Anxiety and depression in women with endometriosis: a comparative study across fertility contexts

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Objective: To assess the prevalence of anxiety and depression in women with endometriosis undergoing ovarian stimulation and oocyte retrieval for in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) or fertility preservation (FP) compared with women without endometriosis.
Design: Observational cohort study conducted in a university hospital-based research center.
Subjects: Women who underwent ovarian stimulation and oocyte retrieval between November 2023 and May 2024 for IVF/ICSI or nononcological FP. Two populations were analyzed: (i) infertile women undergoing IVF/ICSI as part of a current family-building project, and (ii) women undergoing oocyte vitrification for FP.
Exposure: Participants were classified as endometriosis (exposed) or disease-free (unexposed) based on imaging (transvaginal ultrasound and/or magnetic resonance imaging). All patients completed a 55-item questionnaire, including the validated Hospital Anxiety and Depression Scale (HADS), on the day of oocyte retrieval.
Main Outcome Measures: Prevalence of anxiety and depression, defined as a HADS-A or HADS-D score ≥ 11.
Results: The study included 324 women: 196 IVF/ICSI patients (73 with endometriosis and 123 controls) and 128 FP patients (38 with endometriosis and 90 controls). Overall, 111/324 (34.3%) had endometriosis. Anxiety prevalence was higher in women with endometriosis in both populations, but did not reach significance. In patients undergoing IVF/ICSI, depression was significantly more frequent in those with endometriosis vs. controls (5.5% vs. 0.8%). In the FP population, women with endometriosis more often reported prior psychological support (21.1% vs. 4.4%) and psychotropic use (13.2% vs. 2.2%). Multivariate analysis identified severe deep dyspareunia as a factor independently associated with anxiety and/or depression (adjusted odds ratio 2.7; 95% confidence interval, 1.1–7.2).
Conclusion: Among patients undergoing IVF/ICSI, depression was significantly more prevalent in women with endometriosis, whereas no significant difference was observed in the FP population. These findings underscore the importance of integrating psychological support into assisted reproductive technology management for women with endometriosis, particularly those experiencing severe pain and/or infertility. (Fertil Steril® 2026;125:688–97. ©2025 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Endometriosis, IVF, fertility preservation, anxiety, depression

Endometriosis is a benign gynecologic condition that affects approximately 10% of women of reproductive age and significantly impacts women's health. It primarily manifests through gynecological symptoms such as dysmenorrhea, chronic pelvic pain, and infertility (1). However, it can also present with nongynecological symptoms, including gastrointestinal, thoracic, neurological, and psychological

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manifestations, thereby compromising women's quality of life (2, 3).

The management of endometriosis presents a considerable clinical challenge, requiring a multidisciplinary approach to address the complex needs of affected individuals (4). Assisted reproductive technology (ART) is often employed in this population, either through in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) to treat infertility, or through oocyte cryopreservation for fertility preservation (FP), given the higher prevalence of infertility among women with endometriosis (5).

Anxiety and depression are among the most common psychological disorders reported in women with endometriosis, both showing a high prevalence in this population (6). A previous study found moderate to severe anxiety symptoms in nearly one-third of women with histologically confirmed endometriosis, regardless of the severity of the disease or symptoms. Depressive symptoms were observed in approximately one in six patients (7). Understanding and addressing these psychological conditions is particularly important in the comprehensive management of women undergoing ovarian stimulation for ART, as these factors can influence treatment adherence, quality of life, and ART outcomes (8, 9).

The primary objective of this study is to assess the prevalence of anxiety and depression in women with endometriosis undergoing ovarian stimulation and oocyte retrieval for IVF/ICSI or FP compared with unaffected women. A secondary objective is to identify the factors associated with the risk of anxiety and depression in the context of ART.

MATERIALS AND METHODS

Study design and population

We conducted an observational single-center cohort study at our institution between November 1, 2023, and May 1, 2024. All consecutive women undergoing ovarian stimulation and oocyte retrieval for IVF/ICSI or nononcological FP during this period were invited to participate. A 55-question survey was distributed on the day of oocyte retrieval, after the procedure. The questionnaire was designed to collect both clinical and psychological data. Inclusion criteria were women aged 18 years or older who underwent ovarian stimulation and oocyte retrieval for IVF/ICSI or nononcological FP during the study period and who completed the study questionnaire. Exclusion criteria were oocyte donation or incomplete responses to the questionnaire regarding the assessment of anxiety and depression.

Two populations were analyzed: (i) infertile women performing IVF/ICSI treatment for infertility and actual family project, and (ii) women undergoing oocyte vitrification for FP. In each population, we compared the "exposed" women with endometriosis (endometriosis group) to the ''unexposed'' women without any evidence of endometriosis (disease-free group).

