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Full length article

Multidimensional factors increase menstrual distress in patients with endometriosis

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ABSTRACT

Background: Endometriosis is a chronic endocrine and inflammatory disease commonly presenting with dysmenorrhea, pelvic pain, and/or infertility. Despite the importance of menstrual symptoms, the impact of menstruation on stress is still poorly assessed. This study aims to objectively measure menstrual distress and identify its determinants in patients with endometriosis.

Materials and methods: A cross-sectional study was conducted over one year, including 75 patients newly diagnosed with endometriosis and an age-matched control group (n = 75) of healthy women. All participants completed the Menstrual Distress Questionnaire (MEDI-Q), which explores 25 items and provides a total score along with subscales: Menstrual Symptoms (MS), Menstrual Symptoms Distress (MSD), and Menstrual Specificity Index (MESI). Scores were compared between cases and controls. A sub-analysis among endometriosis patients identified the key contributors to distress.

Results: Women with endometriosis showed significantly higher score for MEDI-Q Total (median = 14.00, interquartile range: [5.00—30.50] vs 12.00 [2.00—20.00], $p < 0.05$) as well for the subscale MSD (2.24 [1.67—2.81] vs 1.71 [1.00—2.30], $p < 0.01$) compared to controls. Menstrual distress was primarily associated with dyspareunia, dyschezia, dysuria, gastrointestinal symptoms (nausea, diarrhea, constipation, decreased appetite), reduced sexual drive, impaired concentration, and insomnia. A heightened perception of discomfort with bleeding, particularly in the presence of adenomyosis, further increased distress.

Conclusion: Menstrual distress is significantly higher in women with endometriosis and involves multidimensional factors beyond pain. These findings support the need for a personalized and comprehensive approach in the clinical management of endometriosis.

Introduction

Endometriosis is a chronic gynecological condition diagnosed in more than 10 % of reproductive age women and characterized by the presence of endometrial-like tissue outside the uterus, often resulting in inflammation, pain, and infertility [1,2]. Dysmenorrhea and cyclic pelvic pain are frequently normalized or dismissed in clinical settings, leading to significant delays in endometriosis diagnosis [3]. Furthermore, endometriosis often present with nonspecific symptoms, which may further contribute to a delayed identification of the disease [4]. Persistent symptoms can also contribute to central sensitization and chronic pain syndromes [5]. The great burden of pain and the implications for fertility impair physical, mental, and social well-being, reducing quality of life (QoL) [6,7]. Furthermore, prolonged symptom burden may impair educational and occupational performance, contributing to significant socioeconomic impact [8].

From a psychosocial perspective, patients often experience frustration, psychological distress, and feelings of invalidation, which can lead to anxiety and depression [9,10]. Endometriosis and stress share a complex, bidirectional relationship, wherein the chronic symptoms of the disease act as persistent stressors, and stress itself may exacerbate symptom severity and disease progression [11].

Menstruation plays a pivotal role in the presentation of endometriosis, considering that a significant proportion of clinical manifestation

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are menstrual-related or exacerbated during the period. Emerging research emphasizes the importance of assessing menstrual distress—the physical, emotional, and psychological burden associated with menstruation [12,13] — as a critical, yet underexplored, component of the diagnostic process [14]. However, the evaluation of menstrual distress has been challenging for years, because of the paucity of standardized and validated instruments specifically designed to objectively measure this parameter. Recently, the development of a new tool, the Menstrual Distress Questionnaire (MEDI-Q), has allowed a comprehensive and objective assessment of menstrual distress, providing a representative score of stress perception [15,16]. Moreover, MEDI-Q distinguishes the distress specific to the menstrual phase from that of premenstrual and intermenstrual phases and explores the multifaced symptomatology of menstruation, in terms of mood, emotions, energy, nutrition, sleeping and sexuality, other than pain and bleeding.

Given the key role of menstruation in endometriosis onset and development, the present study aimed to evaluate the menstrual distress in patients with newly diagnosed endometriosis compared to a control group, by using the MEDI-Q instrument.

