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ORIGINAL ARTICLE

Diagnostic Office Vaginohysteroscopy in Evaluation of Infertility Prior to IVF: A Retrospective Analysis of 1000 Cases

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Abstract

Aim The aim of this study was to analyze the utility of routine use of diagnostic office vaginohysteroscopy in the evaluation of uterine cavity in infertility patients prior to IVF-ET.

Materials and Methods We conducted a retrospective analysis of 1000 women who had undergone routine diagnostic office vaginohysteroscopy as an institutional protocol in the evaluation of infertility prior to IVF-ET cycle at a tertiary care hospital. They were divided into two groups: primary infertility (group I) and secondary infertility (group II). The primary outcome was the finding of an abnormal uterine cavity (congenital abnormality vs acquired abnormality).

Results One thousand women underwent routine diagnostic office vaginohysteroscopy in the evaluation of infertility prior to IVF-ET. There were no intraoperative or postoperative complications. Vaginohysteroscopy revealed an abnormal uterine cavity in 13.8% (1000 patients) of women. Primary infertility group (I) had 13.19% (811 patients), and secondary infertility group (II) had 16.4% (189 patients) abnormal uterine cavities.

Conclusion Diagnostic office vaginohysteroscopy has a definite role in the uterine cavity evaluation in infertility patients prior to IVF, but routine use should not be recommended considering the low incidence of abnormal uterine cavity findings. Moreover, the majority of these

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uterine cavity abnormalities can be detected by less invasive tests such as HSG, TVS, SSG and 3D ultrasound.

Keywords Diagnostic office vaginohysteroscopy · Primary and secondary infertility · IVF-ET · Abnormal uterine cavity

Introduction

Hysteroscopy is considered the gold standard procedure for uterine cavity evaluation. However, the World Health Organization (WHO) recommends HSG alone for the management of infertile women. Office hysteroscopy (OH) is only recommended by the WHO when clinical or complementary examinations (ultrasound, HSG) suggest intrauterine abnormality or after in vitro fertilization (IVF) failure [1, 2].

Approximately 15% of married couples experience infertility. The success of in vitro fertilization (IVF) treatment depends on embryo quality, uterine receptivity and uterine integrity. Benign endometrial pathologies, such as endometrial adhesions, polyps, submucous myoma and uterine mullerian abnormalities, have an adverse effect on endometrial receptivity and consequently in pregnancy rate, and correction of these anomalies has been associated with improved pregnancy rates. Therefore, complete infertility workup should include an evaluation of the uterine cavity. The possibility to perform hysteroscopy using no anesthetic or local anesthesia allows use of outpatient settings and speeds recovery. The vaginoscopic, or "no-touch," technique is performed without a speculum or tenaculum and without anesthesia. Bettocchi introduced the "no-touch" transvaginal approach, where no instruments expose or grasp the cervix. Most diagnostic and brief or minor operative procedures can be performed without anesthetic or with a local anesthetic. Due to improved endoscopic developments and evolving techniques, hysteroscopy can be performed reliably and safely as an office procedure without anesthesia with minimal complications [3–5].

The prevalence of minor intrauterine abnormalities identified at hysteroscopy in cases with a normal transvaginal sonography has been recorded to be as high as 20–40%. Diagnosing and treating such pathology prior to initiating IVF/ICSI have been widely advocated without high-quality evidence of a beneficial effect [6].

The aim of this study was to analyze the utility of routine use of diagnostic office vaginohysteroscopy in the evaluation of uterine cavity in infertility patients prior to IVF-ET as well as to compare its use in primary versus secondary infertility.

Materials and Methods

This retrospective analysis was performed on 1000 infertility patients from August 2015 to September 2016, prior to IVF, who underwent routine diagnostic office vaginohysteroscopy as part of institutional protocol for infertility evaluation in a tertiary care center. They were divided into two groups: primary infertility (group I) with 811 patients and secondary infertility (group II) with 189 patients. Written informed consents were taken from each patient. As a protocol, 200 mcg of Tab Misoprostol was given orally to all the patients 12 h prior to the procedure along with Tab Azithromycin 500 mg and Tab Ornidazole 500 mg. Postprocedure single dose of diclofenac rectal suppository was given to all the patients. Diagnostic office vaginohysteroscopy was performed between D6 and D10 of the menstrual cycle for all the patients with 2.9 mm/30° hysteroscope (Karl Storz) using normal saline as the distension media. Hysteroscopy was performed by no-touch technique without anesthesia. The procedure was considered complete only when both the entire uterine cavity and tubal ostia were visualized. Patients with hypertension, heart disease, anemia (Hb < 7.0 gm/dl), posthysteroscopic surgery and canceled cases due to non-negotiation of cervix were excluded from the study. The primary outcome of abnormal uterine cavities (acquired and congenital) was noted for all the cases. Uterine anomalies were diagnosed according to the American Society of Reproductive Medicine classification within the limits of hysteroscopy [7, 8].

