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ORIGINAL ARTICLE

Deep endometriosis: clinical and epidemiological findings of diagnosed women according to the criteria of the International Deep Endometriosis Analysis (IDEA) group

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Abstract

Introduction: endometriosis occurs when tissue similar to the endometrium affects the peritoneum, which can infiltrate structures and organs such as the bowel, ureter, bladder or vagina and is usually accompanied by an inflammatory process. It is estimated that the disease affects 6 to 10% of women of reproductive age and more than 50% of infertile women. The clinical and epidemiological data of patients with deep endometriosis (DE) available in the literature come from studies whose samples were selected by surgery, therefore subject to selection bias. Transvaginal pelvic ultrasound with bowel preparation (TVUBP) has high specificity and sensitivity values.

Objective: to analyze the clinical and epidemiological profile of patients with DE diagnosed through the TVUBP.

Methods: it is a cross-sectional study of 227 patients with an ultrasound diagnosis of deep endometriosis.

Results: infertility affected 43.8% of women. Painful symptoms considered as moderate or severe (visual analogue scale, VAS, ≥3) had the following prevalence and mean values on the VAS scale, respectively: dysmenorrhea in 84.7% (6.9), dyspareunia in 69.1%, (4.5), menstrual dyschezia in 60.7% (4.3) and menstrual dysuria in 35.7% of patients. A history of multiple surgeries occurred in 10.4% and only 6.8% of patients had undergone physiotherapy for the pelvic floor.

Conclusion: the DE population had a high prevalence of infertility and pain symptoms, which reflect the social impact on these women's quality of life and family planning. The high frequency of history of multiple surgical approaches and the low incidence of history of pelvic physiotherapy in the population with DE, contrary to the currently established ideal treatment recommendations, indicate the difficulty of access for patients to specialized centers.

Keywords: endometriosis, epidemiology, ultrasonography, dysmenorrhea, dyspareunia, pelvic pain, infertility.

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Authors summary

Why was this study done?
Generate information to contribute of alerting healthcare professionals who treat patients with deep endometriosis (DE) . The study was carried out to characterize the population with DE, a disease of high prevalence and social and economic impact worldwide. Most of the evidence that characterize the population with DE comes from samples submitted to surgical procedures (laparoscopy or laparotomy).Knowing the characteristics of women with DE can contribute to build strategies for organizing a network focused on public health, optimizing financial resources.

What did the researchers do and find?
We collected data from ultrasound reports in women with DE following the most up-to-date international protocol (IDEA group, 2016) to increase the specificity of the study sample selection. We collected information on the characteristics of patients with DE through a targeted clinical questionnaire. Our findings revealed a 43.8% of infertility prevalence. Painful symptoms considered moderate or severe had the following prevalence and mean values on the VAS scale, respectively: dysmenorrhea in 84.7% (6.9), dyspareunia in 69.1% (4,5), menstrual dyschezia in 60.7 % (4.3) and menstrual dysuria in 35.7% of patients. The study revealed a history of previous surgery to treat endometriosis in 29.5% of the patients. Only 6.8% of women with DE had undergone physiotherapy for the pelvic floor.

What do these findings mean?
The high prevalence of patients with multiple surgical approaches and the low prevalence of a history of pelvic physiotherapy (in contrast to the high prevalence of pain symptoms) indicate failure in the initial therapeutic approach currently recommended, reflecting the need for awareness of professionals in the area and encouragement the organization of reference centers. Some data reveal the social impact of DE and serve as an alert for the negative effect that the disease can have on the reproductive life of DE patients, reinforcing the importance of multidisciplinary care.

INTRODUCTION

Endometriosis is defined by the presence of endometrium-like epithelium and/or stroma outside the uterus, usually associated with an inflammatory process, which can infiltrate organs such as the intestine, vagina, and bladder[1]. It is a chronic, progressive, and complex disease, affecting about 10% of women of reproductive age and more than 50% of infertile patients[2,3].

The classic clinical picture of deep endometriosis (DE) may present symptoms as progressive dysmenorrhea, menstrual dyschezia, menstrual dysuria, dyspareunia, chronic pelvic pain, and infertility, among other urinary and gastrointestinal symptom[4,5]. However, the clinical diagnosis is challenging because, in addition to some women being asymptomatic, DE can also present nonspecific symptoms[4,6].

In public health, DE should be considered a problem, as the symptoms lead to loss of work productivity, causing a significant economic burden, and inducing costs comparable to other chronic diseases to treat pain and infertility problems. In addition, DE also impairs patients' quality of life with negative consequences on sexual function and personal relationships[6,7].

