



Investigating Hysteroscopy Implementation in Infertile Women Candidate With a Normal Uterine Cavity for Laparoscopy in Hysterosalpingography

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Abstract

Objectives: Endometrial pathologies inside the cavity can occur simultaneously with gestational unpleasant consequences but are not always capable of being diagnosed by the hysterosalpingography (HSG). This study aimed to examine the value of performing diagnostic hysteroscopy beside diagnostic laparoscopy among infertile women with normal uterine cavities in HSG.

Materials and Methods: A total of 103 infertile women with normal uterine cavities in the HSG and within the age range of 18-40 who referred to Imam Reza hospital for laparoscopy during 2016-2017 were included in this cross-sectional study. Hysteroscopy was performed simultaneously with diagnostic laparoscopy. Then, the existence of uterine pathologies like endometrial polyps, submucous myoma, and uterine endometrial adhesions and their relationship with the patient's age, infertility type and duration, and cycle time were evaluated. A *P* value less than 0.05 was considered statistically significant.

Results: Overall, 64 patients (63.1 %) had a normal uterine cavity in the hysteroscopy while 39 of them had an abnormal uterine cavity, the HSG false negative cases of whom were reported 37.9%. The pathologies found in the hysteroscopy were endometrial polyp (16 cases), submucous myoma (1 case), uterine septum (6 cases), asherman syndrome (7 cases), bicornuate uterus (4 cases), polyp + asherman (3 cases), polyp + submucous myoma (1 case), and septum + submucous myoma (1 case). Patients' age, type of infertility, and menstruation time during performing hysteroscopy made no particular difference in diagnosing pathologies of the uterine cavity in the hysteroscopy.

Conclusions: Based on the findings, conducting hysteroscopy in infertile women who are candidates of laparoscopy and have normal uterine cavities in HSG can result in recognizing some cases of uterine pathologies which influence the outcomes of future pregnancies is not dependent upon the patient's age, menstruation time, type and duration of infertility, and result of laparoscopy.

Keywords: Hysterosalpingography, Hysteroscopy, Laparoscopy, Infertility, Uterine factor

Introduction

Infertility means that a woman does not conceive despite the unprotected intercourse for one year, which has 2 types, namely, primary and secondary infertility (1,2). Infertility has different causes such as male factors (20%-40%), tubal (30%-40%) or uterine (10%-15%) factors, and ovarian problems (2,3). Based on the significance of investigating uterine disorders, it is estimated that 34%-62% of the uterine factors are related to intrauterine pathologies in which routine evaluation of uterine cavity is conducted using initial evaluation tests such as hysterosalpingography (HSG) and hysteroscopy (1,4).

Uterine disorders are among approximately uncommon causes of infertility thus, their possibility should always be considered as these disorders can unpleasantly influence the consequence of fertility even if no infertility is occurred (5). Uterine pathological disorders which may affect the fertility involve congenital disorders, submucous myomas, intrauterine adhesions, and endometrial polyps (1,2).

During the last three decades, the total amount of infertility has remained almost unchanged while its

diagnostic and treatment methods have increased. As a result, today infertile couples mostly attempt to use infertility diagnostic and treatment workup (1,6).

The HSG and hysteroscopy are among the main methods of investigating the uterine cavity, each having several advantages and weaknesses. Therefore, each of these methods should be selected according to the infertile woman's requirement (2,6).

As HSG is a simple, easy, and low-aggressive method, it is often the best primary alternative which determines the shape and size of the uterine cavity and uterine tubes. However, its diagnostic accuracy for recognizing uterine pathological disorders varies among the infertile women based on the nature of the disorder (4,7). In the majority of the studies, the sensitivity of HSG was reported 44%-77%, with a specificity of 35%, false negative cases of 8%, and false positive cases of 30%. In most cases diagnosed with hysteroscopy (as the main standard method), wrong diagnoses were related to submucous myomas, polyps, and intrauterine adhesions (4).

As mentioned above, the HSG has some weaknesses such

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as time scheduling, using antibiotics, and being discomfort and painful. In addition, HSG somehow exposes the patients to ionizing radiation as well as radiocontrast substances and involves infectious complications which may result in more gestational disorders (4,6,8). Conversely, however, HSG has several advantages which include being performed on an outpatient basis, having low cost, acceptable treatment value, and imaging uterine cavity, intrauterine structure, and tubes simultaneously (6,7).

