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Original Article

Detection of intracavitary lesions in 436 infertile women by office hysteroscopy and comparison with histopathology results

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Abstract

Aim: To examine the importance of office hysteroscopy in detecting and treating endometrial pathologies of infertile patient groups.
Materials and Methods: For this retrospective observational study, first, electronic hospital records were examined in order to identify patients who underwent office hysterescopy at our clinic, between 2003 and 2020, for infertility. The office hysteroscopy findings of 436 patients were included in the study, and examined and compared with the histopathological results.
Results: The age distribution of the patients included in the study was homogeneous in terms of group variances. Thehysteroscopy findings of the patients were as follows: normal cavityin 137 patients(31.4%), endometrial polyps in 199 patients(45.6%), synechia in 14 patients(3.2%), subseptum or arcuate uterus in 32 patients (7.3%), t-shaped uterus in 28 patients (6.4%), cervical polyps in 6 patients (1.4%), Asherman's syndrome in 6 patients (1.4%), and submucous myoma in 14 patients (3.2%). The most frequently detected lesion with office hysteroscopy was polyps,at a rate of 47% with 205 patients. In the pathology results, of the 137 patients who were diagnosed with normal endometrium via office hysteroscopy and underwent biopsy, 119were reported as normal (89.6%), while 6 were diagnosed with polyps (4.4%). The sensitivity and specificity of office hysteroscopy in detecting endometrial polyps were 94% and 56%, respectively.
Conclusion: Office hysteroscopy may be one of the first alternative methods that can be used for safe and practical outpatient diagnosis and treatment in infertile patient groups.

Keywords: Histopathology; infertility; office hysteroscopy

INTRODUCTION

Infertility is defined as the absence of pregnancy despite 1year of unprotected sexual intercourse (1). The main causes of infertility include male factors, decreased ovarian reserve, tubal factors, uterine factors, cervical factors, immunological factors, and unexplained factors (2). Uterine factorshave been reported as the cause of infertility in 3%–10% of infertile women (3,4). These uterine factors include some congenital and acquired pathologies that cause some problems, such as migration of spermatozoa, implantation, and miscarriage (4,5). The uterine factors that play a role in infertility include endometrial polyps, submucous myoma, intrauterine adhesions, mullerian anomalies, and previous exposure to diethylstilbestrol (2). Analysis of the endometrium is an important step in the treatment of women with infertility (6). Until recently, hysterosalpingography (HSG), transvaginal ultrasonography (TVUSG), and hysterosonography were the primary diagnostic methods in the detection of uterine pathologies, while hysteroscopy was used as the secondary diagnostic method (7,8). Presently, however, office hysteroscopy has become the gold standard diagnostic method, which can be easily tolerated by patients, used in the detection of uterine pathologies and in the treatment of pathologies that result in infertility (9-11).

The objective in this retrospective study was to examine the hysteroscopy findings of patients with infertility and compare these findings with the pathologic examinations of the tissues obtained.

MATERIALS and METHODS

Patients

The study protocol was approved after obtaining the necessary permission by the Ethics Committee (register number KA20/216). For this retrospective observational

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study, firstly, electronic hospital records were examined in order to identify infertile patients who underwent office hysterescopy in our clinic between 2003-2020. All of 436 infertile patients were included the study and then, these patients data includes ages, office hysterescopic findings and clinicians who performed the procedure were extracted from the medical records of this cohort. Patients without pathology results were not included in the study. Hysteroscopic findings and pathology results of the patients, who underwent check-up procedures or had been referred due to suspicious lesions that had beendetected by ultrasound and HSG findings, were evaluated. Hysteroscopy was performed in patients who had recurrent implantation failure with normal ultrasonography and HSG findings. A biopsy was performed on patients with a normal endometrium on hysteroscopic observation to investigate the presence of possible infections.CD138 plasma cells were studied in biopsy samples for the diagnosis of chronic endometritis.

At our clinic, The National Institute of Health and Care Excellence (NICE) guidelines were used to assess the infertile patients (12). In this guideline, infertility is defined as being unable to get pregnant despite unprotected sexual intercourse for at least a year in the absence of any known cause of infertility, and it recommends clinical assessment and investigation after this period. Additionally, if a woman is >35 years of age, and has a known cause of infertility or a history of predisposing factors, earlier investigation for infertility treatment is recommended.

