Mental health in women with endometriosis: Searching for predictors of psychological distress

Running head: ENDOMETRIOSIS AND MENTAL HEALTH

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Abstract

Study question: What factors affect the mental health of women with endometriosis?

Summary answer: Not only pelvic pain, but also individual characteristics (i.e. self-esteem, body esteem, and emotional self-efficacy), time from diagnosis, and intimate relationship status influence the psychological health of endometriosis patients.

What is known already: Endometriosis negative impact on mental health has been widely demonstrated by the research literature, as well as the fact that presence and severity of pelvic pain are associated with anxiety and depression. However, endometriosis is a complex multidimensional disease and factors other than pelvic pain, including individual differences, may contribute to explain the variability in women's mental health.

Study design, size, duration: This cross-sectional study was conducted between 2015 and 2017 at an Italian academic department of obstetrics and gynaecology.

Participants/materials, setting, methods: A total of 210 consecutive endometriosis patients (age: 36.7 ± 7.0 years) were included. Demographic and endometriosis-related information was collected. Individual differences were assessed using validated measures evaluating self-esteem, body esteem, and emotional self-efficacy. The Hospital Anxiety and Depression Scale (HADS) and the Ruminative Response Scale (RRS) were used to evaluate mental health.

Main results and the role of chance: Based on the extant literature, we identified three categories of putative predictors (demographic variables, endometriosis-related factors, and individual differences [i.e. 'self']), whose psychological impact was examined using a hierarchical multiple regression approach. Being in a stable relationship (coded 1 ['yes'] or 0 ['no']) was associated with decreased rumination (RRS: β = -.187; P = .002). A shorter time from diagnosis was associated with greater anxiety (HADS-A: β = -.177; P = .015). Pelvic pain severity and 'self' were associated with all mental health variables (*Ps* < .01). Greater self-esteem, body esteem, and emotional self-efficacy were correlated with better psychological outcomes (*Ps* < .01).

Limitations, reasons for caution: Sexual functioning, pregnancy, cultural differences, and gender beliefs have been found to be important in women with endometriosis. In our regression model we did not test the psychological impact of these variables and this should be acknowledged as an important limitation. Moreover, the cross-sectional (rather than longitudinal) nature of this study does not allow to fully examine the temporal relationship between endometriosis and psychological outcomes.

Wider implications of the findings: Factors other than pelvic pain can significantly affect the mental health of women with endometriosis, and the role of individual differences requires further investigation. Targeted multidisciplinary interventions should include evaluation and enhancement of self-esteem and self-efficacy to improve women's psychological health.

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Keywords: Endometriosis / Mental health / Pelvic pain / Self-efficacy / Self-esteem

Introduction

As demonstrated by several studies, either quantitative or qualitative, endometriosis can lead to impaired mental health and quality of life (Culley *et al.*, 2013; Pope *et al.*, 2015). Due to the nature of endometriosis itself—i.e. a chronic gynaecological disease frequently associated with both chronic and cyclic pelvic pain, as well as with infertility—, women are exposed daily to high levels of stress and uncertainty (Denny, 2004, 2009; Jones *et al.*, 2004). A large study by De Graaf *et al.* (2013) revealed that women with endometriosis (n = 931) had lower quality of life as compared with norm-based scores from a general American population. Moreover, quality of life was negatively affected by number of comorbidities, chronic pain, and dyspareunia. De Sepulcri and do Amaral (2009) found that of 109 endometriosis patients, 86% and 87% reported depressive and anxiety symptoms respectively, with substandard quality of life; a significant positive correlation emerged between age and depression, while current pain intensity was positively associated with anxiety.

A grounded theory study by Facchin *et al.* (2017) highlighted that endometriosis involves initial disruption, conceptualized as an interruption of one's regular life, for almost all women and in multiple life domains, such as education, work, and intimate relationships (see also Gilmour *et al.*, 2008; Hudson *et al.*, 2016). However, some women are able to restore a sense of biographical continuity that entails for instance reorganized identity and life meanings, and therefore leads to more positive mental health outcomes. In this process, the emotional support provided by the intimate partner represents an important protective factor (Facchin *et al.*, 2017).