All patients underwent a comprehensive pre-ART evaluation to accurately diagnose and stage endometriosis (10). Although most women with endometriosis are diagnosed before ART initiation, exceptional cases could be newly identified during this evaluation. In such cases, patients were informed of the diagnosis and systematically received additional gynecologic counseling to discuss disease implications and personalized management before proceeding with ART. The diagnosis and characterization of endometriosis were based on specific imaging criteria by expert radiologists, which included transvaginal sonography (TVS) and/or magnetic resonance imaging (MRI). Endometriotic lesions were categorized into three phenotypes: superficial peritoneal endometriosis (SUP), endometrioma (OMA), or deep infiltrating endometriosis (DIE). For the DIE and OMA phenotypes, the diagnosis and staging of endometriosis were based on previously published imaging criteria using TVS (11–13) or MRI (14–17). Endometrioma was defined as a cystic mass arising from the ectopic endometrial tissues and growing in the ovaries. It could be observed by TVS as a cystic mass with a homogeneous low-echogenic fluid content with scattered internal echoes, and without papillary proliferations (1). The MRI characteristics of endometrioma included (i) a round ovarian structure with a high signal intensity on T1 and a characteristic shading sign or (ii) low signal intensity on T2 (16, 18). For each patient, the cyst laterality (i.e., left, right, or bilateral) and size (cm) were assessed by pre-ART TVS (19). In case of bilateral and/or multiple cysts, the largest endometrioma diameter was selected. Deep infiltrating endometriosis lesions were classified into five locations (i.e., the bladder, uterosacral ligament(s), vagina, intestine, and ureter) (20). In cases of multiple DIE lesions, the patients were classified according to the worst finding (least to most severe: uterosacral ligament(s), vagina, bladder, intestine, and ureter) (20). Additionally, in women with a history of previous endometriosis surgery, the diagnosis was confirmed through histological evidence of endometriosis. For cases of SUP, as the pre-ART evaluation did not reveal OMA or DIE lesions, the diagnosis relied on surgical findings. As these phenotypes are often co-occurring, patients were categorized into the group corresponding to their most severe lesion, according to a previously published classification (21), in the following order from least to most severe: SUP, followed by OMA, and then DIE. The presence of adenomyosis was diagnosed using imaging criteria based on TVS or MRI as previously detailed (22–24).

Women with no evidence of endometriosis were allocated to the disease-free group: This group encompasses women who undertake ART treatment for nonendometriosis-related infertility or FP. In those women, endometriosis was ruled out in a pre-ART workup assessment, after questioning about their level of pelvic pain, clinical examination, and pelvic imaging (25).

Data collection

Clinical and psychological assessment of patients. The patients received a digital questionnaire to assess anxiety and depression on the day of oocyte retrieval, which they completed at home. Anxiety and depression were measured using the HADS questionnaire, a well-validated self-report questionnaire in medical settings (26, 27). It demonstrates

good reliability and construct validity (26–28) and has been previously validated and used in endometriosis and infertile patients (29, 30). It has been translated and validated in French (31, 32). The HADS score consists of a total of 14 items related to the patient's psychological state over the past week. Seven items evaluate depression, and seven items evaluate anxiety. The scores for each HADS category are summed up to determine an anxiety score (HADS-A) or a depression score (HADS-D). Each item is rated on a 4-point scale (from 0 to 3), resulting in a total score ranging from 0 to 21 for each subscale. A score of 0 to 7 in each category indicates the absence of symptoms, a score of 8 to 10 indicates questionable symptomatology, and a score of ≥ 11 indicates definite symptomatology (26).

The presence of painful symptoms over the past 6 months was also assessed, using the questionnaire, including dysmenorrhea, deep dyspareunia, noncyclic chronic pelvic pain, gastrointestinal symptoms, and urinary symptoms. Noncyclic chronic pelvic pain was defined as intermittent or constant pelvic pain not related to the menstrual cycle. Gastrointestinal symptoms included pain associated with issues such as diarrhea, painful defecation, rectal bleeding, proctitis, or isolated rectal colic (33). Similarly, urinary symptoms were defined as pain associated with hematuria, urinary infections, pollakiuria, dysuria, nonmicrobial cystitis, or isolated pain during urination, whether chronic or menstruation-related (34). The intensity of painful symptoms was assessed using a 10-cm visual analog scale (VAS) ranging from 0 to 10, where 0 indicated no pain, and ten represented the highest level of pain (35). Severe pain was defined as a VAS score of ≥ 7 at the time. The questionnaire also gathered information on menstrual duration, school absenteeism, and history of fainting during menstruation. Data on lifestyle (profession, tobacco consumption), psychological support, and the current use of psychotropic medication (antidepressants or anxiolytics) were also collected. Other clinical data (clinical characteristics, ovarian stimulation characteristics, and oocyte retrieval outcomes) were retrospectively extracted from the clinical center's software database.

