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Original Article

Mood spectrum in patients with endometriosis

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SUMMARY

Objective

To assess the relationship between endometriosis-related pain, and mood symtoms.

Method

Forty-seven outpatients diagnosed with endometriosis were assessed using the MOODS-SR questionnaire for mood symptoms and VAS score for pain. Statistical analyses included Pearson's correlation coefficient (r) and linear regression models.

Results

Dyspareunia correlated positively with depressive mood (p = . 020), energy in depressive (p = . 002) and manic (p = . 045) states, cognition in depressive states (p = . 028), and rhythmicity (p = . 001). Chronic pelvic pain correlated with depressive mood (p = . 003), energy (p < .001) and cognition (p = . 005) in depressive states and rhythmicity (p = . 016). Linear regression models demonstrated dyspareunia's predictive relationship with depressive mood (p = . 020), energy levels during depressive (p = . 002) and manic (p = . 045) states, cognitive dysfunction during depressive phases (p = . 028) and rhythmicity (p = . 001). Chronic pelvic pain was correlated with depressive mood (p = . 003), energy level (p < . 001) and cognitive dysfunction (p = . 005) in depressive states, and rhythmicity (p = . 016).

Conclusion

The study suggests an association between dyspareunia, chronic pelvic pain and mood disturbances emphasizing the necessity for a multidisciplinary approach to endometriosis management that considers mental health of patients.

Key words: mood, mood spectrum, endometriosis, pelvic pain

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Introduction

Endometriosis is a chronic estrogen-dependent inflammatory disease characterized by the presence of ectopic endometrial glands and stroma, predominantly, but not exclusively, in the pelvic region. It is marked by the presence of pain and infertility [1] with an estimated prevalence of approximately 10% in women of reproductive age [2]. The etiopathogenesis of endometriosis is still unknown, although there is increasing evidence that it results from interactions between immunological, genetic, hormonal, and environmental factors [3]. The primary clinical manifestations of the disease are the presence of painful symptoms such as dysmenorrhea, chronic pelvic pain (somatic pain), dysuria, dyschezia, dyspareunia, and infertility, which may occur alone or, more commonly, in various combinations [4]. Pelvic pain symptoms are often associated with a higher risk of developing other chronic painful syndromes involving bladder dysfunction, vulvodynia, and irritable bowel syndrome, which involve multiple systemic mechanisms and negatively affect the quality of life and psychosocial functioning of these patients [5].

According to the literature, women with endometriosis, especially those

with chronic pelvic pain, appear to have a higher susceptibility to developing psychiatric disorders, especially mood and anxiety disorders [6].
However, the relationship between mental health and endometriosis remains unclear and poorly understood. Given that chronic pelvic pain is the most commonly reported symptom of endometriosis, some studies have hypothesized that mental health and quality of life tend to correlate with pain intensity [7].
Other studies have reported that women with endometriosis and chronic pelvic pain present a higher prevalence of depression compared to those with asymptomatic endometriosis. This suggests that the link between endometriosis and depressive symptoms is largely determined by chronic pain symptoms, and may also be influenced by individual and environmental vulnerability factors [8].
Our study aims to assess whether endometriosis and chronic pelvic pain influence the onset and/or the exacerbation of affective symptoms and whether there is a significant association between endometriosis and mood disorders.