Results

The profiles of the patients were similar as regards age in both primary and secondary infertility groups. The majority of the patients with primary infertility (811 patients) as well as secondary infertility (189 patients) was in the age group of 21–30 years (Table 1; Fig. 1). Primary indication for diagnostic office vaginohysteroscopy was uterine cavity evaluation for infertility.

Abnormal uterine cavities were found in 107 patients (13.19%) in primary infertility group (I) and 31 patients in the secondary infertility group (II). Polyps were the main abnormal findings in both the groups, 5.05% in group (I) and 5.29% in group (II) followed by septate uterus, submucous myoma, unicornuate uterus, bicornuate uterus and uterus didelphys. Uterine synechiae were found in 0.36% in primary infertility group (I) and 2.64% in the secondary infertility group (II). Uterus didelphys were found in two patients in group (I) and 1 patient in group (II) (Table 2).

Table 1 Agewise distribution in the two groups

Age (years)	Primary infertility (group I)	%	Secondary infertility (group II)	%
21–25	234	28.85	50	26.45
26–30	331	40.81	81	42.85
31–35	137	16.89	32	16.93
>35	109	13.44	26	13.75
Total	811		189	

The total numbers of abnormal uterine cavities were found in 138 patients out of 1000 completed office vaginohysteroscopy making it 13.8% in our study.

Acquired abnormal uterine cavity, i.e., endometrial polyps, submucous myoma and uterine synechiae, was found in 62 (7.64%) patients in primary infertility group (I) and 17 (8.99%) in secondary infertility group (II), whereas congenital abnormal uterine cavity, i.e., septate, arcuate, bicornuate, unicornuate and uterus didelphys, was found in 45 (5.54%) patients in group (I) and 14 (7.40%) in group (II) (Table 3; Fig. 2). Acquired abnormal uterine cavity findings had increased percentage of patients in both the groups as compared to congenital abnormalities. Polyps were the commonest acquired abnormality in both the groups followed by submucous myomas and uterine synechiae, whereas septate uterus was the commonest congenital abnormality and uterus didelphys had the least incidence (Table 2). There were no intraoperative or postoperative complications noted in this study.

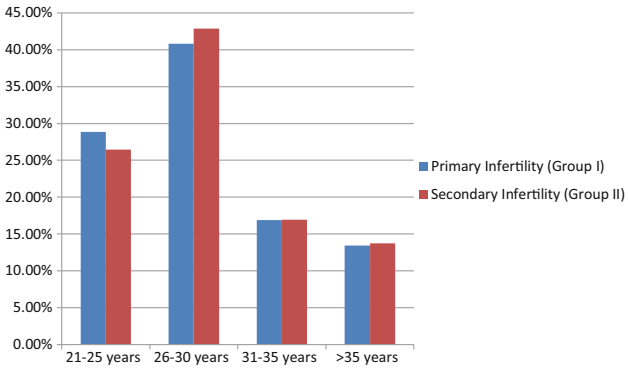

Fig. 1 Agewise distribution in the two groups

Discussion

The basic step of an infertility workup is to evaluate the shape and regularity of the uterine cavity. Acquired uterine lesions, such as uterine fibroids, endometrial polyps and intrauterine adhesions, may cause infertility by interfering with proper embryo implantation and growth. Congenital uterine malformations are also thought to play a role in delaying natural conception. Diagnostic office vaginohysteroscopy is a feasible, safe, simple, tolerable and quick outpatient procedure. It can diagnose intrauterine abnormalities in 23.7% of infertile women with normal HSG. Diagnostic office vaginohysteroscopy has an additional value to HSG and diagnostic laparoscopy in diagnosing uterine abnormalities and even tubal patency. Diagnostic indices including accuracy of either HSG or diagnostic laparoscopy would increase if combined with office vaginohysteroscopy [2, 5, 9].

In our retrospective study, the main indication for performing diagnostic vaginohysteroscopy was uterine cavity evaluation in infertility patients prior to IVF-ET as per the institutional protocol (Figs. 3, 4, 5, 6).

