

Epidemiological profile of women with endometriosis: a retrospective descriptive study

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Abstract

Objectives: to describe the epidemiological and clinical profile of women with endometriosis and to determine the association with the prognostic characteristics of the disease.

Methods: retrospective descriptive study involving 237 women attended at two referral hospitals for endometriosis, between 2011 and 2017. Associations between groups were estimated using logistic regression models.

Results: most women (65.4%) were of reproductive age (29-39 years), with a body mass index in the range of 18.5-24.9 kg/m² and a high prevalence (23-81%) of symptoms of the disease, with 49.5% being infertile. The average time of diagnosis was 5 years. Ovarian endometrioma and/or deep infiltrative endometriosis (DIE) were the most frequent type of endometriosis (87%), and 59% of patients were in the III/IV stage of the disease. Approximately 87% of women with surgical diagnosis were aged over 30, married (70%) and had lower parity. Dyspareunia was negatively associated with superficial endometriosis. Infertility was positively associated with age (30-39 years) and DIE in the uterine tubes; dysmenorrhea with DIE in the uterosacral ligament; cyclic intestinal complaints with DIE in the rectosigmoid and intestine, and with DIE classification and III/IV stage.

Conclusions: knowing the epidemiological and clinical profile of Brazilian women with endometriosis can help in diagnosis and treatment planning.

Key words Endometriosis, Epidemiology, Prognosis, Symptoms



Introduction

Endometriosis is a gynecological disease defined by the presence of endometrial tissue outside the uterus, associated with different symptoms such as dysmenorrhea, chronic pelvic pain, dyspareunia, infertility and cyclical intestinal and urinary complaints.¹ The disease's prevalence is not clearly established; however, it is estimated to affect approximately 10% of the premenopausal women,² and 35-50% of infertile women.^{3,4} Endometriosis is a disease that entails a significant burden on women's quality of life and on healthcare systems, mainly due to the incapacitating symptoms of pain, the presence of infertility and the delay and high cost of diagnosis and treatment.^{1,5,6} In addition, all health care costs involved with endometriosis were comparable to the other chronic conditions.¹

The etiology of endometriosis remains unknown, although the most accepted theory is regarding retrograde menstruation, described by Sampson, in 1927. However, many factors could be involved in the development and maintenance of ectopic implants,¹ such as hormonal,⁷ inflammatory,⁸ genetic⁴ and environmental ones.³ Studies have shown that body mass index (BMI),^{3,9} smoking¹⁰ and physical activity¹¹ have an inverse association with endometriosis, although the mechanisms of these associations remain unclear. Other factors have also been associated with endometriosis, such as early age at menarche³ and infertility,¹² all conferring an increased risk, while parity¹³ and oral contraceptive use³ are associated with a decreased risk. However, it is not known whether these associations are causes or consequences of endometriosis, and therefore should be interpreted with caution, mainly due to the inability to diagnose it before the onset of symptoms.¹

Despite some studies have addressed the association between endometriosis and demographic factors, personal habits, menstrual and reproductive factors, the pathophysiology of the disease remains an enigma and the appropriate counseling of patients regarding prognosis is still challenging.^{3,14,15} Thus, the aim of this study was to describe the epidemiological and clinical profile of women with endometriosis treated at two reference hospitals in Rio de Janeiro and to determine their relationship with prognostic values, diagnosis and symptoms of the disease.

Methods

This hospital-based retrospective descriptive study included 237 women recruited, between 2011 and 2017, from two reference hospitals in Rio de Janeiro. A convenience sampling was chosen to list the accessible population over a significant period for the clinical condition under study. All followed procedures were approved by the Brazilian Ethic Committees of the Hospital Federal dos Servidores do Estado (HFSE - 414/2011) and of the Hospital Moncorvo Filho da Universidade Federal do Rio de Janeiro (HMF/UFRJ -1.244.294/2015). The patients took part in a face-to-face interview, then provided written informed consent to allow their medical data to be collected, analyzed, and shared, and completed a demographic questionnaire during appointments.