Materials and methods

An observational cross-sectional study was conducted in a group of patients newly diagnosed with endometriosis referred to our center over a 1-year period. The inclusion criteria for the study population were: reproductive age, nulliparity, newly established first diagnosis of endometriosis by ultrasound and/or magnetic resonance imaging (MRI) or surgery. Patients with concurrent uterine fibroids or PCOS were excluded. As *per* requirements of MEDI-Q applicability, patients included were fluent in Italian and having had at least three menstruations in the past 12 months. Additional exclusion criteria were pregnancy, overt menopause, illiteracy, or inability to provide informed consent.

Demographics and clinical history were collected, including menstrual cycle characteristics and data on endometriosis (diagnosis by imaging or surgery, lesions localizations, use of hormonal contraceptives). The presence of endometriosis-related pain (dysmenorrhea, non-menstrual pelvic pain, dyspareunia, dyschezia and dysuria) was evaluated by using the visual analogue scale (VAS): no pain (VAS $\leq$ 4), mild pain (VAS 5–6), moderate pain (VAS 6–7), severe pain (VAS $\geq$ 8). The presence of other symptoms and systemic comorbidities was also recorded.

In all patients the MEDI-Q was administered in a digital format on local or online platforms through computers, smartphones or tablets and scores were matched to deidentified patients' information. The MEDI-Q aims to assess and score the distress related to menstruation across the last 12 months. This instrument investigates 25 items, covering the following stress-related areas: pain, discomfort, psychic/cognitive changes, gastrointestinal symptoms, and changes in physiological functions. MEDI-Q Total Score evaluates the global menstruation-related distress, whereas the other 3 additional subscales investigate the number of menstrual symptoms (MS) that exacerbate during menstruation, the average distress related to menstrual symptoms (menstrual symptom distress, MSD), and the specificity of menstrual symptoms (menstrual specificity index, MESI) [15,16].

An age-matched group of healthy fertile age nulliparous women attending the gynecology clinic for routine gynecological checkups was used as control group.

Statistical analysis

The data extrapolated from the questionnaires and baseline characteristics of the cases and controls were entered in an electronic database and analyzed using the software SPSS (Statistical Package for Social Science) (IBM SPSS Statistics 23, IBM Corporation). Characteristics of the sample were reported using means and standard deviations. Pearson's chi-square test or Fisher's exact test was used to compare the qualitative variables, depending on the size of the sample. For the quantitative variables, the *t*-test or the Mann–Whitney test was used, depending on whether or not the distribution of the data was normal. Shapiro-Wilk tests highlighted non-normality for all MEDI-Q variables; consequently, descriptives were reported using medians and 25th–75th interquartile ranges for these outcomes, and comparisons between groups were performed using the Mann-Whitney test. Regarding the report of data on individual MEDI-Q items divided by groups, since these are data that are heavily skewed and zero-inflated by the questionnaire design, a combination of descriptives was used to describe the distribution as accurately as possible: mean, standard deviation, median, 25th and 75th percentiles, and percentage of subjects who reported absence of that specific symptom. A multivariate logistic regression model was used to explore the determinants of menstrual distress. Statistical significance was considered in case of $p < 0.05$. More statistical details are reported in the original articles on MEDI-Q development and English validation [15,16].

Ethical approval

The study protocol was approved by the Ethics Committee of our Institution (*protocol n.14558_oss approved on 28 May 2019*). A written informed consent was requested for participation to the study.

Results

Following the inclusion criteria, the study population resulted of 75 patients with endometriosis, with mean age 31.2 ± 7.7 years, compared to 75 age-matched controls. Baseline characteristics and menstrual history of cases and controls are reported in Table 1. Irregular menstrual cycles and heavy menstrual bleeding (HMB) were significantly more frequent among patients with endometriosis (Table 1). The use of hormonal contraception was also more common in this group; however, contraceptives had been initiated prior to the diagnosis of endometriosis and were not prescribed for disease management. Table 2 shows information about pain symptoms, other non-specific symptoms and comorbidities of cases. Patients with endometriosis had coexistent adenomyosis in 38.7 %, whereas ovarian and mixed were the most frequent phenotypes (Table 2).

