Association of Dysmenorrhea with Endometriosis: a Literature Review

Ramiro Cabrera[1]*, Andrea Carrillo[2], Felipe Esparza[3] and Sylvia Salmun[3]

[1]*Director del Departamento en Cirugía Pélvica, Doyenne High Quality and Multidisciplinary Treatment Center for Endometriosis, Mexico*

[2]*Departamento en Cirugía Pélvica, Doyenne High Quality and Multidisciplinary Treatment Center for Endometriosis, Mexico*

[3]*Centro de Investigación en Ciencias de la Salud (CICSA), Facultad de Ciencias de la Salud Universidad Anáhuac México Norte, Mexico*

*Corresponding Author: Ramiro Cabrera, Director del Departamento en Cirugía Pélvica, Doyenne High Quality and Multidisciplinary Treatment Center for Endometriosis, Mexico.

Abstract

Endometriosis is a chronic and inflammatory disease that affects women of any age. It is a benign inflammatory condition in which endometrial-like tissue is located outside the endometrial cavity. In women of reproductive age, the global incidence of endometriosis is approximately 10-15%, but it can escalate to as high as 35-50% in women experiencing infertility. Presentation varies widely, ranging from asymptomatic individuals to those experiencing varying levels of dysmenorrhea, chronic pelvic pain, dysuria, dyschezia, dyspareunia, asthenia, headaches, and infertility. Diagnostic supporting tools such as imaging studies, primarily ultrasound and magnetic resonance imaging with an endometriosis mapping protocol, demonstrate exceptional sensitivity and specificity when utilized by expert professionals. However, there is a significant delay in diagnosis, typically ranging from 7 to 12 years. Multiple factors contribute to this delay, including challenges in making differential diagnoses, insufficient expert healthcare professionals, lack of clinical judgment and social awareness regarding the disease, and difficulties accessing necessary resources. Today, there is a solid effort to minimize this delay by training healthcare professionals and promoting social awareness among patients, as well as developing easily accessible tools to identify high-risk patients enabling the prompt initiation of appropriate study protocols. Implementing symptom-based questionnaires has been a subject of ongoing debate, primarily due to the controversial results obtained from previous studies. This review aims to contribute to the scientific literature by providing robust evidence to validate their utilization as a first-line tool.

Keywords: Endometriosis; Dysmenorrhea; Pelvic Pain; Dyspareunia; Health Questionnaires and Diagnostic Tools

Introduction

Endometriosis is a chronic and inflammatory disease that affects women of any age. It is a benign inflammatory condition in which endometrial-like tissue is located outside the endometrial cavity [1,2]. According to the literature, endometriosis is known to be more prevalent among women of reproductive age; however, it can occur at any age. It affects over 200 million women worldwide, with a global incidence ranging from 10-15% in women of reproductive age, escalating to as high as 35-50% in women experiencing infertility [3-5]. It significantly impacts on patients' productivity and quality of life, encompassing multiple aspects such as economic, psychological, physical, work-related, and interpersonal.

The economic burden on referral centers is comparable to other chronic diseases, such as diabetes, Crohn's disease, and rheumatoid arthritis [6].

Given the heterogeneous presentation and varying severity of symptoms, limited information and awareness about the disease among healthcare professionals and patients, and scarcity of specialists in this specific field, primary care physicians often encounter challenges in promptly diagnosing this condition [5]. Several articles have shown that many women with endometriosis experience a significant delay in diagnosis ranging from 7 to 12 years from the onset of symptoms. In addition, the clinical presentation exhibits significant variability, with potentially misleading symptoms that may concur with those of other common pathologies like irritable bowel syndrome or interstitial cystitis, thereby complicating the process of differential diagnosis and hindering prompt recognition of the disease [7-9].

Chronic pelvic pain and infertility are significant clinical problems in women with endometriosis. The correlation between the extent and location of the disease with the frequency and severity of symptoms has been debated for many years since numerous studies focused on this relationship have shown contradictory results [10]. As we have already mentioned, there is a great variety and heterogeneity of presentation, with cases of asymptomatic women seeking medical attention due to primary or secondary infertility and women with a long history with varied symptoms ranging from dysmenorrhea, pelvic pain, dysuria, dyschezia, dyspareunia, asthenia, adynamia, and headaches [10].

Association of dysmenorrhea with endometriosis

Women's reproductive health is a prime issue in the medical and social fields due to its direct influence on the quality of life, economic aspects, and public health. For example, endometriosis affects more than 200 million women worldwide, with a global incidence of 10-15% in reproductive-aged women and 35-50% in women with infertility [3,5].

