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Association of the presence of adenomyosis and clinical characteristics in post-hysterectomy patients

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Abstract

Introduction: *It has been estimated that the prevalence of adenomyosis is 5-70% in Mexico. For the correct study of adenomyosis, the histopathological study of the hysterectomy specimen remains the only confirmatory diagnosis. For this reason, there are not many current studies that tell us the prevalence of this pathology, which is why it is important to carry out intentional searches.* **Objective:** *To estimate the prevalence of adenomyosis in patients undergoing total and subtotal hysterectomy, abdominal, laparoscopic, and vaginal hysterectomy in the period from 2019 to 2021 in Ciudad Juárez and to determine whether there are clinical factors associated with the presence of adenomyosis.* **Material and methods:** *Cross-sectional, retrospective, descriptive study. This study was conducted in patients who underwent total and subtotal abdominal, laparoscopic, and vaginal hysterectomy, whose histopathological reports were collected from January 2019 to December 2021. Patients with a subtotal hysterectomy were excluded.* **Results:** *A total of 332 patients were studied, in which a prevalence of 29.5% was observed, like that established in the general bibliography.* **Conclusions:** *Adenomyosis is the second gynecological pathology in order of frequency, only below leiomyomatosis, by histopathological diagnosis. According to the study, the clinical profile of patients to be ruled out for adenomyosis would be a history of previous uterine surgery, multiparity, in the fifth decade of life (specifically between 40 and 50 years of age), overweight, or obese.*

Keywords: *Adenomyosis. Hysterectomy. Uterine hemorrhage. Uterine diseases. Mexico.*

Introduction

Dysfunctional uterine bleeding is the main cause of bleeding in adult women; its diagnosis is the exclusion of anatomical alterations, so the clinician must initially rule out any organic or endocrinological pathology. It is estimated that around 10 million women in Mexico suffer from uterine bleeding, and annually, only 6 million of them seek medical attention[1].

The exact pathogenesis of adenomyosis has not been established, but some theories have been widely accepted and adopted by physicians[2]. The most common theory suggests that adenomatosis results from the invagination of endometrial glands and stroma in the thickness of the myometrium, together with hyperplasia and hypertrophy of smooth muscle fibers of the latter[3]. Another possible theory is that the adenomyotic lesions are due to the metaplasia of displaced Müllerian remains or to the differentiation of adult stem cells[4].

The prevalence of adenomyosis as an anatomopathological finding is highly variable, ranging from 5% to 70%, depending on the depth limit considered in the microscopic finding of foci in myometrial thickness[1]. Arellano Pichardo et al. in a study carried out in the Mexican population, they showed that the prevalence of

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adenomyosis in hysterectomy specimens was 33.33% (86 out of 258 patients)[3], as well as a study carried out in the United States in which a total of 135,162 women between 16 and 60 years of age were analyzed in 2015, in which 1,068 women had a previous diagnosis of adenomyosis. Thus, the prevalence of adenomyosis in 2015 was observed to be 0.8-1.5%; being higher among women aged 41-45 years[5].

The confirmatory diagnosis requires hysterectomy, in order to study the entire piece. The minimum distance required to make the diagnosis has remained under debate, but ranges from half to two low-power fields from the endomyometrial junction or a minimum depth of invasion ranging from 1 to 4 mm. The involvement of at least 25% to one-third of myometrial thickness is another diagnostic criterion that has been used in magnetic resonance imaging (MRI)[6,7].

Hysterectomy is the only definitive treatment for adenomyosis, which allows us to perform the histopathological study of the specimen and thus obtain the microscopic result and obtain the definitive diagnosis[8].

The objective of this study is to determine if there is an association between clinical variables and the presence of adenomyosis in patients undergoing total abdominal and subtotal hysterectomy at the Ciudad Juárez Women's Hospital, with the following specific objectives: (1) to know the age groups with the highest frequency of adenomyosis at the Ciudad Juárez Women's Hospital, (2) to identify the comorbidities present in patients diagnosed with adenomyosis at the Women's Hospital of Ciudad Juárez, (3) to perform inference between patients with adenomyosis and without adenomyosis, and (4) to perform a multivariate model to identify variables associated with the presence of adenomyosis.

Material and methods

An observational, retrospective, cross-sectional, descriptive, and analytical study was conducted in 332 women after total and subtotal non-obstetric hysterectomy at the Hospital de la Mujer of Ciudad Juarez, from January 01, 2019, to December 31, 2021. Clinical records were reviewed, and a database was built in Microsoft Excel 2019. As selection criteria, patients undergoing hysterectomy, both of obstetric and gynecological origin, with total or subtotal technique, from January 01, 2019 to December 31, 2021, had a histopathological report, as well as patients who had in their clinical history the variables studied (age, multigestation, and body mass index [BMI], history of previous gynecology and obstetrics, adenomyosis, diabetes mellitus, and systemic arterial hypertension), as non-inclusion criteria we take patients who are not in the virtual or physical clinical record, patients whose clinical history lacks the previously mentioned variables and finally because they do not have a pathology report.

