ORIGINAL RESEARCH

Chronic Pelvic Pain in Women with Endometriosis is Associated with Psychiatric Disorder and Quality of Life Deterioration

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Background: Endometriosis is a condition associated with pelvic pain, infertility, and possibly with decreased quality of life as well as psychiatric disorder. The purpose of our study was to evaluate the association between pain characteristic, psychiatric disorder, and quality of life in women with endometriosis.

Methods: A cross-sectional study was done involving 160 women with medical diagnosis of endometriosis. Pain intensity was evaluated using Visual Analog Scale (VAS), Quality of Life with Endometriosis Health Profile (EHP-30), and psychologic condition with Mini International Neuropsychiatric Interview International Classification of Diseases (Mini-ICD).

Results: VAS and psychiatric disorder were associated with higher EHP-30 score (β = 9.3 (95% CI: 7.15–11.45; p < 0.001 and β = 28.51 (95% CI: 20.06–36.05; p < 0.001), respectively) and hence, lower quality of life. The strongest correlation between VAS and EHP-30 was in pain (r=0.586; p<0.001) and 'control and powerlessness' (r = 0.583; p < 0.001). VAS was also higher in subjects with depression (49.5 (25.4–77.8) vs 34.4 (6.1–74.6); p < 0.001).

Conclusion: We conclude that severe endometriosis-related pain and the presence of psychiatric disorder were associated with lower quality of life. Comprehensive management of endometriosis is crucial to improve patients' quality of life.

Keywords: endometriosis, pain, depression, psychiatric disorder, quality of life

Introduction

Endometriosis is a condition in which endometrium-like tissue is located outside the uterus. It is estimated that 176 million women worldwide suffer from endometriosis and 1.5 to 10% of them were in the reproductive age.[1,2] Endometriosis is associated with reduced quality of life due to chronic pelvic pain, dysmenorrhea, and dyspareunia as well as with infertility. It has been reported that 35 to 50% of women with endometriosis suffer from pain, infertility, or both.[3,4] Endometriosis symptoms can progressively impair a woman's ability to carry out some daily activities and result in a perception of worsening health status and overall wellbeing.[5]

Pain associated with endometriosis can persist after medical treatment and/or surgery, and similarly with the quality of life.[6,7] Since chronic pelvic pain is the most common symptom of endometriosis, people who suffer from a chronic illness or condition are exposed to a negative challenge for a long time.[8] Accordingly, pain management should be initiated at the beginning of the treatment. In view of endometriosis-related infertility, reproductive health is not commonly discussed in Indonesia. It appears that Indonesian parents feel awkward discussing reproduction with their children.[9] This cultural obstacle may cause participants to have little knowledge of their own parent's reproductive health history.

The purpose of our study was to evaluate the association between pain characteristic, psychiatric disorder, and quality of life in women with endometriosis using the EHP-30 and Mini ICD-10 questionnaire.

Methods

This was a cross-sectional study conducted at National Referral Hospital Cipto Mangunkusumo (RSCM), Jakarta. Between June 2019 and August 2020, we consecutively recruited women aged 18–49 years diagnosed with endometriosis. We included only those with a confirmed diagnosis of endometriosis and suffered from chronic cyclic pelvic pain for at least 6 months. The diagnosis of endometriosis was established by history taking, physical examination, visual detection of endometriotic lesions during previous surgeries, ultrasound examination, or histopathology.

All participants provided a written consent before taking part in the study. Women with chronic pelvic pain due to diseases other than endometriosis were excluded. The women who were excluded, were not undergo endometriosis evaluation. We evaluated demographic data including age, education, history of surgery, parity, body mass index (BMI), and previous medical history. Visual Analogue Scale (VAS) was used to measure pain intensity (scale 1–10); 1: no pain and 10: the worst pain imaginable.

