# Role of Office Hysteroscopy and Histopathologic Evaluation of Endometrium in Patients with Unexplained Infertility

Heba Elsayed Eldeeb¹, Mahmoud Thabet Mahmoud², Mohamed Hassan Bedairy², Mona Gad Mostafa Elebeidy³, Ahmed Abdelhamid Elzayadi²¹Sinbelawen Central Hospital, Mansoura, Egypt²Department of Obstetrics & Gynecology, Faculty of Medicine, Mansoura University, Egypt³Department of Anaesthesia and Intensive care, Faculty of Medicine, Mansoura University

## **Abstract**

**Background:** Infertility affects about 15% of couples. There are several etiologies of infertility, which comprise ovulatory disorders, tubal diseases, and semen abnormalities in males. Hysteroscopy (HS) has been considered as the best approach for uterine assessment, in particular when there is a suspicion of unexplained infertility (UEI). It plays an essential role as regards both taking biopsies and management of pathological conditions in the same diagnostic context.

**Aim:** To explore the uterine cavity using of office hysteroscopy (oHS) and take endometrial biopsy to evaluate the endometrial pathology in patients with UEI.

Methods: This study was observational cross-sectional study. This study included fifty-three women with UEI with normal ovulation and they had healthy patent tube as revealed by Hysterosalpingography (HSG). Entire cases were divided into two subgroups; primary and secondary, which represented 49.1% and 50.9% of cases respectively. Histopathological biopsy and findings of HS were documented.

**Results:** There was no statistically significant difference detected between cases with normal and abnormal hysteroscopic findings in terms of other complaints, pathological findings and pregnancy rate. There was statistically significant difference is detected between cases with normal and abnormal pathological findings as regard type of infertility. Every increase in one year in age increases the risk of 2ry infertility by 1.14. Urban residence has increased risk of 2ry infertility by 3.33 times than rural residence, abnormal pathological findings increase risk of 2ry infertility by 3.58 times than normal pathological findings.

**Conclusion:** Hysteroscopy is considered as a routine step in the fertility work-up program and becomes obligatory before the final diagnosis of UEI. It is an ideal diagnostic approach to several undiagnosed intrauterine pathologies after failure of different routine approaches.

**Keywords:** Hysteroscopy, Histopathologic examination, Endometrium, Unexplained Infertility.

#### Corresponding author:

Heba Elsayed Mohamed Mahmoud Eldeeb, Mobile:01003937229 Email: Baskotam\_90@yahoo.com

## INTRODUCTION

The emerging of hysteroscopy (HS) in the gynecological practice presented a real revolution in the management of the intrauterine diseases that mainly interfered with the management of such pathologic situations. By time, recent technical, and technologic developments have made HS much more successful, economic, safe, and helpful. Additionally, several diagnostic and operative hysteroscopy examination might be currently simply conducted in the office base context, with no need for the operating room or anaesthesia (1).

The existence of uterine anomalies might interfere with the reproductive outcomes by increased frequency of miscarriages, preterm labors, and obstetric adverse events <sup>(2)</sup>. Infertility is the inability of a couple to accomplish pregnancy within a period of one year (among females whose age less than 35 years old) or six months (whose age more than 35 years old) in spite of proper, regular (3-4 times weekly), unprotected sex <sup>(3)</sup>.

Of note, female infertility represents about 48.5 million females globally <sup>(4)</sup>. The existence of uterine pathologies might harmfully interfere with the implantation process. The prevalence of unsuspected uterine pathologies in asymptomatic women with implantation failure is recorded to be about fifty percent <sup>(5)</sup>. UEI could be described as the absence of an evident etiology for a couple's infertility and the females' inability to get pregnant after at least twelve cycles of unprotected intercourse or following six cycles in females beyond the age of 35 for whom all the traditional assessments are normal <sup>(6)</sup>.

Hysteroscopy provides precise visual evaluation of the uterine cavity and give a possibility to manage any pathology determined throughout the examination and availability of HS with smaller diameter has made the use of oHS of great importance as a routine examination (7). Hysteroscopy

also has an important role in terms of the establishment of precise diagnosis, in comparison with HSG and even transvaginal sonography (TVS), minor intrauterine disorders that might interfere with fertility. In brief, it is clear why several investigators think that uterine and endometrial integrity must be assessed mostly by HS in the infertile and IVF managed subjects (8, 9).

