ENDOMETRIOSIS, PAIN AND MENTAL HEALTH

Bernarda Škegro[1], Sarah Bjedov[2], Mislav Mikuš[3,4], Filip Mustač[2], Joško Lešin[3,4], Valentina Matijević[1,5], Mario Ćorić[3,4], Vesna Elveđi Gašparović[3,4], Filip Medić[6] & Vesna Sokol Karadjole[3,4]

[1]*Department of Rheumatology, Physical Medicine and Rehabilitation, University Hospital Center Sestre milosrdnice, Zagreb, Croatia*
[2]*Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb, Zagreb, Croatia*
[3]*Department of Obstetrics and Gynecology, University Hospital Centre Zagreb, Zagreb, Croatia*
[4]*University of Zagreb, School of Medicine, Zagreb, Croatia*
[5]*Libertas International University, Zagreb, Croatia*
[6]*Ministry of Defence of the Republic of Croatia, Zagreb, Croatia*

SUMMARY

Background: Endometriosis is a chronic and progressive disease which can significantly affect a woman's personal, as well as intimate and professional aspects of life. The aim of this study was to asses health-related quality of life and mental health status in patients with endometriosis, investigating also their relationship with endometriosis-related comorbid symptoms and conditions, such as pain and infertility.

Subjects and methods: An observational cross-sectional study involved 79 women with endometriosis. All patients filled the Endometriosis Health Profile (EHP-5), the Depression Anxiety Stress Scales (DASS-21) and the Visual Analogue Scale (VAS). Their medical data were retrieved from medical records. Data was analyzed using the SPSS 23.0 (IBM Corp., Armonk, NY).

Results: Of all the patients evaluated in our study, 44.3% presented depressive symptoms and 25.3% presented anxiety, while 31.7% reported stress symptoms. Moderate correlations were found between results on EHP-5 and depression (r=0.515), stress (r=0.558) and VAS score (r=0.565). Furthermore, weak positive relationship was observed between EHP-5 and anxiety (r=0.295) and infertility (r=0.267). Additionally, moderate correlation was found between depression and infertility (r=0.519), while there was weak association between VAS score and stress (r=0.236).

Conclusions: This study showed complex relationships between symptoms and conditions manifesting in patients with endometriosis. Due to diversity of symptoms, potentially including mental health issues, it is important to emphasize the need for combined personalized treatment for these patients, taking into account both physical and psychological aspect of the disease.

Key words: endometriosis - pain - mental health

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INTRODUCTION

Endometriosis is a chronic and progressive disease, characterized by the presence of endometrial glands and stroma like lesions outside of the uterus. The prevalence is 10-15% of all women of reproductive age (Parasar et al. 2017).

Clinical presentation of endometriosis has variety of symptoms - chronic pelvic pain, subfertility, dysmenorrhea, alterations in menstrual cycles, etc. (La Rosa et al. 2019, Aubry et al. 2017). The usual three subtypes of endometriosis refer to peritoneal, cystic ovarian and deep infiltrating endometriosis (DIE) (La Rosa et al. 2019).

According to the WHO definition, quality of life is a complex construct made up of an individual's perception of their own position in life, and depends on goals, expectations, standards and concerns, and is related to a culture and value system, so we can conclude that it is a matter of subjective perception in a social and environmental context (WHO 1999).

People who suffer from a chronic illness or condition are exposed to a negative challenge for a long time, which can be accompanied by a high amount of stress, sometimes discrimination, and this can lead to a predominance of negative effects versus positive ones in people with chronic illness or condition so they are vulnerable and may develop depressive symptoms (Rush & Misajon 2018, Mead & Cummins 2010).

Women suffering from endometriosis often have lower health-related quality of life (HrQoL) compared to women without endometriosis. Recent meta-analysis has shown that women with endometriosis also have more depressive symptoms, while other studies have demonstrated a greater incidence of anxiety in women with endometriosis (La Rosa et al. 2019, Sepulcri et al. 2008, Gambadauro et al. 2018, Laganà et al. 2017, Chen et al. 2016).