Hysteroscopic Procedure

Hysteroscopies were performed using a 5-mm Karl-Storz office hysteroscope (Tuttlingen, Germany), equipped with a 2.9-mm rod lens telescope with a 30°angle of view, and an oval-shaped working channel for 5-French operating instruments (approximately 1.6mm). Semi-rigid hysteroscopic micro scissors and microforceps were used in the study channel. During the process, the images were transferred to a 22-inch monitor with an xenon light source and optic fiber cable. Saline was used for uterine distention. Hysteroscopies were performed by 3 different gynecologists working at the infertility department.

Statistical Analysis

For discrete and continuous variables, descriptive statistics (mean, standard deviation, number, and percentile) were given. In addition, the homogeneity of the variances, which is one of the prerequisites of parametric tests, was checked through the Levene test. The assumption of normality was tested via the Shapiro-Wilk test.To compare the differences between 3 or more groups, 1-way ANOVA was used when the parametric test prerequisites were fulfilled, and the Kruskal-Wallis test was used when such prerequisites were unfulfilled. The Bonferroni correction method, which is a multiple comparison test, was used to evaluate the significant results concerning 3 or more groups.

IBM SPSS Statistics for Windows 25.0 (Armonk, NY, USA) was used for the analysis of the data. Mean±standard deviation were used to express the variables, while percentage and frequency were used to expressthe median (maximum-minimum). Moreover, sensitivity and selectivity values were calculated. P<0.05 was accepted as statistically significant. Categorical data were analysed using the McNemar-Bowker and chisquare tests. Expected to be less than 25% of cells in cases for inclusion in the analysis of those cells Monte Carlo simulation method and the values were determined.

RESULTS

The age distribution of the patients included in the study was homogeneous in terms of the group variances (P> 0.05). (Table 1). The reasons for infertility, distribution of the hysteroscopic findings, and results of the pathological examinations of the patientsare presented in Table 2. The office hysteroscopy findings of the patients were as follows: normal cavity in 31.4%, endometrial polyps in 45.6%, synechia in 3.2%, subseptum or arcuate uterusin 7.3%, t-shaped uterus in 6.4%, cervical polypsin 1.4%, Asherman's syndrome in 1.4%, and submucous myoma in 3.2% (Table 2).

Table 1. Age distribution of the patients withuterine lesions

Group	Control n=137	Endometrial polyps n=199	Synechia n=14	Subseptum or arcuat n=32	Cervical polyps n=6	Asherman n=6	T-shaped uterus n=28	Submucous myoma n=14	P value
Age	32.19±4.62	32.46±5.16	33±4.56	33.06±4.81	31.83±4.96	33.17±4.62	33.39±4.38	35.57±4.07	0.360¥

¥ One-way ANOVA

As patients with several fundal sinechias in hysteroscopy were included in the sinechia group, those with intensive adhesions were included in Asherman group.The most frequently detected lesion via office hysteroscopy was polyps, at a rate of 47%. The pathology results of 205 patients, who were suspected of having polyps after hysteroscopy, indicated that 103 of these patients had polyps, and 90 of these patients had a normal endometrium. Of the remaining 12 patients, 7 were diagnosed with endometritis, 2 with nonatypical hyperplasia, and 3 with myoma (Table 3). In the pathology results, of the 137 patients who were diagnosed witha normal endometrium via office hysteroscopy and underwent biopsy, 119 were reported as normal (89.6%), while 6 were diagnosed with polyps (4.4%) (Tablo 4). The sensitivity and specificity of office hysteroscopy in detecting the endometrial polyps were 94% and 57%, respectively (Table 5).

Table 2. Causes of infertility and distribution of the hysteroscopic andhistopathological findings

	N (%)
Hysteroscopic diagnosis	
Normal endometrium	137(31.4)
Polyp (total)	205(47)
Endometrial	199(45.6)
Cervical	6(1.4)
Synechias	14(3.2)
Uterine anomaly (total)	60(13.7)
Subseptus or arcuat	32(7.3)
T-shaped uterus	28(6.4)
Asherman's syndrome	6(1.4)
Submucous myoma	14(3.2)
Total	436(100)
Histopathologic findings	
Polyp (total)	115(26.4)
Endometrial	108(24.8)
Cervical	7(1.6)
Normal endometrium	280(64.2)
Endometritis	21(4.8)
Nonatypical hyperplasia	2(0.5)
Myoma uteri	17(3.9)
Endometriozis	1(0.2)
Total	436(100)
Causes of infertility	
Unexplained	307(70.4)
Anovulation	49(11.2)
Age factor	3(0.7)
Male factor	53(12.2)
Poor responder	2(0.5)
Tubal factor	20(4.6)
Hipogonadotropic hipogonadizm	2(0.5)
Total	436(100)