Questionnaires

Patients were asked to fill Endometriosis Health Profile (EHP) questionnaire with a total score of 0 (best quality of life) to 100 (worst quality of life). EHP-30 questionnaire consists of two parts. The first part is a core questionnaire with 30 items applicable to women with endometriosis covering five areas including pain, emotional well-being, control and powerlessness, social support, and self-imaging scales. The second part is a modular section containing six domains, which comprised of 23 questions covering areas such as work, relationship with children, sexual activity, infertility, medical profession and treatment that are not necessarily relevant to all women with endometriosis.[10] With the assistance of an interviewer, patients completed Mini ICD-10 questionnaire. The Mini ICD-10 method was chosen because its validity and reliability, and it has been tested using CIDI (Composite International Diagnostic Interview) dan SCID (Structured Clinical Interview for DSM) as gold standards.[11] The study was approved by medical research ethics committee of Faculty of Medicine, Universitas Indonesia (Study number: KET-753/UN.2. F1/ETIK/ PPM.00.02.2019).

Statistical Analysis

Statistical analysis was conducted using SPSS version 23 (IBM, New York). We grouped the participants into two groups based on VAS value: low[3,4] and high VAS.[7–10] Data with normal distribution were presented as mean ± standard deviation while skewed data as median and range. Spearman's rank correlation analysis was used to analyze the relationship between two continuous variables that were not normally distributed. Pearson product moment test was utilized to analyze the normally distributed data. Comparison was measured using t test or Mann–Whitney U-test when appropriate. Multivariate regression analysis was done by including determinant variables with univariate p-value <0.10. A p-value of less than 0.05 was considered significant.

Results

Characteristics of the Study Population and Outcomes Distributions

The study consisted of 160 participants. Their mean duration of formal education was 12 years (56.0%) and most of them were nulliparous (46.3%); 52% had normal BMI, 47.5% were overweight. A half of the participants (50.6%) had a history of surgical treatments. Because the insurance health system in our country did not allow patients to go to a referral hospital, patients were first treated in community hospitals. When we evaluated medical treatment, we found that 45.6% of the participants had been treated with nonsteroid anti-inflammatory drugs (NSAID) and 54.4% with hormonal therapy (DMPA, Leuprorelin acetate, Dienogest, and Goserelin) (Table 1).

Table 1 Characteristic of VAS, EHP-30, and Psychiatric Disorder in Women with Endometriosis-Associated Chronic Pelvic Pain

Variable	Distribution
VAS	8(3–10)*
-3–6 (Mild-moderate pain)	41 (25.6%) **
-7–10 (Severe-very severe pain)	119 (74.4%)
EHP-30	
-Pain	63.63 (2.27–100)
-Control and powerless	54.16 (0–100)
-Emotional well-being	50 (0–100)
-Social Support	31.25 (0–75)
-Self-image	33.33 (0–91.67)
-Work	20 (0–100)
-Relationship with children	12.5 (0–100)
-Sexual Activity	20 (0–100)
-Medical profession	12.5 (0–81.25)
-Treatment	16.66 (0–83.33)
-Infertility	31.25 (0–100)
Total EHP-30 Score***	39.05 ± 14.74
Psychiatric Disorder	
-Depression	45 (28.1%)
-Dysthymia	0 (0%)
-Manic	4 (2.5%)
-Agoraphobia	0 (0%)
-Panic	7 (4.4%)
-Social Phobia	0 (0%)
-Obsessive Compulsive	1 (0.6%)
-General Anxiety	33 (20.6%)
-PTSD	0 (0%)
-Bulimia	0 (0%)
-Anorexia	0 (0%)
-Alcohol Addiction	0 (0%)
-Drug Addiction	0 (0%)
-Psychotic	5 (3.1%)

Notes: *Presented as median (minimum-maximum). **Presented as frequency (percentage). ***Presented as mean ± standard deviation.
Abbreviations: VAS, Visual Analogue Scale; EHP-30, Endometriosis Health Profile; PTSD, Post Traumatic Stress Disorder.

In view of pain score, the median VAS value was 8 (range 3–10) and we found that most participants suffered from severe pain (74%). The mean EHP score was $39 \pm 14.7\%$ with the highest score observed in the pain component (63.6%) and the "control and powerless" component (54.1%).

