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Hysteroscopic evaluation of uterine cavity in women with unexplained infertility

Abstract

Objective: To detect missed uterine abnormalities on primary work up in unexplained infertile women.

Study design: An observational study was performed in the outpatient infertility clinic of Beni-Suef University Hospitals. It included 100 women with unexplained infertility. Diagnostic office hysteroscopy was done for all participants. Women were grouped according to the infertility type and compared as regards uterine abnormalities detected.

Results: Uterine abnormalities were detected by hysteroscopy in 29% of women. No significant difference was found regarding the hysteroscopic findings between primary and secondary infertility groups. However, uterine polyp cases were detected more in women with primary infertility (55.5% /18). A significant difference in intrauterine adhesions between both groups being detected only in secondary infertility group (p value =0.006).

Conclusion: Outpatient preliminary and routine diagnostic office hysteroscopy may be a beneficial part of a primary and secondary infertility workup.

Keywords: uterine cavity evaluation, unexplained infertility, micro office hysteroscopy, diagnostic hysteroscopy

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Introduction

Infertility affects approximately 15% of couples. Causes include ovulatory disorders, tubal disease, and semen abnormalities in men. These causes account for 75% of infertile couples.[1] When all the standard investigations for infertility such as ovulatory, tubal patency tests and semen analysis are normal, a diagnosis is referred to as unexplained infertility. Those couples with unexplained infertility can be found as many as 30% to 40%.[2] Implantation of the blastocyst is crucial for occurrence of pregnancy. The uterine cavity and its inner layer, the endometrium, are important for implantation. The mechanism of successful implantation is still not clearly evidenced. Thus, uterine cavity evaluation is confirmed as the main step in investigating infertile couple especially those with unexplained infertility.[3] It has been found that 10% to 15% of women seeking treatment of fertility may have undiagnosed uterine cavity abnormalities. Endometrial polyp is a common abnormality and can be found in up to 41% of unexplained infertile population.[4] Moreover, 2.4% of infertile women have fibroids without any other apparent cause of infertility.[5] Intrauterine synechia is commonly caused by inflammation or iatrogenic after curettage for example. Up to 14% of unexplained infertile couple may have minimal or undiagnosed intrauterine adhesions interfering with successful implantation.[6] In addition, uterine septum with different degrees has been diagnosed in 1% to 3.6% of women with otherwise unexplained infertility.[7] Hysterosalpingography (HSG) was commonly used traditionally as a reliable assessment method for infertility. It mainly evaluates the morphology and patency of fallopian tubes, giving some helpful information about uterine cavity. HSG may miss 35% of uterine abnormalities. The inability to treat abnormal findings concurrently with the diagnosis has limited the use of HSG to assess the endometrial cavity.[8] It has only a secondary role in evaluation of the uterine cavity especially in unexplained infertility owing to low-positive predictive value and low specificity.[9,10]

Transvaginal ultrasound scan (TVS) allows us to see uterine cavity and endometrial lining. It has been used as a screening method of uterine cavity abnormality. TVS may not show submucosal fibroids in the presence of multiple fibroids, differentiate between a hyperplastic endometrium and a large polyp, or between an arcuate and a septate uterus.[11,12]

It has been concluded that hysteroscopy is the gold standard for the evaluation of uterine cavity, particularly when a pathology is suspected in unexplained infertility. It allows direct visualization of intrauterine abnormalities, exploring their nature, location, shape, size and vascular pattern. Moreover, it allows directed biopsy or treatment of any pathology in the same diagnostic setting. Thus, in women with unexplained infertility, hysteroscopy may be considered a definitive diagnostic tool to assess any abnormality suspected or could not be detected by HSG or TVS in preliminary evaluation of infertile patients.[12–14] Our primary outcome is to detect any uterine abnormalities missed on primary work up of unexplained infertile couple using micro-office hysteroscopy. This may help the possibility that mini hysteroscopy if available in outpatient setting, may become routine preliminary investigation for all infertile couples.