Materials and methods

An observational study was conducted at the Department of Gynecology, University Hospital of Siena, recruiting 47 female outpatients diagnosed with endometriosis, none of them had a diagnosed psychiatric pathology. The study included patients of reproductive age, between 18 and 45 years, with a surgical or ultrasound diagnosis of endometriosis. Exclusion criteria included subjects under 18 or over 45 years of age, postmenopausal patients, patients without evidence of active disease after surgery, patients on medical treatment without disease manifestations, pregnant patients and patients diagnosed with a psychiatric disorder.
Assessment tools included the Mood Spectrum Self-Report (MOODS-SR) - Last Month questionnaire [9, 10], a self-administered test designed to assess mood disorders across a spectrum that includes both manifest and subthreshold symptoms of mania and depression.
It is a self-administered test with a 'yes' or 'no' response to 161 items reflecting mood over a period of at least 3-5 days in the previous month.
The MOODS-SR - Last Month questionnaire is divided into four main domains:
- Mood: This domain assesses the spectrum of depressive symptoms (items 1-27) and manic symptoms (items 29-56).
- Energy: This domain assesses the psychomotor retardation and fatigue associated with depressive states (items 58-66) and contrasts it with the increased energy or agitation characteristic of manic states (items 68-79).
- Cognition: This domain assesses cognitive aspects in depression (items 81-107), including difficulties with concentration, decision-making, and memory, and in mania (items 109-130), such as racing thoughts, distractibility, and grandiose planning.
- Rhythmicity: This domain assesses the cyclicity of mood, energy, and cognitive symptoms (items 132-160) to explore fluctuations in these patterns over time.
The MOODS-SR does not establish a diagnostic threshold; it is a spectrum-focused instrument that delineates the continuum of mood symptomatology, emphasizing the dimensional aspects of mood that do not always meet the conventional criteria for a mood disorder diagnosis [11].
Pain related to endometriosis (specifically dysmenorrhea, dyspareunia, ovulatory pain, chronic pelvic pain, dyschezia and dysuria) was measured using the Visual Analogue Scale (VAS), a 10 cm line where 0 corresponds to no pain and 10 corresponds to the worst possible pain, within which the patient must quantify her pain level.
Statistical analyses were performed using SPSS for Windows, using Pearson's correlation coefficient (r) to analyze the relationship between MOODS-SR questionnaire domains and VAS scores for different types of endometriosis-related pain, and linear regression models to further understand the predictive value of pain severity on mood disturbance.

Results

The mean age of the 47 adult patients participating in the study, all diagnosed with endometriosis, had a mean age of 37.5 years, with an age range of 25 to 45 years. All women included in the analysis of results were on hormonal therapy for disease control and symptom management. Among the painful symptoms associated with endometriosis, dyspareunia was reported by 16 patients (mean VAS: 2.55), while 13 women complained of dysmenorrhea (mean VAS: 2. 69), 10 participants had chronic pelvic pain (mean VAS: 0.88), 8 reported dyschezia (mean VAS: 1.07), 6 patients experienced mid-cycle pain (mean VAS: 1.16), and only 3 perceived dysuria (mean VAS: 0.42).
We examined the relationship between the total scores of the domains of the MOODS-SR scale and the VAS scores for patient-reported pain symptoms. Statistically significant positive correlations were found between the VAS scores for dyspareunia and the MOODS-SR domains for depressive mood ($p = .020$), energy in depressive states ($p = .002$), energy in manic states ($p = .045$), cognitive aspects in depressive states ($p = .028$), and rhythmicity ($p = .001$) (Tab. I). Similarly, chronic pelvic pain was positively correlated with depressive mood ($p = .003$), energy in depressive states ($p < .001$), cognitive aspects in depressive states ($p =$.

TABLE I. *Dyspareunia and MOOD-SR-Last month's domains.*

		Pearson's correlation	Sig. (2-tailed)	R^2
Dyspareunia	Depressive mood	.338	.020 The correlation is significant at the 0.05 level (two-tailed)	.114
	Energy in depressive states	.440	.002 The correlation is significant at the 0.01 level (two-tailed)	.193
	Energy in manic states	.293	.045 The correlation is significant at the 0.05 level (two-tailed)	
	Cognitive aspects in depressive states	.321	.028 The correlation is significant at the 0.05 level (two-tailed)	.103
	Rhythmicity	.451	.001 The correlation is significant at the 0.01 level (two-tailed)	.204

005), and rhythmicity (p = . 016) (Tab. II).