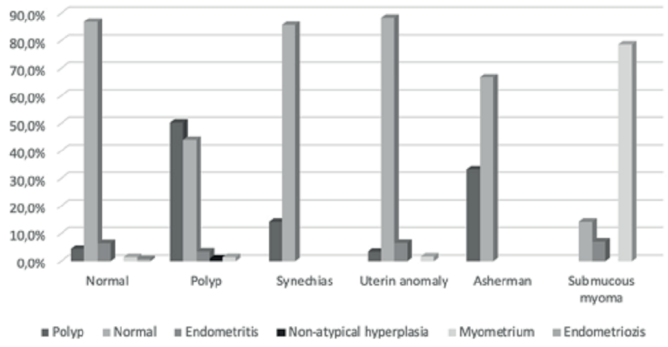

Figure 1. Pathological finding distributionofthe hysteroscopic diagnoses

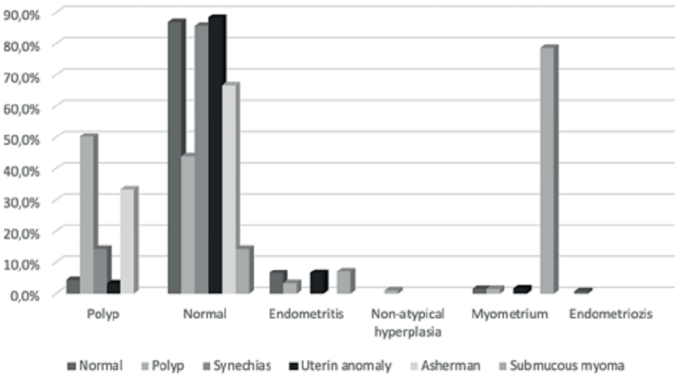

Figure 2. Hysteroscopic diagnoses distribution in the pathological findings

Table 3. Comparison of the hysteroscopic diagnosis and histopathological findings

		Hystopathologic findings					
		Polyp	**Normal**	**Endometritis**	**Nonatypical hyperplasia**	**Myometrium**	**Endometriosis**
Hysteroscopic diagnosis	Normal	6a (0.044)	119b (0.869)	9b (0.066)	0a,b (0)	2a (0.015)	1b (0.007)
	Polyp	103a (0.502)	90b (0.439)	7b,c (0.034)	2a,c (0.01)	3b (0.015)	0b,c (0)
	Synechias	2a (0.143)	12a (0.857)	0a (0)	0a (0)	0a (0)	0a (0)
	Uterine anomaly	2a (0.033)	53b (0.883)	4b (0.067)	0a,b (0)	1a,b (0.017)	0a,b (0)
	Asherman's syndrome	2a (0.333)	4a (0.667)	0a (0)	0a (0)	0a (0)	0a (0)
	Submucous myoma	0a (0)	2a,b (0.143)	1b (0.071)	0a,b,c (0)	11c (0.786)	0a,b,c(0)
	Total	115 (0.264)	280 (0.642)	21(0.048)	2 (0.005)	17 (0.039)	1(0.002)

P <0.05 (chisquare, Monte Carlo simulation method)
a,b,c (There areno statistically significant differences between the same letters.)

Table 4. Comparison of hysteroscopic diagnosis of the endometrial polyps with the histopathological findings

		Histopathological findings			
		Polyp	**Normal**	**Others**	**Total**
Hysteroscopic diagnosis	Polyp	103	90	12	205
	Normal	6	119	12	137
	Others	6	71	17	94
	Total	115	280	41	N=436

P <0.05 (McNemar-Bowker test)

The pathology results of the patients with synechia and uterine anomalies were reported as normal, at 85.7% and 88.3%, respectively. Of the 14 patients who were diagnosed with submucous myoma, the histopathology of 11 of these patients was accordingly reported as myoma, in 2 patients it was reported as anormal endometrium, and in 1 patient it was reported as endometritis (Table 3; Figure 1,2).