Despite the diagnosis evolution, which currently can be performed with high accuracy by transvaginal ultrasound[8,9], the technique can be optimized when performed after bowel preparation[10-12]. Knowledge about the clinical and epidemiological characteristics of women living with DE comes from samples taken from women diagnosed during a surgical procedure[13-18], being, therefore, susceptible to selection bias.

Thus, this research aims to analyze the epidemiological and clinical characteristics of women living with DE diagnosed with a non-invasive protocol by transvaginal ultrasound.

METHODS

Study design

This was a cross-sectional study, carried out in Recife, Pernambuco, Brazil, between May 2019 and May 2021, approved by the Institutional Review Board of the Hospital das Clínicas of the Federal University of Pernambuco (Letter of approval No. 4,883.90).

Eligibility criteria

Women with suspected endometriosis who underwent transvaginal ultrasound after bowel preparation (TVUBP) for DE research in a public university service and two private clinics in the city of Recife were eligible. They were consecutively invited by convenience before the procedure was performed by a research assistant. Inclusion criteria were patients who underwent transvaginal ultrasound with a complete bowel preparation protocol and responded to the clinical questionnaire. Exclusion criteria were: history or suspicion of pelvic neoplasia and whose ultrasound result was negative, that is, without specific criteria for deep endometriosis. Only women with deep endometriosis diagnosed by transvaginal ultrasound remained in the final sample.

Procedures

Clinical history such as time of symptoms, time to diagnosis, obstetric and surgical history, and past and current medication history. Eligible participants completed a questionnaire on clinical and epidemiological aspects based on the international visual analog pain scale (VAS)[19,20], assembled for this research. On a scale from 0 to 10, it addresses pain such as the menstrual period, dysmenorrhea, dyspareunia, dysuria, and dyschezia. Concerning pain symptoms, the women were instructed to consider the symptoms prior to using hormone blockade if they were using clinical treatment at the time of the

examination.

Each exam was performed and interpreted in real-time by the same radiologist (C.P), who has had experience in gynecological ultrasound for nine years and in endometriosis research for five years (at baseline). Exams were performed with a 5-9 MHz probe (Logic E9 and Voluson E8, GE Healthcare®, Milwaukee, WIS).

Participants used two doses of oral laxative the day before the test (Bisacodyl, at 8:00 and 14:00), a low-residue diet for 24 hours before the test, and a rectal enema one hour before[21].

All participants were evaluated according to the protocol of the International Deep Endometriosis Analysis Group, IDEA GROUP[22].

Statistical analysis

Data were entered into an Excel 2010 spreadsheet and transferred to SPSS 13.0 software (Statistical Package for the Social Sciences) for statistical analysis. The variables were represented by measures of central tendency and adequate dispersion.

RESULTS

We recruited 398 women. Of these, 171 were excluded because they did not show specific signs of DE on TVUBP or were neoplasia suspected (Figure 1). Our

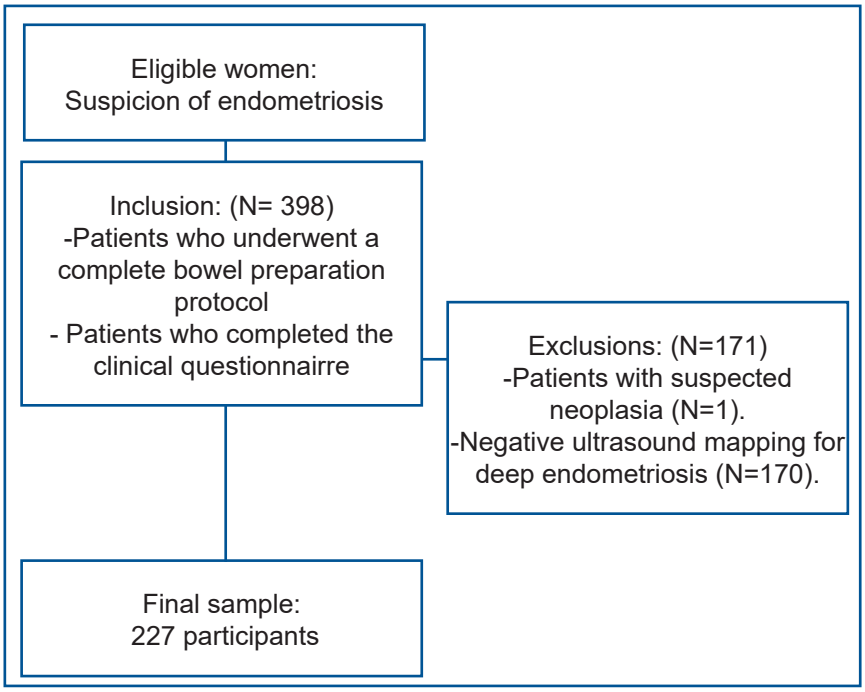

Figure 1:Flowchart of sample selection

Table 1: Characterization of the quantitative variables of women with DE (n=227)