Patients with endometriosis showed significantly higher score for MEDI-Q Total (14.00 [5.00—-30.50] vs 12.00 [2.00—-20.00], $p < 0.05$) as well for the subscale MSD (2.24 [1.67—-2.81] vs 1.71 [1.00—-2.30], $p < 0.01$), indicating significantly higher average menstrual distress than matched controls (Fig. 1). On the contrary, the median number of MEDI-Q MS was not significantly different between the two groups (6.00 [2.00—-12.50] vs 6.00 [2.00—-9.00], $p > 0.05$), as well as MEDI-Q MESI (0.80 [0.50—-1.00] vs 0.71 [0.33—-1.00], p >

Table 1
Baseline and menstrual characteristics of cases and controls. BMI: body mass index.

	Endometriosis (n = 75)	Controls (n = 75)	p
BMI	21.8 ± 3.9	22.4 ± 4.6	0.524
Age of menarche (years)	11.9 ± 2.0	12.9 ± 4.0	0.744
Menstrual cycle length (days)	22.3 ± 12.3	28.5 ± 8.1	0.04
Regular menstrual cycle	46 (61.3 %)	61(81.3 %)	0.007
Menstrual bleeding			0.005
Light	22 (29.3 %)	17(22.7 %)	
Moderate	26 (34.7 %)	45 (60 %)	
Heavy	27 (36 %)	13 (17.3 %)	
Duration of menstrual bleeding	4.2 ± 3.5	5.5 ± 6.5	0.535
Use of hormonal contraceptives	43 (57.3 %)	26 (34.7 %)	0.005

Table 2
Characteristics of patients with endometriosis. OMA, ovarian endometriosis, DIE, deep infiltrating endometriosis; SUP, superficial endometriosis.

		%
Endometriosis phenotypes (%)	OMA	32(42.7)
	DIE	14(18.7)
	SUP	11(14.7)
	Mixed phenotypes	18(24)
	Adenomyosis	29(38.7)
Pain symptoms (%)	Severe dysmenorrhea	47(62.7)
	Dyspareunia	25(33.3)
	Chronic Pelvic Pain	29(38.7)
	Dyschezia	15(20)
	Dysuria	2(2.7)
	Fatigue	27(36)
	Sleeping disturbances	12(16)
	Gastro-intestinal disorders	12(16)
Systemic comorbidities (%)	Mental Health diseases	21(28)
	Migraine	19(25.3)
	Irritable bowel syndrome	8(10.7)
	Autoimmune diseases	15(20)

Data are expressed as n(%).

0.05). By performing a sub-analysis of each single item, the menstrual distress resulted highly related to dyspareunia, dyschezia and dysuria ($p < 0.001$) (Table 3). Furthermore, gastrointestinal symptoms (nausea, diarrhea, constipation) and decreased appetite showed an additional impact ($p < 0.01$). Furthermore, a reduced sexual drive, concentration impairment and insomnia also contributed to the menstrual distress. Finally, the feeling of being uncomfortable with bleeding increased the stress perception (Table 3). This item was significantly associated with coexistence with adenomyosis ($p < 0.01$). The 3 different MEDI-Q scores did not show any significant difference when stratified for endometriosis phenotype, previous surgery and hormonal contraception.

Discussion

The present study showed that patient with endometriosis have higher level of global menstrual distress than healthy women, as resulting from MEDI-Q and subscales. The major determinants of menstrual distress in endometriosis were not only related to dysmenorrhea, but to the presence of dyspareunia, dyschezia and dysuria. Furthermore, nausea, decreased appetite, altered bowel habits, along with reduced sexual drive, cognitive impairment and insomnia have an additional impact on global distress. The significantly higher scores also for the MSD subscale support the exacerbation of these symptoms during menstruation compared to the intermenstrual phase. In addition, the feeling of being uncomfortable with bleeding resulted significantly associated with the coexistence with adenomyosis.

