



Evaluation of pre-cycle hysteroscopy findings and its pathological results of 458 patients undergoing IVF: A retrospective cohort study

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Abstract

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Aim: To evaluate the hysteroscopy results performed before IVF treatment and its pathological findings that may affect pregnancy outcomes in patients undergoing the first IVF cycle.

Materials and Methods: This descriptive study was carried out retrospectively at Gazi University Hospital and a private IVF Clinic between January 2016 and December 2021. A total of 458 patients who had hysteroscopy procedures prior to the planned IVF cycle were analyzed. Appropriate surgery was performed simultaneously during hysteroscopy in patients with uterine cavity abnormalities. Outcome measures were the frequency of uterine abnormalities detected during the hysteroscopy and confirmation of these abnormalities with their pathological findings.

Results: Unexplained infertility was the most frequent infertility etiology among patients (50.9%). The most finding abnormality was endometrial polyp detected in 45.2% of patients during hysteroscopy. The second frequent abnormal finding was intrauterine adhesion, with a ratio of 15.9% of patients. The uterine cavity was seen as normal in 9.6% of patients during the hysteroscopy procedure. Endometrial sampling was performed in 75.5% of patients. The most common pathological result was endometrial polyp that was consistent with hysteroscopy findings (44.3%). Only 20.8% of patients had normal findings after pathological examination on the endometrial tissue samples.

Conclusion: Evaluating the uterine cavity before the IVF cycle is necessary to reach successful outcomes. Undetected intrauterine lesions are frequently observed during hysteroscopy in asymptomatic patients previously examined by conventional methods. Hysteroscopy may be a reasonable approach to assess and restore the uterine cavity in patients undergoing the first IVF cycle.



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Introduction

Despite improvements in assisted reproductive techniques, factors contributing to successful implantation are still relatively known. In general, successful in-vitro fertilization (IVF) treatment requires a high-quality embryo and a normal uterine cavity to support the developing embryo (1). Endometrial abnormalities such as adhesions, polyps, fibroids, and uterine Mullerian abnormalities may cause adverse effects on endometrial receptivity and pregnancy success (2, 3). Uterine cavity pathologies have been reported in approximately 25% of infertile women having IVF and as high as 50% of patients with recurrent implantation failure (4, 5).

The uterine cavity can be evaluated by transvaginal ultrasound, hysterosalpingography, sonohysterography, or hysteroscopy to determine the pathologies before IVF treatment (5, 6). Hysteroscopy is one of the best approaches to evaluate the cavity since it takes a close look inside the uterus (7). Besides, it provides an accurate visual assessment of the cavity and an option

to treat any detected pathology during the process. However, the European Society of Human Reproduction and Endocrinology has recommended that hysteroscopy is favorable only in suspicious uterine cavity pathologies in patients planned for IVF (8).

A normal endometrial cavity is crucial for a successful pregnancy, and conventional methods other than hysteroscopy may be insufficient to evaluate the uterine cavity in some patients due to technical problems. However, the impact of pre-cycle hysteroscopy on IVF outcomes is controversial in the literature. Currently, some studies have suggested that performing hysteroscopy before starting IVF treatment could increase the pregnancy rates in the subsequent cycle of patients having one or more failed IVF cycles (7, 9). However, the others have found no significant difference regarding pregnancy outcomes between patients having and not having hysteroscopy before IVF (10, 11). These studies have concluded that hysteroscopy is ineffective in increasing the success of IVF in patients with normal uterine cavities assessed by transvaginal ultrasound in their first cycle and patients with recurrent IVF failure. Thus, recommendations regarding the efficacy and the availability of

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routine hysteroscopy before starting the first IVF treatment cycle are lacking, and there is still no consensus in the literature.

For this reason, we aimed to evaluate the hysteroscopy results performed before IVF treatment and its pathological findings that may adversely affect outcomes in patients undergoing the first IVF cycle. We also aimed the availability of the hysteroscopy by confirming the results of transvaginal ultrasound and sonohysterography with hysteroscopy.

Material and Methods

This cohort study was carried out retrospectively at Gazi University Faculty of Medicine, Department of Obstetrics and Gynecology, and a private infertility clinic (Novaart IVF Center) in Ankara from January 2016 to December 2021. It was performed in compliance with the Helsinki Declaration. Informed consent was not necessary due to the retrospective nature of the study. The local Ethics Committee of Gazi University Faculty of Medicine approved the study's rationale, purpose, approach, and methods (date: January 11, 2022; number: 2022-024).