Variables	Average ± DP	Median - (Q1; Q3)	Minimum- maximum
Age	**35.8 ± 6.3**	36.0 (31.0; 40.0)	17.0 – 50.0
Sickness time (years)	7.7 ± 7.1	**5.0 (2.0; 11.5)**	0.0 – 30.0
Time to diagnosis (years)	4.5 ± 5.4	**2.0 (1.0; 6.0)**	0.0 – 30.0
VAS Scale:			
Level of general pain in the menstrual period*	7.1 ± 3.1	**8.0 (6.0; 10.0)**	0.0 – 10.0
Dysmenorrhea*	**6.9 ± 3.3**	8.0 (5.0; 10.0)	0.0 – 10.0
Dyspareunia*	**4.5 ± 3.4**	5.0 (2.0; 8.0)	0.0 –10.0
Menstrual dyschezia*	**4.3 ± 3.7**	4.0 (0.0; 8.0)	0.0 –10.0
Menstrual dysuria*	2.4 ± 3.1	0.0 (0.0; 5.0)	0.0 –10.0

*Numerical data from the VAS scale. Source: Author, 2021. The numbers in bold indicate the measure of central tendency used.

final sample consisted of 227 women diagnosed with DE.

The mean age was 35.8 years, 80% of the patients were over 30 years old at the examination time. The median times of illness and delay to diagnosis were five and two years, respectively.

The average level of General Pain in the menstrual period by the VAS scale was 7.1. Painful symptoms obtained the following mean scores: 6.9 for dysmenorrhea, 4.3 for menstrual dyschezia, and 4.5 for dyspareunia. menstrual dysuria did not show a linear distribution. Table 1 summarized quantitative clinical and epidemiological characteristics.

Table 2: Characterization of qualitative variables of women with DE (n=227)

Variables	n	% (valid data)
Place examination		
Public hospital	19	8.4
Private clinics	208	91.6
Previous surgeries for endometriosis[a]		
0	158	70.5
1	42	18.8
2	17	7.6
3	5	2.2
4	2	0.9
Previous hormonal treatment[b]	136	60.2
Hormonal treatment at the time of examination[c]	89	61
Pelvic physiotherapy[d]	15	6.8
Number of previous pregnancies[e]		
0	111	49.3
1	71	31.6
2 or more	43	19.2
Desire pregnancy[f]	141	62.4
Abortion[g]		
0	182	83.1
1	27	12.3
2 or more	10	4.6
History of pelvic inflammatory disease[h]	10	12.3
Quality of life		
Good	97	42.7
Regular	102	44.9
Bad	28	12.3
Infertility[i]	99	43.8
Intensity of general pain in the menstrual period[j]		
mild or absent	27	11.9
moderate	65	28.8
severe	134	59.3
Dysmenorrhea[l]		
mild or absent	34	15.2
moderate	58	58.7
severe	131	26
Dyspareunia[m]		
mild or absent	69	30.9
moderate	84	37.7
severe	70	31.4

Continuation - Table 2: Characterization of qualitative variables of women with DE (n=227)

Variables	n	% (valid data)
Menstrual dyschezia [n]		
mild or absent	88	39.3
moderate	75	33.5
severe	61	27.2
Menstrual dysuria		
mild or absent	146	64.3
moderate	59	26
severe	22	9.7

Source: Author, 2021. **note:** Missing data: [a] 3, [b] 1 , [c] 81, [d]7 , [e]2, [f]1, [g] 8, [h]146, [i] 1, [j]1, [l] 4, [m] 4, [n] 3.

Qualitative characteristics are summarized in table 2.

Regarding treatment history, 29.5% of patients had already received surgical treatment for endometriosis, and 10.7% (24 of 224) had a history of 2 or more surgeries for DE. Oral contraceptive drug treatment or estrogen blockade had already been performed in 60.2% of patients, and 61% were using it at the time of the examination. Regarding the previous physiotherapy to relieve symptoms, only 6.8% of the patients had received it.

Concerning the clinical-obstetric history, 49.3% of the patients had no children, 63.6% had a desire to conceive, 4.6% had a chronology of 2 or more previous miscarriages, and 12.3% reported pelvic inflammatory disease.