Management for ART

For ovarian stimulation, patients were managed according to institutional clinical protocols (10). Various controlled ovarian stimulation (COS) protocols were used, involving daily doses of 150 to 450 IU of recombinant or urinary follicle-stimulating hormone. These included the antagonist protocol, the long agonist protocol, the short agonist protocol, or the progestin-primed ovarian stimulation protocol using dienogest (36). The choice of gonadotropin dosage and COS protocol was tailored to each patient's individual characteristics. Monitoring during stimulation involved pelvic ultrasounds and hormonal assessments. Ovulation was triggered using an injection of (i) recombinant human chorionic gonadotropin, (ii) a gonadotropin-releasing hormone agonist, or (iii) a combination of both (dual trigger). Oocyte retrieval was performed under local or general anesthesia, depending on the patient's preference and technical considerations.

Statistical analysis

The primary outcome measure was the prevalence of anxiety and depression, defined as an HADS-A score (anxiety) or HADS-D score (depression) of ≥ 11. Secondary outcomes included the presence of prior psychological support and the use of psychotropic medication within the past 6 months.

A first analysis was conducted to compare patients with endometriosis with those without endometriosis in each population (IVF/ICSI and FP). A second analysis was performed on the total population to identify factors associated with anxiety and/or depression. In this analysis, women with an HADS-A and/or HADS-D score of ≥ 11 were compared with those without a diagnosis of anxiety or depression.

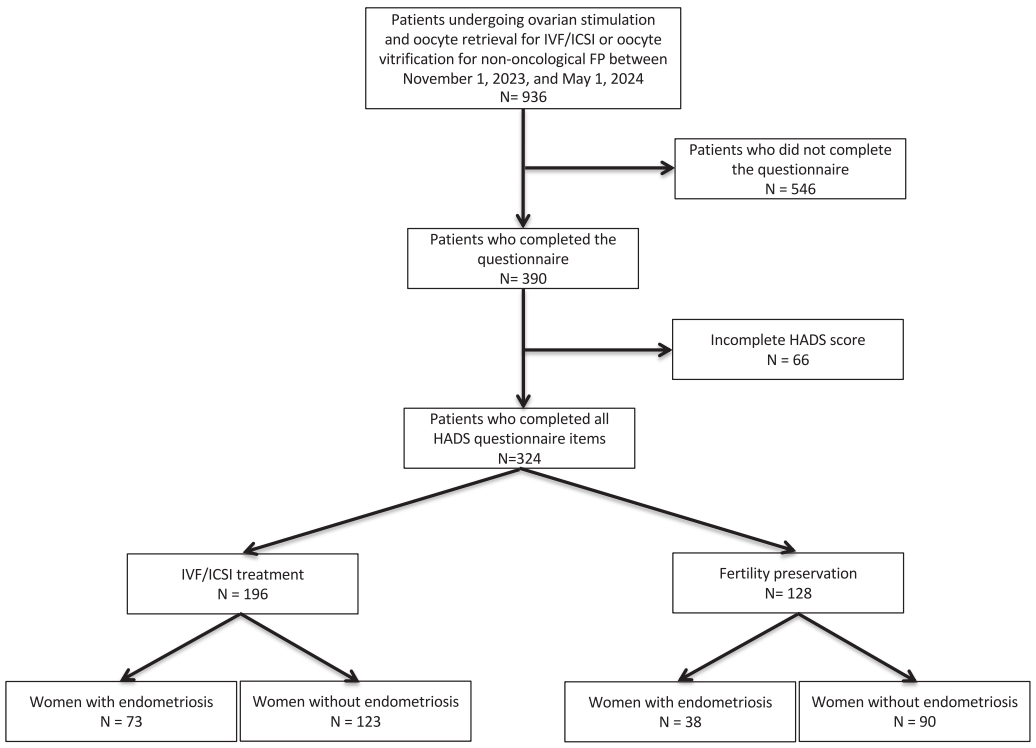
All data were compiled in a digital database and analyzed using IBM SPSS Statistics version 23.0 (SPSS Inc., Chicago, IL). For descriptive analysis, continuous variables were presented as means $\pm$ SD, whereas categorical variables were expressed as numbers (percentages). Group comparisons were performed using Pearson's χ^2 test for qualitative variables and Mann-Whitney U tests for quantitative variables, as appropriate.