A total of 558 patients having a history of hysteroscopy before their first IVF cycle were reviewed from the medical records of the two clinics and included in the study. All included patients had the transvaginal ultrasound or sonohysterography exams before hysteroscopy. Hysteroscopy results were obtained from the surgery notes and pathological findings of the Gazi University database. Patients whose operation notes or pathology results could not be reached were excluded from the study (n = 100).

Infertility etiologies, infertility duration, hysteroscopy findings, and type of pathologies were recorded from the files. The primary outcome measure was the frequency of uterine abnormalities encountered during the hysteroscopy procedure in patients planned for IVF treatment. The secondary outcome measure was confirmation of these abnormalities with their pathological findings.

The hysteroscopy procedures were performed under general anesthesia and dorsal lithotomy position. GmbH Campo Trophyscope and an outer diameter of 2.9 mm Bettocchi office hysteroscopes with 30° views (Karl Storz company, Tuttlingen, Germany) were used as hysteroscopic instruments. Adequate uterine distention was achieved with saline solution (Sterile 0.9% NaCl solution) using the electronic pump (Hysteromat; Karl Storz). At the beginning of the procedure, the cervical canal, uterine cavity, and tubal orifices were visualized consecutively, and detected findings were recorded. In patients with uterine cavity pathologies, suitable treatment was performed during the procedure simultaneously. If polyp, submucous fibroids, or adhesions were found, immediate hysteroscopic resection or adhesiolysis were performed by scissors or resectoscope. The uterine septum was also excised by scissors or the resectoscope. The findings were classified as normal if there was no irregularity in the endometrial cavity. After examining the cervical canal and uterine cavity, endometrial tissue samples were obtained if necessary. All the samples were fixed in formaldehyde and sent for pathology examination. All pathological exams were performed by one experienced pathologist. Statistical Analysis Data were analyzed with Statistical Package for Social Sciences (SPSS, version 21.0, Statistics, 2013, Chicago, IBM, USA). Descriptive statistics, including hysteroscopic findings and pathological results, were presented

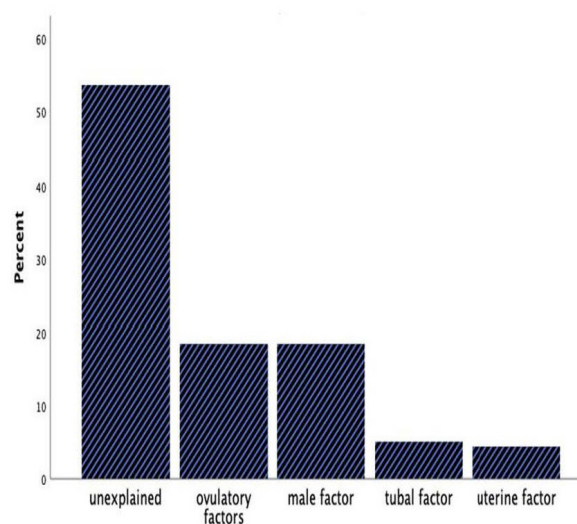


Figure 1. Infertility etiology of study group before undergoing hysteroscopy. Data were presented as frequencies.

as mean (\pm) standard deviation, frequency distribution, and percentage. Characteristics related to fertility history are also presented as mean (\pm) standard deviation, frequency distribution, and percentage.

Results

A total number of 458 patients were evaluated in this study. The age of patients ranged between 19 and 54, and the mean age was 35.58 years. The age range of their partners was between 24 and 58, and the mean male age was 37 ± 6.1 years. Sixty percent of patients were diagnosed with primary infertility, while 40% were diagnosed with secondary infertility. Mean infertility duration was 4.639 years, and approximately 50% (49.1%) of patients were infertile for more than three years.

Infertility etiologies of patients are presented in Figure 1.

Among the causes of infertility, most patients (50.9%) were diagnosed with unexplained infertility. Twelve percent of patients were diagnosed with a suspicious endometrial polyp, and two percent of patients were diagnosed with fibroids by transvaginal ultrasound and sonohysterography before the hysteroscopy procedure. The remaining 86% of patients had a normal uterine cavity assessed by transvaginal ultrasound and sonohysterography.

