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Hysteroscopy findings and epidemiological profile of women experiencing subfertility

LAURA BARROSO CHIARI[1], JULIA FERREIRA LOPES[2], JULIA DE OLIVEIRA ABRAHÃO REIS[3], MARIA ANTÔNIA LOIOLA PACE[4], JOÃO OSCAR ALMEIDA FALCÃO JUNIOR[5]

[1]FACULDADE DE CIÊNCIAS MÉDICAS DE MINAS GERAIS – BELO HORIZONTE, MG-BRASIL
[2]FACULDADE DE CIÊNCIAS MÉDICAS DE MINAS GERAIS E HOSPITAL FELÍCIO ROCHO– BELO HORIZONTE, MG-BRASIL

CORRESPONDING AUTHOR: JOÃO OSCAR ALMEIDA – RUA AIMORÉS, 2480, SALA 309. FUNCIONÁRIOS – CEP: 31140-072 – BELO HORIZONTE, MG - BRASIL
EMAIL: JOFALCOJR@GMAIL.COM

ABSTRACT

Introduction: Infertility is characterized by the inability to establish a pregnancy within 12 months of regular unprotected sexual intercourse. To understand its etiology, a detailed evaluation is necessary, with hysteroscopy considered the "gold standard" for investigating the structural causes of female infertility. **Objective:** To stratify and quantify the endometrial alterations in patients with infertility complaints who underwent hysteroscopy at the University Hospital Ciências Médicas of Minas Gerais (HUCM-MG), correlating these findings with their epidemiological profile. **Method:** A retrospective cross-sectional study was conducted by analyzing 346 medical records of patients with complaints of infertility who underwent hysteroscopy. Patients with complaints of infertility, recurrent miscarriages, or those undergoing follow-up for *in vitro* fertilization were included. **Results:** Among the included patients, the majority had no clinical comorbidities (77.5%) and the mean age was 35.2 years. When present, the most prevalent comorbidities were Systemic Arterial Hypertension (6.5%) and Hypothyroidism (5.6%). In hypertensive patients, a lower proportion of normal findings was observed ($p<0.001$). The most common findings from diagnostic hysteroscopy were polyps (21.3%), endometrial synechiae (13.5%), and submucosal fibroids (8.9%). Among patients with synechiae, a higher proportion had previously undergone intrauterine procedures ($p=0.014$), with most being curettage ($p=0.025$) and a lower proportion being polypectomy ($p=0.004$). **Conclusion:** The results found are supported by current scientific evidence and provide substantial data regarding the epidemiology of uterine cavity pathologies most associated with infertility causes.

Keywords: Uterine Endoscopy; Reproductive Health; Female Infertility; Gynecological Examination.

INTRODUCTION

Infertility is characterized by the inability to establish a clinical pregnancy after 12 months of regular, unprotected sexual intercourse, or due to an impairment in an individual's ability to reproduce, either alone or with a partner. The prevalence of infertility among women of reproductive age is one in every four couples in developing countries. Women are responsible for 20 to 30% of infertility cases but contribute to 50% of cases overall.[18]

Several factors influence women's reproductive capacity, including age, race and ethnicity, nulliparity, access to healthcare services, and lifestyle. Infertility can also be related to hormonal changes in the ovulatory cycle or structural causes in the female reproductive system.[20]

At birth, women have about 2 million oocytes in their ovaries, with half lost by puberty. Approximately 40 to 500 follicles develop in each menstrual cycle, usually with one being released as the dominant follicle and the rest undergoing follicular atresia. With aging, hormonal and structural changes reduce the quality and number of follicles. Thus, the probability of pregnancy remains relatively stable from puberty until age 30, after which the chances decline until menopause when the possibility of pregnancy is zero.[6] With the increased involvement of women in the labor market and the pursuit of professional careers, couples are opting to delay parenthood. Consequently, women are having their first child at older ages, which directly impacts fertility.[19]

Race and ethnicity can also contribute to the prevalence of infertility. However, their relationship is not fully understood as it reflects underlying confounding factors such as socioeconomic disadvantage and access to healthcare services.[16]