Hysteroscopy is an endoscopic method in which a narrow telescope is used to observe the intrauterine cavity. Endoscopic operations, if used appropriately, have such benefits as a decrease in pain, lower cost, and faster improvement. Diagnostic hysteroscopy seeks to evaluate the intrauterine cavity and diagnose the structural and pathological disorders such as a uterine septum, adhesion, polyp or myoma (2,6).

Investigating with hysteroscope has priority in the evaluation of endometrial cavity since it has a sensitivity of 100% and specificity of 95%. Further, it is considered as a gold standard method in diagnosing uterine pathologies and their simultaneous treatment (4).

Using diagnostic hysteroscopy, some information can be achieved that are inaccessible by means of un-purposeful endometrial sampling like diagnosing endometrial polyps or submucous myomas, as well as malignant or hyperplastic polyps or other localized lesions which can be diagnosed by hysteroscopy sampled through purposeful biopsy and completely expelled (3).

Diagnostic hysteroscopic indications in infertility cases encompass abnormal HSG or abnormal transvaginal sonography, unexplained infertility, and in vivo fertilization (IVF) failure which can often be implemented with the lowest amount of irritation and cost (4). Furthermore, laparoscopy is a standard method for exploring the anatomy of pelvic, as well as the size and extent of pelvic diseases in order to investigate uterus and tubo-peritoneal causes of infertility. Moreover, it provides the possibility of treatment along with diagnosis (4,9).

However, the intrauterine cavity cannot be examined by laparoscopy unless it is performed simultaneously with hysteroscopy (4,9). If suspicious cases are found or any disorder is diagnosed inside the endometrial cavity, then hysteroscopy can be used to verify the diagnosis, to describe the disorder in a better way, and to remove the lesion (10). Intrauterine pathological disorders which may have any unpleasant influence on the fertility are evaluated through hysteroscopy which is considered the main standard method for both diagnosis and treatment. Additionally, it is a low-aggressive method for diagnosis and treatment of intrauterine pathologies (1,5).

The role of hysteroscopy together with diagnostic laparoscopy in infertile women is still being discussed and studied (4). Diagnostic hysteroscopy is conducted in infertile women with abnormal HSG. In addition, it is

performed simultaneously with diagnostic laparoscopy in cases of normal HSG as a method of screening to examine intrauterine pathologies such as an endometrial polyp, submucous myoma, uterine, and septum (1,4).

Based on false negative cases of HSG, nowadays, some experts recommend performing hysteroscopy in infertile women as diagnosing and treating uterine pathologies and disorders increase the chances of pregnancy. Further, based on high sensitivity (100%) and specificity (95%) of hysteroscopy in evaluating the uterine cavity, as well as, its low complication, short time of performing, and low cost and little pain, hysteroscopy is advised to be implemented at the time of laparoscopy (4,7).

The present study attempted to investigate the value of performing hysteroscopy simultaneously with diagnostic laparoscopy in infertile women with normal uterine cavities in the HSG. Can this procedure help to discover hidden uterine pathologies which may influence on fertility outcome?

Methods and Materials

After obtaining the code of ethics from the Ethics Committee of Mashhad University of Medical Sciences, the present cross-sectional study was conducted in Imam Reza Hospital of Mashhad University of Medical Sciences from June 2016 to October 2017.

One hundred and three infertile women referring to the infertility clinic who were candidates for diagnostic laparoscopy were included in the study. The inclusion criteria were not getting pregnant despite unprotected intercourse for at least one year, being within the age range of 18-40 years, having a normal semen analysis (spermogram) of the husband, a normal uterine cavity in the HSG, normal hormonal tests (LH-FSH-TSH-PROLACTINE), a normal ovarian reserve, Being a candidate for diagnostic laparoscopy due to tubal obstruction, the possibility of peritubal adhesion, as well as endometriosis or unexplained infertility, and giving a written consent for participation. Furthermore, the exclusion criteria encompassed having a cardiovascular disease or the risk factor for pelvic infection and having a problem during the operation for which an anesthetist diagnoses the operation time to be shorter.

The procedures were first explained to the patients, namely, women patients were informed that diagnostic hysteroscopy and laparoscopy were going to be performed simultaneously. Moreover, if intrauterine pathology was observed, then the treatment was conducted through hysteroscopy. Additionally, the method of doing a hysteroscopy and its benefits and consequences were completely described to the patients and a pamphlet was given to the couple to obtain further information in this regard. In addition, it was emphasized that if the hysteroscopy were diagnostic, the duration of anesthesia would be about 15 minutes and in case of treatment, it would increase based on the given diagnostic pathologies.