Study results show that menstrual distress in individuals with endometriosis encompasses a broad constellation of somatic, gastrointestinal, urogenital, and psychosocial symptoms that significantly impair QoL. Sub-analysis of MEDI-Q variables showed that dyschezia and dysuria are significant determinants of menstrual distress, reflecting typical symptoms of deep endometriosis [17]. Altered bowel habits, including diarrhea, constipation, and bloating are common in patients with endometriosis and may mimic or coexist with bowel disorders [18].

Our results from MEDI-Q support a relevant role played also by dyspareunia and reduced sexual drive in determining menstrual distress, and act as additional factors negatively impacting QoL [19]. Endometriosis entails also a significant impact on psychological side, self-esteem, body image, self-efficacy and social functioning [9]. Furthermore, pain leads to a vicious cycle, inhibiting the sexual response and causing a sexual dysfunction in terms of poor intimacy, arousal, satisfaction and orgasm [20].

Beyond physical symptoms, menstrual distress in endometriosis is frequently accompanied by cognitive impairment (often described as "brain fog"), and insomnia [21], and together contribute to substantial emotional and functional burden. Among women with endometriosis, poorer quality of sleep, higher daytime sleepiness and more severe insomnia are referred, confirming our results from MEDI-Q. The concentration impairment as one of the determinants of menstrual distress in endometriosis is related to the detrimental effect of pain, especially chronic pelvic pain [22] and leads to a substantial fatigue burden and reduced work productivity [23,24]. The higher level of stress could also explain the significant incidence of mental health disorders (mainly depressive and anxiety symptoms) in patient with endometriosis, since some common mental health disabilities are connected with stress [25].

In our study population, menstrual distress was significantly linked to feeling uncomfortable with bleeding, particularly in women with coexistent endometriosis and adenomyosis. HMB, a common symptom among patients with adenomyosis, as well as uterine fibroids [26], is known to increase perceived stress and impair QoL through iron deficiency anemia, fatigue, and iron-related mood changes [31–34]. These findings highlight the importance of assessing bleeding-related symptoms alongside pain to better understand menstrual distress and its impact in endometriosis, especially when adenomyosis coexists [27].

One of the main strengths of this study is its comprehensive assessment of menstrual distress in women with endometriosis, extending beyond dysmenorrhea to include gastrointestinal function, nutrition, sleep, cognition, and sexual drive. The study focused on a well-defined cohort of newly diagnosed patients, minimizing the influence of long-standing disease and prior treatments. MEDI-Q may serve both to identify women at risk and to pinpoint the most affected domains of QoL, supporting a holistic approach to care over the past 12 months.

Despite its contributions, this study has several limitations that should be acknowledged. Its cross-sectional design prevents causal inferences between menstrual distress and disease severity. Longitudinal data would be necessary to understand how symptoms evolve over time and respond to treatment. Reliance on self-reported measures may introduce recall bias. Additionally, cultural factors and social stigma affecting symptom reporting are not fully captured. The small sample size may limit generalizability and the ability to explore relationships between comorbidities and menstrual distress. Future prospective studies with larger, more diverse cohorts are needed to strengthen the evidence and better understand symptom evolution and treatment effects.