Regarding the structural causes of the female reproductive system, the main hysteroscopic findings that impact female fertility are endometriosis, leiomyoma, adenomyoma, and endometrial polyps. Endometriosis is considered one of the primary causes of infertility because it promotes an inflammatory process in the pelvis and increases the formation of fibrosis that hinders the implantation and transport of oocytes and sperm. Polyps and myomas, in turn, distort the anatomy of the uterine cavity, reducing the chances of implantation and maintenance of pregnancy.[18]

The evaluation of female infertility can begin after one year of unprotected sexual intercourse, or six months if the woman is 35 years or older. The initial approach should start with a detailed medical history and physical examination, supported by laboratory and imaging tests to identify the etiology.[15]

Hysteroscopy is considered the "gold standard" for evaluating the uterine cavity and is an important tool in diagnosing and treating infertility. This exam can identify chronic endometritis, polyps, submucosal leiomyomas, intrauterine adhesions, adenomyosis, uterine malformations, endometrial hyperplasia, and many other pathologies that may cause infertility. In addition to its diagnostic value, hysteroscopy can successfully treat intrauterine abnormalities, resulting in a significant increase in pregnancy rates.[9]

Advances in hysteroscopic equipment have made it possible to use these in an outpatient setting. These procedures have become a success in clinical practice as they can directly visualize the uterine cavity and treat less complex pathologies, avoiding the additional risks of anesthesia and the high cost of operating rooms. Besides being cost-efficient, women can quickly return to their work activities, increasing their satisfaction with the procedure.[5]

Thus, this study aims to establish a stratification and quantification of the most commonly found endometrial alterations in hysteroscopy examinations performed on patients with complaints of infertility. From this, the study seeks to compare these findings with the currently available literature, to contribute to a better understanding among healthcare professionals about the profile of infertile women and to optimize the treatment and diagnostic approach for this prevalent issue.

METHOD

This is a retrospective cross-sectional study conducted through the analysis of medical records of patients from the Hospital Universitário Ciências Médicas de Minas Gerais (HUCM-MG) with complaints of infertility who sought diagnostic hysteroscopy. The data analyzed were collected from medical records between the years 2008 and 2022. Data collection began after the approval of the Research Ethics Committee (Certificate of Presentation for Ethical Consideration - CAAE number 62631322.9.0000.5134), with all ethical principles being respected following Resolution 466/12 of the Brazilian National Health Council.

Patients were identified by their medical record numbers, with access to information restricted to the researchers only. The computers used were personal to the researchers, ensuring confidentiality and anonymity of the data. The Free and Informed Consent Form was not collected due to the impossibility of contacting all patients.

For the analysis of medical records, the Diagnostic Hysteroscopy database of the postgraduate service at Faculdade de Ciências Médicas de Minas Gerais (CMMG) was used. The database contains information on all patients who attended the service between 2008 and 2022. The medical records were selected based on the patient's complaints, including women with infertility, recurrent miscarriages, or undergoing investigation for *in vitro* fertilization. Women in post-menopause and records with insufficient information for the research were excluded.

A questionnaire was used as an evaluation tool, covering age, education, weight, height, presence of clinical comorbidities, medications in use, parity, previous uterine surgeries, use of tobacco and alcohol, date of the last menstruation, previous ultrasound data, and the management of the case after the examination. The researchers had access to the ultrasound reports brought by the patients on the day of the diagnostic hysteroscopy and other exams noted in the medical records. The data were transferred to an Excel spreadsheet for subsequent statistical analysis.

Qualitative variables were presented by frequencies, and quantitative variables by minimum, mean, standard deviation (SD), median, first quartile (Q1), third quartile (Q3), and maximum. The association between qualitative variables was assessed using Chi-square and Fisher's exact tests. Odds ratios and their respective 95% confidence intervals (95% CI) were calculated using simple binary logistic regression. The Bonferroni correction was also applied to the significance level in evaluating the association between hysteroscopy findings according to comorbidities. Analyses were performed using R version 4.2.3, with a significance level of 5%.