It has been demonstrated that; infertility due to uterine abnormalities is considered as a causal factor in about 12.5 % of couples seeking treatment. In addition, uterine abnormalities are demonstrated in 34% to 62% of infertile females (10). Recently, HS has been considered as the best approach for assessing the uterus, and owing to an improvement of endoscopic development, could be carried out in a reliable and safe manner as an office approach (11).

Close assessment of the uterine cavity provides considerable advantages in comparison with the previously used blinded approaches, even though hysterosalpingography (HSG) is to be as precise as HS in the context of diagnosis of uterine abnormalities, the natures of the intrauterine filling defects are more precisely demonstrated by HS <sup>(12)</sup>. In general, it is conducted as a conclusive diagnostic approach to assess abnormalities on hysterosalpingogram conducted during the evaluation of sub fertile females <sup>(13)</sup>.

## Aim of the work

To correlate hysteroscopic findings with endometrial histopathology in patients with UEI.

## PATIENTS AND METHODS

This study was observational cross-sectional study. This study included fifty-three women with UEI recruited from the outpatient Clinic of the obstetrics and gynaecology department, Mansoura University hospitals, Egypt, over a period of one year started from March 2021 to March 2022.

## **Population**

Women selected for this study were diagnosed with UEI and had the next criteria; their husbands had normal semen analysis based on WHO 2010, they had normal ovulation (regular menses, confirmed ovulation by using transvaginal sonography (TVS) and the serum progesterone on day 21 of the cycle was more than 3ng/ml indicates ovulation) and they had healthy patent tube determined as evaluated by HSG. But we excluded women with irregular menses, women used hormonal therapy in the past three months, or women with any factor deviating from being UEI as; male factor, tubal blockade, anovulation, previous diagnosis of intrauterine anatomical abnormalities, gynaecological operation in the past six months, and presence of gross uterine pathology.

#### Methods

Patients with UEI were approached to do hysteroscopy to detect any endometrial pathology. They were invited to take part in the study by the investigator. At first visit, history taking included personal, present, past, family, obstetric and menstrual history, clinical examination included heart rate, blood pressure, temperature, cardiac and abdominal examination. Gynaecological examination included normal HSG that was performed four days after menses. The nature of the study was explained, written consent was obtained. All the participants were assured that the information gathered through the study were kept confidential, being collected anonymously.

## **Hysteroscopy Procedure**

Verbal conversation was done to all patients about the procedure and possible adverse events in an understandable form to her. Informed written consent was taken from all patients before their participation. The examination was done by catheterization and bimanual examination. NSAIDS were given before the procedure. The patient was placed in the dorsal lithotomy position. The patient perineum should be just at the edge of the

table. The thighs should be at a 90 angle to the pelvis to form sufficient space for surgeon to conduct the HS. Cleaning of cervix and paracervical block were done. Traction of the cervix with vollsellum was done then office hysteroscope through cervical canal was introduced.

#### **Outcomes**

Histopathological biopsy and findings of hysteroscopy (cervical canal-entery-cavityendometrium-tubal ostia) were reported.

#### **Ethical Considerations**

The collected information as regard the conduct, assessment and documentations were planned to confirm that the authors applied the principles of good practice and the ethical principles based on Declaration of Helsinki. This study was presented to Ethical Committee Mansoura University to be approved. Patient approval for registration in this study was documented.

#### **Statistical Analysis**

Data were entered and analysed by utilizing IBM-SPSS software (Released 2019, Version 26. Armonk, NY). Qualitative data were expressed as N (%). Quantitative data were initially tested for normality using Shapiro-Wilk's test with data being normally distributed if p>0.050. The existence of significant outliers (extreme values) was assessed for by inspecting boxplots. Quantitative data were expressed as median and range (minimum – maximum). Qualitative data between groups; For 2X2 crosstabulation, the chi-square test was utilized to test the association between two nominal variables. The chi-Square test was used when the expected count in all cells was  $\geq 5$ , otherwise, Fisher's exact test was used. Quantitative data between two group; independent samples t-test was utilized for comparison of normal distribution of quantitative data between 2 groups. The Mann-Whitney U-test was utilized for comparison of non-normal distribution of quantitative data between two groups. The results were considered significant when  $p \le$ 0.05.