In our study, 13.8% of women, undergoing infertility evaluation prior to IVF, had abnormal uterine findings on hysteroscopy. Sahu et al. [10] in their study found the rates of abnormal findings at 34.88% in infertile patients who underwent diagnostic hysteroscopy. Siam [11] in her study found the rates of abnormal findings in infertile patient who underwent diagnostic hysteroscopy was 18.4%. In total, 20.37% of women had abnormal uterine cavity findings in the study by El Huseiny et al. [2]. No significant difference in the rate of uterine pathology was found between women with primary and secondary infertility (13.19 and 16.4%, respectively). More percentage of cases of acquired (8.99 vs 7.64%) and congenital abnormalities (7.40 vs 5.54%) were noted in secondary infertility group (II) as compared to primary infertility group (I) (Table 2; Figs. 1, 2)

While the relationship between congenital uterine malformations and impaired pregnancy outcome (such as recurrent pregnancy loss, late abortions, preterm deliveries and malpresentations) is quite established, the issue of these malformations as a cause of infertility is still debatable. The incidence of uterine malformations in other series of infertile patients varies between 1 and 26%, with a mean incidence of 3.4%. We observed an incidence of 5.54% for primary and 7.40% for secondary infertility. Septate uterus was the most common congenital uterine anomaly found in the current study in concordance with other studies. The presence of congenital uterine abnormalities might be associated with a detrimental effect on the probability of pregnancy achievement, spontaneous abortion and

Table 2 Abnormal uterine cavity

Abnormal uterine cavity	Primary infertility (811) group (I)	%	Secondary infertility (189) group (II)	%	Total 1000	%
Polyp	41	5.05	10	5.29	51	5.1
Septate uterus	18	2.21	05	2.64	23	2.3
Arcuate uterus	08	0.98	02	1.05	10	1.0
Bicornuate uterus	07	0.86	03	1.58	10	1.0
Unicornuate uterus	10	1.23	03	1.58	13	1.3
Uterus didelphys	02	0.24	01	0.52	03	0.3
Submucous myoma	18	2.21	02	1.05	20	2.0
Uterine synechiae	03	0.36	05	2.64	08	0.8
Total	107	13.19	31	16.4	138	13.8

Table 3 Acquired versus congenital abnormal uterine cavity

	Primary infertility 811 (group I)	%	Secondary infertility 189 (group II)	%	Total 1000	%
Acquired abnormal uterine cavity	62	7.64	17	8.99	79	7.9
Congenital abnormal uterine cavity	45	5.54	14	7.40	59	5.9

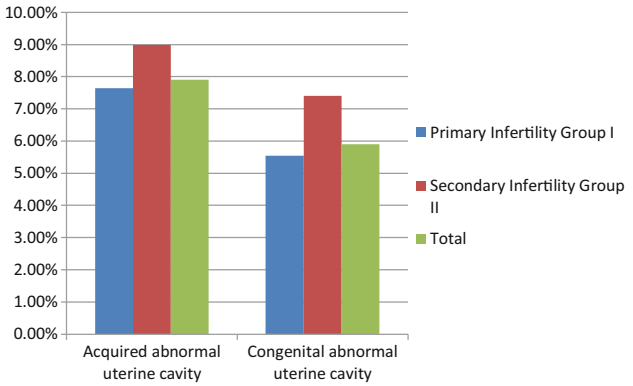

Fig. 2 Acquired versus congenital abnormal uterine cavity

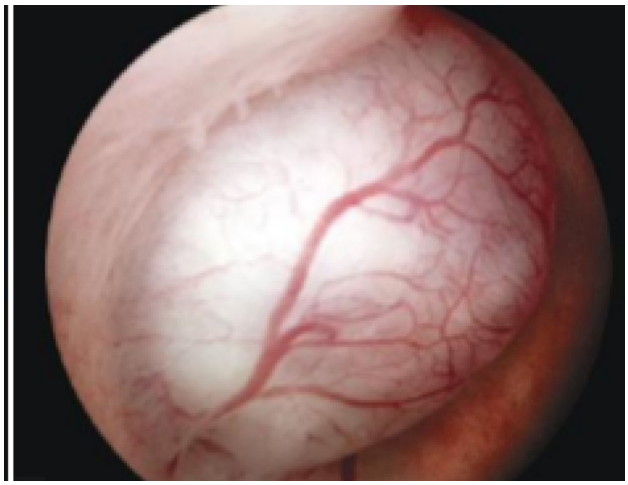

Fig. 3 Submucous myoma

obstetric outcome. Hysteroscopic removal of a septum may reduce the probability of a spontaneous abortion [8, 12].