The patients' demographic characteristics and initial paraclinical information, that is, their age, duration of infertility, type of infertility, and time of cycle during performing hysteroscopy were recorded in a checklist based on the interview conducted with the patients and the existing data in their medical profiles.

Diagnostic hysteroscopy was performed by Bettocchi 5 mm Storz laparoscope (made in Germany) in the women's operating room of Imam Reza Hospital under general anesthesia (GA) and in the lithotomy position. When laparoscopy was finished, the patient was moved out of Trendelenburg position and after gas expulsion and before the expulsion of trocars, hysteroscopy was implemented employing a Storz operative 5-mm hysteroscope in order to examine the intrauterine cavity. Intrauterine pathologies such as an endometrial polyp, submucous myoma, uterine adhesion, and the like, if existed, were recorded and treated at the same time.

The finding related to the uterine pathologies during hysteroscopy was recorded as HSG false negative cases. Further, the value of performing hysteroscopy during diagnostic laparoscopy was evaluated based on a number of false negative cases in the statistical investigation.

Results

The mean age of the attending patients and their duration of infertility were 30.9 ± 5.4 and 4.1 ± 5.2 years, respectively. Patients' demographic information is summarized in Table 1.

As previously explained, 103 infertile women with a normal uterine cavity in HSG underwent diagnostic laparoscopy and hysteroscopy, out of whom the hysteroscopic result of 64 patients (62.1%) was normal while that of the remaining 39 patients (37.9%) was abnormal. The distribution of pathologic findings in the hysteroscopy of 39 patients (37.9 %) with abnormal hysteroscopy is shown in Table 2.

Using the chi-square test, it was revealed that the uterine pathology in the hysteroscopy of infertile patients with normal uterine cavities in HSG who were candidates

Table 1. Demographic Characteristics of Infertile Women Candidates with Normal Cavities in HSG for Laparoscopy

		No. (%)	Total
Age (y)	<35	72 (69.9)	103 (100)
	≥35	31 (30.1)	
Type of infertility	Primary	74 (71.8)	103 (100)
	Secondary	29 (28.1)	
Duration of infertility (y)	<5	85 (82.5)	103 (100)
	≥5	18 (17.5)	
Time of performing hysteroscopy in menstrual cycle	Follicular phase	85 (82.5)	103 (100)
	Luteal phase	18 (17.5)	
Laparoscopic results	Normal	85 (82.5)	103 (100)
	Abnormal	18 (17.5)	

of laparoscopy was not statistically associated with the patient's age ($P = 0.39$), type of infertility whether primary or secondary ($P = 0.77$), duration of infertility less or more than 5 years ($P = 0.33$), time of performing hysteroscopy in the menstrual cycle ($P = 0.5$), and the normal or abnormal result of laparoscopy ($P = 0.90$), the results of which are provided in Table 3.

Discussion

As pointed out, 103 infertile women with a normal uterine cavity in HSG underwent diagnostic laparoscopy and hysteroscopy. The result of hysteroscopy was abnormal in 37.9% of the patients. The endometrial polyp was the most commonly diagnosed pathology. However, the existing uterine pathology was not related to the patient's demographic data. Several studies have been conducted in this respect which are presented in the following sections. Wadhwa et al, for instance, examined 108 infertile women in India. These patients whose age varied from 20 to 40 years were diagnosed normal in gynecologic examinations and hormonal tests and thus underwent both HSG and hysteroscopy. Nearly eighty percent of the patients had

Table 2. Distribution of Uterine Cavity Pathologies in Abnormal Hysteroscopy of Infertile Women Candidates with Normal Cavities in HSG for Laparoscopy

Type of Pathology	Abnormal Cases No. (%)	Patients No. (%)
Endometrial polyp	16 (41)	16 (15.5)
Submucosal myoma	1 (2.6)	1 (1)
Uterine septum	6 (15.4)	6 (5.8)
Asherman syndrome	7 (17.9)	7 (6.8)
Bicornate uterus	4 (10.2)	4 (3.9)
Polyp + submucous myoma	1 (2.6)	1 (1)
Polyp + Asherman syndrome	3 (7.7)	3 (2.9)
Uterine septum + submucosal myoma	1 (2.6)	1 (1)
Total	39 (100)	39 (37.9)

Table 3. The Relationship Between Demographic Information and Uterine Pathology of the Patients in Hysteroscopy of Infertile Women Candidates with Normal Cavity in HSG for Laparoscopy