## **RESULTS**

Table (1) shows that most of the cases of hysteroscopic finding have normal findings by a ratio 56.6%, followed by 13.2% has subseptate uterus, then 11.3 % has endometrial polyp, then 7.5% has partial Asherman Syndrome, 3.8% has partial adhesions of both tubes and finally each of the following; small anterior niche, thick shreddy polypoid endometrium and lateral myoma has the same ratio 1.9%

Table (1): hysteroscopic findings of the studied cases.

	N=53	%
Hysteroscopic Findings		
Normal findings	30	56.6
Subseptate uterus	7	13.2
Endometrial polyp	6	11.3
Small anterior niche	1	1.9
Tubular cavity (partial Asherman syndrome)	4	7.5
Picture of endometriosis	1	1.9
Thick shreddy polypoid endometrium	1	1.9
Partial adhesion both tubes seen	2	3.8
Lateral Myoma	1	1.9

Table (2) shows that there is statistically significant difference is detected between cases with normal and abnormal hysteroscopic results with ratio 21.7% of the cases sof abnormal hysteroscopic finding have parity  $\geq 2$  and 80% of the cases of abnormal hysteroscopic findings have abortion  $\geq 2$  versus 33.3% of the cases with normal hysteroscopic findings

Table (2): Relation between hysteroscopic findings and demographic findings of the studied cases.

	Hysterosco	tost of significance		
	Normal n=30(%)	Abnormal n=23(%)	test of significance	
Age/years	28.77±6.47	31.87±6.72	t=1.70 p=0.095	
Residence				
Urban	16(53.3)	16(69.6)	$\Box^2 = 1.43$	
Rural	14(46.7)	7(30.4)	p=0.231	
Gravidity				
Nulli gravid	10(33.3)	7(30.4)		
Primi gravida	9(30)	5(21.7)	$\Box^2 = 0.761$	
≥2	11(36.7)	11(47.8)	p=0.684	
Parity				
Nulli para	17(56.7)	10(43.5)		
Primi para	13(43.3)	8(34.8)	$\Box^2 = 7.21$	
≥2	0	5(21.7)	p=0.027*	
Abortion				
1	10(66.7)	2(20)	$\Box^2 = 5.23$	
≥2	5(33.3)	8(80)	p=0.02*	
Type of infertility				
1ry	17(56.7)	9(39.1)	$\Box^2 = 1.60$	
2ndry	13(43.3)	14(60.9)	p=0.206	
Infertility duration (years)	4.74±2.55	5.61±3.04	t=1.13 p=0.265	

Table (3) shows that there is no statistically significant difference detected between cases with normal and abnormal hysteroscopic findings as regard other complaints, pathological findings and pregnancy rate. Table (4) shows that there was statistically significant difference is detected between cases with normal and abnormal pathological findings as regard type of infertility 62.5% of cases with abnormal pathological findings have secondary infertility versus 33.3% of cases have normal pathological findings. Table (5) shows that there was no statistically significant difference detected between cases with normal and abnormal pathological findings as regard other complaints, hysteroscopic findings and pregnancy rate. Table (6) shows that there was no statistically significant difference detected between cases with normal and abnormal pathological findings as regard hysteroscopic findings and pregnancy rate. Table (7) shows that every increase in 1 year in age increase the risk of 2ry infertility by 1.14. Urban residence has increased risk of 2ry infertility by 3.33 times than rural residence, abnormal pathological findings increase risk of 2ry infertility by 3.58 times than normal pathological findings.

Table (3): Relation between hysteroscopic findings and other complaints, pathological findings and pregnancy rate among the studied cases.