Statistical analysis

To perform the analysis and graphs of this work, the statistical program IBM Statistical Packages for the Social Sciences V.23 for Windows 10 was used. Kolmogorov-Smirnov normality tests were applied to assess the distribution of variables. The inference analysis for the quantitative variables was performed using Student's t-test or Mann-Whitney's U-test, as appropriate, while Pearson's Chi-square test was used for the qualitative variables. Logistic regression was performed considering statistically significant variables as independent variables for adenomyosis status. The best model was constructed using the backward step technique considering Wald's statistic. A value of $p < 0.05$ was considered to be statistically significant for all statistical tests used.

Results

In a sample of 332 women post-operated obstetric hysterectomy at the Hospital de la Mujer of Ciudad Juarez, from January 01, 2019 to December 31, 2021. A total of 98 (29.5%) patients with histopathological diagnosis of adenomyosis were detected; in this way, it was determined that the prevalence of adenomyosis in the studied population was 29.5% (98 of 332 patients). The sample found a median age of 45 years with an interquartile range of 39-50 years. In our sample, a total of 234 women (70.4%) had a BMI > 25 kg/m^2. A total of 212 women (63.9%) had a history of cesarean section, and 242 (72.9%) were categorized as multigestation. 19% (63) of the women in this study had a diagnosis of diabetes and 28.6% (95) had hypertension. Among the causes of hysterectomy, it was found that 63.6% (211) were due to uterine myomatosis, 11.7% (39) were due to pelvic organ prolapse, 9.9% (33) due to obstetric hemorrhage, and 6.6% (22) due to placental alteration, the rest of the causes are described in table 1.

A total of 98 women (29.5%) had a diagnosis of adenomyosis according to the pathological study (Table 1). Patients were grouped according to the histopathological diagnosis of adenomyosis, finding that the median age in women without adenomyosis was 44 (36-49)

Table 1. General characteristics of the population

Variable	Total (%)	Adenomyosis (%)		p
		No (234)	Yes (98)	
Age (years)	45 (39-50)	44 (36-49)	47 (42-50)	**0.010*u**
BMI > 25 kg/m^2				
Yes	235 (70.8)	161 (68.8)	74 (75.5)	0.220Xi
No	97 (29.2)	73 (31.2)	24 (24.5)	
Previous gynecological and obstetrical surgeries				
Yes	212 (63.9)	156 (66.7)	56 (57.1)	0.099Xi
No	120 (36.1)	78 (33.3)	42 (42.9)	
Multigesta				
Yes	242 (72.9)	173 (73.9)	69 (70.4)	0.510Xi
No	90 (27.1)	61 (26.1)	29 (29.6)	
Causes of hysterectomy				
Placental alteration	22 (6.6)	19 (8.1)	3 (3.1)	
Obstetric bleeding	33 (9.9)	27 (11.5)	6 (6.1)	
Myomatosis	211 (63.6)	145 (62)	66 (67.3)	
NIC 1	3 (0.9)	2 (0.9)	1 (1)	
NIC 2	4 (1.2)	4 (1.7)	0 (0)	**0.035*Xi**
NIC 3	5 (1.5)	5 (2.1)	0 (0)	
Oncologic process	8 (2.4)	5 (2.1)	3 (3.1)	
Pelvic organ prolapse	39 (11.7)	22 (9.4)	17 (17.3)	
Others	7 (2.1)			
Diabetes				
Yes	63 (19)	43 (18.4)	20 (20.4)	0.781Xi
No	269 (81)	191 (81.6)	78 (79.6)	
Hypertension				
Yes	95 (28.6)	67 (28.6)	28 (28.6)	> 0.999pXi
No	268 (81)	167 (71.4)	70 (71.4)	

This table shows median and IQR 25-75% and frequency in number and percentage
*: statistical significance (p < 0.05).
u: Mann Whitney´s U test.
Xi: Pearson´s Chi squared.
BMI: body mass index; NIC: neoplasia intraepitelial cervical.