RESULTS

The sample consisted of 346 patients, with an average age of 35.2 years (SD of 5.8 years) and an average BMI of 26.0 kg/m² (SD 4.5 kg/m²). Most of the women did not have any clinical comorbidities (77.5%); when present, the most prevalent were Systemic Arterial Hypertension (6.5%) and Hypothyroidism (5.6%). In addition to the complaint of infertility, 24 women also presented with chronic pelvic pain, and 36 presented with abnormal uterine bleeding (AUB). Table 1 shows the statistical findings of the analyzed sample profile. The variables Comorbidities and Body Mass Index (BMI) did not show a statistically significant correlation with the analyzed sample.

Table 1. Description of age, body mass index (BMI), years of education, comorbidities, current medications, and complaints.

Variables	Valid N	Statistics
Age	346	
Minimum / Maximum		19,0 / 67,0*
Median (Q1 – Q3)		36,0 (32,0 - 39,0)*
Mean (DP)		35,2 (5,8)*
BMI (kg/m²)	276	
Minimum / Maximum		17,0 / 45,7 **NS**
Median (Q1 – Q3)		25,5 (22,9-28,7) **NS**
Mean (DP)		26,0 (4,5) **NS**
Years of education	234	
Minimum / Maximum		1,0 / 22,0*
Median (Q1 – Q3)		11,0 (8,2 - 12,0)*
Mean (DP)		10,9 (3,3)*
Comorbidities		
None	342	265 (77,5%) **NS**
Diabetes mellitus	340	8 (2,4%) **NS**
Hypertension	340	22 (6,5%) **NS**
Hypercholesterolemia	340	1 (0,3%) **NS**
Hypothyroidism	340	19 (5,6%) **NS**
Tobacco use	338	12 (3,6%) **NS**
Alcohol use	338	16 (4,7%) **NS**
Others	340	31 (9,1%) **NS**
Current medications		
None	344	247 (71,8%)*
Furosemide	342	2 (0,6%)*
Hydrochlorothiazide	342	6 (1,8%)*
Metformin	342	11 (3,2%)*
Losartan	342	13 (3,8%)*
Puran T4	342	17 (5,0%)*
Simvastatin	342	2 (0,6%)*
Others	343	87 (25,4%)*
Complaints		
Asymptomatic	346	244 (70,5%)*
Pelvic pain	346	24 (6,9%)*
Infertility	346	346 (100,0%)*
AUB	346	36 (10,4%)*
Others	346	109 (31,5%)*

*Variables with statistical significance (P < 0.05) analyzed by Chi-square tests, Fisher's exact test, and Bonferroni correction. **NS**: Non-significant variables statistically.

Almost half of the women had previously undergone some type of uterine surgery (47.5%). Among these, 24.1% had a curettage, 21% had a myomectomy, and 13% had a cesarean section. Regarding parity, 59.5% were nulliparous and 40.4% had previously been pregnant. Of the multiparous patients, 36 had previous cesarean sections, and 26 had normal deliveries. Additionally, 14.5% of the women had experienced one miscarriage, and 16.6% had experienced two or more pregnancy losses, as shown in Table 2.

Table 2. Description of previous uterine surgeries, menopause, pregnancy, delivery, and abortion profile.

Variables	Valid N	Statistics
Previous uterine surgeries	341	162 (47,5%)
Curettage	162	39 (24,1%)
Myomectomy	162	34 (21,0%)
Polypectomy	162	26 (16,0%)
Cesarean section	162	21 (13,0%)
Menopause	346	3 (0,9%)
Parity		
Pregnancies	346	
None		206 (59,5%)
One		62 (17,9%)
Two or more		78 (22,5%)
Cesarean section	344	
None		308 (89,5%)
One		24 (7,0%)
Two or more		12 (3,5%)
Vaginal birth	344	
None		318 (92,4%)
One		22 (6,4%)
Two or more		4 (1,2%)
Miscarriages	344	
None		237 (68,9%)

One	50 (14,5%)
Two or more	57 (16,6%)

All variables show statistical significance (p-value < 0.05) analyzed by the Chi-square test, Fisher's exact test, and Bonferroni correction.