		No. (%)	P Value ^a
Age (y)	<35	26 (36.1)	0.39
	≥35	13 (41.9)	
Type of infertility	Primary	32 (31.2)	0.77
	Secondary	7 (6.9)	
Duration of infertility (y)	<5	31 (30.1)	0.33
	≥5	8 (7.8)	
Time of performing hysteroscopy in menstrual cycle	Follicular phase	37 (35.9)	0.5
	Luteal phase	2 (2)	
Laparoscopic results	Normal	34 (33)	0.09
	Abnormal	18	

^aData are chi-square test results.

primary infertility while 26.85% of them suffered from secondary infertility. Furthermore, the HSG was normal in 7.8% of cases while being abnormal in 22.85% of them. Moreover, hysteroscopy was found normal in 64.4% of the patients while it was abnormal in 35.51% of them. False negative cases with HSG who were diagnosed by the hysteroscopy included 15.3% as well. Additionally, the sensitivity and specificity of the HSG were 44.8% and 86.6%, respectively. Similarly, the positive and negative predictive values (PPV & NPV) were 56.5% and 80.2%, respectively. Regarding the hysteroscopic findings, the highest percentages belonged to the endometrial polyp (3.8%), uterine septum (3.8%), and asherman syndrome (1%). Abnormal hysteroscopy existed in 29 (35.44%) women with primary infertility and 10 (35.71%) women with secondary infertility, indicating that the difference between these 2 groups was not statistically significant (1).

In another study by Nigam et al, 128 infertile women with primary infertility received HSG which was found to be abnormal in 100 patients (78.1%) while being normal in 28 other patients (21.9%). Then, laparoscopy and hysteroscopy were conducted in patients with normal HSG. In addition, hysteroscopy was normal in 18 patients whereas being abnormal in 10 patients. The diagnosed pathologies contained uterine adhesions in 9 cases (90%) and an endometrial polyp in 1 case (10%). The false negative percentage was reported 12.69% for the HSG (6).

In the same vein, Chauhan et al conducted a study in which 100 infertile women with normal clinical labs and examinations received HSG and hysteroscopy. The mean age and duration of infertility of the patients were 30 ± 4 and 4.1 ± 2 years, respectively. Sixty-six patients had primary infertility while 34 of them suffered from secondary type. The HSG was abnormal in 13 patients whereas being normal in 87 other patients. Further, hysteroscopy was found abnormal in 10 patients, according to which false negative ratio of HSG was reported 10%. Furthermore, the sensitivity, specificity, PPV, and NPV of the hysteroscopy were 50%, 98%, 76.9%, and 88.5%, respectively. The pathologies diagnosed in the hysteroscopy were submucous myoma (4 cases), endometrial polyp (3 cases), and uterine adhesion (3 cases) (5).

In this study, the means of age and infertility duration of the attending patients were 30.9 ± 5.4 and 4.1 ± 2.5 years, respectively. This is in line with the results obtained by Chauhan et al (5).

In a retrospective study implemented by Taskin et al, 359 infertile patients with a history of one time assisted reproductive technology (ART) or more whose age ranged from 18 to 46 years received HSG and hysteroscopy. The mean age of the patients was 33.3 years and the mean duration of their infertility was 8.3 years. Furthermore, the HSG was abnormal in 82 patients while being normal in 277 others. Hysteroscopy was performed among patients with normal HSG, 81 of whom (36.1%) had pathologies. Pathological findings included uterine septum (36 cases),

endometrial polyp (26 cases), adhesion (11 cases), and submucous myoma (8 cases). Forty-four patients (54.3%) were younger than 35 years old whereas 37 of them (45.7%) were 35 years or older. The number of uterine pathologies discovered was higher among those whose ART number was higher ($P = 0.15$). The highest amount of uterine pathologies in the hysteroscopy which was observed in patients older than 35 years had a significant difference ($P = 0.004$) (11).

Moreover, El-Mazny et al conducted laparoscopy and hysteroscopy in 145 infertile women with a normal hormonal test, normal HSG, and normal semen analysis examinations of the husband, and a history of 2 or more performed ART. Based on the results, the means of age and infertility duration of the patients were 32.2 ± 3.4 and 2.6 ± 1.5 years. Hysteroscopy was found abnormal in 48 patients. Additionally, the false negative ratio of HSG was 33.1%. The highest numbers of uterine pathologies belonged to the endometrial polyp, intrauterine adhesions, and submucosal myoma. Such pathologies were mostly diagnosed among patients older than 35 years and those with higher numbers of ART (3).