	Hysterosco	toot of simulforms		
	Normal n=30(%) Abnormal n=23(%)		test of significance	
Other complaint				
Candidiasis	0	2(40)	MC=4.55	
Secondary amenorrhea	2(25)	0	P=0.208	
AUB	4(50)	2(40)	P-0.208	
Chronic cervicitis	2(25)	1(20)		
Pathological findings				
normal	14(46.7)	7(30.4)	$\Box^2 = 1.43$	
abnormal	16(53.3)	16(69.6)	p=0.231	
Pregnancy rate				
Not pregnant	26(86.7)	20(87.0)	□ <b>²</b> =0.001	
Pregnant	4(13.3)	3(13.0)	p=0.975	

Table (4): Relation between pathological findings and demographic findings of the studied cases.

	Pathology findings		
	Normal n=21(%)	Abnormal n=32(%)	test of significance
Age/years	28.76±6.13	31±6.99	t=1.19 p=0.238
Residence Urban Rural	11(52.4) 10(47.6)	21(65.6) 11(34.4)	□²=0.930 p=0.335
Gravidity Nulli gravid Primi gravida ≥2	6(28.6) 8(38.1) 7(33.3)	11(34.4) 6(18.8) 15(46.9)	□²=2.49 p=0.288
Parity Nulli para Primi para ≥2	14(66.7) 6(28.6) 1(4.8)	13(40.6) 15(46.9) 4(12.5)	□²=3.56 p=0.168

Abortion 1 ≥2	6(54.5) 5(45.5)	6(42.9) 8(57.1)	□²=0.337 p=0.561
Type of infertility 1ry 2ndry	14(66.7) 7(33.3)	12(37.5) 20(62.5)	$\Box^2=4.32$ p=0.038*
infertility duration (years)	4.97±2.62	5.22±2.91	t=0.320 p=0.750

Table (5): Relation between pathological findings and other complaints, hysteroscopic findings and pregnancy rate among the studied cases.

	Pathology findings		tost of
	Normal n=21(%)	Abnormal n=32(%)	test of significance
Other complaint Candidiasis Secondary amenorrhea AUB Chronic cervicitis	1(16.7) 1(16.7) 3(50) 1(16.7)	1(14.3) 1(14.3) 3(42.9) 2(28.6)	MC=0.258 p=0.968
Hysteroscopic findings Normal findings Subseptate uterus Endometrial polyp Small anterior niche Tubular cavity (partial Asherman syndrome) Picture of endometriosis Thick shreddy polypoid endometrium Partial adhesion both tubes seen Lateral Myoma	14(66.7) 4(19) 0 0 1(4.8) 1(4.8) 0 1(4.8) 0	16(50) 3(9.4) 6(18.8) 1(3.1) 3(9.4) 0 1(3.1) 1(3.1) 1(3.1)	MC=9.38 P=0.310
Pregnancy rate Not pregnant Pregnant	18(85.7) 3(14.3)	28(87.5) 4(12.5)	FET=0.035 P=1.0

Table (6): Relation between pregnancy rate and pathological, hysteroscopic findings of the studied cases.

	Pregnancy rate		Asst of siz
	Not pregnant N=46	Pregnant N=7	test of sig- nificance
Pathological findings			FET=0.035
Normal	18(39.1)	3(42.9)	
Abnormal	28(60.9)	4(57.1)	p=1.0
Hysteroscopic findings			
Normal findings	26(56.5)	4(57.1)	
Subseptate uterus	5(10.9)	2(28.6)	
Endometrial polyp	5(10.9)	1(14.3)	
Small anterior niche	1(2.2)	0	MC=3.03
Tubular cavity (partial Asherman syndrome)	4(8.7)	0	P=0.933
Picture of endometriosis	1(2.2)	0	
Thick shreddy polypoid endometrium	1(2.2)	0	
Partial adhesion both tubes seen	2(4.3)	0	
Lateral Myoma	1(2.2)	0	

Table (7): Predictors of secondary infertility among studied cases.