To identify factors associated with anxiety and/or depression, a multivariable logistic regression was performed. Categorical variables with a P value $<.2$ in univariate analyses were included in the model, along with clinically relevant variables such as geographic origin (37) and type of ART treatment (IVF/ICSI vs. FP). Correlations between baseline characteristics were assessed, and in cases of significant correlation, only one variable was retained to avoid redundancy. Specifically, mean VAS scores for dyspareunia, dysmenorrhea, and gastrointestinal pain were excluded due to significant correlations with the categorical variables "severe dyspareunia" and "severe gastrointestinal pain." To ensure model stability and facilitate interpretation, only the categorical variables were included. For each significant association, odds ratios and 95% confidence intervals were calculated based on model coefficients and SEs. A two-sided P value $<.05$ was considered statistically significant. This study received approval from the Ethics Review Committee of the Cochin University Hospital (CLEP) (No. AAA-2025-10045), and all data were fully anonymized before analysis.

RESULTS

Between November 1, 2023, and May 1, 2024, 936 patients underwent oocyte retrieval after COS at our hospital. Of these, 390/936 (41.6%) completed the questionnaire. Three hundred twenty-four patients were included in the study: 196 patients in the IVF/ICSI population (73 with endometriosis and 123 without the disease) and 128 patients in the FP population (38 with endometriosis and 90 without the disease) (Fig. 1).

FIGURE 1



Flow chart. FP = fertility preservation; HADS = Hospital Anxiety and Depression Scale; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization.

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Patients and ovarian stimulation characteristics

All patients' characteristics are presented in Table 1 and Supplemental Table 1 (available online). There was no significant age difference between patients with endometriosis and controls, either in the IVF/ICSI group (35.7 ± 3.6 vs. 35.6 ± 3.8 years, P=.712) or in the FP group (33.2 ± 3.9 vs. 34.2 ± 2.9 years, P=.219). As expected, women with endometriosis more frequently reported severe pain and had higher pain scores for dysmenorrhea, dyspareunia, and noncyclic pelvic pain compared with controls (Table 1).

Details concerning endometriosis characteristics in both populations are described in Table 2. The most frequently observed endometriosis phenotype in our population was DIE, present in 67 out of 73 patients (91.8%) in the IVF/ICSI group and in 28 out of 38 patients (73.7%) in the FP group. A history of surgery was reported in 9 out of 73 patients (12.3%) in the IVF/ICSI group and in 7 out of 38 patients (18.4%) in the FP group. Adenomyosis was associated with endometriosis in 33 out of 73 patients (45.2%) in the IVF/ICSI group and in 12 out of 38 patients (31.6%) in the FP group.

The characteristics of COS are detailed in Supplemental Table 2. The most commonly used protocol was the gonadotropin-releasing hormone antagonist protocol, applied in 159 out of 196 cases (81.1%) in the IVF/ICSI group and in 109 out of 128 cases (85.1%) in the FP group. None of the patients with endometriosis included in this study experienced complications requiring hospitalization or adjustments to their medical treatment to manage disease-related symptoms during stimulation.

Psychological assessment

The evaluation of anxiety and depression using the HADS questionnaire is presented in Table 3. The proportion of women with anxiety was higher in endometriosis groups compared with control groups in both the IVF/ICSI (18/73 [24.7%] vs. 20/123 [16.3%], P=.151) and FP (9/38 [23.7%] vs 17/90 [18.9%], P=.538) populations, although the differences were not statistically significant. In the IVF/ICSI population, the proportion of women with depression was significantly higher among patients with endometriosis compared with controls (4/73 [5.5%] vs. 1/123 [0.8%], P=.045). In the FP population, no statistically significant difference was observed between patients with endometriosis and controls regarding depression (0/38 [0%] vs. 2/90 [2.2%], P=.354). However, in the FP group, prior psychological support (8/38 [21.1%] vs. 4/90 [4.4%], P=.003) and the use of current psychotropic medications (5/38 [13.2%] vs. 2/90 [2.2%], P=.013) were significantly more frequent in patients with endometriosis than in controls. In contrast, no significant differences were observed for these variables in the IVF/ICSI population.

TABLE 1

Characteristics of the 324 patients included in the study.

