DOI: 10.34057/PPj.2026.45.02.80774
Pelviperineology 2026;45(2):73-78

Hysteroscopy before repeated IUI in unexplained infertility: A randomized study

Serhat SARIKAYA[1], Deniz ÖZTEKİN[2], Ceren SAĞLAM PURUT[3], Göktürk Han DOĞAN[1], Anıl Doğukan TUTAL[1], Yunus Emre PURUT[1], Alaattin KARABULUT[1]

[1]Department of Obstetrics and Gynecology, University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, İzmir, Türkiye
[2]Öztekin Women's Health Clinic, İzmir, Türkiye
[3]Department of Perinatology, University of Health Sciences Türkiye, İzmir Atatürk Training and Research Hospital, İzmir, Türkiye

Citation: Sarıkaya S, Öztekin D, Sağlam Purut C, et al. Hysteroscopy before repeated IUI in unexplained infertility: a randomized study. Pelviperineology. 2026;45(2):73-78

ABSTRACT

Objective: To evaluate whether diagnostic hysteroscopy performed before a third intrauterine insemination (IUI) cycle improves clinical pregnancy outcomes in women with unexplained infertility after two previous unsuccessful IUI attempts.

Materials and Methods: This prospective randomized controlled study included 100 women with unexplained infertility who had undergone two unsuccessful IUI cycles. Participants were randomly allocated into two groups. Women in the hysteroscopy group underwent diagnostic hysteroscopy before the third IUI cycle, whereas women in the control group proceeded directly to the third IUI cycle without hysteroscopic evaluation. The primary outcome was clinical pregnancy rate. Secondary outcomes included the detection of intrauterine pathology and procedure-related complications.

Results: Baseline demographic and clinical characteristics were comparable between the groups. Clinical pregnancy was achieved in 10 of 50 women in the hysteroscopy group and 9 of 50 women in the control group, corresponding to pregnancy rates of 20.0% and 18.0%, respectively. The difference was not statistically significant (p=0.79; relative risk: 1.11, 95% confidence interval: 0.52-2.36). Intrauterine pathology was detected in 3 women (6.0%) in the hysteroscopy group, all of whom had endometrial polyps that were resected during the same procedure. No major hysteroscopy-related complications were observed.

Conclusion: Routine diagnostic hysteroscopy before a repeated IUI cycle did not significantly improve clinical pregnancy rates in women with unexplained infertility and previous unsuccessful IUI attempts. Given the low rate of unsuspected intrauterine pathology in this population, hysteroscopy may be more appropriate as a selective rather than routine intervention, particularly in women with abnormal imaging findings or clinical suspicion of intrauterine pathology.

Keywords: Clinical pregnancy; endometrial polyp; hysteroscopy, intrauterine insemination; unexplained infertility

Address for Correspondence: Serhat Sarıkaya, Department of Obstetrics and Gynecology, University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, İzmir, Türkiye
E-mail: sarikayaserat@gmail.com **ORCID ID:** orcid.org/0009-0006-3593-6628
Received: 17 June 2026 **Accepted:** 28 July 2026 **Publication Date:** 04 August 2026

INTRODUCTION

Infertility affects approximately 10-15% of couples worldwide and remains a major clinical and psychosocial challenge despite advances in reproductive medicine.[1,2] Unexplained infertility represents a distinct subgroup in which no identifiable cause is detected after standard diagnostic evaluation, including confirmation of ovulation, tubal patency, and normal semen parameters. This condition accounts for approximately 10-15% of infertile couples and often creates uncertainty regarding the optimal sequence of diagnostic and therapeutic interventions.[3]

Intrauterine insemination (IUI), particularly when combined with ovarian stimulation, is widely used as a first-line treatment option for couples with unexplained infertility. Recent evidence-based guidance also supports IUI with ovarian stimulation as an appropriate first-line active treatment in this population.[4] However, pregnancy rates after IUI remain modest, and the probability of success may decrease after repeated unsuccessful cycles. Therefore, clinicians frequently consider additional diagnostic procedures before proceeding with further IUI attempts or before moving to more advanced assisted reproductive technologies such as in vitro fertilization (IVF).[5]