Menstrual distress, encompassing physical, emotional, and functional symptoms associated with menstruation, holds important clinical implications, especially in the diagnosis and management of endometriosis. Persistent or severe menstrual distress may serve as an early indicator of underlying pathology, yet it is often normalized or overlooked in clinical practice. Recognizing menstrual distress as a legitimate and measurable clinical entity can facilitate earlier identification of conditions that are frequently underdiagnosed, such as endometriosis or adenomyosis. Incorporating systematic assessment of menstrual distress into routine gynecological evaluations could enhance symptom profiling, guide referral for specialized care, and improve patient-clinician communication. Furthermore, addressing menstrual distress holistically may support more personalized treatment strategies, including pain management, hormonal therapies, and psychological support. This approach also aligns with a broader, patient-centered model of care, emphasizing QoL and functional outcomes rather than solely clinical disease markers. As such, menstrual distress should be recognized not only as a symptom but as a critical dimension of reproductive health with direct implications for diagnosis, treatment, and long-term well-being.

The recognition of menstrual distress as a significant component of the endometriosis symptom profile carries important implications for future research. Investigating menstrual distress as a multidimensional construct offers an opportunity to deepen understanding of patient

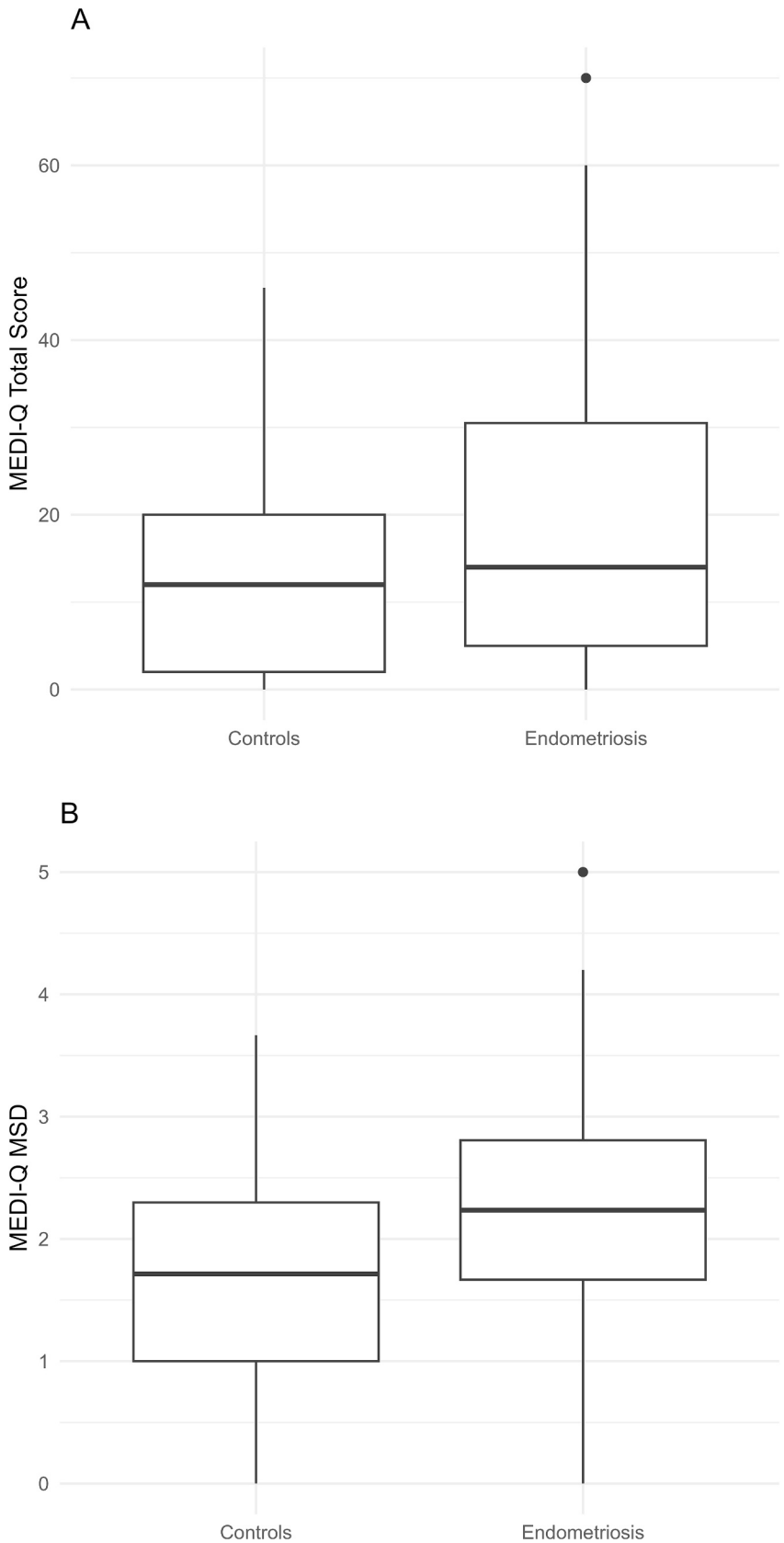

Fig. 1. Box plots for Menstrual Distress Questionnaire (MEDI-Q) Total Score (1A) and subscale Menstrual Symptoms Distress MSD (1B) in patients with endometriosis and controls.

Table 3
Distress score for each item determining the global menstrual distress, reported as mean, standard deviation, median, 25th and 75th percentiles, and percentage of participants in that group reporting absence of that specific symptom. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Item number	Item description	Controls (n = 75)	Endometriosis (n = 75)	Statistic
Item 1	Lower abdominal pain	1.80 ± 1.73 1.00 [0.00—-3.00]; 41.33 %	2.01 ± 1.77 2.00 [0.00—-4.00]; 34.67 %	3.03
Item 2	Urinary pain	0.06 ± 0.39 0.00 [0.00—-0.00]; 97.33 %	0.28 ± 0.88 0.00 [0.00—-0.00]; 86.67 %	14.19***
Item 3	Pain at defecation	0.12 ± 0.53 0.00 [0.00—-0.00]; 94.67 %	0.67 ± 1.36 0.00 [0.00—-1.00]; 73.33 %	38.47***