The most prevalent psychiatric disorder among the participants was depression (28%) followed by generalized anxiety (20%). We did not encounter other psychiatric disorders such as dysthymia, agoraphobia, social phobia, post-traumatic stress, bulimia, anorexia, alcohol dependence, and drug addiction (Table 1).

Correlation Between Pain Intensity and Quality of Life

When we evaluated the correlation between pain intensity as determined by VAS and the EHP-30 score for quality of life, we found that pain intensity significantly correlated with the total score of EHP-30 ($p < 0.001$, $r = 0.573$) (Table S1). There was also a significant correlation between VAS levels and EHP-30 components of pain ($p<0.001$), control and powerlessness ($p<0.001$), emotional well-being ($p<0.001$), social support ($p<0.001$), self-image ($p=0.002$), relationships with children ($p<0.001$), medical profession ($p=0.033$), treatment ($p=0.028$), and infertility ($p=0.001$).

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Factors Associated with Severe Pain

Table 2 shows univariate associations between demographic and clinical characteristics and pain intensity using VAS levels. We found significant associations between VAS levels and surgical history (p<0.001), Body Mass Index (BMI) with p=0.014, and psychiatric disorder (p=0.087). Table 3 shows that surgical history had the strongest significant association with pain intensity (p=0.002).

Factors Associated with Quality of Life

Univariate associations between the characteristics of the subjects and the quality of life using EHP-30 score are shown in Table 4. EHP-30 score was significantly higher, which reflected a lower quality of life, in subjects with than without psychiatric disorders. Subsequently, we found that EHP-30 score was significantly higher in subjects with than without depression 9.84 (6.07–13.60); p<0.001)) (Table S2). Other psychiatric disorders were not significantly associated with

Table 2 Univariate Analysis of the Pain Level (VAS)

Variable	VAS		p-value
	3–6 (Mild–Moderate Pain) (n = 41)	**7–10 (Severe–Very Severe Pain)** (n = 119)	
Age (years)*			0.104[a]
-<35	12 (18.8%)	52 (81.3%)	
-≥ 35	29 (30.2%)	67 (74.4%)	
Education			0.569
-0–12 years	31 (24.6%)	95 (75.4%)	
->12 years	10 (29.4%)	24 (70.6%)	
Surgical history			<0.001
-Any surgical history	11 (13.6%)	70 (86.4%)	
-No surgical history	30 (38%)	49 (62%)	
Parity			0.263
-0	17 (23.0%)	57 (77.0%)	
–1	6 (15.8%)	32 (84.2%)	
->1	18 (37.5%)	30 (62.5%)	
Body Mass Index (BMI)			0.014
-Normal weight	25 (29.8%)	59 (70.2%)	
-Overweight	16 (21.1%)	60 (78.9%)	
Past medication history			0.119
-NSAID	23 (31.5%)	50 (68.5%)	
-Hormonal	18 (20.7%)	69 (79.3%)	
Psychiatric disorder			0.087
-Present	13 (18.8%)	56 (81.2%)	
-Absent	28 (30.8%)	63 (69.2%)	
Type of disorder**			
-Depression	8	37	
-Manic	1	3	
-Agorapanic	0	7	
-Obsessive compulsive	0	1	
-General anxiety	8	25	
-Psychotic	2	3	
Depression			0.155
-Present	8 (17.8%)	37 (82.2%)	
-Absent	33 (28.7%)	82 (71.3%)	

Notes: *Presented as mean (±standard deviation). ** One subject may have multiple psychiatric disorders. [a]Data analysis using coefficient contingency (significant if p <0.1).
Abbreviations: NSAID, Nonsteroidal Anti-Inflammatory Drugs; VAS, Visual Analogue Scale.

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Table 3 Multivariate Analysis for Severe and Very Severe Pain (VAS 7–10) in Women with Endometriosis

Variable	OR (95% CI)	p-value*
Surgical history	3.571 (1.608–7.927)	0.002
Body Mass Index (BMI)	1.315 (0.612–2.824)	0.483
Psychiatric Disorder	1.726 (0.792–3.763)	0.170

Note: * Only variables with univariate p-value <0.1 from logistic regression (Table 2) were included.
Abbreviation: VAS, Visual Analogue Scale.