Patients were eligible if they showed histologically confirmed endometriosis lesions or if they showed images of infiltrative endometrial lesions at magnetic resonance imaging (MRI).¹⁶ Indications for performing surgery were: infertility without access to assisted reproduction techniques, pain refractory to clinical treatment, functional impairment of organs such as large bowel and/or urinary tract or bulky and/or suspected endometriomas.¹⁷ According to the American Fertility Society Score,⁴ patients with endometriosis diagnosed by surgery were divided in stages I/II and stages III/IV. Endometriotic lesions were classified into three groups: superficial endometriosis (SUP), ovarian endometrioma (OMA) or deeply infiltrating endometriosis (DIE), as described elsewhere.³ Patients were excluded in the event of pregnancy or with only clinical suspicion of endometriosis or if surgical findings showed suspicion or evidence of malignancy or adenomyosis (N=32).

The following patients' characteristics were collected for this study: age, BMI, marital status, educational level, contraceptive use, personal habits (smoking, alcohol consumption, physical activity), family history of endometriosis, age at menarche, reproductive history (parity, infertility, spontaneous abortion), symptoms of endometriosis (dysmenorrhea, pelvic pain, dyspareunia, cyclical intestinal and urinary complaints), age at endometriosis diagnosis, diagnosis method, endometriosis staging and classification and ectopic loci affected by the disease.

BMI was categorized according to standard World Health Organization (WHO) cut-off points: underweight (BMI < 18.5kg/m²), normal weight (18.5 - 24.9kg/m²), overweight (25 - 29.9kg/m²), obese (30 - 39.9kg/m²) or morbidly obese (≥40kg/m²). In addition, the women were divided

into two groups for statistical analysis: BMI $<25\text{kg/m}^2$ (underweight and normal weight), and BMI $\geq 25\text{kg/m}^2$ (overweight, obese and morbidly obese). The personal habits were self-reported, and we considered at least one year of practice/consumption. Only severe and incapacitating cyclic and acyclic pains were considered as symptoms of endometriosis. Infertility was defined as a couple not being able to conceive after 12 consecutive months of regular, contraceptive-free intercourse (primary or secondary).⁴

A descriptive study was conducted, presenting relative frequencies for each categorical variable. Women were categorized according to prognostic values, diagnostic method, and presence of clinical symptoms, and evaluated for their association with the personal and clinical features.

Student's t-test was used to compare continuous variables between the studied groups, and results were expressed as mean \pm standard deviation (SD). Chi-square (χ^2) statistic test or Fisher's exact test, when applicable, were used to compare the differences between categorical variables. Multivariable logistic regression analyses were performed to identify possible confounding factors in the associations between variables and endometriosis features, which were estimated by the odds ratio (OR) with a 95% confidence interval (CI95%). To elaborate the final regression model, we considered the biological significance of each variable and the degree of statistical significance in the univariate analysis (p -value less or equal than 0.20). Differences were considered statistically significant when p -value was less than or equal to 0.05. All analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA), version 20.0.

Results

The sociodemographic characteristics of the 237 patients are summarized in Table 1. The mean age was 36.1 ± 7.2 years and more than half of women were married. Most participants had at least finished high school and had a mean BMI of 26.6 ± 5.4 kg/m^2 . In addition, most of them practiced some regular physical activity, were never smokers and had some regular alcohol consumption. Regarding the reproductive history, most patients had at least one child and never had a spontaneous abortion. Besides, the majority of them use oral contraception and some had history of endometriosis in first-degree relatives.

Regarding the age at menarche, it was observed the mean of 12.5 ± 1.7 years, with 43.5% of the patients reaching menarche between 12-13 years. The clinical characteristics of the study population are listed in Table 2. Laparoscopy was the most used diagnostic method and most patients diagnosed by surgery had stage III/IV endometriosis. The most patients presented at least three symptoms of gynecological pain (Figure 1) and almost half of women with endometriosis reported infertility (Table 2). Considering the number of painful symptoms, 32 women had only dysmenorrhea, 20 only deep dyspareunia and 3 only chronic pelvic pain; 40 women had dysmenorrhea and dyspareunia, 33 had dysmenorrhea and chronic pelvic pain and 2 had dyspareunia and chronic pelvic pain. Finally, 86 patients had dysmenorrhea, dyspareunia and chronic pelvic pain (Figure 1).