	В	p value	Odds ratio (95% CI)
Age/years	0.134	0.008*	1.14 (1.04-1.26)
Residence Urban Rural( R )	1.204	0.04*	3.33(1.05-10.58)
Pathological findings Normal (R) Abnormal	2.01	0.03*	3.58(1.05-10.58)
Overall % predicted =64.2%			

## **DISCUSSION**

Infertility affects about 15% of couples. There are several etiologies of infertility, which comprise ovulatory disorders, tubal diseases, and semen abnormalities in males. Such etiologies represent about seventy-five percent of infertile couples. UEI diagnosis could be established when all routine tests for infertility are negative (14).

HS is considered the best approach for the assessment of uterine cavity, in particular when pathologies are suspected in UEI. It permits close visualization of intrauterine pathologies, exploring their nature, site, shape, size and vascular pattern. In addition, it permits directed biopsy or management of any disorder within the same visit. As a result, in females with UEI, HS might be considered a conclusive diagnostic modality to evaluate any abnormality suspected or couldn't be determined by HSG or TVS in initial assessment of infertile cases (15). The present study aimed to properly assess the uterus by utilizing office HS and take endometrial biopsy to assess the endometrial pathology among cases with UEI.

This was a cross-sectional study conducted on a total of 53 women with UEI at Mansoura University Fertility Care Unit within the period from March 2021 to March 2022. Entire cases were divided into two subgroups; primary and secondary which represented 49.1% and 50.9% of cases respectively.

Entire cases were divided into two subgroups; primary and secondary which represented 49.1% and 50.9% of cases respectively. In addition, most of the studied cases (60.4%) were living in urban regions, whole only were living in rural regions (39.6%). In the same line, Makled and his colleagues conducted their study on a total of 100 women with UEI women, in which 40 women had primary infertility, whereas 60 women had secondary infertility. The mean infertility duration was 6 years (16). Also, Matei and his colleagues have demonstrated that; the mean age of subjects was thirty nine years old. Most of cases (88.9%) were living in urban regions; 95.6% of females were in their childbearing period, whereas 4.4% were their menopausal period (17). On the other hand, Hamada and his colleagues have found that; 70 percent of studied women had primary infertility, while only thirty percent were associated with secondary infertility (18).

The current study demonstrated that; the abnormal hystroscpic findings among the studied cases represented 43.4%. Similarly, Makris and his colleagues conducted HS in cases with previous history of abortion, infertility and repeated IVF failure. They revealed that abnormalities in hysteroscopic outcomes were noticed in 40.5% of cases

where intrauterine adhesions, endometrial hyperplasia and polyps were the commonest findings <sup>(19)</sup>. Also, Jain and his colleagues conducted an observational study on one hundred women's with UEI who were examined with oHS and demonstrated that abnormal hysteroscopic findings was recorded in 56% <sup>(20)</sup>.

Khalil Abd El-Shafi and his colleagues have demonstrated that; normal hysteroscopic examination were detected among 65% of subjects, while abnormalities were detected in 35% only <sup>(21)</sup>. Higher incidence was recorded by Mohamed & Elmazzaly who demonstrated that abnormal hysteroscopic examination was detected in 89% of their studied cases <sup>(22)</sup>. Lower incidence was recorded by Makled and his colleagues who displayed that no hysteroscopic abnormalities were detected in 14% of females with UEI <sup>(16)</sup>.

Regarding hysteroscopic findings, most of the cases of hysteroscopic finding have normal findings by a ratio 56.6%, followed by 13.2% has subseptate uters, then 11.3 % has endometrial polyp ,then 7.5% has partial Asherann Syndrome , 3.8% has partial adhesions of both tubes and finally each of the following :small anterior niche thick shreddy polypoid endometrium and lateral myoma has the same ratio 1.9%. Also, Mohamed & Elmazzaly have displayed that; the percentage of cervicitis, cervical stenosis. cervical polyp, uterine septum, arcuate uterus, uniconuate uterus, bicornuate uterus, endemostritis, intrauterine synchcia, endometrial polyp, submucous myoma and hyperplastic were recorded in 2%, 1%, 4%, 3%, 2%, 2%, 1%, 13%, 8%, 30%, 9%, 14% of cases respectively (22). Also, Ahmed et al. displayed that; according to hysteroscopic results, 22 of cases (18.3%) had polyps, six cases had cervical stenosis (5%), one cases has myoma (0.8%), eight cases had intrauterine adhesions (7%) and 19 cases had congenital anomalies of uterus (16%). Cervicitis was revealed in twelve cases (10%), whereas three cases had endocervical cysts (2.5%),