According to the National Population Consensus of 2022, Mexico has a population of 130,118,356 people, with 51.1% being women, which represents 66,425,589 women. Of the total, 52.6% are women aged 15-49, constituting the women of reproductive age group. The delay in diagnosis, from 7 to 12 years from the onset of symptoms, is well-documented and contributes to the deterioration of the quality of life and the significant economic and personal impact associated with the condition [11].

Over the years, laparoscopy with biopsy for histopathological or direct visualization study has been the gold standard for diagnosis. However, with advancements in technology, increased awareness of the disease, and specialized training provided to healthcare professionals who are experts in this field, transvaginal ultrasound and pelvic magnetic resonance imaging with endometriosis mapping studies are now recognized as the first-line methods. These non-invasive approaches offer comparable sensitivity and specificity. However, it is essential to note that endometriosis may not always be visible in imaging studies. Therefore, a high clinical suspicion should not rule out the diagnosis in patients without radiological evidence of the disease [12].

Over the past decade, there has been a significant focus on the development of accessible and non-invasive methods for assessing the probability of developing this disease. The aim is to minimize diagnostic delays, optimize treatment, mitigate surgical risks, and implement a multidisciplinary approach for effective pre-surgical planning [11].

In recent years, there has been significant research interest in harnessing clinical information to predict the presence of diseases such as endometriosis, which has been the subject of extensive research [6,11,13,14]. However, these studies have predominantly relied on relatively small sample sizes, and the predictive models employed have yet to undergo external validation in large-scale databases. Moreover, the clinical utility of predicting endometriosis is hindered by inconsistencies in diagnostic criteria and the variability of presentation and symptoms observed across different studies and populations [14].

The heterogeneity of classification systems has made it challenging to raise awareness and homogeneity in diagnostic criteria among health professionals, emphasizing the need for a consensus classification system for better comparison of research results and facilitate communication among health professionals in the evaluation and management of endometriosis [15].

Elements have been developed based on diaries and symptom-based questionnaires focused on dysmenorrhea and chronic pelvic pain to evaluate the global impact on quality of life. Several studies have shown that experienced physicians can predict the presence of endometriosis based on clinical history and physical examination in up to 80% of cases [16].

As a chronic, inflammatory, estrogen-dependent disease predominantly affecting women of reproductive age, delayed diagnosis of endometriosis can result in a gradual extension of the disease and consequent impact on various aspects of quality of life, including social, physical, psychological, and fertility prognosis. Barriers to early diagnosis encompass high costs, diverse differential diagnoses, lack of clinical judgment, and scarce medical material. Therefore, it is crucial to recognize that in the presence of chronic pelvic pain, gastrointestinal or urinary symptoms, suspicion of endometriosis should be actively considered [17]. Therefore, obtaining a thorough medical history plays a pivotal role in establishing a presumptive diagnosis [17].

Various studies employ questionnaires to assess the relevance of the abovementioned symptoms in suspecting or diagnosing endometriosis. For instance, Ballard conducted a study in 2008 comparing symptom prevalence between women with and without endometriosis in the UK. The study involved 5,540 women diagnosed with endometriosis and 21,239 patients without an endometriosis diagnosis. Their medical records were thoroughly examined to identify key abdominal, menstrual, and pelvic symptoms or signs. The findings indicated that dysmenorrhea occurred more frequently in women diagnosed with endometriosis, with an incidence of 73%. Thus, it was concluded that the presence of dysmenorrhea is significantly higher in patients with endometriosis compared to healthy individuals [1].

The primary symptom of endometriosis is dysmenorrhea, although considerable heterogeneity exists, with reports indicating that up to approximately 30% of patients may be asymptomatic. A common challenge is the fact that these symptoms can resemble or be attributed to other frequently diagnosed conditions, resulting in diagnostic bias and delayed identification, often leading to the implementation of empirical treatments and an incomplete management approach [12].

A significant proportion of adolescents experience menstrual discomfort (70-93%), significantly affecting their quality of life. Studies show that up to 20 to 40% of patients report a negative impact on their daily activities and even limitations in their overall functioning. It is estimated that approximately two-thirds of patients diagnosed with endometriosis experience symptoms before age 20, with dysmenorrhea being the primary symptom present in 64% of patients. Dysmenorrhea is secondary to increased prostaglandin levels, leading to their infiltration into nearby nerves as a consequence of the chronic inflammatory process [18].

Many patients, due to sociocultural aspects, normalize dysmenorrhea, resulting in a delay in seeking primary medical care. Therefore, it is important to have accessible tools so women can identify several red flag symptoms and signs and get an early diagnosis and treatment. Chapron., et al. 2003, establish a correlation between the presence of dysmenorrhea and endometriosis, highlighting that the severity of dysmenorrhea corresponds to the extent of the disease, particularly when involving the ovaries, rectum or vagina [12].

