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ORIGINAL ARTICLE

Hysteroscopic Assessement of Uterine Cavity in Women with Unexplained Infertility

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ABSTRACT

Background: Hysteroscopy is a well-established diagnostic and surgical technique that is widely used to diagnose and treat a wide range of common gynaecological abnormalities involving the uterine cavity. It is also a critical diagnostic step in the treatment of infertility. The aim of this work was to evaluate the role of diagnostic hysteroscopy (DHL) in the comprehensive work-up of unexplained infertility, which would help in planning appropriate management.

Methods: This prospective study was conducted at department of Obstetrics and Gynecology, at Zagazig University Hospital during the period study year July 2020 to December 2020. Included 80 patients infertile women aged between 18 to 42 years with either primary or secondery infertility. All patients had normal Hysterosalpingography, with normal hormone profile and without male factor infertility and normal TVS.

Results: In the current study normal hysteroscopy was found in 50 cases (62.5%) and abnormal hysteroscopy was found in 30 cases (37.5%), 20 (25%) were complaining of primary infertility while 10 (12.5%) were complaining of secondary infertility. the frequency of women with arcuate uterus, bicornuate uterus and very small uterine cavity are significantly increased in Primary infertility group (20%, 15% and 10% respectively) than secondary infertility group. And the frequency of women with intrauterine synechia and bilateral narrow corneal end are significantly higher in secondary infertility group (30 % of both) than Primary infertility group. **Conclusions:** Hysteroscopy remains the gold standard for the evaluation of the uterine cavity.

Key words: Hysteroscopy, Infertility, laparoscopy, Uterine Cavity.

INTRODUCTION

Infertility is defined as the inability to conceive after a year of unprotected regular sexual intercourse. A broader definition of infertility includes the inability to carry a pregnancy to term and have a child. [1]. Unexplained infertility refers to a diagnosis (or lack thereof) made in couples who have normal tubal patency, ovulation, and sperm analysis. Depending on the number of investigations done and degree of evaluation of the couple, this term can be applied to as many as 30% of couples[2].

Hysteroscopy is a well-established diagnostic and surgical technique that is widely used to diagnose and treat a wide range of common gynaecological abnormalities involving the uterine cavity. It is also a critical diagnostic step in the treatment of infertility. Hysteroscopic procedures are popular because they are minimally invasive, suitable for office gynaecology, cost-effective, and safe[3].

It is well known that the intrauterine factor contributes to female infertility by about 15-20%. As a result, ruling out any evidence of intrauterine pathology with hysteroscopy becomes critical. With

the development of miniature hysteroscopes, hysteroscopy can now be performed in an office setting, with or without local anaesthesia, for diagnostic and certain therapeutic interventions[4].

To define the mechanism of infertility caused by intrauterine pathologies, various hypotheses have been proposed. Polyps can cause infertility due to their location, which causes mechanical block (e.g. tubocornual polyp), their association with endometriosis, or their expression of the enzyme aromatase[5]. Protruding myomas into the cavity may reduce the vascular supply to the trophoblastic tissue. Subfertility can also be caused by other pathologies such as synechiae, endometritis, cervical stenosis, and chronic cervicitis[6]. The role of hysteroscopy appears to be critical for patients because intrauterine pathologies and structural uterine abnormalities can be detected and treated, whereas other screening investigations, such as hysterosalpingoraphy, miss the intrauterine pathology. [7].

The aim of this study was to evaluate the role of diagnostic hysteroscopy (DHL) in the comprehensive work-up of unexplained infertility, which would help in planning appropriate management.

METHODS

This prospective study was conducted at department of Obstetrics and Gynecology, at Zagazig University Hospital during the period study year July 2020 to December 2020. The study included patients between the ages of 18 and 42 who had been experiencing primary or secondary infertility for more than a year. Patients with primary infertility had never conceived before, whereas secondary infertile patients had at least one prior conception, regardless of the outcome. Normal hormonal profiles for infertility, for example (serum FSH, LH). Ovulation was suggested by ultrasonic folliculometry. Thyroid function is normal. Prolactin levels are normal. There is no polycystic ovarian syndrome. Normal sperm analysis. **Exclusion Criteria were;** Thyroid dysfunction, hyperprolactinemia, polycystic ovarian syndrome, and other hormonal abnormalities are known to cause anovulation. When combined with abnormal sperm analysis. Women with any contraindications to laparoscopy, such as chronic chest disease, cardiac disease, severe obesity, as well as women with a history of significant adhesions. Suspicion of pregnancy, in order to avoid disrupting an implanting gestation. So, patients examined in the early proliferative phase of the cycle. Symptoms suggestive of pelvic or lower genital tract infection, to avoid exacerbating the symptoms. Intractable cervical stenosis which would make insertion of hysteroscopy difficult and uncomfortable. Patients with advanced or uncontrolled medical disease e.g. DM or rheumatic fever or T.B.