Item 4	Muscle/ osteoarticular pain	0.82 ± 1.29 0.00 [0.00—-1.00]; 60.00 %	0.85 ± 1.39 0.00 [0.00—-1.50]; 64.00 %	0.26
Item 5	Breast tenderness/ widespread swelling sensation	0.72 ± 1.09 0.00 [0.00—-1.00]; 69.33 %	0.83 ± 1.34 0.00 [0.00—-2.00]; 66.67 %	0.69
Item 6	Nausea	0.37 ± 0.95 0.00 [0.00—-0.00]; 86.67 %	0.72 ± 1.39 0.00 [0.00—-1.00]; 73.33 %	12.41***
Item 7	Headache	0.77 ± 1.22 0.00 [0.00—-1.50]; 62.67 %	0.92 ± 1.50 0.00 [0.00—-1.00]; 62.67 %	0.87
Item 8	Pain during sexual intercourse	0.13 ± 0.60 0.00 [0.00—-0.00]; 96.00 %	0.47 ± 1.24 0.00 [0.00—-0.00]; 85.33 %	14.58***
Item 9	Digestive problems	0.36 ± 0.86 0.00 [0.00—-0.00]; 81.33 %	0.45 ± 1.02 0.00 [0.00—-0.00]; 77.33 %	1.16
Item 10	Diarrhea	0.54 ± 1.02 0.00 [0.00—-0.00]; 77.33 %	0.80 ± 1.39 0.00 [0.00—-1.00]; 62.67 %	4.81*
Item 11	Constipation	0.14 ± 0.50 0.00 [0.00—-0.00]; 92.00 %	0.33 ± 0.95 0.00 [0.00—-0.00]; 84.00 %	5.45*
Item 12	Feeling uncomfortable about vaginal blood loss	1.02 ± 1.49 0.00 [0.00—-2.00]; 62.67 %	1.37 ± 1.77 0.00 [0.00—-2.00]; 53.33 %	4.09*
Item 13	Feeling of being impure	0.11 ± 0.55 0.00 [0.00—-0.00]; 94.67 %	0.24 ± 0.75 0.00 [0.00—-0.00]; 86.67 %	2.72
Item 14	Sadness	1.13 ± 1.46 0.00 [0.00—-1.00]; 54.67 %	1.23 ± 1.56 0.00 [0.00—-2.00]; 50.67 %	1.12
Item 15	Emotional lability	1.31 ± 1.50 1.00 [0.00—-2.00]; 46.67 %	1.19 ± 1.59 0.00 [0.00—-2.00]; 56.00 %	0.00
Item 16	Irritability/anger	1.24 ± 1.43 1.00 [0.00—-2.00]; 46.67 %	1.21 ± 1.65 0.00 [0.00—-2.00]; 54.67 %	0.00
Item 17	Impulsiveness	0.24 ± 0.72 0.00 [0.00—-0.00]; 89.33 %	0.44 ± 1.03 0.00 [0.00—-0.00]; 80.00 %	3.41
Item 18	Anxiety	0.48 ± 1.04 0.00 [0.00—-0.00]; 84.00 %	0.71 ± 1.27 0.00 [0.00—-1.50]; 70.67 %	3.78
Item 19	Increased appetite	0.71 ± 1.17 0.00 [0.00—-0.00]; 80.00 %	0.64 ± 1.27 0.00 [0.00—-1.00]; 72.00 %	0.16
Item 20	Decreased appetite	0.15 ± 0.66 0.00 [0.00—-0.00]; 90.67 %	0.36 ± 1.07 0.00 [0.00—-0.00]; 85.33 %	5.82*
Item 21	Insomnia	0.18 ± 0.73 0.00 [0.00—-0.00]; 92.00 %	0.40 ± 1.10 0.00 [0.00—-0.00]; 84.00 %	5.57*
Item 22	Hypersomnia	0.40 ± 0.98 0.00 [0.00—-0.00]; 88.00 %	0.60 ± 1.24 0.00 [0.00—-0.00]; 76.00 %	2.96
Item 23	Fatigue	1.29 ± 1.52 1.00 [0.00—-2.00]; 48.00 %	1.31 ± 1.66 0.00 [0.00—-2.00]; 53.33 %	0.20
Item 24	Decreased sexual drive	0.26 ± 0.79 0.00 [0.00—-0.00]; 84.00 %	0.64 ± 1.32 0.00 [0.00—-0.50]; 74.67 %	8.66**
Item 25	Concentration impairment	0.39 ± 0.97 0.00 [0.00—-0.00]; 82.67 %	0.63 ± 1.28 0.00 [0.00—-0.00]; 77.33 %	4.76*