Similarly, in a study by Hourvitz et al, 91 out of 93 infertile women who had normal uterine cavities in HSG received diagnostic hysteroscopy during the laparoscopy. Hysteroscopy was abnormal in 11 cases (12.1%). The false negative ratio of HSG was 12%. In addition, uterine pathologies involved asherman syndrome (2 cases), arcuate uterus (2 cases), endometrial polyp (3 cases), and endometrial hyperplasia (4 cases) (4).

Further, Godinjak and Idrizbegovic examined 360 infertile patients using hormonal tests, cervical smear, sonography, Chlamydia antibody, and normal semen analysis. Laparoscopy and hysteroscopy were performed in the follicular phase for all the patients within the age range of 23-42 years whose means of age and infertility duration were 31 and 6.3 years, respectively. Based on the results, hysteroscopy was normal in 251 patients (75.11%) while it was found abnormal in the remaining 109 patients (24.89%). Uterine pathologies involved 42 submucosal myomas cases (11.6%), endometrial 26 polyp cases (7.22%), 3 asherman syndrome cases (0.8%), and 19 uterine anomaly cases (5.27%). Furthermore, uterine anomalies contained uterine septum (7 cases), bicornate uterus (5 cases), unicornate uterus (3 cases), and arcuate uterus (4 cases). Based on this study, 20% of uterine pathologies with short time and low complication (less than 0.01%) were diagnosed simultaneously performing hysteroscopy and laparoscopy (2).

In the same vein, Golan et al investigated hysteroscopic results of 324 infertile patients with normal uterine cavities in HSG. Hysteroscopy was abnormal in 156 patients (48.1%). The sensitivity and specificity of HSG in diagnosing uterine pathologies were 97% and 23%, respectively. Moreover, the false negative ratio was 10% and the most frequent pathologies belonged to intrauterine

adhesion and uterine septum (9).

Additionally, Snowden et al, examined the diagnostic precision and treatment value of HSG, hysteroscopy, and laparoscopy among 77 infertile women. The HSG was found to be abnormal in 16 cases (21%). In normal cases of HSG in patients who underwent hysteroscopy, the false negative ratio was 1.3% (12). In the current study, the false negative ratio of HSG was 37.9% which is in conformity with those found by Nigam et al (6), Taskin et al (11), and El-Mazny et al (3). Such consistency may be related to the racial conformities of these studies with our country. The result of this study is different from the European and American studies (4,9,12).

Based on the findings of the present study, the largest number of pathologies which were found in the hysteroscopy while not being diagnosed by means of HSG included endometrial polyp (15.5%) followed by Asherman syndrome (6.8%) and uterine septum (5.8%). These results corroborate with those of Wadhwa et al and Taskin et al (1,11).

In addition, the type of infertility made no significant difference in diagnosing uterine pathology in the hysteroscopy, which is concurrent with the previous report by Wadhwa et al (1). Further, no significant difference was observed with regard to the cycle day while implementing hysteroscopy in diagnosing uterine pathology in the patients. This may be due to the fact that either this issue was not investigated in other studies or all the hysteroscopic cases were conducted in the follicular phase.

In our study, unlike those of Taskin et al and El-Mazny et al, uterine pathology was mostly observed in patients aged less than 35 years old. However, the patients' ages (with a border of 35 years) were not significantly different from each other in diagnosing uterine pathology by hysteroscopy (3,11).

Similarly, the results of this research indicated that implementing hysteroscopy at the same time with diagnostic laparoscopy increased the diagnosis of uterine pathologies even in normal HSG, the point which emphasized by Godinjak et al, Nigam et al and Hourvitz et al (2, 4, 6).

Furthermore, the researchers of this study had to perform the HSG in various centers which may have influenced the number of false negative cases. However, all the operations were conducted by a single gynecology laparoscopist surgeon using the same laparoscopy and hysteroscopy system, which can be regarded as a strong point of the study.

Conclusions

Generally speaking, based on the results, performing hysteroscopy among infertile women who are candidates of laparoscopy and have uterine cavities in normal HSG can result in diagnosing some cases of uterine pathologies which may affect future infertility consequences. However,

this issue does not depend upon the patient's age, cycle time, infertility type and duration, and laparoscopic result.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The study was approved by the Ethical Committee of Mashhad University of Medical Sciences (code: IR.MUMS.fm.REC.1395.384).

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