Table 5. Sensitivity and specificity criteria were calculated using poly and normal columns and rows

	Histopathologic findings		
Histeroscopic diagnosis	Polyp Normal	Polyp 103 6	Normal 90 119
Prevalence	0.34	(0.29-0.4)	
Sensitivity	0.94	(0.88-0.98)	
Specificity	0.57	(0.5-0.64)	
Positive	0.61	(0.55-0.66)	
Negative	0.39	(0.34-0.45)	
True Positive	0.53	(0.46-0.61)	
False Positive	0.47	(0.39-0.54)	

DISCUSSION

Uterine cavity anomalies are frequently observed in infertile patient groups. It is crucial to use an effective, reliable, and practical diagnosis method in these patient groups. In a study conducted by Eloraby et al., endometrial pathologies were determined in 36 of 100 patients who underwent office hysteroscopy for different indications, despite HSG and TVUSG findings that were observed as normal (13). Most of these detected pathologies were endometrial polyps. Similarly, the most frequently detected endometrial pathology in the current study was polyps,at a ratio of 47%. The following conditions suggested that polyps were the cause of infertility, resulting in irregular endometrial hemorrhage, inflammatory endometrial response, inhibition of sperm transport, physical inhibition of the embryo implantation, and an increased concentration of glycodelin that prevented the sperm from binding to the zona pellucida (14,15). In the current study, it was determined that the sensitivity and specificity of office hysteroscopy were 95% and 56%, respectively, for the diagnosis of endometrial polyps. In a study conducted by Radwan et al., these rates were reported as 100% and 96%, respectively (16),while in another study, they were determined as 93.3% and 33.3%, respectively (17). In astudy conducted on 1500 patients to examine conformity between hysteroscopy and histopathology, the sensitivity and specificity of hysteroscopy in separating the endometrium with normal and abnormal histopathology were 94.2% and 88.8%, respectively. These rates were slightly higher only for the diagnosis of polyps (18). The hysteroscopic abnormal findings of the current study also included uterine anomalies with normal biopsy and histopathology. Therefore, sensitivity and specificity could not be calculated for distinguishing normal-abnormal endometrium histopathology. However, the rate of sensitivity observed for the diagnosis of polyps was 95%,which was similar to that reported in the study of Garuti et al., while the specificity rate herein was lower.

It is known that the prevalence of major uterine anomalies is generally 5% in the fertile population, 3% in infertile patients, and 5%–10% in recurrent miscarriages (19). Uterine septum has a 90% effect in inhibiting gestation. This stems from implantation failure in the uterine cavity due to deformity (20). Uterine anomalies were found in 60 patients (13.7%) in the present study, 32 of which were arcuate uterus or subseptum, while 28 were t-shaped uterus.

Endometritis often occurs as an asymptomatic inflammation of the endometrium. Some researchers have reported that it was associated with infertility, recurrent miscarriage, and implantation failure, while others with very small patient groups had opposing views. In a prospective study by Zolghadri et al.,conducted on patients with recurrent miscarriages, 67% of the patients were hysteroscopically reported to have endometritis. Similarly, in another study, low implantation rates were reported in patient groups with endometritis (21,22). These studies indicated that endometritis has an important place in the cause of infertility. In the current study, 21 of the patients (4.8%) who underwent office hysteroscopy were diagnosed with endometritis. The hysteroscopy results of 9 of these patients appeared normal, but were diagnosed histopathologically by biopsy.

Another problem that can be considered among the causes of infertility is intrauterine adhesions. Asherman's syndrome may occur due to adhesions formed by postoperative conditions or some infections. Asherman's syndrome is 90% associated with infertility, abortion, or preterm delivery (23). Many studies have shown that live pregnancy rates increase after the hysteroscopic treatment of adhesions (23,24). Herein, fundal synechia and Asherman's syndrome were detected in 20 patients (4.6%),who were treated by separating the adhesions. Since this study was retrospective, it was possible to access information from patient files. Moreover, the applicability of hysteroscopy by a single physician was not possible. These were the limitations of the study.

CONCLUSION

In conclusion, hysteroscopy has an important role in the detection and treatment of intracavitary pathologies in the infertile patient population. Office hysteroscopy may be one of the first alternative methods that can be used for safe and practical outpatient diagnosis and treatment in infertile patient groups.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: This retrospective study was approved by Baskent University Clinical Research Ethics Committee (register number KA20/216). All participants gave written informed consent to participate.