experiences. It also opens pathways for developing more comprehensive patient-reported outcome measures that can capture the full scope of menstrual-related suffering. Longitudinal studies are particularly needed to assess how menstrual distress evolves over time and in response to interventions, which could inform more personalized approaches to disease management.

Conclusions

Patients with endometriosis report high menstrual distress scores, which extend beyond dysmenorrhea to include dysuria, dyschezia, dyspareunia, as well as disturbances in gastrointestinal function, sleep, sexual activity, cognition, and eating or concentration. Systematically assessing menstrual distress and its determinants and integrating this information into diagnostic frameworks can enable more personalized and timely interventions, ultimately improving patient outcomes and QoL.

CRediT authorship contribution statement

Silvia Vannuccini: Writing – original draft, Data curation, Conceptualization. **Francesco La Torre:** Investigation, Data curation. **Ernesto Gallucci:** Investigation, Data curation. **Anna Rosa Speciale:** Investigation, Data curation. **Eleonora Rossi:** Writing – review & editing, Formal analysis. **Emanuele Cassioli:** Writing – review & editing, Formal analysis. **Valdo Ricca:** Supervision, Conceptualization. **Giovanni Castellini:** Writing – review & editing, Supervision, Conceptualization. **Felice Petraglia:** Writing – review & editing, Supervision, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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