cornu not accessible in four cases (3.3%), while ostia not detected in eight cases (6.6%), three cases had tight isthmus (2.5%) and three cases had polypidal thickness at isthmus (2.5%), while hysteroscopy findings were demonstrated to have no abnormalities in 49 cases (40.8%) (26). In addition, Hamada and his colleagues have displayed that; among the 100 females studied, 29 % had abnormalities by HS in the uterine cavity and cervical stenosis. Moreover, 71% of studied females had no abnormalities. In addition, 14% were detected to have intrauterine polyps (not detected by both HSG and ultrasonography). Eight females were observed to have submucous fibroids with grades from zero to two and small in size, four women had intrauterine adhesions. A single female had small uterine septum. Failed approach happened in two females with cervical stenosis (18).

Moreover, Makled and his colleagues demonstrated that; according to hysteroscopic results, thirty one cases were finally diagnosed with endometrial polyps; 14 endometritis; 15 endometrial hyperplasia; six submucous myomas; seven intrauterine synechiae; seven congenital uterine anomalies, six cervical stenosis and fourteen females with normal uterus. Assessment of specimens by endometrial suction curette was nondiagnostic in sixteen cases; the commonest endometrial pathologic feature determined by this assessment was endometritis (15%). The prevalence of endometrial hyperplasia was 14%, and 3 patients of endometrial polyps were identified (16).

Concerning predictors of secondary infertility among studied cases, the present study demonstrated that; every increase in 1 year in age increase the risk of 2ry infertility by 1.14, Urban residence has increase risk of 2ry infertility by 3.33 times than rural residence, abnormal pathological findings increase risk of 2ry infertility by 3.58 times than normal pathological findings. In the same line, Ono and his colleagues

have demonstrated that; age was recognized as an independent predisposing factor for postsurgical secondary infertility. (28). While, Dhont and his colleagues have demonstrated that; predisposing factors in the obstetric history for secondary infertility were absence of prenatal care in the last pregnancy, adverse pregnancy outcomes, stillbirth, postpartum infections and curettage. (29).

The current study demonstrated that hysteroscopic findings have a significant correlation with parity and abortion only. In addition; there was a significant relation between pathological findings and type of infertility only.

With regard validity of hystroscope as compared to pathological findings, the current study demonstrated that; it showed sensitivity 50%, specificity 66.7%, PPV 69.6%, NPV 46.7% and accuracy 66.7 %. Mohamed & Elmazzaly have demonstrated that HS was significant with sensitivity, specificity, PPV, NPV and accuracy of 97.8%, 100%, 100%, 84.6%, 98% respectively (22).

In the same line, Garuti and his colleagues recorded that HS was of great diagnostic accuracy in the context of endometrial polyp diagnosis (30).

In addition, Hauge and his colleagues revealed that the outcomes of HS and TVS were comparable in 90.9% of cases (31). Draz and his colleagues have displayed that HS was of great sensitivity (, but had the same specificity, and was more precise in comparison with saline infusion ultrasonography. Throughout the assessment of subjects with UEI, HS had a better predictive value in comparison with saline infusion ultrasonography (32).

On the other hand, Zargar and his colleagues revealed that the sensitivity of hysterography and sonography were 48.9% and 48%, respectively, on the other hand false negative rates were 51.1% and 52%. Thus, sonography and hysterography were inadequate in the

context of uterine cavity evaluation (33).

In addition, Preutthipan & Linasmita carried out a comparative study of HSG and HS in the recognition of intrauterine diseases among infertile females and demonstrated that HSG had a higher sensitivity (98%) and mild specificity (34.6%) (34). Our study revealed that, HSG had a higher sensitivity and poor specificity in terms of detection of intrauterine pathologies. Thus, although HSG is a useful screening test for intrauterine lesions as it demonstrates the filling defects, which are obtained by HSG (not specific). Only HS has the ability to precisely demonstrate the natures of the intrauterine filling changes. When an HSG demonstrates any uterine abnormalities, HS is suggested to verify their site and extent (34).