Regarding previous examinations, the ultrasound results were normal in most cases (28.8%), with an average endometrial thickening of 8.1 mm (SD 4.1 mm). When abnormalities were found, the most common findings were intramural myoma (26.4%), submucosal myoma (18.4%), and polyps (13.4%).

Hysteroscopy was indicated and performed in 95.7% of the cases. Among the findings in diagnostic hysteroscopy, the most common were polyps (21.3%), endometrial synechiae (13.5%), and submucosal myoma (8.9%). No woman showed signs suggestive of malignancy, and 40.9% had no visible abnormalities on hysteroscopy. Endometrial fragment biopsy was performed on 19 patients, of whom 3 had polyps (15.8%) and 4 had endometritis. After hysteroscopy, 25% of the women were referred for surgical hysteroscopy, 12.2% were indicated for a second-look hysteroscopy, and 51.2% were referred for outpatient follow-up. Table 3 summarizes the ultrasound findings, hysteroscopy results, and patient follow-up.

Table 3. Description of ultrasound and hysteroscopy findings, and referral.

Variables	Valid N	Statistics
Available ultrasound data	345	242 (70,1%)
Uterine position	239	
Anteverted		209 (87,4%)
Intermediate		2 (0,8%)
Other		1 (0,4%)
Retroverted		27 (11,3%)
Endometrial thickening (mm)	229	
Minimum / Maximum		0,5 / 24,7
Median (Q1 – Q3)		7,1 (5,2 - 9,8)
Mean (DP)		8,1 (4,1)
Ultrasound conclusion		
Normal	243	70 (28,8%)
Polyp	239	32 (13,4%)
Intramural myoma	239	63 (26,4%)
Submucosal myoma	239	44 (18,4%)
Adenomyosis	239	3 (1,3%)
Endometrial thickening	239	13 (5,4%)
Other	240	53 (22,1%)
Hysteroscopy	345	330 (95,7%)
Hysteroscopy conclusion		
Normal	330	135 (40,9%)
Cervical stenosis	330	18 (5,5%)
Polyp	328	70 (21,3%)
Intramural myoma	327	9 (2,8%)
Submucosal myoma	327	29 (8,9%)
Uterine malformation	327	20 (6,1%)
Signs of endometritis	327	26 (8,0%)
Endometrial thickening	327	28 (8,6%)
Signs suggestive of malignancy	327	0 (-)
Synechiae	326	44 (13,5%)
Others	331	122 (36,9%)
Hysteroscopy biopsy	333	19 (5,7%)
Adenomyosis	19	0 (-)
Polyp	19	3 (15,8%)
Endometritis	19	2 (10,5%)
Secretory endometrium	19	2 (10,5%)
Proliferative endometrium	19	2 (10,5%)
Synechiae	19	0 (-)
Biopsy suggestive of malignancy	19	1 (5,3%)
Others	19	4 (21,1%)
Referral		
Second look	337	41 (12,2%)
Surgical hysteroscopy	336	84 (25,0%)
Outpatient	336	172 (51,2%)
Others	336	57 (17,0%)

All variables show statistical significance (p-value < 0.05) analyzed by Chi-square tests, Fisher's exact test, and Bonferroni correction.

Figure 1. Boxplots of age in years according to hysteroscopy findings.