Hysteroscopy findings of patients are shown in Figure 2. The endometrial polyp was detected in 45.2% of patients (207/458). These polyps were removed without difficulties during the procedure. Intrauterine adhesion was found in 15.9% of patients (73/458). We applied adhesion barriers on 26 patients in this group, including intrauterine devices and anti-adhesion gels after adhesiolysis. Chronic endometritis images, including mucosal hyperemia and hemorrhagic spots on the endometrium, mucosal edema, or micropolyps (<1mm in diameter), were identified in 10.5% of patients (48/458). The uterine cavity was screened as normal in 9.6% of patients (44/458). The endometrial tissue sample was performed in 346 patients.

Pathological results of the patients after hysteroscopy are presented in Figure 3. After pathological examination, 20.8% of

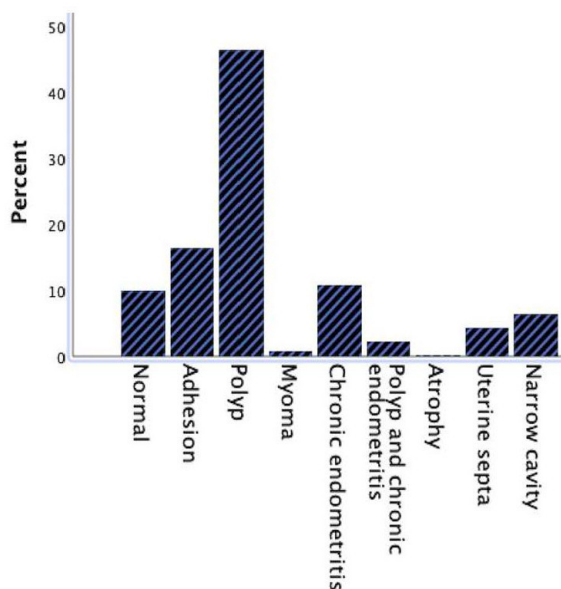


Figure 2. Hysteroscopy findings of study patients. Data were presented as frequencies.

patients have been diagnosed with normal findings of the endometrium. In this group, 17.7% of patients were in the proliferative phase, while 3.1% were in the secretory phase of the endometrium. The endometrial polyp was the most common pathology, with a ratio of 44.3%. Chronic endometritis was seen in 10.9% of patients. Chronic endometritis and endometrial polyp were diagnosed together in 6.1% of patients. One patient had endometrial hyperplasia without atypia, and one had an endometrial cancer diagnosis.

There was not any recorded complication during the hysteroscopy procedure. After hysteroscopy, all patients had IVF treatment.

Discussion

In this study, we evaluated the pre-cycle hysteroscopy findings and the association of these findings with histopathologic results in patients planned for IVF. Our key finding was that endometrial polyps were the most observed uterine cavity abnormalities during hysteroscopy and the most reported pathological results. Besides, approximately 80% of our patients had uterine cavity abnormalities that may adversely affect pregnancy achieved in patients undergoing their first cycle of IVF.

The importance of embryo quality for pregnancy success should not be considered independent of uterine integrity. Besides, the efficacy of hysteroscopy has been accepted for many years to evaluate uterine cavity in patients who have good quality embryos (12, 13). Intrauterine pathologies causing failure of IVF treatments have been determined in the significant number of patients without any pathologies found by diagnostic tools other than hysteroscopy (14, 15).

Endometrial polyps are usually asymptomatic incidental findings in patients planned for IVF/ICSI. The relation between endometrial polyps and subfertility is controversial because patients may reach pregnancy with endometrial polyps. While one study shows polyps in 32% of patients (16), another study showed 6% of patients with polyps in asymptomatic IVF patients (17). In the present study, endometrial polyps were