## **CONCLUSION**

Planning the HS as a routine step in the fertility work-up program has become obligatory before the conclusive diagnosis of UEI. This approach has been considered a perfect approach to diagnose several intrauterine pathologies undiagnosed with different traditional methods. Of note, the marked improvement in the pregnancy outcomes after the hysteroscopic approach, reinforces the formerly reported suggestions.

# Recommendations

Additional researches on large number of cases and different populations are needed to emphasize the current conclusion. There was a need to assess the impact of choice of tubal test on chances of spontaneous conception and therapeutic outcomes in females with UEI. Any patient with UEI must be investigated with hysteroscopy.

Conflict of interest: Nil.

**Sources of funding:** No special grant from funding agencies.

## REFERENCES

- 1. Bakour SH, Jones SE, O'Donovan P. Ambulatory hysteroscopy: evidence-based guide to diagnosis and therapy. Best Practice & Research Clinical Obstetrics & Gynaecology. 2006;20(6):953-75.
- 2. Fedele L, Bianchi S, Zanconato G, et al. Laparoscopic removal of the cavitated noncommunicating rudimentary uterine horn: surgical aspects in 10 cases. Fertility and sterility. 2005;83(2):432-6.
- 3. Cooper TG, Noonan E, Von Eckardstein S, et al. World Health Organization reference values for human semen characteristics. Human reproduction update. 2010;16(3):231-45.
- 4. Mascarenhas MN, Flaxman SR, Boerma T, et al. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS medicine. 2012;9(12):e1001356.
- 5. Cenksoy P, Ficicioglu C, Yıldırım G, et al. Hysteroscopic findings in women with recurrent IVF failures and the effect of correction of hysteroscopic findings on subsequent pregnancy rates. Archives of gynecology and obstetrics. 2013;287:357-60.
- 6. King RB, Davis J. Introduction: health disparities in infertility. Fertility and Sterility. 2006;85(4):842-3.
- 7. De Placido G, Clarizia R, Cadente C, et al. Compliance and diagnostic efficacy of mini-hysteroscopy versus traditional hysteroscopy in infertility investigation. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2007;135(1):83-7.
- 8. Oliveira FG, Abdelmassih VG, Diamond MP, et al. Uterine cavity findings and hysteroscopic interventions in patients undergoing in vitro fertilization—embryo transfer who repeatedly cannot conceive. Fertility and sterility. 2003;80(6):1371-5.

- 9. Pansky M, Feingold M, Sagi R, et al. Diagnostic hysteroscopy as a primary tool in a basic infertility workup. JSLS: Journal of the Society of Laparoendoscopic Surgeons. 2006;10(2):231.
- 10. Brown SE, Coddington CC, Schnorr J, et al. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. Fertility and sterility. 2000;74(5):1029-34.
- 11. Sahu, L., Tempe, A. and Gupta, S. Hysteroscopic Evaluation in Infertile Patients: A Prospective Study. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2012;1, 37-41.
- 12. Shakya, B. Hysterosalpingography Vs Hysteroscopy in the Detection of Intrauterine Pathology in Infertility. Journal of Nepal Health Research Council, 2009;7(1), 6–9
- 13. Penzias A, Azziz R, Bendikson K, et al. Fertility evaluation of infertile women: a committee opinion. Fertility and sterility. 2021;116(5):1255-65.
- 14. Gelbaya TA, Potdar N, Jeve YB, et al. Definition and epidemiology of unexplained infertility. Obstetrical & gynecological survey. 2014;69(2):109-15.
- 15. Genovese F, Di Guardo F, Monteleone MM, et al. Hysteroscopy as an investigational operative procedure in primary and secondary infertility: a systematic review. International journal of fertility & sterility. 2021;15(2):80.
- 16. Makled AK, Farghali MM, Shenouda DS. Role of hysteroscopy and endometrial biopsy in women with unexplained infertility. Archives of gynecology and obstetrics. 2014;289:187-92.
- 17. Matei A, Ionescu C, Gorun F, et al. Insights on Hysteroscopic Procedures and Their Place in Romanian Gynecologic Practice—The Experience of Two Medical Units. Diagnostics. 2020;10(5):281.