Fifteen (6.3%) patients had only SUP endometriosis, 55 (23.2%) only OMA and 56 (23.6%) only DIE, 5 (2.1%) women had SUP and OMA, 10 (4.2%) had SUP and DIE and 72 (30.4%) had OMA and DIE. In addition, 21 (8.9%) patients with SUP and OMA were associated with DIE. Under these circumstances, most women had 2 to 4 affected loci with ovary being the most prevalent loci, followed by uterosacral ligament and by rectosigmoid (Table 2).

Figure 2 shows a comparison between asymptomatic and symptomatic women for dysmenorrhea (A), deep dyspareunia (B-D), cyclical intestinal complaints (E-H) and infertility (I-J), regarding the demographic, clinical and menstrual characteristics of the study population. Women with DIE in uterosacral ligament were more affected by dysmenorrhea (OR = 2.8; CI95% = 3.14 - 7.52). We also observed that patients with BMI higher than 25 kg/m^2 (OR = 1.97; CI95% = 1.10 - 3.53), and who had any alcohol consumption (OR = 2.13; CI95% = 1.20 - 3.82) were more affected by dyspareunia. However, woman with superficial endometriosis were less affected by dyspareunia (OR = 0.25; CI95% = 0.11 - 0.57). The cyclical intestinal complaints were positively associated with DIE in the rectosigmoid (OR = 3.78; CI95% = 1.95 - 7.33) and intestine loci (OR = 2.96; CI95% = 1.31 - 6.65), and with DIE classification (OR = 2.58; CI95% = 1.08 - 6.11) and III/IV stage of the disease (OR = 2.75; CI95% = 1.31 - 5.76). Finally, we found that women between 30 - 39 years old were more likely to be infertile than those younger than 29 years (OR = 2.72; CI95% = 1.02 - 7.24). We also observed that women whose uterine tubes were affected by

Table 1

Sociodemographic characteristics of the studied population (N=237).

Variables	N	%
Age (year)		
≤ 29	44	18.6
30 – 39	111	46.8
≥ 40	73	30.8
Missing	9	3.8
Marital status		
Single	78	32.9
Married	135	57.0
Divorced/separated	13	5.5
Widowed	1	0.4
Missing	10	4.2
Educational level		
Primary school	33	13.9
High school	114	48.1
Higher education	82	34.6
Missing	8	3.4
BMI (kg/m ²)		
< 18.5	12	5.1
18.5 – 24.9	81	34.2
25 – 29.9	78	32.9
30 - 40	60	25.3
> 40	3	1.3
Missing	3	1.3
Physical activity		
No	93	39.2
Yes*	136	57.4
Missing	8	3.4
Smoking status		
Smoker	22	9.3
Never smoked	192	81.0
Ex-smoker	22	9.3
Missing	1	0.4
Alcohol consumption		
No	96	40.5
Yes	100	42.2
Ex-alcoholic	32	13.5
Missing	9	3.8
Parity**		
0	60	32.3
1	59	31.7
2	34	18.3
≥ 3	19	10.2
Missing	14	7.5
Spontaneous abortion**		
No	142	76.3
Yes	37	19.9
Missing	7	3.8

continue

BMI = body mass index; * Past and present physical activity; ** Fifty-one patients were not included because they did not attempt to get pregnant;*** A patient can use more than one contraception type; **** Family history only in first-degree relatives.

