
Role of Diagnostic Hysteroscopy in Infertile Women With Normal Hysterosalpingogram

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Abstract

Objective : To evaluate the Role of Diagnostic Hysteroscopy in Infertile Women With Normal Hysterosalpingogram(HSG).

Methods : We performed a prospective study on 140 women attending Benha university hospitals .women underwent a diagnostic hysteroscopy .All women were having normal HSG, hormonal profile, and their husbands were having normal semen.

Results: Hysteroscopy revealed abnormalities in 48 women (34.3 %), and 56 hystoscopic abnormalities(Endometrial Polyp, Cervical Polyp, Submucous myoma, Cervical stenosis, Intrauterine adhesions, Chronic endometritis. Septum, Hypertrophic endometrium. Atrophic endometrium , Cornual inflammation and Cornual fibrosis). It revealed that hysteroscopy may be a part of routine infertility work up.

Conclusion: We can conclude that HSG is still considered the first line diagnostic tool in infertility work up, however, in infertile women with normal HSG, hysteroscopy is recommended 6 months following the procedure of HSG.

Keywords: primary Infertility - Hysteroscopy - Hysterosalpingography.

Introduction

Infertility means the inability to conceive following 1 year of unprotected intercourse in cases where the female is ≤ 35 years of age or following 6 months of unprotected intercourse for women > 35 years of age (1). Fertility investigations are often based more on tradition and personal preference than on the demonstrated usefulness of the many available components (2).

Today, hysteroscopy is considered the gold standard for evaluating the uterine cavity, and due to improved endoscopic developments, it can be performed reliably and safely as an office procedure. (3). Later studies have shown a correlation of only 65% between findings diagnosed with HSG compared with those diagnosed with hysteroscopy (4). It is widely accepted that a complete infertility workup should include an evaluation of the uterine cavity. Uterine abnormalities, congenital or acquired, are implicated as one of the causes of infertility (5).

In fact, infertility related to uterine cavity abnormalities has been estimated to be the causal factor in as many as 10% to 15% of couples seeking treatment. Moreover, abnormal uterine findings have been found in 34% to 62% of infertile women (6). The presence of uterine pathology may negatively affect the chance of implantation. The prevalence of unsuspected uterine pathology in asymptomatic women with implantation failure has been reported to be as high as 50% Therefore, one of the common investigations proposed for women undergoing IVF treatment is to evaluate the uterine cavity via Hysteroscopy (7).

The role of hysteroscopy in infertility investigation is to detect possible intrauterine changes that could interfere with implantation or growth or

both, of the conceptus (6). The role of congenital uterine anomalies in infertility remains unclear. However, it has been suggested that uterine anomalies may contribute to infertility, possibly by interfering with normal implantation and placentation (8). Little is known about the association between endometrial polyps and fertility. The mechanism by which polyps may adversely affect fertility is also poorly understood but may be related to mechanical interference with sperm transport, embryo implantation, or through increased production of inhibitory factors such as glycodeclin that can inhibit natural killer cell function (9).

There are various potential mechanisms by which myomas could cause infertility. These include chronic endometrial inflammation, abnormal vascularisation, increased uterine contractility, and abnormal local endocrine patterns, all of which may interfere with sperm transport or embryo implantation (10). **Gollan et al., (11)**, confirmed the superiority of hysteroscopy over other diagnostic procedure for accurate and definite diagnosis of IUAs. He also recommended the use of hysteroscopy as a therapeutic tool in treatment of such problem.

The aim of this study was to examine the role of diagnostic hysteroscopy in a basic infertility workup.

Patients and Methods

Patients

This Study was a prospective study that was conducted at Benha University Hospital after the approval of Institutional ethical committee. One hundred forty women were recruited from antenatal clinic starting from November 2013 till April 2015. An informed consent was obtained from every patient. **Inclusion criteria:** Patients having primary infertility age group (20-40 years) with normal HSG. **Exclusion criteria:** 1-Patient age less than 20 years or more than 40 years. 2-Contraindications of hysteroscopy like bleeding, suspected or confirmed pregnancy & history suggestive of active infection like history of cervical or vaginal discharge. 3- patient with abnormal HSG. 4- Couples with male factor infertility (abnormal semen parameters and /or sexual dysfunctions).

