# Endometriosis and dyspareunia: Solving the enigma

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ABSTRACT

*Introduction:* Endometriosis is a chronic oestrogen-dependent disease that affects 1 in 10 women of childbearing age. Half of these women have deep dyspareunia. The presence of this symptom has been shown to negatively affect your quality of life. There are few studies in the literature that address this issue and its pathophysiology remains poorly understood.
*Materials and methods:* A case-control study has been carried out in order to assess the multi-causality of dyspareunia in patients with endometriosis. All the patients were assessed in a unit specialising in endometriosis and pelvic pain and their disease was staged using high-resolution ultrasound following the criteria of the IDEA group. The patients were divided into two groups, patients with dyspareunia n = 45 (cases) and those without it n = 55 (controls).
*Results:* The only element that was statistically significant in explaining the dyspareunia was the presence of nodules in the retrocervical region with p = 0.000. The odds ratio of dyspareunia in the cases group was 5.3 (95 % CI 2.2–12.5).
*Conclusions:* Dyspareunia in patients with endometriosis is strongly dependent on the presence of nodules in the retrocervical region, although there are other factors involved that remain unknown, so more studies are still needed to understand and optimally address this symptom.

## 1. Introduction

Endometriosis is a chronic oestrogen-dependent disease that affects 1 in 10 women of childbearing age [1]. The peak incidence is among women between the ages of 25 and 45 [2]. Since it is one of the most frequent benign gynaecological diseases, it is a debilitating condition with social, occupational and psychological effects. The prevalence of this disease ranges from 30 % to 50 % in patients with infertility and 45 % in patients with chronic pelvic pain [1,2].

Endometriosis is characterised by the implantation and growth of stroma and functional endometrial glands outside the uterine cavity [1]. These ectopic lesions can be classified as superficial peritoneal endometriosis (superficial implants in the peritoneum), deep infiltrating endometriosis (infiltrating nodules > 5 mm in the peritoneum or pelvic organs), and ovarian endometriomas. The most common locations for ectopic endometrial implants are the ovaries, the ovarian fossa, the uterosacral ligaments and the pouch of Douglas, they are rare outside the pelvis, although they can affect any organ including in surgical scars. The presence of these implants can drastically modify the patient's pelvic anatomy [1,2].

Endometriotic tissue is hormone dependent and causes the same bleeding and shedding as menstruation. Periodic bleeding leads to an inflammation response that triggers fibrosis and the formation of secondary adhesions that contribute in part to the symptoms of the disease. It has the ability to grow, infiltrate and even to spread like tumour tissue but its transformation to malignancy is exceptionally rare [2,3].

Endometriosis is one of the main causes of pelvic pain during sexual intercourse. Half of women with endometriosis have deep dyspareunia and it has been shown that this negatively affects their quality of life. However, the mechanisms of the deep dyspareunia associated with endometriosis are still poorly understood [4–6].

Some studies have tried to link dyspareunia with the presence of deep endometriotic nodules, proposing nodules in the rectovaginal septum, uterosacral ligaments and cul-de-sac as one of its causes [5,6].

**Table 1**
Characteristics and history of the patients.

|  | Dyspareunia | Controls | p |
|---|---|---|---|
| **Age** | 34.96 (± 6.8) | 38.16 (± 6.6) | 0.190 |
| **Number of pregnancies** | 0.76 (± 1.25) | 0.85 (± 1.4) | 0.712 |
| **Number of deliveries** | 0.24 (± 0.6) | 0.29 (± 0.6) | 0.694 |
| **Number of caesarean sections** | 0.11 (± 0.3) | 0.27 (± 0.6) | 0.117 |
| **Previous surgery for endometriosis** | 26.7 % | 21.8 % | 0.572 |
| **Assisted reproduction** | 22.2 % | 18.2 % | 0.615 |
| **Hormone Treatment** | 67.8 % | 52.7 % | 0.466 |
| **Combined** | 50 % | 68.96 % | 0.546 |
| **Progestogens** | 50 % | 31.03 % | 0.133 |
| **Amenorrhoea** | 20 % | 27.3 % | 0.397 |