Table 1 concluded

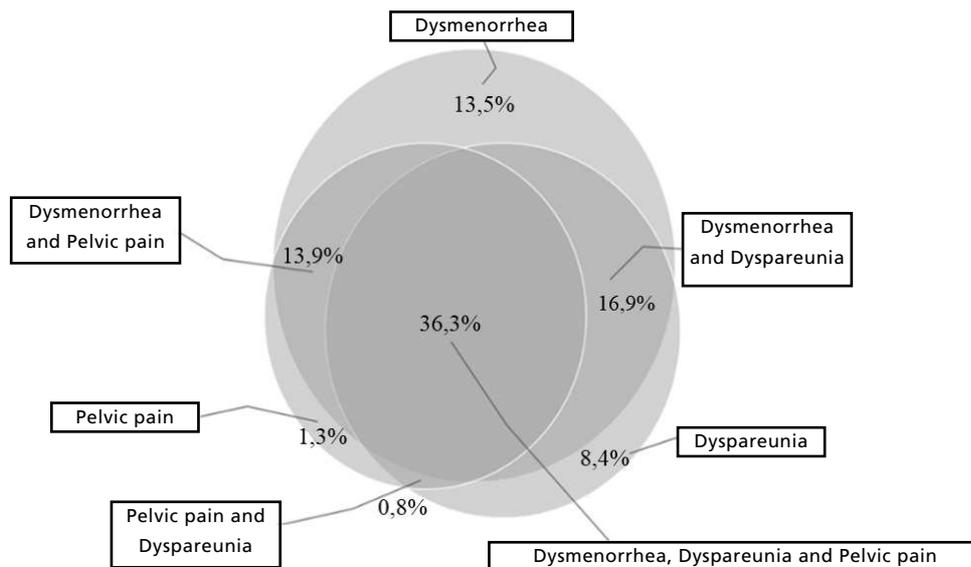
Sociodemographic characteristics of the studied population (N=237).

Variables	N	%
Contraception use***		
Oral	208	87.7
Injectable	67	28.3
DIU	19	8.0
Missing	1	0.4
History of endometriosis****		
No	178	75.1
Yes	47	19.8
Missing	12	5.1

BMI = body mass index; * Past and present physical activity; ** Fifty-one patients were not included because they did not attempt to get pregnant;*** A patient can use more than one contraception type; **** Family history only in first-degree relatives.

Figure 1

Frequency of the individual and concomitant symptoms in the studied population.



endometriosis were more likely to have infertility (OR = 2.91; CI95% = 1.18 - 7.17).

Table 3 shows the demographic and clinical differences between cases diagnosed by surgery and image, DIE and non-DIE cases and between endometriosis stages I/II and III/IV. We found that patients diagnosed by surgery were significantly older (mean age 36.9 ± 7.0 years), were more likely to be married and had a lower parity than those diag-

nosed by image. Women with DIE showed a higher educational level and were more likely to be never smokers than the ones without DIE. We observed that stage III/IV patients were more likely to be married, to practice some regular physical activity than the ones with endometriosis stage I/II.

The mean time between the first endometriosis symptoms and diagnosis was 4.5 ± 6.5 years for all cases. Significant differences were observed

Table 2

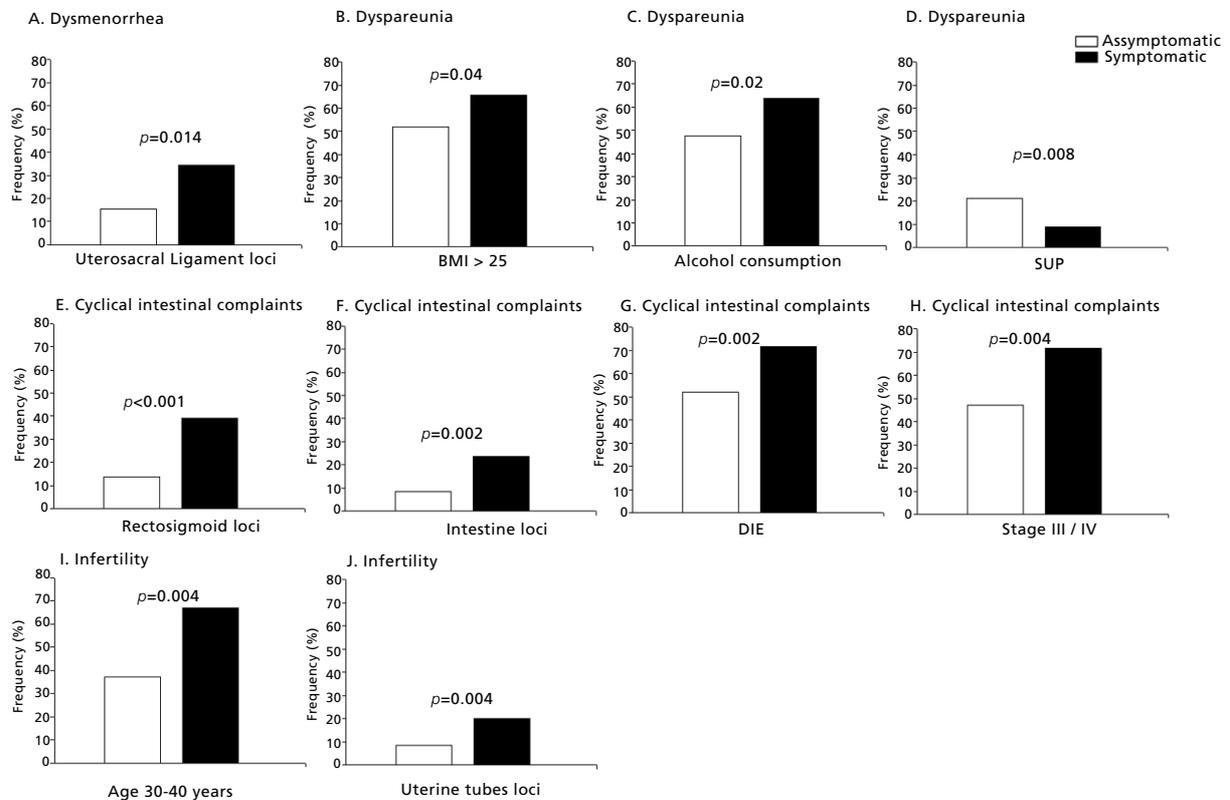
Clinical characteristics of the studied population (n= 237).