Given the observed correlations of both dyspareunia and chronic pelvic pain with four domains of the MOODS-SR scale, three of which concern depressive aspects, we used linear regression models to further examine the relationship between these two symptoms and mood disorders.

For dyspareunia, we observed a significant predictive relationship with the severity of depressive mood symptoms (p = . 020). Higher dyspareunia VAS scores were also significantly correlated with energy levels during depressive states (p = . 002) and during hypo/manic episodes (p = . 045), as well as with cognitive dysfunction during depressive phases (p = . 028) and with rhythmicity (p = . 001) (Tab. I). Chronic pelvic pain was significantly correlated with depressive mood (p = . 003), energy level in depressive states (p < . 001), cognitive dysfunction in these states (p = . 005), and rhythmicity of mood fluctuations (p = . 016) (Tab. II).

According to the coefficient of determination (R^2) values, energy levels during depressive states were significantly influenced by chronic pelvic pain (R^2 value of 0.302). Dyspareunia was also a significant predictor of mood rhythmicity (R^2 = 0.204) and energy in depressive states (R^2 = 0.193), suggesting a significant effect of pain on these mood parameters.

Cognitive disturbances during depressive states were less affected by pain severity, with dyspareunia explain-

TABLE II. *Chronic pelvic pain and MOOD-SR-Last month's domains.*

		Pearson's correlation	Sig. (2-tailed)	R^2
Chronic pelvic pain	Depressive mood	.430	.003 The correlation is significant at the 0.01 level (two-tailed)	.185
	Energy in depressive states	.549	< .001 The correlation is significant at the 0.01 level (two-tailed)	.302
	Cognitive aspects in depressive states	.401	.005 The correlation is significant at the 0.01 level (two-tailed)	.161
	Rhythmicity	.351	.016 The correlation is significant at the 0.05 level (two-tailed)	.123

ing 10.3% of the variance (R^2 = 0.103) and chronic pelvic pain explaining 16.1% (R^2 = 0.161). The influence of chronic pelvic pain on the rhythmicity of mood symptoms was moderate (R^2 = 0.123), reflecting a less pronounced effect on this mood aspect.

Discussion

In this study, we observed positive correlations between the VAS scores for dyspareunia and the MOODS-SR domains for depressive mood (p = . 020), energy in depressive states (p = . 002), energy in manic states (p = .045), cognitive aspects in depressive states (p = . 028), and rhythmicity (p = . 001). Similarly, chronic pelvic pain was positively correlated with depressive mood (p = . 003), energy in depressive states (p < .001), cognitive aspects in depressive states (p = . 005), and rhythmicity (p = . 016).

These findings suggest an association between the experience of pain associated with endometriosis and mood disturbances. Chronic inflammation may additionally disrupt the HPA axis, both of which might also intervene in the relationship among endometriosis, pain, and mood disorders. Increased pro-inflammatory cytokines (such as IL-6 and TNF-α) would thus contribute to pain sensitization and HPA dysregulation, which may lead to an increased risk of mood disorders [12]. Furthermore, the cytokine-induced interference with serotonergic and dopaminergic systems further connects inflammation with depression and anxiety in endometriosis [13] Moreover, serotonin and dopamine dysregulation may underlie the bidirectional relationship between endometriosis-associated pain and mood disturbances. Serotonin dysfunction contributes to decreased pain thresholds and increased affective dysregulation, while dopaminergic alterations, particularly in the mesolimbic system, exacerbate anhedonia and pain perception. Additionally, chronic pain states are associated with increased glutamatergic activity in pain-processing brain regions and impaired descending inhibitory control, promoting central sensitization. [14 15 16 17]. Additionally, chronic pain itself alters neurotransmitter balance, promoting a state of central sensitization that perpetuates both nociceptive processing and affective dysregulation[18]. Although we could not determine the direction of causality – whether endometriosis pain worsens mood symptoms or vice versa – we believe the two conditions negatively influence each other, with mood symptoms intensifying pain perception and pain exacerbating mood disturbances. The inclusion of baseline temperament assessments, such as depressive or anxious temperament, could provide further insights into how pre-existing traits interact with mood disturbances in endometriosis patients. Previous studies have shown that harm avoidance temperament [19], the presence of depressive symptoms, and high levels of trait and state anxiety positively correlate with pain severity in women with endometriosis [20]. Assessing these temperament traits at baseline could help elucidate their role in predisposing individuals to mood disorders and influencing the perception and management of chronic pelvic pain in endometriosis. In this complex interplay, hormonal therapies such as progestins and GnRH agonists represent a key management strategy. While they effectively reduce endometriosis-associated pain, they may also influence mood symptoms. Although some patients experience mood disturbances as a side effect, these symptoms tend to diminish over time, and the overall risk-benefit balance remains favorable, given the significant pain relief and improvement in quality of life they provide [21].