Sample size: Assuming that all cases fulfill the inclusion and exclusion criteria will be included. During the study period (6 months), 12 cases/month, 72 cases will be included as a comprehensive sample. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (IRB#7072). The work was carried out for studies involving humans in accordance with the World Medical Association's Code of Ethics (Helsinki Declaration).

All participants underwent a detailed history including; duration of pregnancy, antenatal care, complication of pregnancy mode of delivery, fetal outcome and postpartum complication. Menstrual history. Abdominal or pelvic surgery particularly involving the uterus, fallopian tubes or ovaries.

Investigations included; Pelvic ultrasound. Laparoscopy. Hysterosalpingography (HSG). Hormonal assay of each case. Recent semen analysis of the husband.

General examination including; body mass index, pulse and blood pressure, chest and heart examination, abdominal examination. Vaginal (P.V) examination for detection of Vaginal discharge. Vaginal bleeding. Cervical abnormalities in the form of cervicitis or cervical polyps. Bimanual examination with palpation of uterus to assess uterine size, position, shape and to exclude clinically detectable pelvic lesions like pelvic masses or pelvic inflammatory diseases.

Hysteroscopic diagnostic examination was done to all patients using diagnostic minihysteroscopy (continuous flow rigid Hamou type II hysteroscope, 30 cm long, 2.8 mm in diameter with zero viewing angle, the outer sheath 3.8 mm in diameter.

Video-monitor system

An endovision video camera, a color camera system karl storz endoscopic 302.0031 Pal" was used during diagnostic procedure. It was applied to the eye-piece of the telescope and connected to a colored monitor equipped with a video-recorder.

Distension medium

Glycine was used in this study. It is supplied in soft plastic bags containing 1000cc put in infusion cuff. To obtain adequate uterine distension, good view and to wash out any tissue particles or gas bubbles.

Cable through an endoscope to the examination site. Specific and particularly powerful halogen or xenon light sources were used in today's cold light projectors.

Statistical Analysis

IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA) and MedCalc version 13 (MedCalc Software bvba, Ostend, Belgium) were used for statistical analysis. For quantitative variables, data were expressed as mean standard deviation, and for qualitative variables, as number and percentage. The results were interpreted using the chi-square, ANOVA, and paired t tests. A P-value of ≤ 0.05 was considered statistically significant.

RESULTS

Hysteroscopy assessment of the uterine cavity was performed on 80 cases of unexplained infertility. All procedures were performed without complications. Normal hysteroscopy was found in 50 cases and abnormal hysteroscopy was found in 30 cases .

Table 1; showed that number and percentage of normal and abnormal hysteroscopy regarding to age groups, there was a highly significant difference in mean (±SD) age between Normal and abnormal hysteroscopy groups; (27.4 ± 4.8 versus 34.8 ± 2.25 respectively; P < 0.001). Also there was significant difference between the study groups in women with age < 30 years and also in women with age >35 years which means that the percentage of normal hysteroscopy was significant among young women and percentage of abnormal hysteroscopy was significant among older women > 35 years.

Table 2; there was no significant difference between normal and abnormal hysteroscopy groups (P > 0.05), as regards type of infertility this means that Infertility, either primary or secondary didn't affect on the hysteroscopic findings.

Table 3; there was a highly significant difference in mean (± SD) between normal and abnormal hysteroscopy groups; (6.7 ± 2.2 versus 11.2 ± 1.7 respectively; P< 0.001). which means that more abnormalities were found with longer duration of infertility.