Variables	N	%
Symptoms*		
Dysmenorrhea	191	80.6
Non-cyclic chronic pelvic pain	124	52.3
Deep dyspareunia	150	63.3
Cyclical intestinal complaints**	111	46.8
Cyclical urinary complaints**	54	22.8
Asymptomatic	14	5.9
Infertility***		
No	93	50.5
Yes	91	49.5
Diagnostic method		
MRI	88	37.1
Laparoscopy	110	46.4
Laparotomy	34	14.4
Laparoscopy and laparotomy	5	2.1
Endometriosis type		
SUP	31	13.1
OMA	60	25.3
DIE	145	61.2
Missing	1	0.4
Endometriosis staging****		
I/II	58	38.9
III/IV	83	55.7
Missing	8	5.4
Organs affected by endometriosis*****		
Ovary	154	65.0
Uterosacral ligament	72	30.4
Rectosigmoid	59	24.9
Peritoneum	50	21.1
Intestine	45	19.0
Bladder	40	16.9
Uterine tubes	29	12.2
Rectovaginal septum	25	10.5
Others	23	9.7
Number of ectopic loci		
1	104	43.9
2 to 4	114	48.1
> 4	16	6.7
Missing	3	1.3

MRI =magnetic resonance imaging; SUP = superficial endometriosis; OMA = ovarian endometrioma; DIE = deeply infiltrating endometriosis; * A patient can have more than one concomitant symptom; ** Pain and bleeding; *** Primary or secondary. Fifty-three patients had no attempt to conceive and were excluded from this analysis; **** Refers to patients diagnosed by surgery (N = 149); *****A patient can have more than one endometriotic foci.

Figure 2

Comparison between asymptomatic and symptomatic women for dysmenorrhea, deep dyspareunia, cyclical intestinal complaints and infertility, regarding the demographic, clinical and menstrual characteristics of the studied population.



(A) dysmenorrhea; (B-D) deep dyspareunia; (E-H) cyclical intestinal complaints; (I-J) infertility. *p*-value from Chi-square test (Pearson *p*-value); SUP = superficial endometriosis; DIE = deeply infiltrating endometriosis; BMI= body mass index.

between endometriosis stages I/II and III/IV (3.3 ± 4.1 and 5.3 ± 7.5 years) and between DIE *versus* non-DIE patients (3.8 ± 5.4 and 5.2 ± 7.0 years), showing that advanced stages and DIE had a longer diagnosis time than initial stage and non-DIE. However, no statistical differences were found between patients with diagnosis confirmed by surgery or by image methods.