Interventions

All eligible patients were well informed regarding the procedure and then they were submitted to the following: 1-Detailed history (Personal history, Menstrual history, Past history) 2-Complete general examination. 3-Complete local examination (Vaginal examination - Bimanual examination and Speculum examination). 4. Blood analysis: for a base line hormonal profile- day 2 serum FSH ,LH, and prolactin.

5- Diagnostic hysteroscopy. The hysteroscopy was done by a well trained staff the hysteroscopy used was rigid continuous flow diagnostic hysteroscopy (Tuttlingen, Karl Storz, Germany). It has a 30° panoramic optic which is 4mm in diameter and the diagnostic continuous flow outer sheath is 6.5 mm in diameter. The patient was placed in lithotomy position with the buttocks projecting slightly beyond the table edge. The perineum and vagina were gently swabbed with povidone-iodine. The cervix was exposed with a posterior wall retractor and a tenaculum was applied to its anterior lip. The telescope was inserted into the sheath then flushed with distension media (saline) to expel any air. The technique used to provide uterine distension involved attaching plastic bags of saline to dual blood infusion tubing. Each bag was then wrapped in a pressure infusion cuff similar to that used to infuse blood under pressure with a pressure used 100mmHg. A reflex camera (Olympus) with an objective that has a focal length varies from f70 to f140 together with (Karl Storz) special zoom length, adapter to Hopkins telescope and a suitable cable ware used with computer flash unit. The hysteroscopic picture which appeared through the optic, transmitted on the monitor by the camera which is fitted on the eyepiece of the optic where the panoramic diagnostic hysteroscopy could be informed with better visualization and accuracy. The light generator which is a metal halide automatic light source with a 150 watt lamp (model G71A, Circon ACMI, Germany) was switched on and the high cable was attached to the hysteroscope. Dilatation of the cervix was avoided whenever possible to avoid leakage of the medium into the vagina. The hysteroscope was then introduced into the external os and advanced under vision along the axis of cervical canal.

Once the cavity was entered, an overview of the uterine cavity was performed. This was followed by systematic examination for fundus then tubal ostia on both sides then the uterine wall through slow rotatory movements of the telescope. Examination was considered normal if the endometrial cavity was easily distended by the medium with complete separation of its walls and vision of both tubal ostia. Agglutination of the uterine walls or the presence of thick bands extending across the cavity or occlusion of ostial area or upper cavity indicated intrauterine adhesions (IUAs). A longitudinal depression extending from the fundus downwards to a variable level indicated a uterine septum. Any other pathological lesions such as polyps, submucous myomas were described according to their site, size and vascularity. At the end of the procedure, the hysteroscope was slowly withdrawn through the cervical canal which was visualized to detect any lesion.

Methods of statistical analysis

Collected data were statistically represented in terms of range, mean, standard deviation (+/- SD) and percentages. Accuracy was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy. All statistical calculation was done using computer programs Microsoft Excel version 7 and statistical package for the social science program version 16.

RESULTS:

The study included 140 patients with primary infertility, proved to be normal on physical examination, All patients had essentially normal hysterosalpingography (HSG).

The mean age of the studied group was 27.64 ± 5.42 years. The mean duration of infertility was 5.64 ± 3.55 years; ranging between 1 and 16 years.

Table (1) : Distribution of the studied group regarding age and years of infertility.

| Variable | Age | Years of infertility |
|-----------------|-------|----------------------|
| Mean | 27.64 | 5.64 |
| \pm SD | 5.42 | 3.55 |
| Range (min-max) | 20-40 | 1-16 |

During hysteroscopic examination, abnormalities were detected in the cervix and uterus in 48 patients (34.3%). More than one abnormality was seen in 8 patients, i.e. 56 abnormalities were recorded, Cervical abnormalities (n = 12) represented 21.4 % of all abnormalities, while uterine abnormalities were 44, representing 78.6 % all abnormalities (Figure 2).