Normal hysteroscopy was found in 50 cases (62.5%) and abnormal hysteroscopy was found in 30 cases (37.5%), 20 (25%) were complaining of primary infertility while 10 (12.5%) were complaining of secondary infertility table 4.

Table 5; showed that the frequency of women with arcuate uterus, bicornuate uterus, and very small uterine cavity is significantly higher in the Primary infertility group than in the Secondary infertility group. Furthermore, the prevalence of women with intrauterine synechia and bilateral narrow corneal end is significantly higher in the Secondary infertility group than in the Primary infertility group.

Table 6; showed hysteroscopic interventions had been made to infertile patients with abnormal hysteroscopic findings. As it shows 13.3% of those cases had been operated for myomectomy, polypectomy in 6.8% and 6.8% % operated for septal resection as well as 10% had adhesiolysis.

Table (1): Age in the studied groups

Age groups	Total	Normal hysteroscopy (50)		Abnormal-hysteroscopy (30)		X^2	P-value
		N	%	N	%		
< 30	38	32	64	6	20	8.79	0.003 (S)
30-35	22	10	20	12	40	0.20	0.64 (NS)
> 35	20	8	16.0	12	40	6.81	0.009 (S)
$\bar{X}$ ± SD	80	27.4 ± 4.8		34.8 ± 2.25		t=5.3	<0.001 (HS)
Range		20-36		29-37			

Table (2): Types of infertility in the studied groups

Type of infertility	Total	Normal hysteroscopy (50)		Abnormal hysteroscopy (30)		X^2	P-value
		N	%	N	%		
Primary infertility	56	36	72	20	66.7	0.04	0.83 (NS)
Secondary infertility	24	14	28	10	33.3		

Table (3): Duration of infertility in the studied groups

Duration of infertility	Normal hysteroscopy (50)	Abnormal hysteroscopy (30)	t-test	P-value
$\bar{X} \pm SD$	6.7 ± 2.2	11.2 ± 1.7	6.96	< 0.001 (HS)
Range	2-10	8-14		

Table (4): Hystroscopic findings of the studied groups as regard type of infertility

Finding	Primary infertility (56)	Secondary infertility (24)	Total(80)
Normal hystroscopic findings	36 (45%)	14 (17.5%)	50(62.5.5%)
Abnormal hystroscopic findings	20 (25%)	10 (12.5%)	30 (37.5%)

Table (5): Abnormal hysteroscopic findings in both two groups

Abnormal hysteroscopic findings	Primary infertility (20)		Secondary infertility (10)		X^2	P
	N	%	N	%		
Arcuate uterus	4	20.0	0	0.0	5.21	0.02*
Subseptate uterus	2	10.0	0	0.0	1.89	0.033*
Bicornuate uterus	3	15.0	0	0.0	4.13	0.04*
Infantile uterine cavity	2	10.0	0	0.0	5.1	0.02*
Submucou smyoma	0	0.0	2	20.0	0.0	0.001*
Intrauterine synechia	0	0.0	3	30.0	4.54	0.04*
Single endometrium polyp	1	5.0	1	10.0	3.33	1.1
Multiple endometrium polyp	2	10.0	0	0.0	1.0	0.012*
Atrophic endometrium	1	5.0	0	0.0	0.0	1.0
Hypertrophic endometrium	2	10.0	0	0.0	1.04	0.8
Bilateral narrow corneal ends	2	10.0	3	30.0	6.07	0.001*
Unilateral narrow corneal end	1	5.0	1	10.0	0.54	0.06*

***** significance

Table (6): Hysteroscopic interventions in infertile patients :

Myomectomy	4 (13.3%)
polypectomy	2 (6.8%)
Septal resection	2 (6.8%)
Adhesiolysis	3 (10%)
Tubal cannulation	5 (16.8%)
Removal of abnormal endometrial tissue	2 (6.8%)

DISCUSSION

All patients had normal HSG, with normal hormone profile and without male factor infertility and normal TVS. In current study, women are in the age group (18_42) years. |{38(47.5%) patients were < 30, 22 (27.5|%) patients were 30-35 while 20 (25%)patients were > 35}. As regards to female age in our study, abnormal hysteroscopy was significant among old women > 35 years. This observation was in agreement with the study carried by ***Karayalcin et al.*** [8], who observed significant abnormal hysteroscopy with advanced age.