In recent years, there has been a growing number of studies suggesting that not all women with endometriosis are necessarily more distressed than healthy women, despite the indisputable number of challenges involved by the disease (see for example Facchin *et al.*, 2015, 2017). Among the various factors associated with greater distress, pelvic pain—dysmenorrhea, dyspareunia, dyschezia, and chronic pelvic pain (Bloski and Pierson, 2008)—which affects up to 80% of women with endometriosis (Bulletti *et al.*, 2010), represents a major concern (Cox *et al.*, 2003; Pope *et al.*, 2015). Pain severity affects mental health (Facchin *et al.*, 2015), but it is not directly associated with type or stage of endometriosis

(Vercellini *et al.*, 2007) and does not necessarily decrease after medical and/or surgical treatment (Vercellini *et al.*, 2009). The pathway to diagnosis is also important (Facchin *et al.*, 2017; Manderson *et al.*, 2008) given that endometriosis is often misdiagnosed, especially because of pain normalization by either doctors or patients (Culley *et al.*, 2013).

Another study (Facchin *et al.*, 2016) showed that the severity of chronic pelvic pain can be increased by a tendency towards anxiety and catastrophism (i.e. Harm Avoidance). There is also evidence that distressed endometriosis patients (i.e. with high levels of anxiety and depression) present an overall negative sense of female identity, with lower self-esteem and worse body image relative to non-distressed patients (Facchin *et al.*, 2017). These findings suggest that individual differences may contribute to explain the variability in women's subjective experience of endometriosis, as demonstrated for other chronic diseases. For instance, a number of studies showed that self-esteem—referred to as one's beliefs about one's self-worth in different domains, such as physical, mental, and social functioning (Rosenberg, 1989)—may shape the illness experience of individuals with rheumatoid arthritis (Nagyova *et al.*, 2005), asthma (Hesselink *et al.*, 2004), and multiple sclerosis (Dlugosnki and Motl, 2012) by influencing the levels of stress and negative affects (Dlugonski and Motl, 2012; Juth *et al.*, 2008; Penninx *et al.*, 1998). Emotional self-efficacy—i.e. one's beliefs about one's capacity to manage emotions and feelings, either positive or negative—is another important trait characterizing individual differences in reacting to and exerting control over life events (Bandura, 2001; Caprara *et al.*, 2008). Although research has shown that good self-esteem and feelings of self-efficacy may enhance the ability to cope with chronic disease and therefore lead to greater mental health, with lower anxiety and depression (see Mann *et al.*, 2004 for review), very little is known about the role played by these individual characteristics in women with endometriosis.

Overall, the fact that endometriosis can significantly affect women's mental health is now ascertained, but we are still far from a complete understanding of what specific factors (either related or unrelated to the disease) may lead to positive or negative psychological outcomes—which is pivotal to the implementation of targeted multidisciplinary treatment strategies. The current study aims at taking a step

forward in the development of such an explanatory model by systematically testing the psychological impact of putative predictors identified on the basis of the extant literature. Specifically, we hypothesized that mental health could be affected by three categories of factors: demographic variables (age and intimate relationship status); endometriosis-related variables (hormonal treatment, surgical interventions, current infertility, time from diagnosis, pain severity); individual differences (self-esteem, body esteem, emotional self-efficacy).