The reported incidence of myomas in infertile women without any obvious cause of infertility is estimated to be between 1 and 2.4%. In the current study, submucous myomas were diagnosed in 2.21% of patients with primary infertility and 1.05% in secondary infertility. Submucous myoma influences fertility, mainly based on the favorable pregnancy rates obtained after myomectomy. Submucous and intramural myomas distort the cavity, impairing implantation and pregnancy rates in women undergoing IVF. Several theories have been proposed regarding this issue, including alteration of uterine contractility or induction of inflammatory and vascular changes leading to a less receptive implantation site [13–15]. Removal of large myomas (more than 3 cm) has a much more beneficial effect on fertility than small ones. Zayed et al. revealed in their study that hysteroscopic myomectomy is a safe and effective management for submucous myomas up to 6 cm in diameter [14–17].

Endometrial polyps were diagnosed in the highest percentage in our study in both primary and secondary infertility groups with no significant difference (5.05 vs 5.29%). The true incidence of endometrial polyps in the general population is difficult to determine, because many of them are clinically asymptomatic. Hysteroscopic polypectomy remains the gold standard for both the diagnosis and treatment of endometrial polyps [18, 19].

The effect of polyps on the endometrium was evaluated using *HOXA10* and *HOXA11*, established molecular markers of endometrial receptivity. Significantly lower *HOXA10* and *HOXA11* expression was identified in

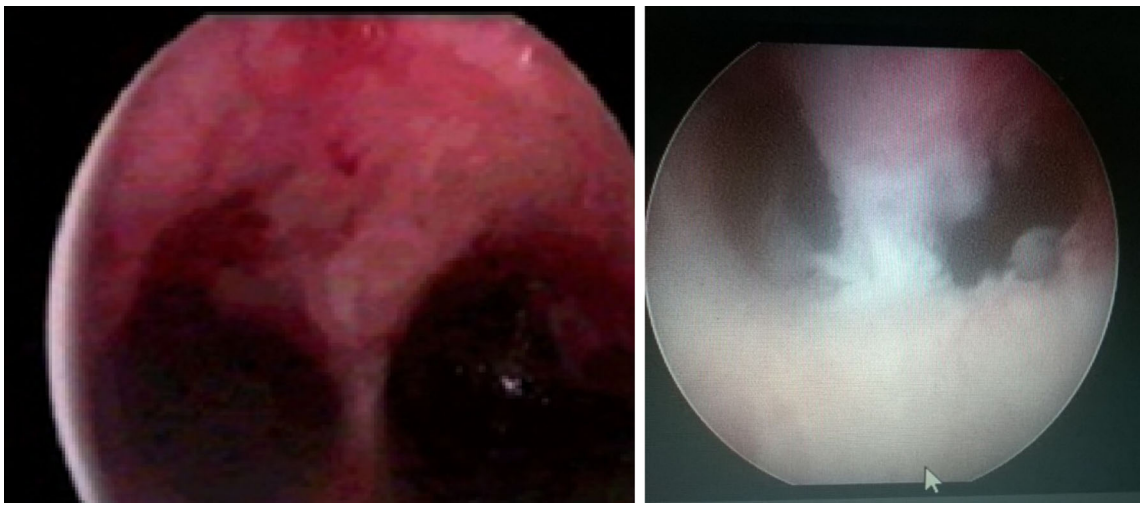

Fig. 4 Septate uterus

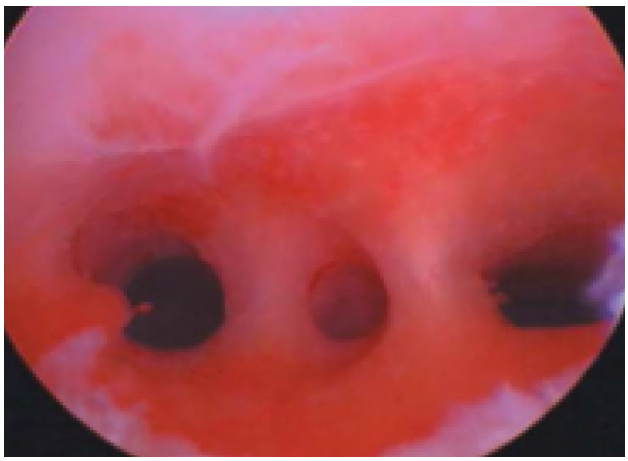

Fig. 5 Asherman's syndrome

Fig. 6 Endometrial polyp

endometrium from uteri with polyps compared to controls, suggestive of impaired endometrial receptivity in uteri with polyps. Endometrial polyps can produce glycodelin, a glycoprotein that has been shown to inhibit natural killer cell activity, rendering the endometrium less receptive to implantation [15]. The effect of asymptomatic endometrial polyps on infertility is unclear. However, it is plausible that polyps can cause infertility due to mechanical interference with sperm and embryo transport, impairment of embryo implantation or altered endometrial receptivity. Furthermore, the size, number or location of polyps may influence any effect on reproductive outcomes [20]. The possible role of these polyps in infertility is yet unclear, although follow-up on these women revealed improved reproductive outcomes after polypectomy. Waiting for two or more menstrual cycles after hysteroscopic polypectomy for IVF cycle does not necessarily yield superior outcomes; patients can undergo ovarian stimulation after their next menses without affecting IVF-ET outcomes [18].