Another similar observation by ***Fatemi et al.***[9] was found that regarding female age, also old women associated with the significant occurrence of unsuspected intrauterine abnormalities. ***Rama Raju et al.*** [10] was in disagreement with our result, as they found no significant abnormal hysteroscopy with advanced age.

As regards type of infertility in our study, there was no significant difference between normal and abnormal hysteroscopy groups (P > 0.05), this means that infertility, either primary or secondary didn't affect on the hysteroscopic findings. In another similar retrospective study carried by ***Karayalcin et al***[8], there was agreement with our results that no significant difference between normal and abnormal hysteroscopy groups regarding type of infertility was found. ***Fatemi et al***[9], also agreed that no significant difference between normal and abnormal hysteroscopy groups regarding type of infertility was found.

Regarding to duration of infertility in our study, there was a highly significant difference between normal and abnormal hysteroscopy groups, which means that more abnormalities were found with longer duration of infertility. In agreement with our results ***Karayalcin et al***.[8], found that there was significant difference between normal and abnormal hysteroscopy groups regarding duration of infertility. On the contrary ***Fatemi et al.*** [9], found that there was no significant difference between normal and abnormal hysteroscopy groups regarding duration of infertility.

In the current study Normal hysteroscopy was found in 50 cases (62.5%) and abnormal hysteroscopy was found in 30 cases (37.5%). Women with arcuate uterus, bicornuate uterus, and very small uterine cavity are more common in the primary infertility group (20%, 15%, and 10%, respectively) than in the secondary infertility group. Furthermore, the prevalence of women with intrauterine synechia and bilateral narrow corneal end is significantly higher in the Secondary infertility group (30% of both) than in the Primary infertility group.

Karayalcin et al. [8] conducted a similar study to assess the diagnostic accuracy, findings, and feasibility of office-based diagnostic hysteroscopy in unexplained infertility. A total of 2500 infertile patients were enrolled in the study. A 4-mm continuous-flow Bettocchi office hysteroscope with an integrated working channel for mechanical and electrosurgical instruments was used for all hysteroscopies. The use of 30-degree lenses ensured a thorough examination of the cavity. Each subject underwent diagnostic hysteroscopy. On hysteroscopy, 1927 patients (77.1 percent) had a normal uterine cavity, while the remaining sample (n = 573) had endometrial pathology (22.9 %). There were 192 patients with intrauterine synechia (7.68 %), 96 patients with submucosal fibroids (3.84 %), 31 patients with polypoid endometria (1.24 %), and 73 patients with uterine septa (2.92%). Also this difference in percentage between this study and our study may be attributed to the large number (2500) of cases however, similar to our study, intrauterine synechia are found most frequently in this group of patients. In cases of unexplained infertility, diagnostic office-based hysteroscopy is used to evaluate the endometrial cavity. A significant proportion of patients in such an uncontrolled population had uterine pathology. Office-based

hysteroscopy is an ideal procedure due to its safety, ease of use, high diagnostic accuracy, and high patient tolerance. In addition, the study found that patients with abnormal hysteroscopic findings had lower pregnancy rates after IVF treatment than those with no abnormalities. The authors concluded that office hysteroscopy is still a very effective diagnostic procedure for assessing intrauterine pathologies. Office hysteroscopy is an ideal procedure for evaluating the uterine cavity in patients with unexplained infertility due to patient tolerance, safety, and the feasibility of operative management.

The observation in our study was in agreement with ***Fatemi et al.*** [9] who observed a total of 678 unselected, asymptomatic, infertile women with a regular indication for a first IVF/ICSI treatment who underwent office hysteroscopy. Only asymptomatic patients, aged ≤42 years, with a normal TVS and no previous hysteroscopy were included. The presence of pre-defined intrauterine abnormalities was recorded and described in a standardized manner, only 11% abnormalities were found. intrauterine synechia were identified in 41 cases (6%). Submucous myomas were found in six cases (1%). Also 14 cases with a septum (2%) were diagnosed, ***Fatemi et al.*** [9] were also in agreement with our observation that TVS did not reveal any of the predefined abnormalities in the included patients. The overall prevalence of abnormalities described by ***Fatemi et al.*** [9] differs from the prevalence reported in previously published articles ***Rama Raju et al.,*** [10] (11 versus 20-45%), and also differs from our overall prevalence of abnormal hysteroscopy (37.5% VS 62.5%). This difference could be explained by study design and patient inclusion criteria. Unfortunately, most authors only reported that they investigated women with normal TVS or HSG, but did not provide a detailed description of the patient characteristics.