These findings are consistent with existing literature linking chronic pain conditions to psychiatric morbidity, particularly mood disorders. A large cohort study that endometriosis increases the risk of psychiatric disorders, particularly in the years immediately following the diagnosis reinforcing the role of chronic inflammation and stress-system dysregulation in mood disturbances [22]. The findings were in line with our results, further strengthening the involvement of neuroimmune interactions and neurotransmitter dysregulation in the bidirectional relationship between endometriosis, pain, and affective symptoms.

Chronic pain, such as that experienced in endometriosis, can lead to a decrease in quality of life and contribute to the development or exacerbation of mood disorders such as depression and anxiety [23]. Dyspareunia can also have a profound psychosocial impact by affecting intimate relationships and self-image, and can lead to avoidance behaviors, reduced sexual satisfaction, and impaired partner relationships, all of which can contribute to mood disturbances [24,25]. Dyspareunia can also lead to the development or exacerbation of mood disorders such as depression and anxiety. The relationship between increased energy in manic states and dyspareunia is not well-established and requires further investigation. While the positive correlation between manic hypersexuality and unprotected sex may potentially influence pain perception during sexual intercourse, this hypothesis remains speculative. Further studies are needed to explore this connection in more detail and clarify its implications for patients experiencing both manic states and dyspareunia.

The small sample size, although adequate for preliminary findings, may limit the generalizability of the results and the absence of a control group may have contributed to the underpowering of it.

Conclusions

In conclusion, the aim of this study was to investigate

the influence of endometriosis on affective symptoms and their association with mood spectrum disorders. The significant associations found between pain intensity and mood symptoms reflect the complex interplay between physical and psychological aspects of endometriosis. Future research should examine these relationships longitudinally and in larger cohorts, incorporating the assessment of temperament traits, to further understand the mechanisms underlying this association and to develop comprehensive treatment strategies that consider both psychological and temperament-related factors, ultimately improving quality of life and psychosocial outcomes for women with endometriosis. The identification of biological factors of psychological vulnerability (such as premorbid temperaments), stress response, and pain sensitivity allows for early intervention on pelvic pain and a personalized treatment approach based on the characteristics of patients with endometriosis. These findings have important implications for clinical practice, highlighting the need for a multidisciplinary approach to endometriosis management that does not underestimate the importance of these women's mental health, but rather considers it as an element to be investigated during the gynecologic examination.

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Conflict of interest statement

None.

Authors' contributions

Conceptualization: AM, EZ, AF, IC, LL; data curation: SB; formal analysis SB; investigation: IC; methodology: EZ, AF, FV, SB, AG, LL; project administration: EZ, AF, FV, SB, AG, LL; resources: IC; supervision: AG, LL; writing – original draft: AM, FV; Writing – review and editing: AM, AF, FV, AG, AC, SP.

Ethical consideration

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the Regional Ethics Committee for Clinical Experimentation of Tuscany (Approval Reference Number: 25699).

Written informed consent, including research objectives and procedures, was obtained from each participant before their inclusion in the study. Confidentiality and anonymity of the participants were strictly maintained throughout the study, and all collected data were used solely for research purposes.

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