In our study, intrauterine adhesions/synechiae were found in 2.64% of cases in secondary infertility, which was higher than in primary infertility (0.36%), being mostly the result of uterine curettage for postpartum or postabortion residua. The patients of intrauterine adhesions (IUA) generally present with amenorrhea or other menstrual aberrations, recurrent pregnancy loss and infertility. During the last two decades, the advent of hysteroscopy has revolutionized the diagnosis and management of Asherman's syndrome. Historically, the use of hysterosalpingography (HSG) has been widespread in the diagnosis, but hysteroscopy is now the gold standard of diagnosis and treatment of Asherman's syndrome. Women who underwent hysteroscopic adhesiolysis showed significant

improvement in the menstrual pattern and increased rates of conception as well as live birth rate per conception [21].

It is evident that the introduction of hysteroscopy in the diagnosis of intrauterine lesions has helped us to realize that IUA is much more frequent than we had previously thought. Moreover, the incidence of this pathology seems to be significantly influenced by the number of abortions performed, the high incidence of genital tuberculosis in some countries and the different criteria used to detect intrauterine adhesions. Hysteroscopy provides a real-time view of the uterine cavity, allowing for a meticulous definition of the site, extent and character of any adhesions, and it is the optimum tool for assessing the endometrium [22].

In our study, we used Tab Misoprostol 200 mcg orally 12 h prior to the procedure. Misoprostol, a synthetic prostaglandin E1 analog, has been used for cervical priming prior to its use in office hysteroscopy, but there is still no agreement on the recommended dose, route (oral or vaginal) or time of administration [23, 24].

While debating the need for routine diagnostic office vaginohysteroscopy in the evaluation of the infertile woman, one must keep in mind that this procedure today is a simple, fast, outpatient procedure, requiring short training with high success rates. The incidence of pathologic abnormalities based on hysteroscopic diagnosis was high, especially with repeated IVF failure. Improvement in implantation and clinical pregnancy rates was observed after office hysteroscopy prior to ICSI [6].

Diagnostic office vaginohysteroscopy allows complete, accurate identification of intrauterine abnormalities that might negatively affect endometrial receptivity and implantation. The information derived from vaginohysteroscopy helps to institute appropriate therapy and by doing so to improve conception rates over shorter intervals. However, routine use should not be recommended considering the relatively low incidence of abnormal uterine cavity findings in our study and invasive nature of the procedure. A variety of less or non-invasive modalities such as hysterosalpingography (HSG), transvaginal sonography (TVS), diagnostic hysteroscopy, two-dimensional hysterosonography (2-DHS) and three-dimensional hysterosonography (3-DHS) can be used for the diagnosis of uterine abnormalities. However, diagnostic hysteroscopy has remained the gold standard in infertility investigation. Compared to hysteroscopy, 3-DHS has a reliable specificity for diagnosis of uterine abnormalities, and it can be introduced as a first-line investigation tool in an infertility workup. Sensitivity and specificity of 3-DHS and hysteroscopy in detecting polyp or hyperplasia regarding histopathology as the gold were the same [25, 26].

Conclusion

Our study shows that the incidence of uterine pathologies (congenital and acquired) in women with primary or secondary infertility approximates 13.8%. Diagnostic office vaginohysteroscopy has a definite role in the uterine cavity evaluation in infertility patients prior to IVF, but routine use should not be recommended considering the invasive nature of the procedure and low incidence of abnormal uterine cavity findings in our study. Moreover, the majority of these uterine cavity abnormalities can be detected by less invasive tests such as HSG, TVS, SSG and 3D ultrasound. Therefore, this diagnostic modality should be used judiciously in patients with abnormalities of uterine cavity detected by noninvasive tests and in infertility patients with recurrent implantation failure post-IVF-ET, though it has a similar importance in the evaluation of patients with both primary infertility and secondary infertility.

Compliance with Ethical Standards

Conflict of interest There is no potential conflict of interest for any author.

Ethical Standards Since this study is a retrospective analysis of diagnostic office vaginohysteroscopies performed in a tertiary care center as an institutional protocol in the evaluation of infertility patients prior to IVF, no ethical issues are involved.

Informed Consent Written informed consent was taken from each patient in the study.

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