As there is no effective tool to assess the severity of pain in patients with endometriosis, the most commonly used standard tool is the clinical severity scale from 1 to 10, which may introduce bias since each patient has a different pain threshold. In their study, Deal., et al. used the Endometriosis Pain and Bleeding Diary [EPBD] scale, where a total of 38 women diagnosed with endometriosis were evaluated, all of whom had dysmenorrhea, and 18 patients reported severe pain. Therefore, the EPBD scale was able to differentiate between patients with severe and mild pain [19].

Multiple studies have identified the main symptoms of endometriosis, but all of them have a retrospective design and thus do not show a predictive value of the symptoms. Dysmenorrhea, pelvic pain, and dyspareunia exhibit high sensitivity in raising suspicion of an endometriosis diagnosis. Therefore, using technological apps with questionnaires could support the early and prompt diagnosis of endometriosis. It is important to emphasize that the purpose is not diagnosing but rather identifying patients at higher risk of developing endometriosis through clinical history and self- assessment. This approach enables a systematic approach and makes an adequate distribution of resources. Hence, the utilization of digital techniques could support the physician in suspecting the disease [20].

The leading cause of secondary dysmenorrhea is endometriosis, which raises suspicion of this condition in patients with persistent dysmenorrhea that does not improve after three months of treatment with NSAIDs and hormonal agents. Another crucial aspect to consider when assessing dysmenorrhea is the evaluation of first- degree family history of this condition, as there is evidence that a family history of first-degree relatives increases the risk of developing endometriosis by 7 to 10 times [21].

Different studies estimate the prevalence of dysmenorrhea in adolescent patients, ranging from 41% to 91.5%, contributing to an annual loss of 140 million hours in school and an inability to perform daily activities. Dysmenorrhea presents a higher intensity during the first 24 to 48 hours of menstruation. After that, associated symptoms such as asthenia, headaches, abdominal distension, nausea, and vomiting may occur [22,23]. In addition, patients with dysmenorrhea have up to twice the risk of developing endometriosis compared to patients without dysmenorrhea [24].

In their study, Gater., *et al*. enrolled a cohort of 45 patients diagnosed with endometriosis and applied a comprehensive health questionnaire on daily endometriosis symptoms. The study's findings revealed that dysmenorrhea was present in 92% of the patients, making it the most frequent and severe symptom. In addition, the patients reported experiencing dyspareunia; finally, they mentioned that this pain was so incapacitating that it had repercussions on their household chores, school activities, work, and sexual activities [25,26].

There is compelling evidence, supported by previous studies on various diseases, regarding the efficacy of applying technology and medical apps for monitoring, raising awareness of the condition, and promoting treatment adherence. In a study that evaluated the integration of pharmacists in the management of cardiovascular diseases using digital technologies, it was concluded that this approach is a valuable tool to improve treatment adherence, patient education about the disease, and outcomes in terms of systemic blood pressure control and cardiovascular risk reduction [27].

A meta-analysis assessing the efficacy of smartphone-based mental health interventions for managing depressive symptoms concluded that mobile apps incorporating cognitive-behavioral therapy and mindfulness techniques could be valuable in reducing depressive symptoms [28].

Another systematic review and meta-analysis examining the effectiveness of digital interventions in promoting self-care among adults with systemic arterial hypertension yielded findings indicating that remote monitoring technology utilizing mobile apps can improve blood pressure control and treatment adherence [29].

While health apps and technological tools can be helpful in monitoring and managing diverse health conditions, it is crucial to bear in mind that they serve as initial tools for promptly identifying and filtering high-risk patients. However, further individual research is required to evaluate their long-term effectiveness and applicability in different populations and contexts.

Conclusion

The reduction of diagnostic delay plays a crucial role enhancing the management and treatment of endometriosis, ultimately impacting the quality of life and prognosis. This can be accomplished by providing access to a screening tool that accurately predicts endometriosis in women presenting within a specific clinical setting. While the overall predictive ability for any stage of endometriosis is relatively low, symptom-based models developed and validated in multiple studies have demonstrated satisfactory accuracy in predicting the relationship of symptoms with specific stages of the disease. Still, there is an ongoing debate among the different diagnostic methods for an unequivocal diagnosis of endometriosis, in which the challenges in establishing an ideal screening method for all populations arise form limited access to diagnostic methods, inadequate availability of trained health professionals in the field, lack of social awareness of the disease, and heterogeneity of presentation and its relationship to disease extent. Nevertheless, this screening tool can be a useful initial tool to guide health professionals and patients in identifying abnormalities early and having prompt access to health services.

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