As for the quality of life, 44.9% classified it as regular, 42.7% as good, and 12.3% as poor. Regarding classic symptoms, infertility occurred in 43.8% of women, and pain symptoms were subclassified as absent (VAS 0), mild (VAS 1.2), moderate (VAS 3,4,5,6, 7), and severe (VAS 9 and 10).

Painful symptoms considered moderate or severe had the following decreasing prevalence: Dysmenorrhea in 84.7%, Dyspareunia in 69.1%, menstrual Dyschezia in 60.7%, and menstrual Dysuria in 35.7%.

DISCUSSION

Our findings indicate a high prevalence of infertility and pain symptoms (mainly dysmenorrhea, dyspareunia, and menstrual dyschezia), revealing particularities compared to outcomes reported in other countries[2,10,15,18,23].

The mean age of patients was 35.8 years, similar to other studies[24-26]. Although the disease is typically diagnosed in this age group, probably when there are symptoms that cause repercussions or these patients seek diagnostic investigation, many studies have already shown that the onset of DE is early since adolescence[27].

Infertility occurred in 43.8% of the patients in our sample, a higher number than that found by Leonardi *et al.*[24] (20.9% in Australia), Bazot *et al.*[28] (22.85% in France), or Morgan-Ortiz *et al.*[26] (26%, in Austria). Our number is expected to be higher when compared to such studies that exclusively studied operated patients and possibly excluded those with infertility referred for assisted reproduction therapy.

The higher prevalence of infertility in this Brazilian region may be due to our sample selection. It was focused on those still looking for diagnostic investigation such as pain, infertility, or altered findings in routine exams.

It is noteworthy that there is a difference in methodology between this manuscript and previous researchers, who evaluated the records of patients in tertiary centers or interviewed women undergoing laparoscopy. The delay time between the onset of symptoms and the moment of diagnosis in this study (2.0 years) was lower than the value found by European researchers (which varied between 4 and 10 years)[29-31]. Therefore, a naturally longer delay in indicating a laparoscopy is expected than in requesting an ultrasound, due to the invasive nature of the former. Another issue is that most of the sample in this study was collected in private clinics (91.6%), whose access time to the diagnostic investigation exam should be much shorter when compared to patients in the public health system, as already demonstrated by Nnoaham in 2011[31].

Despite this, the fact that 60.2% of the patients had already used oral contraceptives or estrogen blockade makes us believe that probably many patients in this study already had an asymptomatic disease and the perception of the onset of symptoms may have occurred when the patients discontinued the treatment to try to conceive. The concept is already well established that the previous history of oral contraceptives is associated with more severe cases of endometriosis, possibly masking the symptoms but without preventing the progression of the disease in these patients[32,33].

Patients in this study exhibited pain symptoms with a mean score of 6.9 for dysmenorrhea and 4,3 for menstrual dyschezia (other researchers found values that ranged between 6.9 and 7.7 for the first and, 6.6 for the last[23,32,34]). The slightly higher values in studies published in the literature may be justified because these authors consider only patients with surgical indications, potentially more severe than those in this research.

The high prevalence of moderate or severe pain symptoms (>85%) and infertility (43.8%) must be some of the reasons why 57.2% of the patients included in the study considered their quality of life moderate or poor.

On the other hand, some patients with moderate or severe pain levels on the VAS scale but responsive to clinical treatment explain the almost 43% of patients who judged their quality of life to be good. Future studies that investigate the correlation between pain intensity and

prolonged use of contraceptives, which could interfere with the perception of quality of life, may be helpful.

Our data reflect the difficulties women face in accessing specialized treatment. It is essential to highlight that 29.5% of patients with DE had 1 to 4 previous surgeries for endometriosis treatment[16,23], and, among these, 10.7% (24 of 224) had a history of 2 or more surgeries for DE, but persisted with ultrasound findings compatible with the disease. Since these women are usually seen by generalist gynecologists and have an early indication for surgery, without initial staging using an acceptable imaging method, there is a detriment to the planning of an excellent surgical team and, therefore, an increase in the rate of residual disease. The current concept of good practices seeks a smaller number of approaches, with a single and complete surgery being ideal, as advocated by Chapron[6].

The role of pelvic physiotherapy in assessing and treating muscle disorders involving the pelvic floor, with consequent improvement in pain symptoms and the quality of life of women with DE, is already well established[6,35]. Still, in the treatment of DE, only 6.6% of the participants in this study had already performed pelvic physiotherapy. Our findings warn and reveal how this method has been underused in Pernambuco.