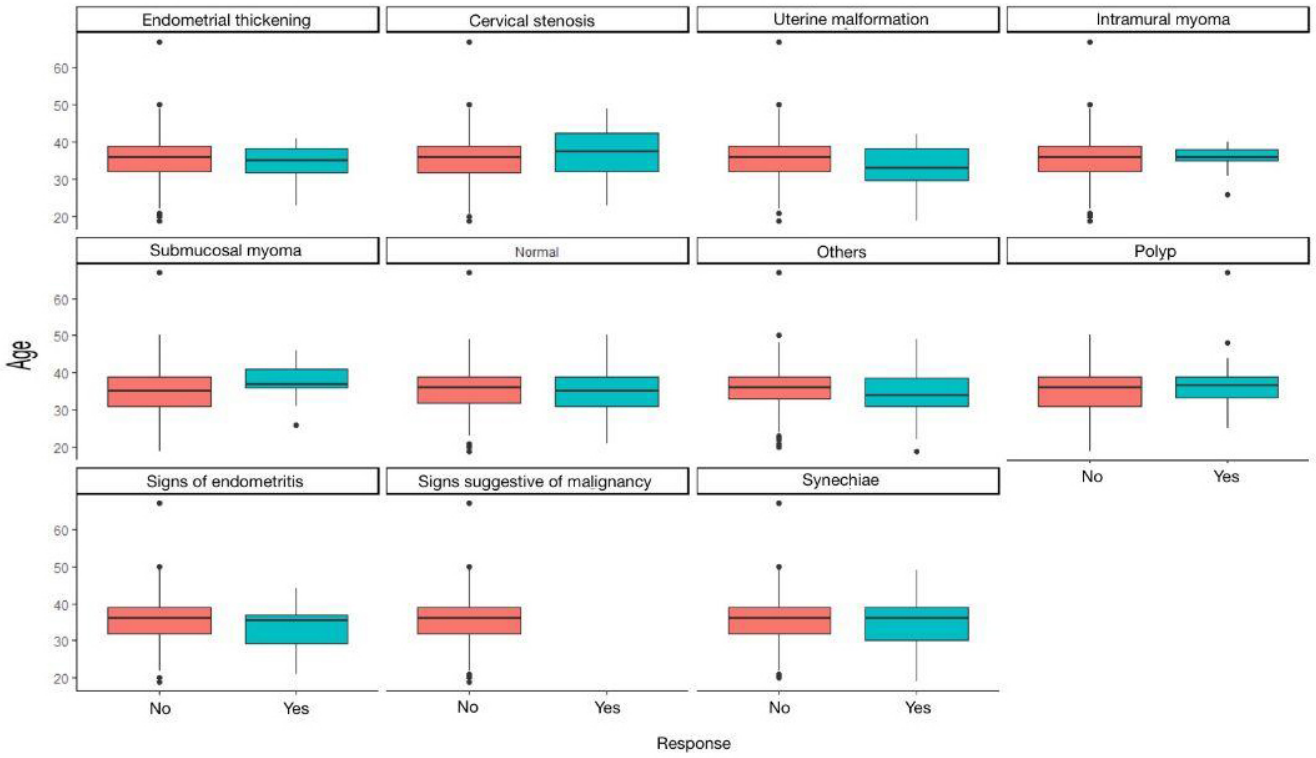
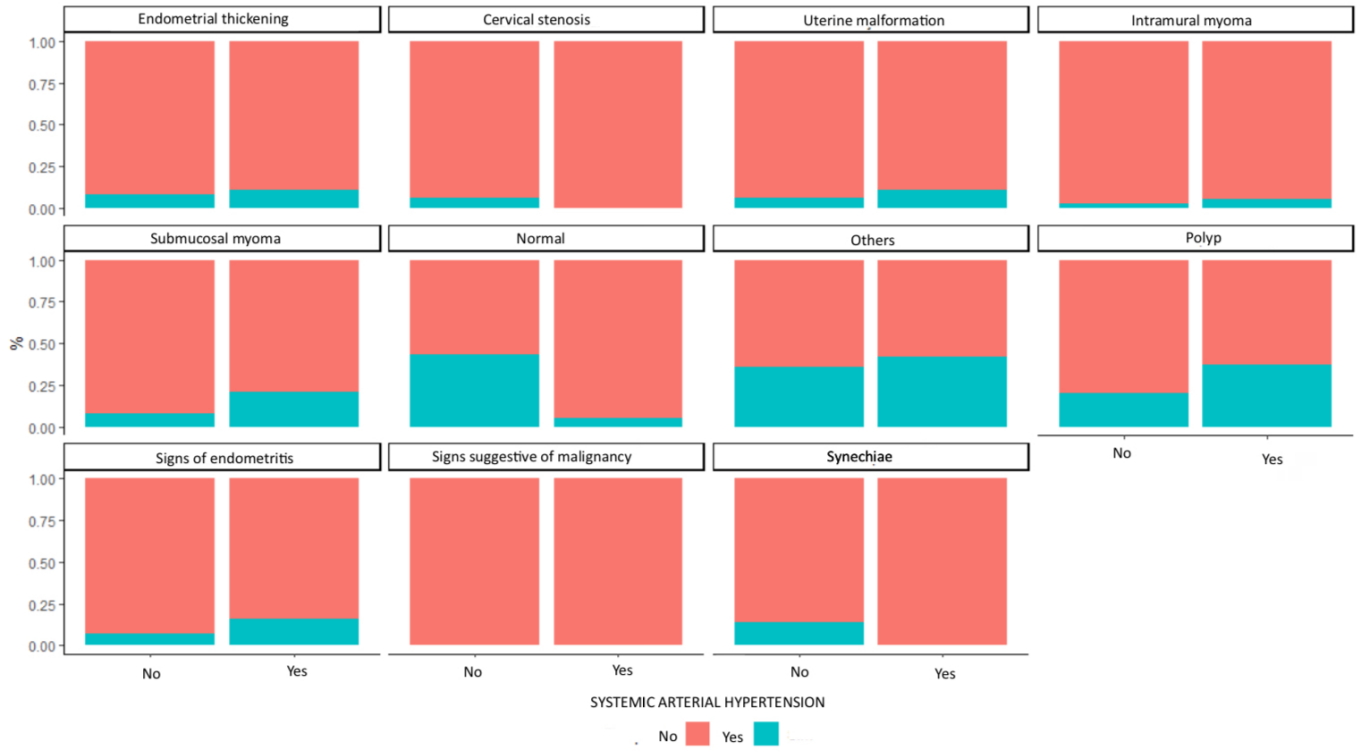


