4	0.6	3	9.7	4	1.7
History STIs								
No	304	84.2	481	77.5	28	90.3	185	79.4
Yes	57	15.8	140	22.5	3	9.7	48	20.6
History of abnormal pap smear								
No	281	77.8	461	74.2	26	83.9	165	70.8
Yes	80	22.2	160	25.8	5	16.1	68	29.2

Ever seek infertility treatment								
No	239	66.2	514	82.8	23	74.2	211	90.6
Yes	122	33.8	107	17.2	8	25.8	22	9.4
Surgical indication								
Pelvic pain	228	63.2	188	30.3				
Pelvic mass	49	13.6	107	17.2				
Menstrual irregularity	38	10.5	97	15.6				
Fibroids	17	4.7	95	15.3				
Tubal ligation	15	4.2	89	14.3				
Infertility	14	3.9	45	7.2				
Menarche, y								
≤11	168	46.5	325	52.3	15	48.4	64	27.5
12–13	121	33.5	189	30.4	11	35.5	131	56.2
≥14	72	19.9	107	17.2	5	16.1	38	6.3
BMI (mean±SD)	27.6 ± 7.7		29.4	± 8.2	27.2	± 5.5	27.8	± 6.4

Table 1. Cont.

SD, standard deviation; STIs, sexually transmitted disease; BMI, Body Mass Index.

diagnosis and staging using the revised criteria from the American Society for Reproductive Medicine (rASRM) [17]. rASRM staging was categorized as: stage I, minimal (scores 1–5); stage II, mild (scores 6–15); stage III, moderate (scores 16-40); or stage IV, severe (scores >40) [17]. All women in the population cohort (patients without prior surgery) underwent a pelvic MRI to assess any gynecologic pathology including endometriosis. Using protocol for pelvic imaging, 1 radiologist supervised and evaluated all MRI. These results were confirmed by a second radiologist with expertise in gynecologic imaging. In present study endometriosis among women diagnoses were derived from visualization by the surgeon in the operative cohort and from MRI in the population cohort (patients unexposed to surgery). Histologically confirmed endometriosis required the presence of endometrial glands and/or stroma.

ETHICS

The study was approved by the Institutional Ethics Committee of the Ukrainian center of maternity and childhood of the National Academy of Medical sciences of Ukraine. All participants provided informed consent before any data collection.

STATISTICAL ANALYSIS

In this study was performed by using SPSS program (Version 18, Chicago, IL, USA). Descriptive statistics

were reported in numbers and percentages. In this study the associations between categorical variables were assessed by x2 statistic or the Student t test. Odds ratio (OR) and 95% confidence interval were also calculated for all factor. Factors associated with endometriosis were investigated using logistic regression analysis model. We used stepwise logistic regression in a backward manner. In ordinal regression analysis, predictors which probably reflect symptoms of endometriosis (such as dyspareunia, dysmenorrhea and pelvic pain) were examined. Logistic regression estimated the adjusted odds ratios (AORs) and 95% confidence intervals for each cohort. We in each category compared the mean predicted probability in that particular category with the observed probability. In this study P values less than 0.05 (< 0.05) were considered to be statistically significant.

RESULTS

PREVALENCE OF ENDOMETRIOSIS

A total the study cohort comprised 1,246 women, who were evacuated from the Eastern Ukrainian military conflict regions. The overall prevalence of endometriosis among these women was 31.5% [95% confidence interval (Cl), 30.2-32.8]. The number of surgically visualized endometriosis among women in the operative cohort was 361/982 and 31/233 in the population cohort based on MRI. MRI-visualized endometriosis in the population cohort consisted of primarily ovarian