while in women with adenomyosis it was 47 (42-50), p = 0.010 (Fig. 1). In the group of women without adenomyosis, 68.8% had a BMI > 25 kg/m^2 and in the group of women with adenomyosis, 75.5% had a BMI > 25 kg/m^2 (p = 0.220). Regarding the history of previous obstetric surgeries, the history was present in 57.1% of the women in the group with a diagnosis of adenomyosis, whereas the history was present in 66.7% of the women without adenomyosis (p = 0.099) (Table 1). Regarding the categorization of multigest, 73.9% and 70.4% of the group without adenomyosis and with a diagnosis of adenomyosis were found to be multigest, respectively (p = 0.510). 18.4% of women without adenomyosis had diabetes, and the same diagnosis occurred in 20.4% of women with adenomyosis (p = 0.667). 28.6% of women with and without adenomyosis had hypertension (p = 0.991). 2 logistic models were performed, in the first (Table 2), all binary variables were entered, taking the presence of adenomyosis as a dependent variable, finding statistical significance with age (B = 0.026 [odds ratio (OR) = 1.026 95% confidence interval (CI) = 1.002-1.051], p = 0.035). Due to the result obtained, the elimination of covariates was carried out using Wald's statistical criterion (Table 3), finding statistical significance for age (B = 0.026 [OR = 1.026 95% CI = 1.003-1.049], p = 0.026].

Discussion

Total hysterectomy is the most common gynecological surgery in the world. In our study, hysterectomies performed in 1 year (n = 332) were considered, using laparotomy, laparoscopy, and vaginality. The type of surgery to be performed is decided according to the characteristics of the uterus and the concomitant pathologies[3,9].

Table 2. Multiple logistic regression for the presence of adenomyosis in women after hysterectomy obstetric

Variable	B	Wald	p	OR (95% CI)
BMI > 25 kg/m^2	0.307	1.189	0.275	1.359 (0.783-2.359)
Previous gyneco-obstetrical surgeries	0.306	1.436	0.231	1.358 (0.823-2.240)
Multigesta	–0.259	0.871	0.521	0.772 (0.448-1.329)
Diabetes	0.111	0.124	0.725	1.117 (0.603-2.068)
Hypertension	–0.188	0.430	0.512	0.829 (0.473-1.452)
Age	0.026	4.442	0.035*	1.026 (1.002-1.051)

B: logistic regression coefficient; Wald: Wald statistic; p: value of p;
OR: *odds ratio*; 95% CI: Confidence interval at 95%. ; BMI: body mass index.
*: statistical significance ($p < 0.05$).

Table 3. Multiple logistic regression for the presence of adenomyosis in women after obstetric hysterectomy

Variable	B	Wald	p	OR (95% CI)
Age	0.026	4.935	0.026*	1.026 (1.003-1.049)

B: logistic regression coefficient; Wald: Wald statistic; p: value of p; OR: *odds ratio*; 95% CI: confidence interval at 95%.
*: statistical significance ($p < 0.05$).

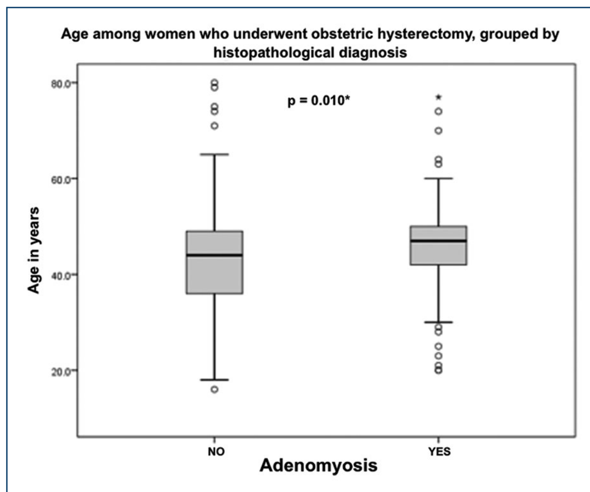

Figure 1. Age of the patients included in the study according to diagnosis of adenomyosis. The p value corresponds to the Mann's U-test.

In the literature, abnormal uterine bleeding with or without leiomyomatosis is reported as the main cause of hysterectomy. Leiomyomatosis is the cause of up to 55%[10]. In our study, uterine leiomyomatosis was the most frequent definitive diagnosis, with 211 cases, representing 63.5% of the sample, a percentage higher than what was reported worldwide. Either alone or in combination with other conditions, was the second most frequent diagnosis, with a prevalence of 29.5%. This finding is consistent with global reports, where prevalence ranges from 2.6% to 70% in pathology specimens. However, in none of the procedures was adenomyosis the primary indication for hysterectomy, as it was diagnosed histopathologically and justified by other clinical causes[11,12].

Endovaginal ultrasound is the most important imaging technique in gynecological patients. The radiologist requires experience to identify adenomyosis. This is explained by the great difficulty in making the prior diagnosis. There are studies that mention that ultrasound and MRI can establish the diagnosis with a sensitivity of 89%[13-15]. However, to suspect adenomyosis, a detailed description of the myometrium described in the morphological uterus sonographic assessment criteria is required, which is not done routinely and only has the experience of some physicians assigned to gynecology; for this reason, it is emphasized that each of these criteria is made known to all personnel and thus be able to carry out an adequate approach to this pathology[16].