**Table 2**
Ultrasound findings.

|  | Dyspareunia | Controls | p |
|---|---|---|---|
| **Adenomyosis** | 48.9 % | 36.4 % | 0.207 |
| **Endometrioma** | 40 % | 38.2 % | 0.853 |
| **Hydrosalpinx** | 24.4 % | 10.9 % | 0.073 |
| **Retrocervical region nodule** | 64.4 % | 25.5 % | **0.000** |
| **Rectosigmoid nodule** | 17.8 % | 12.7 % | 0.482 |
| **Uterosacral ligaments Nodule** | 26.6 % | 7,3 % | **0.008** |
| **Abdominal nodule** | 0 % | 1.8 % | 0.363 |
| **Bladder nodule** | 0 % | 0 % | 1 |
| **Positive anterior slide** | 97.8 % | 94.5 % | 0.412 |
| **Positive posterior slide** | 60 % | 67.3 | 0.451 |

An over-expression of nerve growth factor (NGF) has also been postulated as one of its possible mechanisms [4]. However, more recent reviews indicate that its pathophysiology remains poorly understood and the research published on it is very diverse [7].

The response of these patients to medical treatment is very diverse, with most of them not responding adequately to hormonal treatment. This unclear response of deep dyspareunia to the standard treatment could be due to a lack of knowledge of the mechanisms of pain in endometriosis, which are especially relevant in this subgroup of patients [1,7].

The aim of this study is to determine the main causes of dyspareunia in patients with endometriosis.

## 2. Materials and methods

A case-control study has been carried out in order to assess the multicausality of dyspareunia in patients with endometriosis. The participants have been divided into two groups, patients with endometriosis and dyspareunia (n = 45), who are the cases, and patients with endometriosis without dyspareunia (n = 55), who are the controls.

The sample size of the study was calculated for an alpha error of 0′05 and a statistical power of 80 %. A minimum sample size of 26 patients was obtained in each group. Finally, the study was extended to 100 patients to increase its statistical power. Patients were included consecutively among those who met the inclusion criteria.

The diagnosis of endometriosis was made by laparoscopy, magnetic resonance imaging or high-resolution ultrasound by expert gynaecologists.

Women who attended the Endometriosis and Pelvic Pain Unit who were of legal age, without established menopause, who still had their uterus and at least one ovary, and who were sexually active, were included. Minor patients, hysterectomised patients, patients undergoing double adnexectomy, menopausal patients, and those who were not sexually active were excluded. Careful anamnesis was carried out to take into account other possible conditions that could cause dyspareunia and act as confounding variables, such as myofascial syndrome, fibromyalgia, low back pain, etc.

Dyspareunia was classified using the Visual Analogue Scale (VAS) from 0 to 10.

The staging, classification, and follow-up of the nodules in these patients was performed using the IDEA group criteria [8].

The IBM SPSS Statistics v25 program was used to perform the statistical analysis. For the analysis of the qualitative variables, the Chi-squared test was used and for the analysis of the quantitative ones, the Student's T test. The increased risk was calculated using the Odds Ratio and linear regression techniques were used to see the relationship between the symptoms and the possible causes.

All the patients gave their consent to participating in this study and likewise the study was approved by the Malaga Provincial Comité de Ética de Investigación (CEI) [Research Ethics Committee].

## 3. Results

The chosen sample size was 100 patients divided into 45 cases and 55 controls. As can be seen in Table 1, the groups were homogeneous with respect to their demographic characteristics and backgrounds.

At the time of the physical examination, contracture of the pelvic floor muscles was identified in 4 % of the patients with dyspareunia but only in 1.8 % of the patients in the control group (p = 0.444), likewise the presence of vaginal endometriotic nodules was not statistically significant, being present in 2.2 % of the cases and in 1.8 % of the patients without dyspareunia (p = 0.886).