	IVF/ICSI (n = 196)			Fertility preservation (n = 128)		
Variables	**Endometriosis group (n = 73)**	**Control group (n = 123)**	***P***	**Endometriosis group (n = 38)**	**Control group (n = 90)**	***P***
Age			.545			.211
<35 (y)	30 (41.1)	56 (45.5)		24 (63.2)	46 (51.1)	
≥35 (y)	43 (58 .9)	67 (54.5)		14 (36.8)	44 (48.9)	
BMI (kg/m^2)	23.6 ± 4.3	24.5 ± 4.4	.128	22.7 ± 3.9	22.5 ± 3.8	.964
Smoking habits			.570			.195
Current user	21 (28.8)	44 (35.8)		9 (23.7)	11 (12.2)	
Previous user	2 (2.7)	4 (3.3)		10 (26.3)	34 (37.8)	
Never smoked	50 (68.5)	75 (61)		19 (50)	45 (50)	
Profession			.015			.077
Farmers, growers	0 (0)	0 (0)		0 (0)	0 (0)	
Craftsmen, shopkeepers and company directors	5 (6.8)	9 (7.3)		2 (5.3)	5 (5.6)	
Executives and higher intellectual professions	21 (28.8)	35 (28.5)		13 (34.2)	43 (47.8)	
Intermediate professions	27 (37)	25 (20.3)		12 (31.6)	33 (36.7)	
Employees	15 (20.5)	51 (41.5)		7 (18.4)	6 (6.7)	
Workers	0 (0)	1 (0.8)		0 (0)	0 (0)	
Unemployed	3 (4.1)	2 (1.6)		2 (5.3)	0 (0)	
Student	2 (2.7)	0 (0)		2 (5.3)	3 (3.3)	
Geographic origin			.582			.989
European	48 (65.8)	69 (56.1)		28 (73.7)	67 (74.4)	
Asian	2 (2.7)	3 (2.4)		1 (2.6)	3 (3.3)	
African	14 (19.2)	32 (26)		5 (13.2)	12 (13.3)	
Other	9 (12.3)	19 (15.4)		4 (10.5)	8 (8.9)	
Gravidity	0.7 ± 1.2	0.96 ± 1.2	.053	0.13 ± 0.3	0.23 ± 0.7	.766
Parity	0.14 ± 0.3	0.28 ± 0.6	.187	0 ± 0	0.02 ± 0.1	.356
AFC	19.9 ± 12.6	19.6 ± 13.1	.829	19.7 ± 9.6	19.3 ± 10.8	.605
AMH (ng/mL)	2.49 ± 2.6	2.52 ± 2	.432	2.3 ± 1.5	2.5 ± 1.9	.960
No. of previous oocyte retrieval	1.85 ± 1	1.99 ± 1.5	.744	1.2 ± 0.5	1.3 ± 0.5	.255
First rank of oocyte retrieval	35 (47.5)	68 (55.3)	.320	32 (84.2)	67 (74.4)	.228
Severe dysmenorrhea	23 (31.5)	18 (14.6)	.005	11 (28.9)	5 (5.6)	<.001
Severe dyspareunia	4 (5.5)	4 (3.3)	.446	10 (26.3)	3 (3.3)	<.001
Severe noncyclic chronic pelvic pain	6 (8.2)	4 (3.3)	.127	4 (10.5)	0 (0)	.002
Severe gastrointestinal pain	11 (15.1)	6 (4.9)	.014	8 (21.1)	3 (3.3)	.001
Severe urinary pain	1 (1.4)	0 (0)	.193	3 (7.9)	0 (0)	.007
Mean VAS dysmenorrhea	4.25 ± 3.3	2.60 ± 3	<.001	4.58 ± 3.3	2.44 ± 2.6	<.001
Mean VAS dyspareunia	1.9 ± 2.7	1.0 ± 2.1	.012	2.97 ± 3.5	0.59 ± 1.7	<.001
Mean VAS noncyclic pelvic pain	1.4 ± 2.5	0.5 ± 1.8	.003	2.1 ± 3.0	0.44 ± 1.3	<.001
Mean VAS gastrointestinal pain	2.55 ± 3.1	1.1 ± 2.2	<.001	3.87 ± 3.1	1.36 ± 2.2	<.001
Mean VAS urinary pain	0.38 ± 1.5	0.22 ± 0.9	.624	1.18 ± 2.5	0.12 ± 0.6	<.001
Duration of menstruation (d)	5.28 ± 3.8	5.49 ± 4	.809	5.86 ± 3.6	4.69 ± 1.1	.003
History of fainting during menstruation	10 (13.7)	3 (2.4)	.002	6 (15.8)	2 (2.2)	.004
Absenteeism from school during menstruation	29 (39.7)	23 (18.7)	.001	18 (47.4)	22 (24.4)	.011
Oral contraceptive use	12 (16.4)	3 (2.4)	<.001	19 (50)	2 (2.2)	<.001

Note: Data are means ± the SE or n (%), unless specified otherwise. Group comparisons were performed using Pearson's χ^2 test for qualitative variables and Mann-Whitney *U* tests for quantitative variables, as appropriate. Severe pain is defined by a VAS score ≥7. AFC = antral follicle count; AMH = antimüllerian hormone; BMI = body mass index; VAS = visual analog scale.