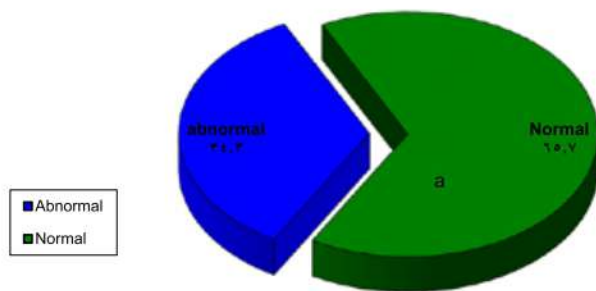


Fig. (1): Percentage of patients with abnormal hysteroscopic findings among the studied group (n = 48)

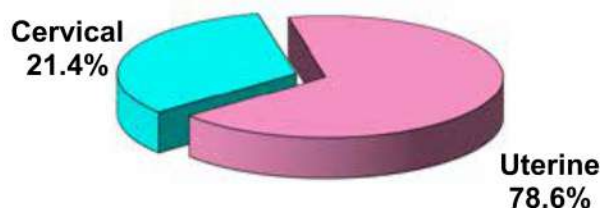


Fig. (2): Distribution of abnormalities detected by hysteroscopy (n = 56) in the studied group

Table (2) shows detailed list of hysteroscopic abnormalities. Cervical stenosis was the most frequent hysteroscopic findings, 9 cases was detected. Cervical stenosis and cervical polyp were seen in 21.3 % of cases.

Table (2): Hysteroscopic abnormalities detected in 48 patients.

| | Number | Percentage |
|--------------------------|--------|------------|
| Endometrial Polyp | 7 | (12.5) % |
| Cervical Polyp | 3 | (5.3)% |
| Submucous myoma | 6 | (10.7)% |
| Cervical stenosis | 9 | (16)% |
| Intrauterine adhesions | 8 | (14.3)% |
| Chronic endometritis | 5 | (8.9)% |
| Septum | 2 | (3.6)% |
| Hypertrophic endometrium | 4 | (7.1)% |
| Atrophic endometrium | 3 | (5.3)% |
| Cornual inflammation | 3 | (5.3)% |
| Cornual fibrosis | 6 | (10.7)% |
| Total | 56 | 100 % |

The 2 cases with uterine septa had small septum. Intrauterine adhesions were found in 8 patients; 6 with mild adhesions and 2 with moderate adhesions. Cervical stenosis did not hinder passage of the hysteroscope to inspect the uterine cavity in the 9 cases.

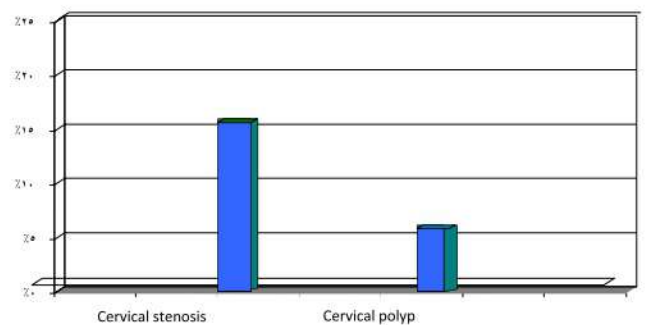


Fig. (3): Types of cervical abnormalities detected by hysteroscopy (n = 12)

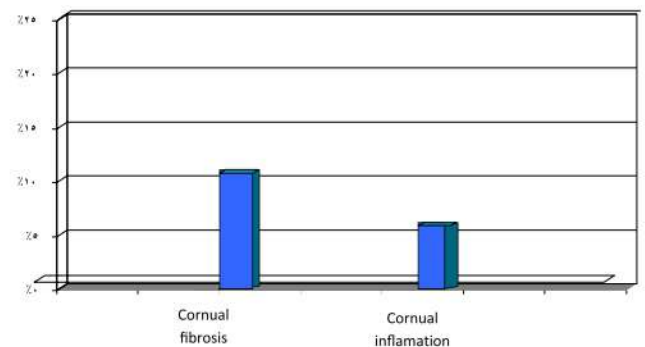


Fig. (4): Types of ostial abnormalities detected by hysteroscopy (n=9)