For the ultrasound evaluation, 100 % of these patients were evaluated by expert endometriosis sonographers. The distribution of the ultrasound findings in the various groups is shown in Table 2. In this same table you can see how the only elements that reaches statistical significance is the presence of nodules in the retrocervical region and the uterosacral ligament.

Within the cases group, the distribution of pain was as follows: patients with mild dyspareunia (VAS 1–3) 20 %, patients with moderate dyspareunia (VAS 4–6) 35.5 % and patients with severe dyspareunia (VAS 7–10) 44.4 %.

The odds ratio of presenting dyspareunia with an endometriotic nodule in the retrocervical region is 5.3 (95 % CI 2.2–12.5). The mean size of these nodules in both groups was assessed, it was 3.7 mm in the asymptomatic group and 7.6 mm in the group with pain, with p = 0.013. This difference in size was not observed, however, in the subgroups of symptomatic patients. The mean size of the nodules in patients with severe dyspareunia was 7.8 mm vs the mean for patients with mild or moderate dyspareunia which was 7.4 mm p = 0.860.

The odds ratio of presenting dyspareunia with an endometriotic nodule in the retrocervical region is 4.6 (95 % CI 1.4–15.6). The mean size of these nodules in both groups was assessed, it was 10.7 mm in the asymptomatic group and 11.3 mm in the group with pain, with p = 0.230.

Among the patients with a uterosacral ligament nodule 93.8 % also had an endometriotic nodule in the retrocervix. This percentage rises to 100 % in the case of patients with dyspareunia.

When performing a multiple linear regression between dyspareunia, presence of nodules in the retrocervical region and presence of nodules in the uterosacral region, only the retrocervical nodules obtained a statistical significance p = 0.032 vs. the uterosacral nodules which obtained p = 0.124. This single factor manages to present an $R^2$ of 0.49.

## 4. Discussion

Dyspareunia is a condition that drastically limits the quality of life of patients. It can have a significant impact on their physical and mental health, as well as their body image, relationships and fertility. It is estimated that it affects between 10 % and 20 % of the population [9]. This situation is even more serious in patients with endometriosis where up to 50 % of them may have deep dyspareunia [5,6].

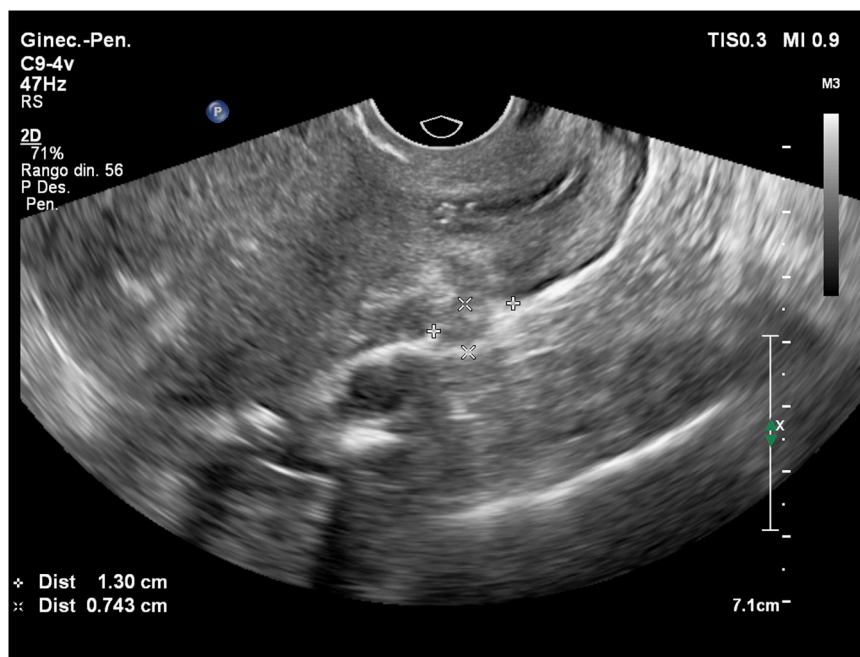Dyspareunia is an aspect of endometriosis that has barely been