Discussion

Endometriosis is usually present in women of reproductive age,^{2,3} according to the mean age (36 years) described in the present study. The endometriosis risk associated to a lower BMI has been described

but remains an enigma.^{2,3,9} Our findings agree with earlier large cross-sectional and case-control studies linking an inverse association between endometriosis and BMI.^{2,3,9} A cross-sectional study, in 2017, involving surgical cohort (273 women) found endometriosis was inversely associated with anthropometric measures and body composition indicators.⁹ However, the biosynthesis of estrogen, an important hormone that contributes to endometriosis progression, occurs primarily in the ovaries, but also occurs in the adipose tissue and subcutaneous fat in the body.¹⁸ Thus, biologically, the low BMI cannot be explained in women with endometriosis. Therefore, the relationship between endometriosis and BMI, and the genetic and mole-

Table 3

Distribution of demographics and clinical characteristics in subgroups of patients with endometriosis by diagnosis and classification of disease.

Variables	Surgery (N=149)		Image (N=88)		p*	Non-DIE (N=91)		DIE (N=145)		p*	I / II Stage (N=58)		III / IV Stage (N=83)		p*
	n	%	n	%		n	%	n	%		n	%	n	%	
Age (year)															
≤ 29	18	12.7	26	30.2	0.005	-	-	-	-	NS	-	-	-	-	NS
30 – 39	76	53.5	35	40.7		-	-	-	-		-	-	-	-	
≥ 40	48	33.8	25	29.1		-	-	-	-		-	-	-	-	
Marital status															
Single	36	25.9	42	47.7	0.01	-	-	-	-	NS	20	38.5	14		0.049
Married	97	69.8	38	43.2		-	-	-	-		31	59.6	60		
Divorced/separated	5	3.6	8	9.1		-	-	-	-		1	1.9	4		
Widowed	1	0.7	0	0.0		-	-	-	-		0	0.0	1		
Educational level															
Primary school	-	-	-	-	NS	19	22.1	14	9.9	0.02	-	-	-	-	NS
High school	-	-	-	-		45	52.3	68	47.9		-	-	-	-	
Higher education	-	-	-	-		22	25.6	60	42.2		-	-	-	-	
Smoking status															
Smoker	-	-	-	-	NS	23	25.3	20	13.9	0.03	-	-	-	-	NS
Never smoked	-	-	-	-		68	74.7	124			-	-	-	-	
Physical activity															
No	-	-	-	-	NS	-	-	-	NS	29	53.7	25	31.6	0.01	
Yes**	-	-	-	-		-	-	-			25	46.3	54		68.4
Parity															
0	50	41.3	10	19.6	0.02	-	-	-	NS	-	-	-	-	NS	
1	38	31.4	21	41.2		-	-	-			-	-	-		
2	24	19.8	10	19.6		-	-	-			-	-	-		
>3	9	7.5	10	19.6		-	-	-			-	-	-		

DIE = deeply infiltrating endometriosis; NS and (-) = Non-significant results; * Chi-square test or Fisher's exact test; ** Past and present physical activity.

cular effects upon body weight still needs to be elucidated. Regarding the hereditary influence in endometriosis features, positive associations about family history of endometriosis have been suggested in several studies.^{1,19}

Patients with endometriosis reported to be married and had higher educational level, corroborating with previous qualitative and case-control studies.^{3,15,20} Chapron *et al.*³ conducted a multi-country case-control study, in 2016, comprising 1008 women with endometriosis and showed a higher frequency of married and university-educated women among endometriosis cases in comparison with disease free women. Nowadays, women use contraceptives more often and for a longer period, therefore only discover the presence of the disease when they decide to get pregnant.²¹ We also observed that most women used contraceptives, and had menarche around 12 years old, in agreement with recent studies.^{3,13,22}

Regarding lifestyle features, we found that patients had the habit of practicing physical activity and alcohol consumption, also most of them never smoked. Some studies have reported that women with endometriosis consume more alcohol,^{11,23} perform more physical activities²² and usually don't smoke in accordance with our findings.^{3,9} However, other articles have found different results,^{11,24} showing that there are some controversies and, therefore, further studies are needed to better understand the relation between these variables and endometriosis.