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Factors associated with anxiety and/or depression in ART management

To identify factors associated with pathological psychological states during ART management, 67 patients with anxiety and/or depression (HADS-A and/or HADS-D ≥11) were compared with 257 patients without either condition (HADS-A and HADS-D <11) (Supplemental Tables 3 and 4). The presence of endometriosis (29/67 [43.3%] vs. 82/257 [31.9%], *P*=.081) or adenomyosis (16/67 [23.9%]

TABLE 2

Endometriosis characteristics.

Variables	IVF/ICSI (n = 73)	Fertility preservation (n = 38)
Endometriosis phenotype		
SUP	5 (6.8)	1 (2.6)
OMA	1 (1.4)	9 (23.7)
DIE	67 (91.8)	28 (73.7)
Deep infiltrating endometriosis		
With OMA	21 (31.3)	15 (53.6)
Without OMA	46 (68.7)	13 (46.4)
Subtype of DIE		
Uterosacral ligament(s)	44 (65.7)	18 (64.3)
Vagina	2 (3)	1 (3.6)
Bladder	3 (4.5)	2 (7.1)
Intestine	18 (26.9)	7 (25)
Ureter	0 (0)	0 (0)
Endometrioma laterality		
Unilateral	17 (77.3)	18 (75)
Bilateral	5 (22.7)	6 (25)
Endometrioma size (cm)	3.8 ± 4.1	4.4 ± 3.4
Adenomyosis	33 (45.2)	12 (31.6)
Pelvic MRI performed	51 (69.9)	13 (34.2)
Previous surgery of endometriosis	9 (12.3)	7 (18.4)

Note: Data are means ± the SE or n (%), unless specified otherwise. DIE = deep infiltrating endometriosis; OMA = endometrioma; SUP = superficial peritoneal endometriosis.

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vs. 50/257 [19.5%], $P=.381$) was not significantly associated with anxiety or depression. Similarly, the number of oocytes retrieved did not differ between women with and without anxiety and/or depression (10.7 ± 8.3 vs. 11.6 ± 8.0; $P=.190$) (Supplemental Table 3). After adjusting for age, geographic origin, presence of severe deep dyspareunia, severe gastrointestinal pain, endometriosis, and type of ART (IVF/ICSI vs. FP), severe deep dyspareunia remained the only factor significantly associated with anxiety and/or depression (adjusted odds ratio 2.7, 95% confidence interval, 1.1–7.2) (Supplemental Table 4).

DISCUSSION

Main results

This study highlights a significantly higher prevalence of depression among women with endometriosis undergoing IVF/ICSI, compared with those without endometriosis. No significant difference was found regarding anxiety in this population. Among patients undergoing FP, the prevalence of anxiety and depression did not differ according to the presence or absence of endometriosis, although those with endometriosis more frequently reported a history of psychological support or use of psychotropic medication. Finally, severe deep dyspareunia was identified as an independent factor associated with anxiety and/or depression, across all types of ART (ICSI or FP).

Strengths and limitations

To our knowledge, this is the largest study to date evaluating the psychological impact of endometriosis in the context of ART, including both women undergoing IVF/ICSI and those opting for elective oocyte cryopreservation for nononcological indications. The use of a validated questionnaire (HADS), administered in a standardized manner at the time of oocyte retrieval, helps limit recall bias. The precise characterization of endometriosis phenotype through expert imaging further strengthens the robustness of the data.

However, several limitations must be acknowledged. First, the single-center design may limit the generalizability of the findings. In addition, the high proportion of DIE observed in our cohort likely reflects the specific profile of patients referred to our tertiary endometriosis center, rather than the general ART population. This particular recruitment should be considered when interpreting our findings, as the severity of endometriosis could influence patients' psychological experience and the way they completed the questionnaire. Second, only 41% of patients completed the questionnaire, introducing a potential inclusion bias, as women who agreed to participate may differ from nonrespondents. Third, no a priori sample size calculation was performed; the study included all eligible patients during the

TABLE 3

Assessment of anxiety and depression.

	IVF/ICSI (n = 196)			Fertility preservation (n = 128)		
Variables	Endometriosis group (n = 73)	Control group (n = 123)	*P*	Endometriosis group (n = 38)	Control group (n = 90)	*P*
HADS-A			.151			.538
0–10	55 (75.3)	103 (83.7)		29 (76.3)	73 (81.1)	
11–21	18 (24.7)	20 (16.3)		9 (23.7)	17 (18.9)	
HADS-D			.045			.354
0–10	69 (94.5)	122 (99.2)		38 (100)	88 (97.8)	
11–21	4 (5.5)	1 (0.8)		0 (0)	2 (2.2)	
Psychological support	11 (15.1)	14 (11.4)	.454	8 (21.1)	4 (4.4)	.003
Psychotropic treatment	0 (0)	3 (2.4)	.179	5 (13.2)	2 (2.2)	.013

Note: Data are means ± the SE or n (%), unless specified otherwise. Group comparisons were performed using Pearson's χ^2 test for qualitative variables and Mann-Whitney *U* tests for quantitative variables, as appropriate. HADS = hospital anxiety and depression scale (score ≥11 = definite symptomatology); ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization.