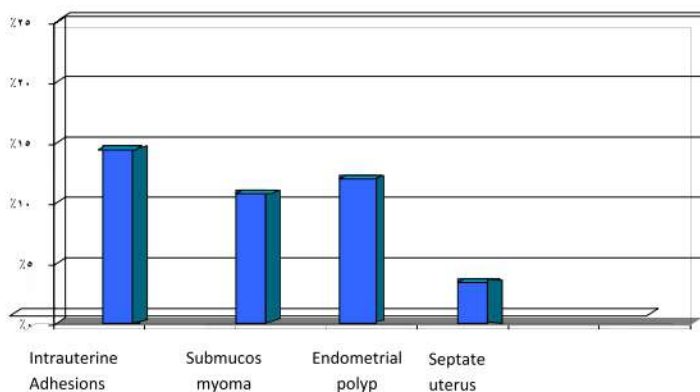


Fig. (5): Types of uterine cavity lesions detected by hysteroscopy

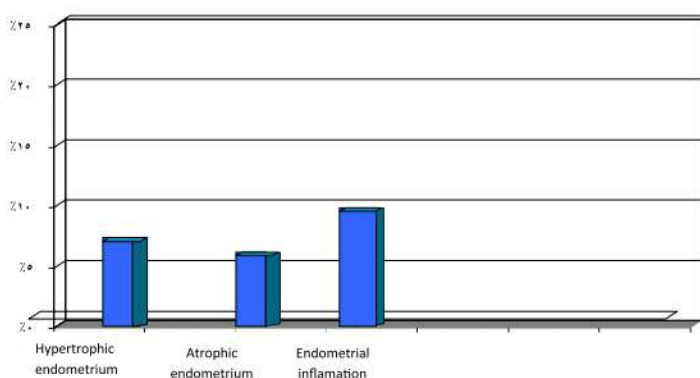


Fig. (6): Types of Endometrial abnormalities detected by hysteroscopy

Discussion

Infertility is a highly prevalent global reproductive health problem, affecting at least 15% of reproductive-aged couples worldwide (12). A global study utilizing data from 47 Demographic and Health Surveys (DHS) in low-resource countries estimated that, in 2002, more than 186 million ever-married women of reproductive age (15-49 years) in such countries (except China) were infertile. This number includes both primary infertility (i.e., infertility in the absence of a prior history of pregnancy) and secondary infertility (i.e., infertility following a prior pregnancy). According to the global DHS study, this number represents more than one-fourth of the ever married women of reproductive age in these countries (13). In a WHO-sponsored community-based prevalence study of infertility, based on a random sample of married women aged 18-49 in 20,000 rural and urban Egyptian households, the total infertility prevalence rate was 12 percent, with 4.3 percent of cases suffering from primary infertility and 7.7 percent from secondary infertility (Egyptian Fertility Care Society, 1995). DHS Comparative Report (2004), reported 2.7% primary infertility rate among married women age 25-49 who have been married for at least five years between 1994 and 2000 (13).

In the current study we selected infertile women normal hysterosalpingographic study denoting

bilateral tubal patency and apparently normal uterine cavity. As hysteroscopy provides direct visual to the uterine cavity, we ask the question; *Do hysteroscopy add to the infertility work-up?* This study demonstrated abnormalities in hysterosalpingographically “normal” infertile women. Hysteroscopy detected abnormalities in 34.3% of women, 65.7 % of women had normal hysteroscopy in agreement with the normal HSG. This relatively large zone of disagreement may be exaggerated if taken collectively. Some detected abnormalities may not have a direct effect to be considered a cause of infertility. It is better to discuss it in terms of individual diagnoses. The list of abnormalities detected with hysteroscopy involved polyps,(endometrial and cervical), submucous myomas, small septa, cervical stenosis – allowed passing the hysteroscope – in addition to intrauterine adhesions, and evidence of chronic endometritis. The last two defects are thought to affect infertility in some way. These were detected in 13 women (9.3%). We think this is the direct additive value of hysteroscopy to diagnosis of infertility in the studied group. However, submucous myomas and endometrial polyps (13 cases) might be a cause of implantation failure.

Around 10% of women presenting with infertility have endometrial polyps (14). Endometrial polyps may be associated with increased miscarriage rates, but there is no evidence of lower pregnancy rates in this group (15,16,3). Fibroids have rarely been shown to be a direct cause of infertility but might affect fertility indirectly (15). Some studies indicate high success rates in both pregnancy and live births following removal of fibroids in women with otherwise unexplained infertility (17,18). Intrauterine adhesions are usually the result of intraoperative or postoperative complications during uterine evacuation, termination of pregnancy or hysteroscopic surgery. It can also be caused by uterine infections. Ashermann’s syndrome has been found in 13% of women undergoing routine infertility investigations (19). Uterine cavity abnormalities are thought to contribute to subfertility in 10% of women (5). Other investigators found uterine factors representing only 2-3% of infertility causes, but intra-uterine lesions are much more common in infertile women (40-50%). These lesions can interfere with spontaneous fertility and can compromise pregnancy rates in assisted reproduction (20).