Since chronic pelvic pain is the most common symptom of endometriosis, as well as the primary reason for treatment, it has been thought that HrQoL and mental health tend to correlate with the intensity of pain (Gambadauro et al. 2018, Gerlinger et al. 2010, Facchin et al. 2015).

However, later research has concluded that the intensity of pain does not really depend on the severity of the degree of endometriosis, which raises the question of whether mental health has a modulating effect because it has been shown that psychoemotional distress and alexithymia may change pain perception in patients with endometriosis (La Rosa et al. 2019, Cavaggioni et al. 2014).

Furthermore, endometriosis is often accompanied by infertility which affects sexual functioning, self-confidence and relationship of the couple which can certainly further derive the propensity for anxiety and depressive symptoms (La Rosa et al. 2019, Fassino et al. 2002)

Overall, endometriosis can significantly affect a woman's personal, as well as intimate and professional aspects of life (Friedi et al. 2015).

Therefore, the aim of this study was to asses health-related quality of life and mental health status in patients with endometriosis, investigating also their relationship with endometriosis-related comorbid symptoms and conditions, such as pain and infertility.

SUBJECTS AND METHODS

Participants and study design

This observational cross-sectional study involved 79 women who were treated at the Department of Obstetrics and Gynecology, University Hospital Centre Zagreb, Croatia between January 2020 and June 2020. Mean age of our sample was 35.03±7.11 years (range 20-52 years).

Inclusion criteria were: 1) females ≥18 years; 2) surgically diagnosed/histopathologically confirmed endometriosis; 3) literate in Croatian; 4) ability to independently understand the questions in the questionnaires.

Exclusion criteria were as following: 1) women who could not read Croatian; 2) women with associated pelvic pathology; 3) women who were initially referred for other reasons than endometriosis associated pain symptoms; 4) lack of informed consent.

The purpose of the study was stated in informed consent and all the subjects signed it before inclusion. After that participants completed questionnaires and their medical data were retrieved from Department's medical records. The study was approved by the Institutional Review Board (No. 2020/0034-1) and adhered to all the principles of the Declaration of Helsinki. This study is part of study protocol available at clinicaltrials.gov (Identifier: NCT04491305).

Questionnaires

The EHP-5 (Endometriosis Health Profile) is an instrument for measuring health-related quality of life in endometriosis. It is a two-part questionnaire reffering to the last 4 weeks. The first part is a 5-item core questionnaire including questions about pain, control and powerlessness, emotions, social support and self-image. The second part is a 6-item modular questionnaire that consists questions that may not be applicable to every woman with endometriosis. Those 6 items reffer to work life, relation with children, sexual intercourse, medical profession, treatment and infertility. Each of the 11 items is scored on a Likert-type scale with the range from 0=never to 4=always. The second part also has an option not applicable. Scores are then transformed on a scale 0-100, with 0=best possible health status, 100=worst possible health status (Jones et al. 2004, Aubry et al. 2017, Goshtasebi et al. 2011). The translation of the EHP-5 to Croatian followed standardized procedure in which expert group, consisted of two gynecologists, a methodologist and an authorized translator, ensured cross-cultural equivalence of questionnaire. The initial translation was carried out independently by the two gynecological surgeons, experts in the field of endometriosis. After that they met and discussed discrepancies in translation and created a new, joint version of EHP-5 questionnaire. A new version was then sent to an authorized translator who did not have access to the original version. Finally, an expert group met to review all versions of the translations and concluded that there were no major discrepancies and to ensure that the final version of a translated questionnaire is culturally congruent. Preliminary pilot-testing was conducted on a small sample (N=20) in order to check if participants understood questions and were asked for suggestions on how to improve the questionnaire. Preliminary results showed that all items from EHP-5 were easily understandable and that the questionnaire was well received.