**Fig. 1.** Ultrasound evaluation of a nodule in the retrocervix.

studied. There are few articles or trials that address this issue and the mechanisms that cause these symptoms remain unclear [7]. There is also a component of taboo or reluctance when it comes to talking about sexuality during a medical consultation, in both patients and professionals. This often leads women to use harmful strategies to deal with pain during sex, such as interrupting or avoiding intercourse or even enduring pain to try to become pregnant [10].

Therefore, understanding the seriousness of the problem and the mechanisms that cause it is the first, and fundamental, step in being able to deal with it.

It had previously been postulated that deep endometriotic nodules in the posterior compartment could be one of the causes of deep dyspareunia [5,6]. However, these studies were carried out prior to the consensus of the IDEA group [8] in which the endometriosis study system was classified and standardised to allow us all to use the same language. This causes many older studies to combine or mix deep endometriosis nodules into a single entity. Currently works such as those of Ros [11] or Leonardi [12] have validated the evaluation of these nodules by means of high-resolution ultrasound and their clear differentiation into retrocervical region nodules, uterosacral ligaments nodules, rectovaginal septal nodules and rectosigmoid involvement.

Our research allows us to clearly and unequivocally link the presence of dyspareunia with the presence of endometriotic tissue in the retrocervical region. Of special relevance is the fact that neither rectosigmoid involvement nor pouch of Douglas obliteration, assessed using the uterine slide technique, have shown statistical significance for this effect. The increased risk, with an odds ratio of 5.3 (95 % CI 2.2–12.5), shows a much higher likeliness of dyspareunia in the cases group. The difference in size of the nodules between the patients who have pain and those who are asymptomatic is also striking. It is possible that larger nodules do modulate an increase in biomarkers such as NGF, as proposed by Barcena et al. [4] and that this is one of the pathophysiological mechanisms of this symptom (Fig. 1).

It is also important to take into account the linear regression model that shows an R squared of 0.49 between retrocervical region nodules and dyspareunia. This means that these nodules alone are capable of explaining 50 % of the appearance and intensity of this symptom but we still do not know what other elements justify the remaining 50 %.

The effect of the presence of nodules in the uterosacral ligaments on

dyspareunia is doubtful. While it is true that individually they reach statistical significance, they fail to do so in the multiple linear regression model. This may be due to the fact that 100 % of patients with dyspareunia and nodules in the uterosacral ligaments also have nodules in the retrocervix. It is possible that it is the retrocervical nodules that actually cause dyspareunia. Studies with larger cohorts of patients would be necessary to elucidate the influence of nodules in the uterosacral ligaments.

The main characteristics of this type of patient have been reviewed, both the medical history and treatments and the exploration and ultrasound with no other element that reached statistical significance found. It is therefore necessary to continue carrying out studies into this in order to understand 100 % of the causes and mechanisms of this symptom.

Our study also shows a series of limitations that must be taken into account. It is a retrospective case-control study. However, the study was designed this way precisely to be able to assess the multi-causality of dyspareunia. Patients with previous surgeries have been included. This can sometimes make it difficult to correctly assess the posterior compartment, since postoperative adhesions or scars can be misinterpreted as endometriotic lesions due to their hypoechoic appearance. However, since the percentage of patients operated on is similar in both groups, we think that this bias is partially controlled. Another possible limitation of this study is that it was carried out in a reference centre for endometriosis, with a population with a high prevalence of nodules in the posterior compartment. Therefore, the findings may not be fully generalisable to the general population.

## 5. Conclusions

We can conclude that dyspareunia in patients with endometriosis is strongly dependent on the presence of nodules in the retrocervical region, although there are other factors involved that remain unknown, so more studies are still needed to understand and optimally address this symptom.

**Declaration of Competing Interest**

The authors declare that they have no conflicts of interest and

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