Materials and Methods

The current study reports findings from analyses of data derived from a research project on endometriosis and its association with psychological and relational variables. The research was approved by the local Institutional Review Board and these data were collected between 2015 and 2017. Of the 215 women originally recruited, 210 (98%) returned complete measures that were included in our statistical analyses. Final participants were 210 Caucasian women aged from 19 to 51 with clinical and/or surgical diagnosis of endometriosis (for details regarding the reliability of non-surgical diagnosis of endometriosis see Nisenblat *et al*., 2016; Somigliana *et al.*, 2010; Vercellini *et al.*, 2015), consecutively recruited at an Italian academic department of obstetrics and gynaecology. We did not include women who reported alcohol or drug use; diagnosed mental illness or physical diseases other than endometriosis, including sexually transmitted, urologic, gastrointestinal, orthopaedic, rheumatologic, and autoimmune diseases; genital malformations, obstructive uropathy or bowel stenosis.

A structured interview was administered to collect demographic data and gynaecological information pertaining to: current infertility, hormonal therapy, and surgical interventions (dichotomous variables coded 0 = “no”; 1 = “yes”); time from diagnosis; severity of pain (chronic pelvic pain, dysmenorrhea, dyspareunia, dyschezia) assessed on a 0-10 numerical rating scale (*NRS*; 0 = “no pain”; 10 = “the worst imaginable pain”). Clinical information was entirely retrieved from medical records or directly asked to participants when necessary.

Individual differences (self-esteem, body-esteem, emotional self-efficacy) were assessed using the validated Italian version of four different self-report questionnaires: the *Rosenberg Self-Esteem Scale*

(*RSES*; Prezza *et al.*, 1997; Rosenberg, 1989), that includes 10 items (e.g. "On the whole, I am satisfied with myself") with responses scored on a 0-3 scale (0 = "Strongly Disagree", 3 = "Strongly Agree" or vice versa); the *Body Esteem Scale* (*BES*; Mendelson *et al.*, 2001), whose Italian version (Confalonieri *et al.*, 2008) includes 14 items (0 = "Never", 4 = "Always") organized in three subscales—Weight (i.e. one's satisfaction about weight: "I really like what I weigh"), Appearance (i.e. one's feelings about general appearance: "I worry about the way I look"), and Attribution (i.e. the opinions attributed to others: "Other people consider me good looking")—and a full scale score; the scale of *Emotional Self-Efficacy in Regulating Negative Emotions* (*ESE-NEG*; 8 items) and the scale of *Emotional Self-Efficacy in Expressing Positive Emotions* (*ESE-POS*; 7 items) that measure respectively one's capacity to manage negative emotions (e.g. "To what extent are you able to avoid to get discouraged in the face of difficulties") and to express positive emotions (e.g. "To what extent are you able to express joy when good things happen to you?") on a 5-point scale (1 = "Not at all"; 5 = "Extremely"; Caprara and Gerbino, 2001). In this study, all individual differences scales showed good internal consistency, with Cronbach's α ranging from .83 to .90.

Mental health was assessed using the *Hospital Anxiety and Depression Scale* (*HADS*; Costantini *et al.*, 1999; Zigmond and Snaith, 1983) that comprises two 7-item scales—HADS anxiety (HADS-A) and HADS depression (HADS-D), plus a full scale score—on which respondents have to rate the frequency of symptoms ranging from 0 to 3 (higher scores indicate poorer mental health), and the *Ruminative Response Scale* (RRS; Nolen-Hoeksema and Morrow, 1991; Palmieri *et al.*, 2007)—22 items with scores ranging from 1 = "Never" to 4 = "Always"— that evaluates the intensity of depressive rumination conceptualized as one's repetitive thoughts about one's depressed mood and its causes (e.g. "You think about how you feel sad"). The internal consistency of mental health variables ranged from .79 to.92 in the current study.