More than one third of the patients had all three symptoms of gynecological pain combined, according to a cross-sectional study, published in 2008, with a cohort of 1000 women from Britain, Ireland, and the United States, whose frequency of dysmenorrhea, dyspareunia and chronic pelvic pain combined was 34.4%.¹⁴ Regarding all disease symptoms (dysmenorrhea, dyspareunia, chronic pelvic pain, intestinal and urinary complaints), a few patients in this study were asymptomatic, which does not corroborate with a qualitative descriptive study, with 35 participants, published by Moradi *et al.*²⁰

However, this finding can be explained by the fact that our two recruiting hospitals are specialized centers for the diagnosis and treatment of endometriosis and, thus, most women sought medical attention there due to the occurrence of any symptom. In addition, the recruitment time between the first symptoms of endometriosis and the diagnosis was similar (~ 5 years) to that found in other

recent studies.^{25,26}

Women with SUP had decreased risk of dyspareunia, according to Chapron *et al.*,³ since the peritoneum area is less likely to be struck during intercourse. Endometriosis may cause dyspareunia by tension on the infiltrated uterosacral ligament during intercourse, since the distance between ectopic endometrial growths and nerve fibers in women with this symptom is shortened.²⁷ We have also observed that intestinal symptoms are positively associated with DIE in the rectosigmoid and intestine loci, and with DIE classification and the advanced stages of the disease. It is to be considered the pain to evacuate may be due to infiltrative lesions.²⁸ Finally, infertile women had almost a 3-fold increase in the risk of endometriotic lesions in uterine tubes. Previous reports have described that uterine tube's diseases accounts for 25-35% of all female primary infertility cases and can be associated with endometriosis.²⁸⁻³⁰ In addition, women between 30-39 years were associated with increased risk of infertility. Briceag *et al.*²⁹ performed a review through an international database and showed that the risk of having a diagnosis of tubal factor infertility at 35-39 years was 2 times higher than those under 30 years. In addition, in present study, women at this age group may have searched the doctor due to infertility, leading to a selection bias.

As expected, most patients were diagnosed by laparoscopy, in agreement with recent multi-country case-control studies with large hospital and population samples,^{3,24} since it is the gold standard for endometriosis diagnosis.¹ Currently, laparoscopy treatment is recommended preferably in cases of infertility, untreatable pain and/or those with significant involvement of the intestine or urinary tract with risk of functional impairment.¹⁷ In our study, 37% of women were diagnosed by MRI, which have been described as an accurate method for the detection of deep endometriosis due to its high specificity and sensibility.¹⁶ Nevertheless, SUP cases, mainly, can be underdiagnosed.¹⁶ The present study showed that most sociodemographic and clinical variables had similar frequencies between women who underwent surgery *versus* imaging diagnosis; however, those diagnosed by image were younger, had greater parity and were most likely to be single. We hypothesized that older women perform surgical diagnosis to treat possible infertility, which also explains the fact that they are, for the most part, married and therefore trying to conceive a child.

A larger sample size would be required to detect more associations and provide more confidence in

the findings. Additionally, as this is an observational study, it is possible that there are still unmeasured variables, which forbids the complete exclusion of residual confounding. However, this bias has minimal effect given the adjustment by various confounding factors. A referral bias has also to be raised: patients included in this study are treated in two reference institutions for endometriosis. These patients may have more severe symptomatology as they were probably referred to these centers, biasing the results. It is not possible to assure that these associations are causal, however, this epidemiological analysis is an important tool in the identification of endometriosis' etiology. Furthermore, by understanding endometriosis' epidemiological profile, it would be possible to determine a guideline to improve diagnosis, prognosis and treatment of the disease.

In summary, dysmenorrhea, dyspareunia, cyclical intestinal complaints, surgical diagnosis, DIE and advanced stage endometriosis were associated with either sociodemographic or clinical variables of endometriosis.

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Author's contribution

Cardoso JV carried out the research, recruited the patients from the *Hospital Moncorvo Filho* and *Hospital dos Servidores do Estado*, analyzed data and wrote the manuscript. Machado DE contributed to critical discussion of manuscript. Silva MC recruited the patients from the *Hospital dos Servidores do Estado*, contributed to data collection and contributed to writing the manuscript. Berardo PT followed the patients from the *Hospital dos Servidores do Estado*, contributed to data collection and to critical discussion and to edit the manuscript. Ferrari R recruited and followed the patients from the *Hospital Moncorvo Filho*. Abrão MS contributed to critical discussion of manuscript. Perini JA conceived and designed the research, supervised the data collection, analyzed data, wrote the manuscript and obtained funding. All authors approved the final version of the article.

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