Adenomyosis is a condition with variable frequency depending on the population studied. It is most commonly diagnosed between 40 and 50 years of age, accounting for up to 80% of cases. For the purposes of this study, and to better localize the pathology, patients were grouped by decades. The highest frequency of diagnosis was found in the 40-50-year age group, with a rate of 63.2%, which is consistent with findings reported in the global literature[9]. Regarding obstetric history, 70.4% of patients with adenomyosis were multigested. Patients with 2 or fewer gestates accounted for 29.6% of reported cases of adenomyosis. According to several authors, most cases of adenomyosis occur in multigestation patients (90%), consolidating itself as one of the main risk factors[4,7,17].

Regarding the history of previous uterine surgery and the presence of adenomyosis, it occurred in 57.1% of the patients, specifically the history of cesarean section and instrumented uterine curettage. Uterine trauma during a cesarean section, curettage, or myomectomy are the classic risk factors[17]. BMI also plays an important role[18]. Overweight patients or with some degree of obesity make up 70.7% of the total number of patients

studied in our sample, of which 75.5% were diagnosed with adenomyosis. In adenomyosis, the role of hyperestrogenism plays an important role, as it is a risk factor and is frequently found in overweight or obese women[11].

The presence of diabetes mellitus or systemic arterial hypertension are variables that in our study, we did not find with statistical significance, a total of 63 patients presented a diagnosis of diabetes mellitus (18.9%), of which twenty presented a diagnosis of adenomyosis (20.4%), similar figures with systemic arterial hypertension, in which we have 95 reported cases (28.6%) of which 28 patients presented a diagnosis of adenomyosis (28.6%). However, we found that age is associated with the presence of adenomyosis (OR = 1.026, [95% CI = 1.003-1.049], p = 0.026).

Clinical diagnosis is difficult, due to nonspecific signs and symptoms, which often coexist with other pelvic diseases[1]. In the present study, most of the patients had abnormal uterine bleeding as their main antecedent; in 73.4% of them, so in all patients with a study protocol for abnormal uterine bleeding, adenomyosis should be considered as a diagnostic probability, and the appropriate protocol for its diagnosis should be performed.

Currently, there is a limited series of studies, but important to perform for presurgical diagnosis, which are, in addition to clinical suspicion, ultrasound and, in some cases, MRI, this in an attempt by gynecologists to define the various characteristics resulted in the criteria for morphological sonographic evaluation of the uterus[19]. In these cases, adenomyosis is considered when the uterus has a globular configuration and multiple areas of shadow, sometimes described as fan-shaped, are visible, with difficulty in differentiating the myometrium from the junction zone and cystic changes in the junction zone and myometrium[20]. Additional features that can be observed include an irregular or interrupted area of conjunction with islands[18,20]. Unfortunately, there are no classic findings on physical examination or laboratory studies that identify it as a probable diagnosis[20].

Future applications of artificial intelligence (AI) in medicine, specifically related to our topic of adenomyosis classification[16,18], and need to be discussed. Systems based on conjunction zone anomalies have shown promising results in terms of observer agreement and correlation with clinical symptoms. Recently, there has been growing interest in the potential of AI to improve the accuracy and consistency of the diagnosis and classification of adenomyosis. It has been suggested that AI-based ultrasound or MRI image analysis could accurately identify and classify different types of adenomyosis based on the abnormalities of the conjunction zone[16]. This approach has the potential to improve the standardization and reproducibility of presurgical diagnosis of adenomyosis, as AI algorithms can analyze large datasets and identify patterns that may not be immediately apparent to human physicians[15,16,21]. However, as in many areas of medicine, more research is needed to evaluate these approaches and explore whether they provide answers to clinically relevant questions.

Conclusions

The prevalence of adenomyosis at the Ciudad Juárez Women's Hospital is 29.4%. Adenomyosis is the second gynecological pathology in order of frequency, only below leiomyomatosis, by histopathological diagnosis. According to the study, the clinical profile of patients to be ruled out for adenomyosis would be a history of previous uterine surgery, multiparity, in the fifth decade of life (specifically between 40 and 50 years of age), overweight, or obese. Previous uterine surgery is an important factor, found in 57.2% of patients. The most common surgery is cesarean section. It is essential to include in the study protocol of patients with suspected adenomyosis, an ultrasound that includes a complete description of the myometrium, subendometrial space, and endometrium. The outpatient service does not have sonography equipment, so the diagnosis of adenomyosis is impossible. In none of the patients who underwent hysterectomy was the presence of adenomyosis diagnosed before the surgical event. Training is required for the resident and affiliated physicians of our institute due to the evident lack of knowledge and expertise for the preoperative diagnosis of adenomyosis. None of the patients was the suspicion of adenomyosis contemplated in the clinical file. Age may be a factor associated with the presence of adenomyosis; however, more observational studies are required to corroborate these findings.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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