Table 4 Univariate Analysis of Quality of Life

Variable	EHP-30 Score*	p-value
Age		0.897
-<35	39.23 (± 14.11)	
-≥ 35	38.92 (± 15.22)	
Education		0.163
-0–12 years	39.89 (± 14.08)	
->12 years	35.91 (±16.83)	
Surgical history		0.268
-Any surgical history	85.41 (± 3.27)	
-No surgical history	80.10 (± 3.70)	
Parity		0.194
-Nullipara	36.83 (± 14.64)	
-Primipara	42.06 (± 14.36)	
-Multipara	40.09 (± 14.97)	
Body Mass Index (BMI)		0.002
-Normal weight	35.70 (±13.79)	
-Overweight	42.75 (± 14.97)	
Previous medication history		0.047
-NSAID	36.57 (± 12.75)	
-Hormonal	41.13 (± 16.01)	
VAS		<0.001
−3–6 (mild – moderate pain)	27.23 (± 13.44)	
−7–10 (severe – very severe pain)	43.12 (± 12.90)	
Psychiatric disorder		<0.001
-Present	96.47 (± 28.37)	
-Absent	72.41 (± 29.43)	
Type of disorder**		
-Depression	50.51 (± 12.18)	
-Manic	42.33 (± 13.59)	
-Agorapanic	39.35 (± 7.78)	
-General anxiety	41.59 (± 12.35)	
-Psychotic	44.52 (± 17.43)	

Notes: *Presented as mean (±standard deviation). **One subject may have multiple psychiatric disorders.
Abbreviations: EHP-30, (higher the values reflect lower the quality of life); NSAID, Nonsteroidal Anti-Inflammatory Drugs.

EHP-30 score. We also found that VAS (p<0.001) and depression (p<0.001) were independently associated with quality of life in women with endometriosis (Table S3).

There was no significant difference between history of medical management and VAS (p=0.288), EHP-30 (p=0.254), or depression (p=0.380) (Tables S4 and S5). Of interest, history of surgical management was significantly associated with VAS (p<0.001), but not with EHP-30 or depression (Tables S6 and S7).

Table 5 Multivariate Analysis of Quality of Life (EHP-30 Score) in Endometriosis Patients

Variable	Unstandardized β Coefficient (95% CI)	p-value*
Body Mass Index	5.52 (1.82–9.27)	0.007
Previous medication history	2.97 (−0.78–6.77)	0.125
VAS	13.33 (9.01–17.65)	<0.001
Psychiatric disorder	9.84 (6.07–13.60)	<0.001

Note: *Only variables with univariate p-value <0.1 from linear regression (Table 4) were included.
Abbreviations: EHP-30, Endometriosis Health Profile (higher the values reflect lower the quality of life); VAS, Visual Analogue Scale.

Multivariate analysis demonstrated that VAS and psychiatric disorders were independently associated with EHP-30 score (Table 5). Based on the formula for this linear regression model, a point increase in VAS would increase EHP-30 score by 9.30 (95% CI: 7.15–11.45; p<0.001) and psychiatric disorders would increase EHP-30 score by 28.51 (95% CI: 20.06–36.05; p<0.001).

Discussion

We found that pain and "control and powerless" were the components with the highest score in women with endometriosis. The high pain score indicates severe pain among our patients. Lower score of pain has been reported previously.[12] The high level of control and powerlessness could be attributed to the pain experienced suggesting impairment in their life control. Emotional well-being component scored high as well. This component evaluated emotional disturbances faced by the participants as well as their perception of psychiatric disorders. The components that scored low in our study were relationship with children, treatment, and medical profession, substantially lower than other studies.[12] This might be due to the unique Indonesian culture.

Depression and anxiety disorder were the most prevalent psychiatric disorder among our patients. Previous study showed that depression was higher in women due to hormonal changes.[13] Depression and generalized anxiety disorders are common in women with endometriosis.[14,15] It has been reported that those women have a high risk of developing generalized anxiety disorder and depression, alcohol addiction, and attention deficit hyperactivity disorder.[16] Endometriosis women were at highest risk of depression with a hazard ratio of 1.98 and[16] about 23% of them suffered from depression.[17] In our study, 28.1% of the participants were found to have depression.