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recruitment period, which may have limited statistical power to detect small differences. Fourth, anxiety and depression were assessed at a single time point using self-reported measures, without longitudinal follow-up. Moreover, although the results suggest an association between endometriosis and psychological symptoms, no causal relationship can be established. Finally, our control group included women with no clinical symptoms or radiological signs of endometriosis; however, it is possible that some cases of asymptomatic superficial endometriosis were misclassified as disease-free. We acknowledge that selecting an ideal control group in studies on endometriosis is inherently challenging. However, the absence of severe pelvic pain symptoms in these women reduces the likelihood of a significant bias.

Interpretation

Our study confirms a higher prevalence of depression in women with endometriosis undergoing IVF/ICSI, in line with previous findings. In a prospective case-control study including 93 women (37 with endometriosis and 56 without), Ceran et al. (38) showed significantly higher depression scores in women with endometriosis, whereas no significant differences were found regarding anxiety or psychological quality of life. Similarly, Mori et al. (39) conducted a cross-sectional study including 201 infertile women, of whom 81 had endometriosis, and found significantly higher depression scores among infertile women with endometriosis compared with infertile women without endometriosis. These results should also be interpreted in light of the psychological burden already associated with infertility itself. As highlighted by Verhaak et al. (40) in a systematic review, women undergoing IVF often report elevated levels of anxiety and depression, particularly after treatment failure, largely driven by the emotional impact of infertility and fear of permanent childlessness.

In contrast, in our cohort, the presence of endometriosis did not appear to influence anxiety or depression rates in the FP group—despite a higher prevalence of past psychological follow-up or psychotropic treatment—suggesting a distinct emotional profile and care dynamic in these patients. One hypothesis could be that women undergoing FP for endometriosis benefit from early multidisciplinary care and access to psychological support, potentially contributing to better emotional stability. Such proactive or preventive psychological care, including counseling and fertility education provided by physicians, may help women with endometriosis better anticipate and manage reproductive challenges, thereby mitigating anxiety or depressive symptoms. Another hypothesis may explain this observation: FP patients did not experience prolonged infertility, which could reduce psychological vulnerability. In contrast, the association between endometriosis and infertility in the IVF/ICSI group may amplify emotional distress (41). Moreover, this burden does not only affect women themselves but may also have a significant psychological impact on their partners (42). The psychological context indeed differs between women undergoing IVF/ICSI and those undergoing FP. In vitro fertilization/intracytoplasmic sperm injection patients are actively engaged in infertility treatment, a situation often accompanied by time pressure and repeated treatment exposure, which may contribute to the higher level of depression observed among IVF/ICSI patients with endometriosis. In contrast, FP patients are generally women anticipating possible future fertility loss and may face less immediate treatment-related stress. This contextual difference may partly explain why the association between endometriosis and depressive symptoms was not observed in the FP cohort.

Psychological distress appeared particularly marked in patients experiencing pain, as highlighted by the independent association between severe deep dyspareunia and the presence of anxiety and/or depression. A link between dyspareunia and psychological distress has also been documented in a large multicenter observational study (43), which reported that deep dyspareunia and depressive symptoms were independently associated with impaired sexual function. Moreover, this could support the hypothesis that pain symptoms, more than the diagnosis of endometriosis itself, are key determinants of psychological health, as previously suggested by Van Barneveld et al. (44). In their meta-analysis, they found that women with endometriosis exhibited more symptoms of anxiety and depression than healthy controls, but these differences were not significant when compared with women with chronic pelvic pain from other causes (44). These findings are further supported by a large cross-sectional survey of 449 individuals with self-reported endometriosis, which demonstrated a direct linear relationship between pain severity and psychological distress, including depression and anxiety (41). However, the question remains open as to whether chronic pain leads to psychological distress or whether pre-existing psychological vulnerability may heighten the perception and severity of pain. This bidirectional relationship was discussed by Laganà et al. (6), who emphasized that anxiety and depression could amplify pain through emotional and cognitive mechanisms, contributing to a vicious cycle of pelvic pain and psychological suffering. In line with those data, Spinoni et al. (45) showed that negative illness perceptions and pain-focused coping strategies, such as catastrophizing, were strongly associated with increased psychological distress in women with endometriosis.