Figure 2. Distribution of hysteroscopy findings according to the occurrence of systemic arterial hypertension (SAH).



When evaluating the data from Figure 1, it is noted that older age was associated with a higher proportion of submucosal fibroids (p = 0.002), considering the Bonferroni correction at the significance level (significant p-value < 0.0045).

Figure 2 compares endometrial findings in women with and without hypertension (HAS). It is observed that women without hypertension have a higher proportion of normal hysteroscopies (p < 0.001), considering the Bonferroni correction at the significance level (significant p-value < 0.0045).

Regarding BMI, Diabetes Mellitus, Hypercholesterolemia, Hypothyroidism, and the use of tobacco and alcohol, no statistically significant association was found with the results obtained in diagnostic hysteroscopy.

When evaluating the research results, it is noted that the average age of the study patients is relatively high. Most patients do not have clinical comorbidities and, consequently, do not use medications. In most hysteroscopies performed, the examinations were normal. Among the patients with abnormalities in diagnostic hysteroscopy, the most common findings were polyps, endometrial synechiae, and submucosal fibroids.

DISCUSSION

The women in the analyzed sample who underwent hysteroscopy had an average age of 35.2 years, which is considered relatively high. Aging is associated with various hormonal and structural changes that negatively affect the quality and quantity of oocytes. Recent studies have shown that age can also harm endometrial functionality, impairing endometrial receptivity. Endometrial cell senescence can jeopardize the initial implantation phase and is also associated with chronic inflammatory conditions, creating a pro-inflammatory environment and tissue fibrosis that hinder embryonic development.[2]

Uterine leiomyomas are the most common benign tumors found in the female genital tract. A meta-analysis by Pritts *et al* demonstrated that submucosal myoma are associated with lower rates of endometrial implantation.[7] Other studies have also associated submucosal myoma with recurrent miscarriages and decreased endometrial receptivity, with their removal being associated with increased pregnancy rates. The mechanisms are not well established in the literature, but some theories point to chronic endometrial inflammation, abnormal vascularization, increased uterine contractility,[18] and hormonal alterations such as decreased IL-2 as possible pathophysiological explanations.[9] In the analyzed sample, women with uterine myomas had a higher mean age, which can be explained by the fact that leiomyomas increase in incidence with age, being found in up to 80-90% of women by age 50.[14]