There is growing evidence that hysteroscopy is helpful in the diagnosis of uterine cavity abnormalities, which are often missed on previous ultrasound scans, and are found in a significant proportion (25–50%) of such women [11].

Pathology of the uterine cavity, including RIFs, has been linked to poor reproductive outcomes. Endometrial polyps and submucous myomas can interfere with implantation by increasing uterine contractility, inducing inflammatory or vascular changes with irregular growth factor release impairing endometrial receptivity, or mechanically impairing gametes and/or embryo transportation and implantation. Uterine septa have been linked to an increase in abortion rates due to endometrial vascularity or endometrial structure changes, but it is theoretically possible that septum tissue is also unsuitable for blastocyst implantation. Endometrial adhesions can interfere with implantation for purely mechanical reasons or because they change the endometrial environment.

In line with our findings, **Makrakis et al. [12]** observed 1475 women with RIF and discovered an abnormality in the uterus in 36.6 % of these women (16.7 endometrial polyps, 12.5 % endometrial adhesions, 1.5 % endocervical adhesions, 4.3 % endometritis, 0.9 % uterine septa, and 0.8 percent submucous fibroids). According to the study, 22.2 % of the population had a prior ultrasound screening that resulted in a false negative and subsequent hysteroscopy intrauterine pathology (endometrial adhesions in 12.5 %, endometritis in 4.3%, endometrial polyps in 3.3 % , endocervical adhesions in 1.5 % , uterine septa in 0.5%, and submucuos myomas in 0.1%). The same study compared the use and non-use of hysteroscopy for women with RIF in a new IVF attempt and found that the former group had a significantly higher implantation and pregnancy rate. It strongly recommends hysteroscopy for women with unexplained infertility for two reasons: I a significant number of uterine pathologies are undetected by ultrasound, and (ii) hysteroscopy has a significant success rate of ongoing pregnancy.

Aletebi [13] agreed with our findings as well. She studied 132 women, with the majority of patients (62 %) showing no visible pathology on hysteroscopy, while a third of the population (38 %) showed some degree of uterine pathology. Endometrial polyps were found in 22 % of patients, endometrial adhesions in 9.8 %, endometritis in 3.7%, submucous myomas in 1.5%, and uterine septa in 0.7 %. Following hysteroscopy, 43 women (32.5 %) became pregnant. The majority of these pregnancies occurred in women who had corrected endometrial pathology, the majority of which were endometrial polyps.

On the contrary, **De Placido et al. [6]** stated that the role of routine hysteroscopy in the management of infertile women with no other diagnosed or suspected intrauterine pathologies is still debatable.

In agreement with our study, **Crosignani and Rubin[14]** stated that the two main problems that argue against the ease of hysteroscopy are: first, it is an invasive procedure, and second, there is still debate about the true significance of the observed intrauterine pathology on fertility. They also stated that, according to the European Society of Human

Reproduction and Emberiology (ESHRE) guidelines from the year 2000, hysteroscopy is unnecessary unless it is used to confirm and treat doubtful intrauterine pathology.

Recentlly hysteroscopy is considered one of the evidence-based managements of infertile couples [15].

The study could be criticized of being limited only to diagnose the intrauterine pathology and did not proceed to observe the pregnancy rate after correction of the pathology

Conclusion

Hysteroscopy is still the gold standard for assessing the uterine cavity. When hysteroscopy is used to diagnose unexplained infertility, a significant proportion of patients are found to have uterine pathology. Office hysteroscopy is an ideal procedure and the gold standard in the diagnosis and treatment of intrauterine pathology due to patient tolerance, safety, and the feasibility of simultaneous operative correction.

Hysteroscopy can be added as a step in the routine infertility work up. Hysteroscopy has an advantage of being able to treat a lesion once detected in the same session.

Further prospective randomized trials in unexplained infertility and no suspicion of intrauterine pathology are needed and warranted to allow further insight and to delineate the role of hysteroscopy in such patients.

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