REFERENCES

1. Female infertility. In: Fritz MA, Speroff L. Clinical gynecologic endocrinology and infertility. 8th ed. Philadelphia: Woltres Kluwer Health/Lippincott Williams & wilkins, 2012. p. 1137-90
2. Practice Committee of American Society for Reproductive Medicine.Diagnostic evaluation of the infertile female: a committee opinion. Fertil Steril 2012;98:302-7.
3. Hatasaka H. Clinical management of the uterine factor in infertility. Clin Obstet Gynecol 2011;54:696-709.
4. Taylor E, Gomel V. The uterus and fertility. Fertil Steril 2008;89:1-16.
5. Grimbizis G, Gordts S, Di Spiezio Sardo A, et al. The ESHRE-ESGE consensus on the classification of female genital tract congenital anomalies. Gynecol Surg. 2013;10:199-212.
6. Balić D, Balić A.Office hysteroscopy, transvaginal ultrasound and endometrial histology: a comparison in infertile patients. Acta Medica Academica 2012;40: 34-8.
7. Brown SE, Coddington CC, Schnorr J, et al. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. Fertil Steril 2000;74:1029-34.
8. Soares SR, dos ReisMMBB, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 2000;73: 406-11.
9. Amer-Cuenca JJ, Marín-Buck A, Vital SG, et al. Non-pharmacological pain control in outpatient hysteroscopies. Minimally Invasive Therapy & Allied Technologies 2020;29:10-9.
10. Shokeir TA, Shalan HM, El Shafei MM. Significance of endometrial polyps detected hysteroscopically in eumenorrheic infertile women. Aust N Z J Obstet Gynaecol 2004;30:84-9.
11. Vitale SG, Sapia F, Rapisarda AMC, et al. Hysteroscopic morcellation of submucous myomas: a systematic review. BioMed research international. Published online: 2017.
12. O'Flynn, N. Assessment and treatment for people with fertility problems: NICE guideline. British J of General Practice 2014;64:50-1.
13. Mohammed Eloraby N, Elnory MA, Eldeen AAS, et al. Journal homepage: http://www. journalijar. com ınternatıonal journal journal doı: 10.21474/ıjar01 of advanced research research artıcle dıagnostıc hysteroscopy as a prımary tool ın basıc ınfertılıty workup. Int J 2016;4:1716-21.
14. Richlin SS, Ramachandran S, Shanti A, et al. Glycodelin levels in uterine flushings and in plasma of patients with leiomyomas and polyps: implications for implantation. Hum Reprod 2002;17:2742-7.
15. Oehninger S, Coddington CC, Hodgen GD, et al. Factors affecting fertilization: endometrial placental protein 14 reduces the capacity of human spermatozoa to bind to the human zona pellucida. Fertil Steril 1995;63: 377-83.
16. Radwan P, Radwan M, Polać I, et al. Detection of intracavitary lesions in 820 infertile women: comparison of outpatient hysteroscopy with histopathological examination. Ginekol Pol 2013;84: 857-61.
17. Yantapant A. Comparison of the accuracy of transvaginal sonography and hysteroscopy for the diagnosis of endometrial polyps at Rajavithi Hospital. J Med Assoc Thai 2012;95:92-7.
18. Garuti G, Sambruni I, Colonnelli, et al. Accuracy of hysteroscopy in predicting histopathology of endometrium in 1500 women. J Am Assoc Gynecol Laparosc 2001;8:207-13.
19. Lin PC. Reproductive outcomes in women with uterine anomalies. J Womens Health 2004;13:33-9.
20. Kormányos Z, Molnár BG, Pál A. Removal of a residual portion of a uterine septum in women of advanced reproductive age: obstetric outcome. Hum Reprod 2006;21:1047-51.
21. Zolghadri J, Momtahan M, Aminian K, et al. The value of hysteroscopy in diagnosis of chronic endometritis in patients with unexplained recurrent spontaneous abortion. European J Obstetrics & Gynecology and Reproductive Biology 2011;155: 217-20.
22. Johnston-MacAnanny EB, Hartnett J, Engmann LL, et al. Chronic endometritis is a frequent finding in women with recurrent implantation failure after in vitro fertilization. Fertil Steril 2010;93:437-41.
23. Goldenberg M, Sivan E, Sharabi Z, et al. Reproductive outcome following hysteroscopic management of intrauterine septum and adhesions. Hum Reprod 1995;10: 2663-5.
24. Capella-Allouc S, Morsad F, Rongieres-Bertrand C, et al. Hysteroscopic treatment of severe Asherman's syndrome and subsequent fertility. Hum Reprod 1999;14:1230-3.