Patients and methods

In this cross-sectional observational study, a total of 100 women with unexplained infertility referred to office micro hysteroscopic session from 2018 to 2019 at outpatient infertility clinic of Beni-Suef University Hospitals were included. The study was approved by the local ethical committee and informed verbal consent was obtained from all participants. All women included, were in reproductive age. Inclusion criteria were normal ovulatory, tubal patency and semen analysis tests.[2] Hysteroscopy examination was done 7-10 days from the start of menstruation.[15] The woman was placed in the dorsal lithotomy position. Normal saline was used for uterine distension

connected to the inflow channel on the sheath with intravenous tubing. The uterine cavity was systematically explored by rotating the fore-oblique scope in order to identify any anomaly in the uterine walls and/or the right and left tubal ostia. At this stage it was crucially important to avoid lateral movements as much as possible to reduce patient discomfort to a minimum. After that, the scope was removed. Finally, the evaluation and the data that had been found were written in details by the surgeon. Operative intervention was done if needed under general anaesthesia. Any complication in the form of pain, bleeding, vasovagal attack and perforation, were registered in the patient's sheet.[16] Our secondary outcome was documentation of any complications resulting from the procedure. A 2-mm rigid fibreoptic, 30-degrees angled hysteroscope was used for diagnostic indication (Karl. Storz-GmbH and Co. Tuttlingen, Germany). Women were grouped according to type of infertility (primary or secondary) and compared according to hysteroscopic findings.

For this cross-sectional study, one group of women was studied. We established a type I error α=0.05, effect size w=0.3 and a calculated power (1-β err prob) =0.90 by G*Power statistical analysis program [G* Power 3.1 manual 1 March, 2017]. Sample size was designed to detect number of uterine cavity abnormalities by hysteroscope in the studied group for example uterine fibroids.[17] In that study, it was concluded that 90% of infertile women showed uterine cavity pathologies mainly submucous myomas. Based on these criteria and the use of G* Power statistical analysis, 100 women were included taking into consideration failed hysteroscopy in some women.

Data were statistically described in terms of mean and standard deviation, median, frequencies and relative frequencies (%). Also, the data was analysed by using the following tests as t-test for comparison between each two groups, non-parametric data and chi-square test. A correlation is a single number that describes the degree of relationship between two variables. The most common type, called the Pearson correlation. A probability (p-value) <0.05 will be considered statistically significant.

Results

The duration of couples' infertility ranged from 2-9years. The mean age of women was 24years old (Table 1). Among the 100 women studied, 29 % had abnormal findings by hysteroscope in the uterine cavity and cervical stenosis. Seventy one percent of studied women had normal uterine cavity and cervix. Fourteen percent were discovered to have intrauterine polyps whose diagnosis was missed by hysterosalpingography and ultrasound. Eight women were noted to have submucous fibroids with grades from 0 to 2 and small in size, four women had mild intrauterine adhesions. One woman had small uterine septum. Failure of procedure occurred in two women with cervical stenosis due to difficult insertion (Table 2). Figure 1 showed hysteroscopic findings distribution among study population.

Table 1 General characteristics among study population

Variables	No. of women (n=100)
Age (years) Range, mean± SD	(20-35), (24±3.36)
Duration of infertility(years) Range, mean± SD	(2-9), (2.86±2.14)

Table 2 Hysteroscopic findings among the study population

Findings	Percent of women (%)
Normal	71%
Polyp	14%
Fibroids	8%
Adhesions	4%
Uterine Septum	1%
Cervical stenosis	2%
Total	100%