Assessment of the uterine cavity is an important component of infertility evaluation because intrauterine abnormalities, including endometrial polyps, submucosal fibroids, adhesions, and congenital uterine anomalies, may impair implantation and reduce pregnancy rates. Hysterosalpingography (HSG) is commonly used as an initial screening tool because it provides information about both tubal patency and the uterine cavity. Nevertheless, HSG has limitations in detecting subtle intracavitary lesions. In contrast, hysteroscopy allows direct visualization of the uterine cavity and offers the possibility of simultaneous treatment when pathology is identified.[6]

Previous studies in infertile women undergoing assisted reproductive treatment have reported that hysteroscopy may detect unsuspected intrauterine abnormalities even when previous imaging appears normal.[7,8] This has led some clinicians to advocate hysteroscopic evaluation before assisted reproductive treatment, particularly in patients with recurrent implantation failure or suspected uterine pathology. However, the clinical value of routine hysteroscopy in asymptomatic women with unexplained infertility remains uncertain. In the context of IUI, the potential benefit of detecting and treating occult uterine lesions must be balanced against the invasiveness, cost, discomfort, and resource utilization associated with the procedure.[9,10]

Data specifically evaluating the role of hysteroscopy before repeated IUI cycles are limited, and the routine use of hysteroscopy in this setting remains controversial. Therefore, the aim of the present randomized controlled study was to evaluate whether diagnostic hysteroscopy performed before a third IUI cycle improves clinical pregnancy outcomes in women with unexplained infertility who had previously undergone two unsuccessful IUI attempts.

MATERIALS AND METHODS

Study Design and Participants

This prospective randomized controlled study was conducted at a tertiary referral centre between May 2013 and December 2014. Ethical approval was obtained from the Local Institutional Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital with the approval number 03/05, dated 12.05.2013. All procedures were performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

A total of 100 women diagnosed with unexplained infertility were included in the study. Unexplained infertility was defined as the absence of an identifiable cause after standard infertility evaluation, including confirmation of ovulation, assessment of tubal patency, and semen analysis. Eligible women were between 20 and 38 years of age, had undergone at least two previous unsuccessful IUI cycles, had evidence of ovulation based on regular menstrual cycles and/or mid-luteal serum progesterone levels greater than 3 ng/mL, and had bilateral tubal patency confirmed by HSG. Male partners had normal semen parameters according to World Health Organization criteria.[11]

Patients with known intrauterine pathology, endometriosis, severe male factor infertility, previous uterine surgery, or systemic or endocrine disorders that could affect fertility were excluded.

Randomization and Study Groups

Eligible patients were randomly assigned in a 1:1 ratio to one of two groups using a computer-generated randomization sequence. Allocation concealment was ensured using sealed opaque envelopes. In Group A, patients underwent diagnostic hysteroscopy before the third IUI cycle. In Group B, patients proceeded directly to the third IUI cycle without hysteroscopic evaluation.

Hysteroscopy Procedure

In the hysteroscopy group, the procedure was performed during the early proliferative phase of the menstrual cycle, between cycle days 6 and 10. A rigid hysteroscope with an outer diameter

of approximately 4 mm was used, and normal saline served as the distension medium. The uterine cavity, endometrial surface, and tubal ostia were systematically evaluated.

When intrauterine abnormalities were detected, they were treated during the same session using operative hysteroscopic techniques. The procedure was performed under minimal analgesia when required.

Ovarian Stimulation and IUI Protocol

All patients in both groups underwent controlled ovarian stimulation with gonadotropins followed by hCG triggering. Gonadotropin stimulation was performed using human menopausal gonadotropin with individualized dosing.

Follicular development was monitored by transvaginal ultrasonography starting from cycle days 8-10. When at least one dominant follicle reached a mean diameter of 18 mm or greater, ovulation was triggered with an intramuscular injection of 5,000-10,000 IU human chorionic gonadotropin. IUI was performed 34-36 hours after ovulation trigger using prepared semen samples processed by standard density gradient centrifugation.

Outcome Measures

The primary outcome measure was the clinical pregnancy rate. Clinical pregnancy was defined as the presence of a gestational sac with fetal cardiac activity detected by transvaginal ultrasonography at 6-7 weeks of gestation. Pregnancy follow-up was limited to the confirmation of clinical pregnancy; therefore, miscarriage and live birth outcomes were not systematically recorded.