Statistical analyses

All statistical analyses were conducted with SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) software version 17. Continuous variables are reported as mean ± standard deviation

and qualitative variables as frequencies. In this study we used a hierarchical multiple regression approach to test our hypotheses, and assumptions (including normality of data) were tested as appropriate. Two separate principal component analyses were also run for two categories of predictors: individual differences (i.e. RSES, BES total score, ESE-NEG, ESE-POS) and severity of pain (i.e. chronic pelvic pain, dysmenorrhea, dyspareunia, dyschezia). One single component was extracted for each category, specifically: '*self*' (KMO test = .70, Bartlett's test of sphericity = 114.55, *Ps* < .001), representing the information provided by the RSES, the BES total, the ESE-NEG, and the ESE-POS; and '*pelvic pain severity*' (KMO test = .69, Bartlett's test of sphericity = 83.89, *Ps* < .001), summarising the scores of the four NRSs used to evaluate the severity of pelvic pain. The identification of these two components allowed to synthetize data information and avoid subsequent multicollinearity problems due to the presence of correlations between putative predictors within each of these two categories.

Hierarchical multiple regression was used to examine the psychological impact of demographic factors (age and intimate relationship status), endometriosis-related factors (hormonal treatment; surgical interventions; current infertility; time from diagnosis; 'pelvic pain severity'), and 'self'. Three models were tested for each dependent variable (HADS-A, HADS-D, HADS total, and RRS) by entering demographic data in the first regression step, endometriosis-related variables in the second step, and 'self' in the third step. The changes in R^2 (ΔR^2) from step 1 to step 3 and their significance allowed to evaluate the predictive power of each set of predictors. Moreover, because we wanted to collect further information regarding the association between individual differences and mental health, which is unexplored in the endometriosis psychological literature, separate Pearson correlations were conducted for each of the four scales, including the three BES subscales. Significance tests were performed at $P < .05$. Consistently with Cohen's guidelines for power analysis (Cohen, 1992), our sample was large enough to detect a medium effect size ($f^2 = .15$) for the F test of the multiple R^2 at $Power = .80$.

Results

Participant characteristics

The mean ± SD age of the 210 participants was 36.7 ± 7.0 years. Of these, 167 (80%) were in a stable intimate relationship. The majority of participants had a job (186 [89%]) and a high school degree (102 [49%]), 85 (40%) went to university and a small percentage (23 [11%]) had a middle school diploma. Time from diagnosis (7.0 ± 5.7 years) ranged from less than one year (12 [6%]) to 25 years (2 [1%]). Most participants (117 [56%]) were currently under hormonal therapy, with overall low pain severity (NRS; chronic pain: 1.0 ± 2.4; dysmenorrhea: 3.0 ± 3.6; dyspareunia: 2.6 ± 3.2; dyschezia: 1.2 ± 2.6). A larger percentage of patients underwent surgery (130 [62%]), of these only 4 (3%) had hysterectomy. The majority of women (142 [68%]) were childfree and current infertility was reported by 53 women (25%). Means and standard deviations for individual differences variables (RSES, ESE-NEG, ESE-POS, BES [Weight, Appearance, Attribution, and total score]) and mental health (HADS anxiety, HADS depression, HADS total score, RRS) are displayed in Table 1.

Associations between selected predictors and mental health

An overview of the findings obtained with the hierarchical multiple regressions performed is provided in Table 2 and Table 3. As regards the first set of putative predictors, we found that the fact of being in a stable intimate relationship was associated with decreased rumination (RRS: β = -.187; P = .002); however, Model 1 (i.e. demographic variables alone) was never significant (P > .05). Model 2 (i.e. demographic factors *and* endometriosis-related variables) and Model 3 (i.e. demographic factors *and* endometriosis-related variables *and* 'self') were statistically significant for all mental health variables (*Ps* < .001). Among the endometriosis-related factors included in Model 2, a shorter time from diagnosis was associated with more severe anxiety (HADS-A: β = -.177; P = .015), and a higher 'pelvic pain severity' with poorer mental health, with *Ps* < .01 in all dependent variables.