Intrauterine adhesions are associated with worse reproductive outcomes, as they can lead to obstruction of the tubal ostia, decrease endometrial surface area, and generate mechanical obstruction in the uterine cavity and cervical canal.[13] Additionally, adhesions are more common in women with recurrent pregnancy loss due to insufficient endometrial support for placental fetal growth. In the sample, it was observed that women with synechiae at hysteroscopy had also been more frequently subjected to intrauterine procedures. Adhesions are commonly caused by previous uterine surgeries such as dilation, curettage, operative hysteroscopy, and myomectomy. Any intrauterine surgery can traumatize the basal layer of the endometrium, leading to granulation tissue formation. Subsequent healing on opposing surfaces of the uterus can eventually fuse, forming tissue bridges. These can range from transparent adhesions composed of endometrial tissue to dense connective tissue fibers resulting in total or partial obliteration of the uterine cavity. Moreover, trauma can compromise endometrial vas-

cularization, contributing to decreased fertility and recurrent pregnancy losses.[9]

Endometrial polyps are linked to a decrease in embryonic implantation potential and early pregnancy losses. In the analyzed sample, polyps were the most frequent endometrial abnormality found (21.3%). The literature has shown similar results, such as Fatemi *et al*'s study, which found a 45% prevalence of polyps in infertile women.[10] Potential mechanisms explaining how polyps may contribute to infertility include endometrial bleeding and inflammation, spatial alteration of sperm transport, endocrine changes such as reduction of IGFBP-1 and TNF-alpha during the mid-menstrual cycle, decreased uterine receptivity, and inhibition of sperm binding to the zona pellucida through increased glycodelin levels.[9]

Establishing a relationship between decreased fertility and high BMI was not possible with the research findings. However, studies show that being overweight increases the chance of anovulation in infertile patients with regular menstrual cycles.[4] Additionally, it was not possible to define the impact of systemic arterial hypertension on infertility. The lack of studies showing this relationship corroborates the research findings.

As a retrospective cross-sectional study, it is common for confounding factors to interfere with the researched outcomes. To mitigate these factors, statistical methods were used, such as setting a significance value of less than 0.05 to avoid mistaken associations. Another possible bias is sampling bias, as most of the sample consisted of women who underwent the exam between 2013 and 2016. This can be explained by the fact that the postgraduate diagnostic hysteroscopy service at HUCM is not a reference service for infertility, resulting in a variety of complaints from patients. In recent years (2018-2019), most patients were excluded from the study because they were postmenopausal at the time of the exam.

Hysteroscopy is considered the gold standard for evaluating factors related to infertility, being a safe technique compared to others for accurate diagnosis. This exam allows for early recognition of pathologies, which can lead to a greater chance of treatment and subsequently, a greater chance of pregnancy. Therefore, the present study showed that the most common pathologies found in patients with complaints of infertility were polyps, synechiae, and submucosal myomas, findings that are in agreement with similar studies, thus reinforcing the importance of the role of hysteroscopy in the diagnosis of infertility[11].

CONCLUSION

This retrospective cross-sectional study analyzed the medical records of 346 patients with complaints of infertility. It addressed the definition and epidemiology of fertility and infertility, as well as presenting the main alterations of the uterine cavity related to this condition.

The mean age of the sample was relatively high, at 35.2 years, with most women not presenting clinical comorbidities. The main pathologies found on diagnostic hysteroscopy were polyps (21.3%), followed by endometrial synechiae (13.5%) and submucosal myomas (8.9%). All these intrauterine pathologies contribute to infertility, as already described in the literature.

Finally, the findings are in line with current scientific evidence and provide substantial data regarding the epidemiology of uterine cavity pathologies that contribute to infertility. However, it is noted that further studies are needed to clarify the correlation between comorbidities, lifestyle, and endometrial findings on hysteroscopy in women with complaints of infertility.

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THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.