Secondary outcome measures included the detection and characterization of intrauterine pathology during hysteroscopy and procedure-related complications.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. The normality of distribution was assessed using the Kolmogorov-Smirnov test.

Comparisons between groups were performed using the independent samples t-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. In addition, the absolute risk difference and relative risk for clinical pregnancy were calculated with corresponding 95% confidence intervals (CIs). A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 women with unexplained infertility were enrolled and completed the study protocol. Patients were randomly assigned into two groups, with 50 women in the hysteroscopy group and 50 women in the control group. No dropouts or protocol deviations were recorded.

Baseline demographic and clinical characteristics were comparable between the two groups. There were no statistically significant differences in age, body mass index, duration or type of infertility, basal follicle-stimulating hormone levels, endometrial thickness, or dominant follicle count between the groups (Table 1). All patients in both groups received the same ovarian stimulation protocol with gonadotropins followed by hCG triggering; therefore, there was no difference between the groups regarding the stimulation protocol.

Table 1. Baseline demographic, infertility-related, and cycle characteristics of the study groups

	Group A (hysteroscopy + IUI) (n=50)	Group B (IUI only) (n=50)	*p*
Age (years)	29.8±4.2	30.1±4.5	0.72
BMI (kg/m²)	24.6±2.8	24.9±3.1	0.65
Duration of infertility (years)	3.2±1.1	3.4±1.3	0.58
Primary infertility, n (%)	32 (64.0%)	30 (60.0%)	0.68
Basal FSH (IU/L)	6.8±1.9	7.0±2.1	0.61
Endometrial thickness (mm)	8.7±1.2	8.5±1.3	0.47
Dominant follicle count	1.8±0.6	1.7±0.5	0.39

Values are presented as mean ± standard deviation or number (percentage), as appropriate. BMI: body mass index; IUI: intrauterine insemination; FSH: follicle-stimulating hormone

Clinical pregnancy was achieved in 10 of 50 women in the hysteroscopy group and in 9 of 50 women in the control group, corresponding to clinical pregnancy rates of 20.0% and 18.0%, respectively. The difference between the groups was not statistically significant (p=0.79). The absolute risk difference for clinical pregnancy was 2% (95% CI: -13% to 17%), and the relative risk of clinical pregnancy in the hysteroscopy group compared with the control group was 1.11 (95% CI: 0.52-2.36). Miscarriage and live birth outcomes were not analyzed because follow-up was limited to the confirmation of clinical pregnancy.

In the hysteroscopy group, intrauterine pathology was detected in 3 of 50 women (6.0%). All detected abnormalities were endometrial polyps and were resected during the same hysteroscopic procedure. No intrauterine adhesions, uterine septa, or submucosal fibroids were identified.

No major hysteroscopy-related complications, including uterine perforation, infection, or fluid overload, were observed. Because intrauterine pathology was detected in only three patients, subgroup analysis according to hysteroscopic findings was not performed.

DISCUSSION

In the present randomized controlled study, diagnostic hysteroscopy performed before a third IUI cycle did not significantly improve clinical pregnancy rates in women with unexplained infertility who had previously undergone two unsuccessful IUI attempts. Clinical pregnancy rates were similar between the hysteroscopy and control groups, and the relative risk estimate did not demonstrate a clinically meaningful benefit. These findings suggest that routine hysteroscopic evaluation before repeated IUI cycles may not provide additional reproductive benefit in women with unexplained infertility and no prior suspicion of intrauterine pathology.