- 18. Hamada AA Ali, Rabab Ashour, El MZ, et al. Hysteroscopic evaluation of uterine cavity in women with unexplained infertility. Obstetrics & Gynecology International Journal. 2021;12(6):375–8.
- 19. Makris N, Xygakis A, Michalas S, et al. Day clinic diagnostic hysteroscopy in a state hospital. Clinical and Experimental Obstetrics & Gynecology. 1999;26(2):91-2.
- 20. Jain N, Manchanda R, Lekhi A, et al. Role of hysteroscopy in evaluation of infertility: A retrospective study of 100 cases. Journal of Gynecology. 2016:1:000117.
- 21. Khalil Abd El-Shafi A, Talaat El-Garhy I, Mohamed Labeb M, et al. Comparison between 2D transvaginal ultrasonography and hysteroscopy in detection of inrauterine pathology in patients with infertility. Al-Azhar Medical Journal. 2022;51(1):309-20.
- 22. Mohamed MA, Elmazzaly SM. Role of Diagnostic Hysteroscopy in Cases with Unexplained Infertility. Al-Azhar International Medical Journal. 2022;3(9):88-95.
- 23. Dickey RP, Olar TT, Taylor SN, et al. Relationship of follicle number and other factors to fecundability and multiple pregnancy in clomiphene citrate-induced intrauterine insemination cycles. Fertility and sterility. 1992;57(3):613-9.
- 24. Nagele F, O'connor H, Davies A, et al. 2500 outpatient diagnostic hysteroscopies. Obstetrics & Gynecology. 1996;88(1):87-92.
- 25. Arefi S, Soltan GH, Zarnani AH, et al. Repeated IVF/ICSI-ETs failures and impact of hysteroscopy. Iranian Journal of Reproductive Medicine 2008;6(1): 19-24.
- 26. Ahmed F, Khalifa E, Ahmed A, et al. Hysteroscopic detection of intrauterine pathology in women with unexplained infertility. The Medical Journal of Cairo University. 2018;86:1287-94.
- 27. Hamouda EFA, Farahat MAE-R, Shaheen

- KAE-F. Hysteroscopic evaluation of chronic endometritis and its relation to unexplained infertility. Tanta Medical Journal. 2022;50(3):194.
- 28. Ono S, Yonezawa M, Watanabe K, et al. Retrospective cohort study of the risk factors for secondary infertility following hysteroscopic metroplasty of the uterine septum in women with recurrent pregnancy loss. Reproductive Medicine and Biology. 2018;17(1):77-81.
- 29. Dhont N, Luchters S, Muvunyi C, et al. The risk factor profile of women with secondary infertility: an unmatched case-control study in Kigali, Rwanda. BMC women's health. 2011;11:32.
- 30. Garuti G, Sambruni I, Colonnelli M, et al. Accuracy of hysteroscopy in predicting histopathology of endometrium in 1500 women. The Journal of the American Association of Gynecologic Laparoscopists. 2001;8(2):207-13.
- 31. Hauge K, Flo K, Riedhart M, et al. Can ultrasound-based investigations replace laparoscopy and hysteroscopy in infertility? European Journal of Obstetrics & Gynecology and Reproductive Biology. 2000;92(1):167-70.
- 32. Draz MH, El-Sabaa TM, El Shorbagy SH. Saline infusion sonography versus hysteroscopy in the evaluation of uterine cavity in women with unexplained infertility. Tanta Medical Journal. 2017;45(3):155.
- 33. Barati M., Mahvash Zargar, Sara Masihi, Leila Borzoo and Bahman Cheraghian: Office Hysteroscopy in Infertility. Int. J. of Fertil & Steril. 2009;3: 17-20.
- 34. Preutthipan S, Linasmita V. A prospective comparative study between hysterosalpingography and hysteroscopy in the detection of intrauterine pathology in patients with infertility. Journal of Obstetrics and Gynaecology Research. 2003;29(1):33-7.