Data are represented in (%) percent

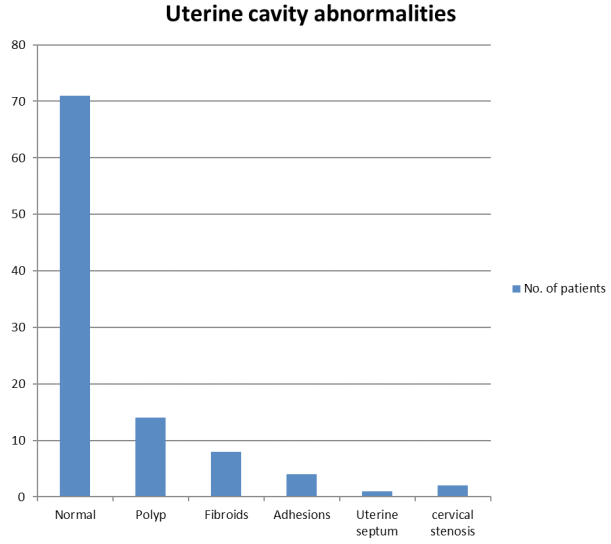

Figure 1 Bar chart of hysteroscopic findings among the study population.

Distribution of hysteroscopic abnormalities among study population according to different age groups was shown in Table 3. The commonest age range of women involved in the study was between 20 and 25 years (44%). Seventy percent of studied women had primary infertility (Figure 2). Table 4 showed the difference between women with primary and secondary infertility concerning uterine cavity abnormalities by hysteroscope. Both groups showed no statistical significance as regards uterine cavity abnormalities (p value=0.303). Table 4 showed uterine cavity abnormalities distribution in primary and secondary infertility among study population. Uterine polyp was the most common abnormality in primary infertility group (55.5% out of 18 women). The intrauterine adhesions were more common in secondary infertility group with statistical significance between both infertility groups (P value=0.006).

Table 3 Distribution of lesions among study population according to different age groups

	Between 20 and 25 years	Between 25 - 30 years	Between 30 -35 years
	(N=43)	(N=35)	(N=20)
Normal	31(72.0%)	25(72.3%)	14(70%)
Abnormal	11(25.5%)	10(27.7%)	7(35%)

Data are represented in number (n) and (%) percent

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Table 4 Comparison between primary and secondary infertility groups concerning hysteroscopic findings

Hysteroscopic findings	Primary infertility (N=70)	Secondary infertility (N=28)	P value
Normal findings	53(75.7%)	18(64.3%)	
Abnormal findings	17(24.3%)	10(35.7%)	P=0.383
Polyps	10(14.3%)	4(14.3%)	P=0.333
Submucous fibroid	6(8.6%)	2(7.1%)	P=0.408
Intrauterine adhesion	0%	4(14.3%)	P=0.006*
Uterine septum	1(1.4%)	0%	P=0.597

Data are represented in number (n) and (%) percent, (>0.05, non-significant)

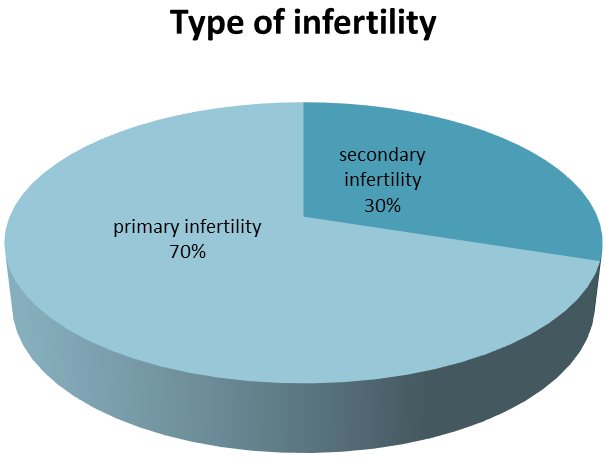

Figure 2 Type of infertility percentage among the study population.