The role of hysteroscopy in infertility management remains a matter of debate. Hysteroscopy is widely regarded as the most accurate method for direct evaluation of the uterine cavity because it allows both visualization and simultaneous treatment of intrauterine abnormalities.[6] However, whether this diagnostic advantage translates into improved reproductive outcomes in unselected infertile women is less certain. In patients with unexplained infertility, current evidence-based recommendations support IUI with ovarian stimulation as an appropriate first-line active treatment, while additional invasive diagnostic procedures should generally be individualized according to clinical findings and previous evaluation results.[4]

Previous studies in infertile women scheduled for assisted reproductive treatment have shown that office hysteroscopy may detect unsuspected intrauterine abnormalities even when conventional imaging findings are normal.[7] Reported rates of occult pathology vary widely, depending on patient selection, previous imaging methods, and whether the population includes women with recurrent implantation failure or other risk factors. In the present study, the prevalence of intrauterine pathology was low, with abnormalities detected in only 6.0% of women undergoing hysteroscopy. All detected lesions were endometrial polyps and were resected during the same procedure. This low rate of pathology may explain why routine hysteroscopy did not lead to a significant improvement in clinical pregnancy rates.

Endometrial polyps are among the most frequently reported intracavitary lesions in infertile women and may interfere with implantation through mechanical effects, altered endometrial receptivity, or local inflammatory changes.[12] In selected infertile women with identified polyps, hysteroscopic polypectomy has been associated with improved reproductive outcomes.[13] Similar observations have also been reported in assisted reproductive treatment populations after outpatient hysteroscopy.[14] Nevertheless, the potential benefit of polypectomy or hysteroscopic treatment should not be extrapolated to women with a normal uterine cavity or to routine hysteroscopic screening of all patients. In our cohort, the small number of detected polyps limited any possibility of subgroup analysis and suggests that the overall benefit of routine hysteroscopy in this setting would be small.

The available literature also supports a selective rather than routine approach to hysteroscopy before assisted reproductive treatment. Earlier reviews suggested that hysteroscopy might be useful before IVF, particularly in women with recurrent implantation failure or suspected uterine abnormalities.[15] An earlier systematic review and meta-analysis also suggested that hysteroscopy before the first IVF cycle might be associated with improved reproductive outcomes, although the authors emphasized the need for more robust randomized evidence.[16] However, subsequent large randomized trials have challenged the routine use of hysteroscopy in unselected patients. The inSIGHT trial reported that routine hysteroscopy before a first IVF cycle did not improve live birth rates in women with a normal transvaginal ultrasound of the uterine cavity.[17] Similarly, the TROPHY trial found no improvement in live birth rates after routine outpatient hysteroscopy in women with recurrent IVF failure and normal ultrasound findings.[18] Although these trials were conducted in IVF populations rather than IUI populations, they reinforce the broader concept that routine hysteroscopy is unlikely to improve reproductive outcomes when there is no clinical or imaging suspicion of intrauterine disease.

Evidence specifically addressing screening hysteroscopy before IUI remains limited, and current systematic review data do not provide high-certainty support for its routine use in unselected patients.[10] This is consistent with our findings and supports an individualized approach. Patients with abnormal HSG or ultrasound findings, abnormal uterine bleeding, previous intrauterine surgery, recurrent pregnancy loss, or a strong clinical suspicion of intracavitary pathology may still benefit from hysteroscopic evaluation.

The present study has several strengths. Its randomized design reduced selection bias, and the study population was relatively homogeneous, consisting of women with unexplained infertility who had already undergone two unsuccessful IUI cycles. In addition, all patients completed the study protocol, and both groups were comparable in baseline demographic and clinical characteristics. These features strengthen the internal validity of the findings.

Study Limitations

However, several limitations should also be acknowledged. First, the sample size was relatively small and may not have been sufficient to detect small differences in clinical pregnancy rates. Second, the study was conducted at a single tertiary centre, which may limit the generalizability of the findings. Third, miscarriage and live birth outcomes were not systematically recorded because some pregnancies were followed in other centers. Therefore, follow-up was limited to the confirmation of clinical pregnancy. This should be considered an important limitation, since live birth represents the most clinically meaningful reproductive outcome. Fourth, the prevalence of intrauterine pathology was low, preventing meaningful subgroup analysis of women with detected abnormalities. Finally, although the study evaluated clinical pregnancy after the third IUI cycle, it did not assess cumulative pregnancy outcomes over subsequent treatment cycles.