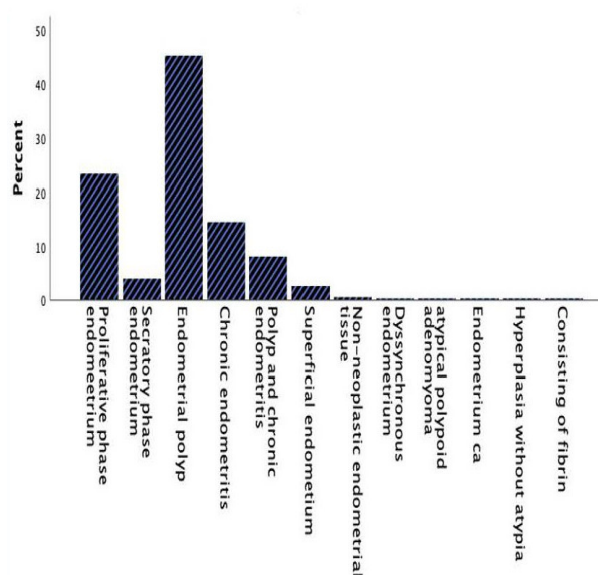


Figure 3. Pathological findings of study patients. Data were presented as frequencies.

found in 45.2% of the study population that was confirmed by histopathology (44.3%). In addition, it was the most common pathology consistently with hysteroscopy. However, we could detect 12% of these endometrial polyps by transvaginal ultrasound and sonohysterography before hysteroscopy. Considering that these structural pathologies have the potential to reduce the chance of pregnancy, hysteroscopy might be a useful diagnostic tool to detect the smaller size of polyps that may adversely affect implantation. In addition, hysteroscopy may allow the simultaneous treatment of these pathologies during the procedure. Therefore, hysteroscopy may be more advantageous than routine transvaginal ultrasound in IVF patients.

The impact of routine hysteroscopy before IVF treatment has been investigated in the literature so far. However, the results are controversial to draw an accurate conclusion. In a recent Cochrane review, it has been reported with low-quality evidence that pre-cycle hysteroscopy may be a favorable attempt regarding clinical pregnancy (CPR) and live birth rates (LBR) in patients with the first IVF cycle and recurrent IVF failure in addition to unselected patients (18). Another review found higher CPR and LBR after hysteroscopy performed just before the first IVF cycle in asymptomatic patients diagnosed by transvaginal ultrasound than those who did not have pre-cycle hysteroscopy. The authors also expressed a possible increase in endometrial receptivity after hysteroscopy due to the stimulation of the endometrium during the procedure (19). However, a large randomized controlled inSIGHT trial was found a similar LBR among the hysteroscopy and immediate IVF groups in patients undergoing their first IVF cycle after diagnosed with a normal uterine cavity by transvaginal ultrasound (11). Another large randomized controlled TROPHY trial also reported no significant difference regarding LBR between the hysteroscopy and non-hysteroscopy groups in patients with recurrent IVF failure while the endometrial cavity was normal on the ultrasonographic exam (10). These controversial results may be attributed to heterogeneous study populations. Given that undetected uterine cavity pathologies such as polyps, fi-

broids and septa might be encountered up to 50% in asymptomatic patients during hysteroscopy and the adverse impact of these lesions on implantation (19), hysteroscopy may be a reasonable option before IVF to restore the endometrial cavity. Besides, since difficult embryo transfer may adversely affect IVF results, hysteroscopy can improve IVF results by correcting cervical canal stenosis and facilitating optimal transfer for future embryo transfer (20).

The main strength of the current study is the evaluation of the incidence of uterine abnormalities in a large cohort of patients undergoing the first cycle of IVF. Another strength is confirming the results of transvaginal ultrasound and sonohysterography with hysteroscopy procedure. Hysteroscopy findings were also confirmed with pathological findings in this study. The major limitations are retrospective design and the bias potential of medical records. We did not declare the pregnancy outcomes of patients in this study because we wanted to draw attention to the availability of the hysteroscopy prior to IVF treatment. So, we planned to present the IVF outcomes in another study.

Conclusion

The use of diagnostic tools before fertility treatment is essential to investigate subfertility in patients applying to infertility centers. However, the choice of the optimal method is challenging for clinicians. Although transvaginal ultrasound and sonohysterography are commonly preferred methods to evaluate the endometrial cavity, abnormal findings undiagnosed by these conventional methods are frequently seen on hysteroscopy in asymptomatic patients before their first cycle of IVF. Besides, hysteroscopy allows the diagnosis and the correction of these pathologies that may lead to successful implantation. Thus, hysteroscopy may be considered to be a reasonable method to evaluate the uterine cavity prior to the first cycle of patients undergoing IVF treatment.

Ethical Approval:

This study was approved by the Local Ethics Committee of Gazi University Faculty of Medicine (date: January 11, 2022; approval number: 2022-024) and conducted in accordance with the Helsinki Declaration.

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