Exploration of the uterine cavity is actually one of the basic explorations in infertility workup. Traditionally HSG is known to be helpful in evaluating uterine cavity abnormalities. When compared with hysteroscopy, HSG is considered to have a high sensitivity (60–98%), but a low specificity (15–80%) in detecting

uterine abnormalities and is, therefore, associated with relatively high false-positive and false-negative rates (21,22,5,23).

One of the studies comparing HSG with hysteroscopy reported a sensitivity of 81% and a specificity of 80% with a false-negative rate of 9% and a false-positive rate of 22% (23). Another study conducted to assess the diagnostic reliability of hysteroscopy and HSG, demonstrated HSG to have a sensitivity of 79% and a specificity of 82%, with an 18% false-positive rate and a 19% false-negative rate. They concluded that even though HSG is mainly used for the assessment of tubal patency, it has a secondary role in the assessment of the uterine cavity (21). In the current study, we could not calculate sensitivity or a false positive rate, as all women were proved to be normal on HSG. We found a false negative rate of 34.3%.

In fact HSG can detect a filling defect inside the uterus, for differential diagnosis. The differential diagnosis includes polyps, submucosal fibroids, intrauterine adhesions and uterine septa. Hysteroscopy, here, is necessary to confirm pathology. A pronounced advantage in these cases is the possibility to treat these lesions with operative hysteroscopy.

HSG results may also be influenced if the procedures are performed at different phases of the menstrual cycle due to the variable trophic changes of the endometrium. False-positive findings can be caused by air bubbles, mucus and menstrual debris that could mimic filling defects. False-negative findings can result from an excessive amount of contrast media in the uterus obliterating shadows caused by small endometrial lesions (23).

Previous studies reported that 10–35% of women undergoing fertility investigations, who have a normal cavity at HSG, have been reported to have abnormal hysteroscopic findings (21,22). We had nearly the same rate, 34.3%.

In addition, HSG does not provide information about trophic, inflammatory and infectious lesions that may be responsible for poor reproductive outcome in nearly 25% of subfertile women (23). In the current study we found 5 women with chronic endometritis and 8 women with adhesions, most probably post-inflammatory because women of the studied group had primary infertility with no history of previous intrauterine surgery or procedures apart from HSG.

In view of the low-positive predictive value and low specificity of the HSG, Golan et al. suggested HSG should be replaced by the diagnostic hysteroscopy as a first-line infertility investigation (22).

Hysteroscopy is the gold standard for evaluating the uterine cavity and can be performed reliably and safely as an outpatient procedure. However, standard hysteroscopy often elicits significant discomfort. Mini-hysteroscopy uses a traumatic insertion technique, saline or lactated Ringer's solution for distension of the uterine cavity, and a small diameter hysteroscope of ≤ 3.5 mm in outer diameter. A prospective study of 530 outpatient mini-hysteroscopies, performed without any form of anesthesia, reported high patient acceptability (24). Mini-hysteroscopy is not more invasive than hystero-contrast sonography (HyCoSy) (25) and, for detection of abnormalities of the uterine cavity, both techniques are equally effective but superior to transvaginal sonography (26).

Hysteroscopy, with the development and miniaturization of equipment, is currently simple, outpatient cost-effective exploration and it is considered the gold standard for diagnosis of intrauterine lesions. However, the benefit of the systematic use of hysteroscopy in the initial assessment of infertility remains unclear and the exploration of the uterine cavity in the initial assessment of infertility should be based on hysterosalpingography or hysterosonography. Systematic hysteroscopy before IVF is widely accepted practice that is supposed to improve pregnancy rates but still lacks scientific evidence. After repeated implantation failure in IVF cycles, uterine cavity should be reevaluated by hysteroscopy and this practice has been demonstrated to improve pregnancy rates (20).

Conclusion

We can conclude that HSG is still considered the first line diagnostic tool in infertility work up, however, in infertile women with normal HSG, hysterolaparoscopy is recommended 6 months following the procedure of HSG.

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