Multivariate analysis indicated that VAS score was independently associated with EHP-30 and its components consisting of pain, control and powerless, emotional well-being, social support, self-image, relationships with children, medical profession, treatment, and infertility. Components with moderate correlation in our study were pain, control and powerless, and emotional well-being, while others showed weak correlations with VAS score. The association between chronic pelvic pain and reduced quality of life has been previously described.[18] Patients that affected by posterior DIE (Deep Infiltrating Endometriosis) usually have severe painful symptoms (dysmenorrhea, chronic pelvic pain, dyspareunia, pain on defecation, and pain on micturition) that severely reduce the quality of life.[19] Yela et al reported that chronic pelvic pain was the only factor associated with poor quality of life, and quality of life improved following pain control.[20] Although the EHP-30 and VAS both measure pain scale, the EHP-30 questionnaire contains other components such as control and powerless. The results show that pain influences patient's perception of disease control.

We found that endometriosis patients with psychiatric disorder had a higher EHP-30 score (by almost 30 points) than those without. This means endometriosis patients with psychiatric disorder had lower quality of life.[21] In this context, endometriosis patients diagnosed with psychiatric disorder, especially depression, may require psychiatric management to prevent psychiatric disease progression and deterioration of quality of life.

Limitations

The limitations of our study included the fact that some participants were previously treated before data collection. Further, 37% of them were treated with dienogest, which could be associated with depression in long term usage.[22] However, the mean duration of dienogest treatment was less than six months. Further, primary and secondary health care

providers in Indonesia do not use of dienogest or GnRH agonists. As a result, patients seek treatment at tertiary care centers. The implementation of stepwise approach in Indonesian healthcare system led to the difficulty in excluding participants who had received treatment. Accordingly, most patients had received treatment before they were referred to our institution. Also, the cross-sectional nature of our study prevents causation identification and the lack of visual confirmation at laparoscopy and pathological confirmation of endometriosis.

The strength of our study was that we included both quality of life and the presence of psychiatric disorder and correlate them with the degree of pain assessed by VAS score. This may add additional information that when dealing with endometriosis patients diagnosed with psychiatric disorders, especially depression, a multidisciplinary approach is necessary to prevent the progression of psychiatric disorders and deterioration of the quality of life. To the best of our knowledge, this is the first study correlating the level of pain score, quality of life and psychiatric disorders among women with endometriosis. The use of Mini ICD-10 in this study allowed a quick and easy process for screening psychiatric disorders. Yet, diagnosis of psychiatric disorder still requires an in-depth interview by a psychiatrist. Accordingly, patients with psychiatric disorders discovered by Mini-ICD 10 questionnaire should be referred to a psychiatrist for further evaluation and treatment.

Conclusion

We conclude that severe endometriosis-related pain and the presence of psychiatric disorder were associated with lower quality of life. Comprehensive management of endometriosis is crucial to improve patients' quality of life.

Abbreviations

BMI, Body Mass Index; CIDI, Composite International Diagnostic Interview; EHP, endometriosis health profile; GnRH, gonadotropin-releasing hormone; Mini-ICD, Mini International Neuropsychiatric Interview International Classification of Diseases; NSAID, nonsteroid anti-inflammatory drugs; RSCM, National Referral Hospital Cipto Mangunkusumo; SCID, Structured Clinical Interview for DSM; VAS, visual analog scale.

Ethics Approval

Ethical approval was granted by the Ethics Committee at the Faculty of Medicine, University of Indonesia (KET-753/UN2.F1/ETIK/PPM.00.02/2019). Informed consent was obtained from all patients. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent to Participate

Written informed consent was obtained from all participants.

Consent for Publication

Not applicable.

Author Contributions

MR designed the project. TA, GP, AKH, and FA took part in the acquisition and management of data. TA and MA performed the analysis under the supervision of KS, HW, BW, and AH. MR, TA, and MM drafted the manuscript. TT, ES critically reviewed the manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there is no conflict of interest.

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