The knowledge dissemination among general gynecologists about new treatments, ideal diagnostic methods, and the creation of endometriosis reference centers are strategies with an expected positive impact on the affected population.

Some of our figures reveal the social impact of DE and alert the negative effect that the disease can cause on the reproductive life of DE women: 80% of the patients studied were over 30 years old, 62.4% had a desire to conceive, 43.8% already fulfilled the infertility criteria and 69.1% complained of deep dyspareunia (moderate and severe). Together, these data reinforce the importance of multidisciplinary care, of a broader look at these patients and their couples, who need to manage many issues arising from the emotional and financial impacts associated with infertility[6,7].

However, some limitations of this study must be considered. First, the sample is susceptible to selection bias, as women were recruited from specialized sites to investigate endometriosis. On the other hand, it is noteworthy that our analysis is less susceptible to selection biases presented by most previous researchers whose samples were selected by indication of surgical treatment[7,32]. Therefore, our sample is more representative of the general population, which has a suggestive clinical history but did not undergo surgery for the diagnosis.

Another factor to consider is that the clinical questionnaires were answered by the participants, who may have had difficulty interpreting the terms used. We reiterate that the research instrument was built with language for lay people; thus, we believe that we have reduced the bias of the interviewer's interference.

On the other hand, the main strength is that the selected sample came from patients diagnosed in reference centers, using a non-invasive method, following international criteria, which made the chance of a false positive low (IDEA, 2016).

CONCLUSION

The analyzed sample of women living with DE had a high prevalence of infertility and pain symptoms (mainly dysmenorrhea, dyspareunia, and menstrual dyschezia), reflecting the social impact of impairing on quality of life and family planning for these women. The high frequency of history of multiple surgical approaches and the low incidence of history of performing pelvic physiotherapy in the population with DE, contrary to the recommendations of ideal treatment, indicates the difficulty of access of patients to specialized centers. Selecting the sample based on ultrasound diagnostic criteria opens the horizon for a new methodology for analyzing patients with DE, possibly bringing them closer to the general population.

Author Contributions

Cicília: lead author, writing the text; Cicília, Mauro, Simone: idealization and elaboration of the questionnaires; Cicília, Mauro, Luciana, E. Just, Débora Leite and Jóse Luíz: text review.

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Conflicts of Interest

None of the authors have a conflict of interest to declare.

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Resumo

Introdução: endometriose ocorre quando o tecido semelhante ao endométrio acomete o peritônio, podendo infiltrar estruturas e órgãos como o intestino, o ureter, a bexiga ou a vagina e geralmente está acompanhado de processo inflamatório. Estima-se que a doença acometa 6 a 10% das mulheres em idade reprodutiva e mais de 50% das mulheres inférteis. Os dados clínicos e epidemiológicos das pacientes com EP disponíveis na literatura são provenientes de estudos cujas amostras foram selecionadas por cirurgia, portanto passíveis de vieses de seleção. A ultrassonografia pélvica endovaginal com preparo intestinal (USGTVP) tem valores de especificidade e sensibilidade elevados.

Objetivo: analisar o perfil clínico e epidemiológico das pacientes portadoras de EP diagnosticadas através da USGTVP.

Método: estudo transversal, que analisou 227 pacientes com diagnóstico ultrassonográfico de endometriose profunda.

Resultados: infertilidade acometeu 43,8% das mulheres. Sintomas álgicos considerados como moderado ou grave (escala visual analógica, EVA, ≥3) apresentaram respectivamente a seguinte prevalência e valores médios na escala de EVA: dismenorreia em 84,7% (6,9), dispareunia em 69,1%, (4,5) disquezia menstrual em 60,7% (4,3) e disúria menstrual em 35,7% das pacientes. Antecedente de múltiplas cirurgias ocorreu em 10,4 % e apenas 6,8 % das portadoras haviam realizado fisioterapia para assoalho pélvico.

Conclusão: a população portadora de EP apresentou alta prevalência de infertilidade e sintomas álgicos, achados que refletem o impacto social na qualidade de vida e no planejamento familiar dessas mulheres. A alta frequência de antecedentes de múltiplas abordagens cirúrgicas e a baixa incidência de antecedente de realização de fisioterapia pélvica na população com EP, contrariando as recomendações de tratamento ideal atualmente já estabelecidas, sinalizam a dificuldade de acesso das portadoras a centros especializados.

Palavras-chave: endometriose, epidemiologia, ultrassonografia, dismenorreia, dispereunia, dor pélvica, infertilidade.