Discussion

Many observational studies have shown improvement in spontaneous pregnancy rates in couples with unexplained infertility after hysteroscopic diagnosis and treatment of endometrial polyps, submucous fibroids, intrauterine adhesions and intrauterine septum.[3,18,19] Uterine abnormalities, either congenital or acquired are important causes of infertility due to implantation failure. Thus, investigation of uterine cavity is obligatory practice in assessment of couples with unexplained infertility. Hysteroscopy is a gold standard and more accurate for this practice than other tools especially HSG.[4,18] In current study this was also the rationale behind use of micro-office hysteroscopy for further investigation of couples with unexplained infertility. Based on findings of the previous studies, it has been found that more than 1/3 of the women diagnosed as normal following previous workup have a uterine abnormality after diagnostic hysteroscopy, which might be a significant cause of reproductive failure.[18–20] In the current study, 29% of women, undergoing office hysteroscopy, had abnormal uterine findings. These results are comparable to those of the other studies reporting that only 40% to 70% of infertile patients have a normal uterine cavity.[21–23]

Malhorta and Sood,[24] evaluated the diagnostic accuracy and value of hysteroscopy in 32 infertile women aged 21-35 years. In 19 cases (59.4%) visually recognizable abnormalities were detected on hysteroscopy. These included intrauterine adhesions (25%), submucous fibroid (9.4%), uterine septum (6.1%) and Mullerian fusion defect (6.1%). The percentage of those hysteroscopic findings is different from the present study. This difference may be attributed to the smaller sample size in their study.

No significant difference in the rate of uterine pathology was found between women with primary and secondary infertility (70% and 30%, respectively). Yet, more cases of uterine polyps (10/18 (55.5%)) were detected in the group of primary infertility (p value=0.326), while intrauterine adhesions were found only in secondary infertility group (p=0.006).

Endometrial polyps were found in about 25% of women with unexplained primary infertility on hysteroscopy.[25,26] How asymptomatic endometrial polyps affect infertility is unclear. However, it has been concluded that polyps can cause infertility through impairment of embryo implantation or altered endometrial receptivity through studied markers. They can also interfere mechanically with sperm and embryo transport. Furthermore, the size, number or location of polyps may influence any effect on reproductive outcomes.[27] It may be difficult to determine exact incidence for clinically asymptomatic endometrial polyps in general population. However, it has been found that these lesions are more common in the unexplained infertility population compared with fertile women.[26] A study by Shokeir[26] concluded that it is important to do surgical treatment of all endometrial polyps among eumenorrheic infertile women, since even if small, they are likely to impair fertility. Removal of these polyps may enhance reproductive outcome. This supports our findings and that using outpatient office hysteroscopy as a routine investigation for all infertile couples may be beneficial and time saving for women complaining of infertility.[26]

A significant difference was found in the percent of intrauterine adhesions comparing women with primary versus secondary infertility. The relationship between secondary infertility and the existence of adhesions, being mostly iatrogenic as the result of uterine curettage for postpartum or post abortion retained products is well known.[1] Oliveira also found intrauterine adhesions in 10% of patients with repeated failed IVF cycles of whom none had undergone previous abortions or other uterine manipulation. He suggested that other causes of intrauterine adhesions must be excluded.[28] Again, this finding supports that routine micro-office hysteroscopy may be a great substitution for other investigations which may be time consuming for infertile couples.

In current study perforation occurred in one patient who was treated conservatively as there was no bleeding and she was vitally stable. Routine micro-office hysteroscopy in assessment of the infertile women is no longer a complicated procedure. It can be done by a shortly trained gynaecologist as a simple, fast and successful outpatient procedure.[6] Moreover, De Placido concluded that infertile

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couples who were screened systematically by diagnostic hysteroscopy, the incidence of newly detected intrauterine pathology may be as high as 50%.[14]

Thus, results of previous studies in addition to our results justify the use of diagnostic hysteroscopy in the primary routine investigation of infertile women. It has the same value in both primary and secondary infertility as no significant difference was found in uterine abnormalities between both groups in current study. However, National Institute for Health and Clinical Excellence (NICE) guideline on fertility assessment and treatment stated that "women should not be offered hysteroscopy on its own as part of the initial investigation unless clinically indicated because the effectiveness of surgical treatment of uterine abnormalities on improving pregnancy rates has not been established".[29] That is why, large randomized controlled trials and systematic review studies are recommended for supporting our conclusion.

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Conflicts of interest

The authors did not report any potential conflicts of interest.

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