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Diskfaster	Operativ (n =	re cohort 982)	Population cohort (n = 264)		
RISK Idetor	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% Cl)	Adjusted OR (95% CI)	
Sociodemographic					
Age, y	0.97 (0.94–0.99		1.02 (0.95–1.09)		
Poverty level	1.54 (0.83–2.81)	1.89 (1.00–3.53)	0.87 (0.18–4.25)	0.87 (0.18–4.54)	
Educated level	1.63 (1.00–2.64)	1.83 (1.12–3.00)	0.58 (0.11–2.98)	0.58 (0.11–3.13)	
Reproductive history					
Gravid vs nulligravid	0.48 (0.34–0.72)	0.49 (0.33–0.76)	1.25 (0.41–3.95)	1.03 (0.28–3.79)	
Parous vs nulliparous	0.47 (0.33–0.69)	0.42 (0.27–0.65)	1.31 (0.43–4.03)	1.06 (0.27–3.97)	
Infertility history	2.51 (1.62–3.86)	2.44 (1.56–3.78)	7.14 (1.73–29.8)	7.92 (1.67–37.4)	
Age at first consenting sex	1.06 (1.01–1.13)	1.06 (1.02–1.14)	1.08 (0.87–1.31)	1.06 (0.88–1.29)	
Surgical indication for laparoscopy	3.91 (2.64–5.77)	3.66 (2.45–5.51)			
Menstruation					
Early age at menarche, y	2.79 (1.47–5.31)	2.47 (1.29–4.74)	3.97 (2.64–5.73)	3.68 (2.45–5.57)	
Dysmenorrhea (yes/no)	1.07 (0.95–1.19)	1.05 (0.93–1.18)	1.38 (0.28–6.59)	1.42 (0.28–7.16)	
Pelvic pain	3.91 (2.64–5.77)	3.66 (2.45–5.51)	5.48 (2.66–9.88)	5.41 (2.61–7.72)	
Body mass index, kg/m ²	0.95 (0.94–0.98)	0.95 (0.94–0.98)	1.01 (0.93–1.09)	1.01 (0.93–1.09)	

Table 2. Risk factors for endometriosis b	y female evacuated from the Eastern Ukrainian military	y conflict regions, 2022-2024 (n $=$	1,246
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endometriomas, and included nodular implants (stage 3–4 by rASRM). The prevalence of endometriosis by rASRM stage ranged from 4.6% for stage 4 to 23.8% for stage 1. Of all endometriosis cases, 36.8% were peritoneal/superficial endometriosis, 48.4% were ovarian endometriotic cyst/endometrioma and 14.8% were deep infiltrating endometriosis. Prevalence of the three types of endometrioses included peritoneal/ superficial endometriosis, ovarian endometriotic cyst/ endometrioma and deep infiltrating endometriosis was 13.8%, 9.8%, and 4.8%, respectively. Three hundred sixty-one women 36,8% [95% (Cl), 35,4-38,0) in the surgical group and thirty-one women 13.3% [95% (Cl), 12.3-14.3) in the community treatment group (unexposed to surgery, population cohort) were diagnosed with incident endometriosis. Detailed of socio-demographic, gynecological and clinical characteristics of study participants who were evacuated from the Eastern Ukrainian military conflict regions are presented in Table 1.

RISK FACTORS FOR ENDOMETRIOSIS

In this study, logistic regression identified only three consistent risk factors across both cohorts—history of infertility, early age at menarche and pelvic pain. A history of infertility increased the odds of endometriosis diagnosis in the surgical cohort (adjusted odds ratio [AOR], 2.44; 95% CI, 1.56–3.78) and in the popula-

tion-based cohort (AOR, 7.14; 95% Cl, 1.73-29.8), even after adjusting for age. A pelvic pain history increased the odds of an endometriosis diagnosis in the operative cohort (adjusted odds ratio [AOR], 3.66; 95% CI, 2.45-5.51), and in the population cohort (AOR, 5.51; 95% CI, 2.61-7.72). Also, in our study, early menarche history increased the odds of an endometriosis diagnosis in the operative cohort (adjusted odds ratio [AOR], 2.47; 95% CI, 1.47-5.31), and in the population cohort (AOR, 3.97; 95% CI, 2.64–5.73), even after adjusting for age and study site. Data analysis showed that odds were decreased for gravidity, parity, and BMI. Factors that increased the odds of endometriosis diagnosis included dysmenorrhea, older age at first sex, pelvic pain as a surgical indication for laparoscopy, and higher education. In this study, we found no association with endometriosis for any aspect of menstrual history (Table 2).

DISCUSSION

This study was performed to estimate the prevalence and risk factors associated with endometriosis in female evacuated from the Eastern Ukrainian military conflict regions, who admitted to gynecologic departments at regional hospitals located in the Kyiv, Vinnitsa, L'viv and Odesa sites. In this study, women undergoing pelvic surgery were compared to population cohort (unexposed to surgery). The incidence of surgically visualized endometriosis in the operative cohort was 36.8% and 13.3% in the population cohort. The prevalence of endometriosis by rASRM stage ranged from 4.6% for stage 4 to 23.8% for stage 1. Of all endometriosis cases, 36.8% were peritoneal/superficial endometriosis, 48.4% were ovarian endometriotic cyst/endometrioma and 14.8% were deep infiltrating endometriosis. Prevalence of the three types of endometrioses included peritoneal/ superficial endometriosis, ovarian endometriotic cyst/ endometrioma and deep infiltrating endometriosis was 13.8%, 9.8%, and 4.8%, respectively. In this study we found infertility, pelvic pain, and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts. Other risk factors either decreased or increased the odds of an endometriosis diagnosis.