As shown in Table 2, endometriosis-related predictors led to a significant increase in the percentage of variance explained, with ΔR^2 ranging from .096 (9.6% increase) for depression to .12 (12% increase) for rumination. However, we found that individual differences, summarised by the single component 'self', played an important role since they affected all variables with *Ps* < .001(see Table 3) and significantly added greater explanatory power to the overall model, especially in the case of

depression (HADS-D: ΔR^2 from Model 2 to Model 3 = .348, which indicates a 35% increase in the variance explained), relative to endometriosis-related factors (see also the values of the standardised coefficients reported in Table 3). The percentage of variance explained by the overall model ranged from 35% for anxiety to 47% for depression (see the R^2 reported in Table 2).

Correlations between individual differences and mental health

When separate correlation analyses were conducted for each of the variables representing individual differences (see Table 4), we found that lower self-esteem (RSES) and emotional self-efficacy (ESE-NEG, ESE-POS) were correlated with poorer mental health on all dependent variables (*Ps* < .01). A significant negative correlation was also found between two of the BES subscales (Weight and Appearance), as well as BES-total, and all mental health variables (*Ps* < .01), while Attribution was not correlated with any dependent variable.

Discussion

Endometriosis has a negative impact on mental health, as it is often associated with depression and anxiety disorders (Chen *et al.*, 2016; Pope *et al.*, 2015). However, the specific factors involved in the development of psychological impairment in women with endometriosis have not been clarified. For this reason, we conducted this cross-sectional study aimed at contributing to the current understanding of mental health in women with endometriosis, which may also have important implications for treatment. Three sets of putative predictors were identified based on the extant literature, whose findings suggested that age, intimate relationship status, treatment variables, current infertility, and pelvic pain may affect anxiety and depression (De Graaf *et al.*, 2013; De Sepulcri and do Amaral, 2009; Facchin *et al.*, 2017; Huntington and Gilmour, 2005; Jones *et al.*, 2004). The impact of hormonal therapy was systematically tested because there is evidence that it may influence women's mood (Skovlund *et al.*, 2016; Yonkers *et al.*, 2016). We also examined whether mental health was affected by time from diagnosis, which is important to understand the temporal relationship between endometriosis and psychological disorders, as suggested by Chen *et al.* (2016). In addition, we investigated the role played by individual differences in the mental health of women with endometriosis.

Our findings confirmed that pelvic pain severity, which affected all dependent variables, has a negative pervasive impact on women's mental health. There is currently strong evidence that pain is associated with poorer psychological outcomes (Cox *et al.*, 2003; Facchin *et al.*, 2015; Kumar *et al.*, 2010; Pope *et al.*, 2015), which indicates that teaching patients how to manage these symptoms is a fundamental part of endometriosis multidisciplinary treatment. In this regard, mindfulness-based psychological treatment has been found to be effective in helping women deal with endometriosis-related pelvic pain (Hansen *et al.*, 2016; Kold *et al.*, 2012). In our study, pelvic pain was assessed regardless of women's menstrual cycle phase, which may affect pain severity, and future studies should control for the effects of this variable.

Although being fully aware of the role played by pain symptoms is important, our study revealed that factors other than pelvic pain may influence the mental health of women with endometriosis. Among the factors related to the disease, a shorter time from diagnosis was associated with increased anxiety, which seems to be a common endometriosis short-term psychological outcome. These results provide empirical support to the idea that being diagnosed with endometriosis, which involves becoming aware of having a chronic disease with no definitive cure and often associated with infertility, is a disruptive stressful event for women (Facchin *et al.*, 2017; Gilmour *et al.*, 2008; Hudson *et al.*, 2016). On one hand, our findings reaffirm the importance of a well-communicated diagnosis, i.e. extensive, clear, sensitive, and respectful. On the other hand, prompt psychological intervention (such as counselling) may reduce the risk of developing mental disorders by helping women find more effective strategies to cope with the disease and its implications. As also suggested by other authors (Chen *et al.*, 2016), there is need for further research to understand the temporal association between endometriosis and specific psychological symptoms or disorders (i.e. short-term versus long-term psychological outcomes), which would be very important for clinical practice. The time from symptom onset to diagnosis is also an important variable: in a recent qualitative study, Facchin *et al.* (2017) found that the histories of distressed endometriosis patients were characterized by a long pathway to diagnosis (up to 12 years). Future studies should

systematically examine the long-term consequences of diagnostic delays, which frequently occur in women with this disease (Manderson *et al.*, 2008).