Depression Anxiety Stress Scales (DASS-21) is a three-dimensional scale assessing both the presence and intensity of depression, anxiety and stress in last week. Each item is scored on a 4-point Likert scale with values from 0=did not apply to me at all to 3=applied to me very much or most of the time. Each of the scales consists 7 items and the total score for each one of them is calculated by summing these 7 items and then multiplying them by 2. A higher score indicates a higher intensity of depression, anxiety and stress. The authors recommended cut-off scores for each scale and based on them are suggested labels as follows: normal, mild, moderate, severe and extremely severe (Lovibond & Lovibond 1995, González-Rivera et al. 2020). For the purpose of this study, we used Croatian adaptation and translation of the English version of the DASS-21 (Ivezic et al. 2012).

A Visual Analogue Scale (VAS) is an unidimensional measure of pain intensity. Score is based on self-reported measure on a 10 cm (100 mm) line that represents the continuum between the left end 0=no pain and 10=worst pain on the right end of the scale. Scores are expressed as values between 0 and 100, by measuring the line in millimeters. (Klimek et al. 2017, Delgado et al. 2018).

Statistical analysis

Once the data was collected, we analyzed it using the SPSS 23.0 (IBM Corp., Armonk, NY). Continuous data is presented as arithmetic mean ± standard deviation (SD), while discrete data is presented as frequencies and percentages. Pearson's and Spearman's correlation coefficients were calculated in order to establish the relationship between EHP-5 results and demographic, gynaecological and psychological factors. Significance level was set as $p < 0.05$.

RESULTS

As seen from Table 1, majority of our participants graduated from university with either master (38%) or bachelor's degree (35.4%); are married (68.3%) and didn't give a birth (53.2%). 22.8% women in our study were infertile. Body mass index was on average 23.58 (sd=3.89).

On DASS-21 scale, 44.3% women reported mild, moderate or severe difficulties regarding depressive symptoms, while more than half of our sample was classified within range of normal values for depression (55.7%). More than one quarter of woman had disturbances on

Anxiety subscale (25.3%), while 31.7% reported difficulties on Stress subscale. The average score on EHP-5 questionnaire was M=37.03, with the range from 0 to 75 (Table 2).

We found no significant correlation between demographic data and EHP-5 (p>0.05), thus we did not report those correlation in Table 3. As seen from Table 3, we found moderate correlations between results on EHP-5 and depression (r=0.515), stress (r=0.558) and VAS score (r=0.565), indicating that women who have worse health status measured by the EHP-5 have also significantly higher symptoms of depression, stress and pain. Furthermore, weak positive relationship was observed between EHP-5 and anxiety (r=0.295) and infertility (r=0.267), suggesting that those participants who reported worse health status also reported more anxiety symptoms and worse health status was in correlation with infertility. Additionally, moderate correlation was found between depression and infertility (r=0.519), while weak correlation was observed between VAS score and stress (r=0.236).

DISCUSSION

The present study investigated the relationships between health-related quality of life, psychopathological symptoms, intensity of pain and infertility in patients with endometriosis. Our findings show that 44.3% of patients with endometriosis reported difficulties regarding depression. While health related quality of life exhibited a moderate correlation with pain, as well as with depressive symptoms, pain was not found to be significantly linked to depressive symptoms, but was weakly correlated with stress.

Table 1. Demographic data

	N	%
Education		
Secondary school	21	26.6
BA/BSc	28	35.4
M.A.	30	38.0
Marriage status		
Not married	16	20.3
Married	54	68.3
Divorced	9	11.4
BMI (M±sd)	23.58±3.89	
Infertility (yes)	18	22.8
DIE (yes)	11	13.9
Parity		
0	42	53.2
1	20	25.3
2	12	15.2
3	4	5.1
4	1	1.3

Table 2. Results on DASS, EHP-5 and VAS scales

	Depression	Anxiety	Stress	EHP-5	VAS
M ± sd	10.05±8.75	4.30±5.07	10.76±7.98	37.03±22.08	58.48±27.97
Range min-max	0-38	0-26	0-32	0-75	0-100
Normal (%)	55.7%	74.7%	68.3%		
Mild (%)	10.1%	10.1%	16.5%		
Moderate (%)	25.3%	12.6%	8.9%		
Severe (%)	2.5%	1.3%	6.3%		
Extremely severe (%)	6.4%	1.3%	0.0%		