CONCLUSION

To conclude, our findings underscore the importance of systematically screening for psychological distress, sexual dysfunction, and severe pain in ART pathways (46), particularly in women with endometriosis. Multidisciplinary care, including tailored psychological support and a thorough assessment of pelvic pain, appears essential to improve patient experience and optimize ART outcomes (47, 48). Prospective longitudinal studies are needed to better understand how anxiety and depression evolve throughout ART care, and to assess the efficacy of targeted interventions in this at-risk population.

CRediT Authorship Contribution Statement

Mathilde Bourdon: Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Laure Bolac:** Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Celie Cervantes:** Validation, Conceptualization. **Chloé Maignien:** Writing – original draft, Validation. **Rhea Aoun-Clavel:** Visualization, Validation. **Marianne Reynaud:** Visualization, Validation. **Catherine Patrat:** Visualization, Validation. **Charles Chapron:** Visualization, Validation, Methodology. **Pietro Santulli:** Writing – original draft, Validation, Conceptualization.

Declaration of Interests

M.B. reports personal fees from Gedeon Richter, IBSA, Organon, Vifor, outside the submitted work. L.B. has nothing to disclose. C. Cervantes has nothing to disclose. C.M. has nothing to disclose. R.A.-C. has nothing to disclose. M.R. has nothing to disclose. C.P. reports personal fees and nonfinancial support from Ferring, outside the submitted work. C. Chapron has nothing to disclose. P.S. reports personal fees from Merck, Ferring, Besins, Gedeon Richter, Theramex, IBSA, General Electrics Medical Systems, other from Board Member of the SEUD, Editorial Board Member RBMO, GOF, outside the submitted work.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be found online at https://doi.org/10.1016/j.fertnstert.2025.12.011.

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Ansiedad y depresión en mujeres con endometriosis: un estudio comparativo de contextos en fertilidad

Objetivo: Evaluar la prevalencia de ansiedad y depresión en mujeres con endometriosis sometidas a estimulación ovárica y recuperación de ovocitos para fertilización in vitro/inyección intracitoplasmática de espermatozoides (FIV/ICSI) o preservación de la fertilidad (PF), en comparación con mujeres sin endometriosis.

Diseño: Estudio de cohorte observacional realizado en un centro de investigación de un hospital universitario.

Sujetos: Mujeres que se sometieron a estimulación ovárica y recuperación de ovocitos entre noviembre de 2023 y mayo de 2024 para FIV/ICSI o PF no oncológica. Se analizaron dos poblaciones: (i) mujeres infértiles sometidas a FIV/ICSI como parte de un proyecto actual de formación de familia, y (ii) mujeres sometidas a vitrificación de ovocitos para PF.

Exposición: Las participantes se clasificaron como con endometriosis (expuestas) o sin enfermedad (no expuestas) según estudios de imagen (ultrasonido transvaginal y/o resonancia magnética). Todas las pacientes completaron un cuestionario de 55 ítems, incluida la escala validada *Hospital Anxiety and Depression Scale (HADS)*, el día de la recuperación de ovocitos.

Medidas principales de resultado: Prevalencia de ansiedad y depresión, definidas como una puntuación HADS-A o HADS-D ≥ 11.

Resultados: El estudio incluyó 324 mujeres: 196 pacientes de FIV/ICSI (73 con endometriosis y 123 controles) y 128 pacientes de PF (38 con endometriosis y 90 controles). En total, 111/324 (34.3%) tenían endometriosis. La prevalencia de ansiedad fue mayor en mujeres con endometriosis en ambas poblaciones, pero no fue estadísticamente significativa. En las pacientes sometidas a FIV/ICSI, la depresión fue significativamente más frecuente en aquellas con endometriosis en comparación a los controles (5.5% vs. 0.8%). En la población de PF, las mujeres con endometriosis reportaron con mayor frecuencia apoyo psicológico previo (21.1% vs. 4.4%) y uso de psicofármacos (13.2% vs. 2.2%). El análisis multivariado identificó la dispareunia profunda severa como un factor independientemente asociado con ansiedad y/o depresión (odds ratio ajustado 2.7; intervalo de confianza del 95%, 1.1–7.2).

Conclusión: Entre las pacientes sometidas a FIV/ICSI, la depresión fue significativamente más prevalente en mujeres con endometriosis, mientras que no se observaron diferencias significativas en la población de PF. Estos hallazgos subrayan la importancia de integrar apoyo psicológico en el manejo de las tecnologías de reproducción asistida para mujeres con endometriosis, particularmente en aquellas que experimentan dolor severo y/o infertilidad.