Endometriosis is a common, chronic, gynecological condition that affects approximately 5-10 % of women of reproductive age worldwide [18]. According to the literature, endometriosis is estimated to affect approximately from 176 million [8] to 190 million of reproductive-age women worldwide [19]. The true prevalence of these disease in women is unknown. Literature data on the prevalence of endometriosis vary widely among population samples and diagnostic approaches, and on characteristics of the study population. In addition, differences in prevalence and diagnosis of female endometriosis patients are caused by differential access to healthcare, views, society, economy, education, medical conditions, and security systems and other factors. Moradi Y, et al. reported that the prevalence of endometriosis by the continent ranged from 17% for Europe to 36% for Asia [1].

Despite the high prevalence of endometriosis, diagnosing the condition remains challenging. In USA during the 10-year study period (2006-2016), among 332,0562863 women incident endometriosis cases were identified for an average incidence 24.3%. The distribution of the 2863 incident cases by the diagnosis modality was as follows: 45.5% surgical, 5.7% imaging, and 48.8% clinical [20]. The results of our study showed that the prevalence of endometriosis diagnosed with laparoscopy, ultrasound and magnetic resonance imaging (MRI) methods was higher than endometriosis diagnosed with other diagnostic methods. Other studies have shown the same results regarding the prevalence of endometriosis. Another study showed the same results prevalence of endometriosis [1, 21].

According to the literature, many women with this pathology are asymptomatic, while others may report non-specific symptoms. Shafrir AL, et al. reported that the prevalence ranged from 2 to 11% among asymptomatic women, 5 to 50% among infertile women, and 5 to 21%

among women hospitalized with pelvic pain [19]. In our study, prevalence of asymptomatic women with endometriosis was 13.3%. A previous study, the prevalence of endometriosis among Ukrainian women was 28.4% [22]. In present study the overall prevalence of endometriosis among women in present study was 31.5%.

Currently, the etiology of endometriosis remains unknown. Prior studies identified a variety of endometriosis risk factors including abnormal or heavy bleeding, dysmenorrhea, dyspareunia, dysuria, and pelvic pain, age, alcohol use, early menarche, family history of endometriosis, infertility, intercourse during menses, low body weight, prolonged menstrual flow [14, 19, 22-26]. In present study, infertility, pelvic pain, and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts. Other risk factors either decreased or increased the odds of an endometriosis diagnosis.

STRENGTH AND LIMITATIONS

Strength: The main strength of this study is the utilization of surveillance data for prevalence and causal inference of endometriosis. This work may be considered the first of epidemiological studies in Ukraine in order to estimate the prevalence and risk factors associated with endometriosis in female evacuated from the Eastern Ukrainian military conflict regions. Our results provide new data for a comprehensive assessment of the prevalence and risk factors of endometriosis in Ukraine.

Limitations: (1) The prevalence and risk factor data are derived exclusively in female evacuated from the Eastern Ukrainian military conflict regions. Therefore, the findings may not be extrapolated to other female groups and regions. More comprehensive studies across different regional groups of female are needed; (2) Although the available large female evacuated from the military conflict regions data, follow-up research efforts should focus on further expanding the sample size to produce more precise assessments on endometriosis.

CONCLUSIONS

Our study findings demonstrate the high prevalence of endometriosis among women in Ukraine. The pelvic pain, infertility and early age at menarche to be a consistent risk factor for endometriosis in both the operative and population cohorts. However, whether these factors are causal or merely represent a feature of the pathophysiological process remains uncertain. The lack of an effective diagnosis of endometriosis in female leads to delayed or missed diagnosis are associated with reduced quality of life and high financial costs to the patient and the healthcare system. An improved understanding of the pathogenesis of endometriosis is needed for the development of targeted medical approaches. Given the high prevalence of endometriosis, the negative effect of the disease on female health and the high associated economic costs, biomarkers are urgently needed, as are new therapeutics that target the varied physiological pathways related to the development and progression of endometriosis. These can be achieved through collaborative, multidisciplinary research and the prioritization of endometriosis as an important public health issue.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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