Because we found that being in a stable intimate relationship was associated with decreased rumination, our results also suggest that partners may represent a resource for women with endometriosis and a protective factor against negative psychological outcomes. The disruptive impact of endometriosis on couple relationships as well as the important emotional support provided by intimate partners have been highlighted by other studies (Facchin *et al.*, 2017; Hudson *et al.*, 2016). However, there is currently paucity of information about couples dealing with endometriosis and future studies should address this issue in order to clarify how endometriosis affects intimate relationships (also in terms of partners' subjective experience) and what relational factors may influence women's response to the disease.

However, our most important findings regard the significant association between individual differences and mental health (especially depression) in women with endometriosis, such that participants with greater self-esteem and self-efficacy were less distressed. Although the association between these variables and psychological health is well known in psychological research, especially in patients with chronic illness, our findings are novel in the study of endometriosis and suggest that multidisciplinary treatments should be tailored to women's individual needs and characteristics. Based on our results, as well as from those of other studies on chronic diseases (Juth *et al.*, 2008; Nagyova *et al.*, 2005), we believe that assessing and enhancing self-esteem and self-efficacy should be considered as important components in the psychological treatment of endometriosis patients.

Indeed, the relationship between endometriosis and "self" variables (for instance, the way in which the disease affects women's self-esteem and sense of femininity, with different mental health outcomes) requires further investigation in future studies including a control condition. This relationship should be conceptualized as a complex mutual interaction rather than a unidirectional causal link. Specifically, we can hypothesise that endometriosis patients with pre-existent poorer self-esteem and self-efficacy may experience more distress due to an increased tendency to self-criticism and overall negative emotions. At the same time, endometriosis—whose potentially devastating impact on sense of female

identity has been described elsewhere (Facchin *et al.*, 2017)—may contribute to further decrease self-esteem and self-efficacy, with augmented psychological disruption. Overall, there is need for more research to identify the specificities of mental health outcomes in women with endometriosis relative to other conditions (i.e., not only healthy controls, but also other types of chronic disease).

Conclusive thoughts

Endometriosis is characterized by remarkable variability in terms of symptoms, types of lesions, psychological and relational outcomes. The 'endometriosis ocean' is vast and our study contributes to navigate only a small portion of it (see the R^2 values presented in Table 2), which represents an important limitation. For instance, we did not examine the psychological impact of sexual functioning, which is very often impaired in women with endometriosis (Barbara *et al.*, 2016). The fact that endometriosis patients with poorer sexual functioning may be more distressed represents a plausible hypothesis that requires investigation. Another limitation is the fact that our study is cross-sectional and does not allow to understand the evolution of women's endometriosis experience, for instance before and after pregnancy. In this regard, we acknowledge the need for longitudinal studies in the field of endometriosis. Moreover, the role of infertility may have been underestimated in our study because we simply compared participants who had and who did not have current infertility, without controlling for the effects of possible past infertility. We also believe that cultural and gender issues may shape women's subjective experience of endometriosis (see for example the relationship between menstrual pain normalization and delayed diagnosis) and thus we encourage research aimed at exploring their role.

Authors' roles

F.F., G.B., Em.S., and P.V. conceptualized, designed and supervised the whole study. F.F. wrote a first draft of the manuscript, which was initially reviewed by P.V. and Ed.S., and subsequently by all authors, including D.D., D.A., and L.B. All authors provided substantial contributions to data analysis, whose findings were extensively shared and discussed, until full consensus was reached regarding the final version.

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Conflict of interest

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