Table 3. Correlations between EHP-5, DASS, infertility and VAS

	EHP-5	DEPR	ANX	STR	INFERT	VAS
EHP-5	1.000	0.515*	0.295*	0.558*	0.267**	0.565*
DEPR	0.515*	1.000	0.539*	0.670*	0.519*	0.164
ANX	0.295*	0.539*	1.000	0.660*	0.070	0.0053
STR	0.558*	0.670*	0.660*	1.000	0.136	0.236**
INFERT	0.267**	0.519*	0.070	0.136	1.000	-0.012
VAS	0.565*	0.164	0.053	0.236**	-0.012	1.000

* p<0.01; ** p<0.05

Our results suggested that intensity of pain (measured by the VAS questionnaire) is associated with worse health status (measured by EHP-5) in patients with endometriosis. Such finding is in line with research of Souza et al., who have used VAS in patients with chronic pelvic pain and concluded that higher pain scores are associated with poorer quality of life. Moreover, they claim that the mere fact of having endometriosis in addition to chronic pelvic pain has no additional impact on quality of life (Souza et al. 2011). Similarly, Facchin et al. (2015) observed that the pelvic pain was associated both with lower quality of life and higher anxiety and depression levels in comparison to patients with asymptomatic endometriosis and healthy controls. Our study did not demonstrate significant correlation between pain and depression and anxiety, even though the intensity of pain was found to be correlated with quality of life, but we observed a weak positive relationship between pain and stress symptoms.

Futhermore, our results indicate the relationship between health related quality of life in endometriosis (EHP-5) and depressive symptoms (evaluated using the DASS-21 questionnaire). Different authors pointed to higher levels of depression in patients with endometriosis, as well as to impaired quality of life (De Graaff et al. 2016, Lorençatto et al. 2006). While some authors suggest pain as a key mediator in the development of depressive symptoms (As-Sanie et al. 2012, Waller & Shaw 1995), there are also other variables proposed to have a role in affecting emotional well-being of women with endometriosis, such as personality traits, sexual dysfunctions and infertility (Vitale et al. 2017a), with the latter being found significantly correlated with depressive symptoms in our study.

The findings of this study reaffirm the importance of multidisciplinary approach in the treatment of patients with endometriosis, due to related spectrum of symptoms regarding mental health and quality of life. Nowadays, certainly advised is psychotherapy, first of all cognitive-behavioural, and then other techniques that will help in reducing anxiety and depressive symptoms. If there is suffering of an infertile couple, sexual or couple therapy should be considered (La Rosa et al. 2020, Vitale et al. 2017b).

The reason for choosing EHP-5 questionnaire for this study lies in the fact that it is a simple and efficient tool for evaluating health-related QoL in women with endometriosis. The EHP-5 is currently in a validation process in Croatia. Considering that women with higher results on EHP-5 reported more depressive symptoms in our study, as well as higher stress levels, gynecologists should be aware of psychological disturbances in women with endometriosis. Since endometriosis is a chronic disease, which can be unpleasant and is sometimes associated with infertility, it is clear that patients with endometriosis may develop mental health problems, which is supported by our results. Furthermore, cooperation between gynecologists and psychiatrists is necessary to achieve the greatest benefit for the patients. Liason psychiatry should certainly be a priority to ease the suffering of patients with endometriosis in coping with the disease itself or its consequences.

CONCLUSION

This study showed complex relationships between symptoms and conditions manifesting in patients with endometriosis. Due to diversity of symptoms, potentially including mental health issues, it is important to emphasize the significance of screening for psychiatric comorbidites, as well as the need for combined personalized treatment for these patients, taking into account both physical and psychological aspect of the disease.

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Correspondence:

Sarah Bjedov, MD
Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb
Kispaticeva 12, 10 000 Zagreb, Croatia
E-mail: sarahbjedov@gmail.com