CONCLUSION

In conclusion, routine diagnostic hysteroscopy before a repeated IUI cycle did not significantly improve clinical pregnancy rates in women with unexplained infertility and two previous unsuccessful IUI attempts. Given the low prevalence of unsuspected intrauterine pathology and the absence of a measurable reproductive benefit, hysteroscopy should not be considered mandatory before repeated IUI in patients with normal prior evaluation. Instead, it appears more appropriate as a selective intervention for women with abnormal imaging findings, clinical suspicion of intrauterine pathology, or other risk factors that may justify direct uterine cavity assessment.

ETHICS

Ethics Committee Approval: This prospective randomized controlled study was conducted at a tertiary referral centre between May 2013 and December 2014. Ethical approval was obtained from the Local Institutional Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital with the approval number 03/05, dated 12.05.2013. All procedures were performed in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants prior to enrolment.

FOOTNOTES

Contributions

Surgical and Medical Practices: S.S., D.Ö., C.S.P., G.H.D., A.D.T., Y.E.P., A.K., Concept: S.S., D.Ö., Y.E.P., Design: S.S., D.Ö., C.S.P., Data Collection or Processing: S.S., G.H.D., A.D.T., A.K., Analysis or Interpretation: S.S., D.Ö., C.S.P., Y.E.P., Literature Search: S.S., G.H.D., A.D.T., Writing: S.S., D.Ö., C.S.P., Critical Review: D.Ö., Y.E.P., A.K.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, et al.; International Committee for Monitoring Assisted Reproductive Technology; World Health Organization. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. Fertil Steril. 2009; 92: 1520-4.
2. Practice Committee of the American Society for Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. Fertil Steril. 2015; 103: e44-50.
3. Crosignani PG, Rubin BL. Optimal use of infertility diagnostic tests and treatments. The ESHRE Capri Workshop Group. Hum Reprod. 2000; 15: 723-32.
4. Guideline Group on Unexplained Infertility; Romualdi D, Ata B, et al. Evidence-based guideline: unexplained infertility†. Hum Reprod. 2023; 38: 1881-90.
5. Cohlen BJ. Should we continue performing intrauterine inseminations in the year 2004? Gynecol Obstet Invest. 2005; 59: 3-13.
6. Bettocchi S, Selvaggi L. A vaginoscopic approach to reduce the pain of office hysteroscopy. J Am Assoc Gynecol Laparosc. 1997; 4: 255-8.

7. Fatemi HM, Kasius JC, Timmermans A, et al. Prevalence of unsuspected uterine cavity abnormalities diagnosed by office hysteroscopy prior to in vitro fertilization. Hum Reprod. 2010; 25: 1959-65.
8. Bahadur A, Malhotra N, Singh N, Gurunath S, Mittal S. Comparative study on the role of diagnostic hysteroscopy in evaluation of the uterine cavity prior to in vitro fertilization in a developing country. Arch Gynecol Obstet. 2013; 288: 1137-43.
9. Bosteels J, van Wessel S, Weyers S, et al. Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities. Cochrane Database Syst Rev. 2018; 12: CD009461.
10. Kamath MS, Bosteels J, D'Hooghe TM, et al. Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. Cochrane Database Syst Rev. 2019; 4: CD012856.
11. World Health Organization. WHO laboratory manual for the examination and processing of human semen. 5th ed. Geneva: World Health Organization; 2010.
12. Pérez-Medina T, Bajo-Arenas J, Salazar F, et al. Endometrial polyps and their implication in the pregnancy rates of patients undergoing intrauterine insemination: a prospective, randomized study. Hum Reprod. 2005; 20: 1632-5.
13. Shokeir TA, Shalan HM, El-Shafei MM. Significance of endometrial polyps detected hysteroscopically in eumenorrheic infertile women. J Obstet Gynaecol Res. 2004; 30: 84-9.
14. El-Toukhy T, Sunkara SK, Coomarasamy A, Grace J, Khalaf Y. Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis. Reprod Biomed Online. 2008; 16: 712-9.
15. Pundir J, El Toukhy T. Uterine cavity assessment prior to IVF. Womens Health (Lond). 2010; 6: 841-7.
16. Pundir J, Pundir V, Omanwa K, Khalaf Y, El-Toukhy T. Hysteroscopy prior to the first IVF cycle: a systematic review and meta-analysis. Reprod Biomed Online. 2014; 28: 151-61.
17. Smit JG, Kasius JC, Eijkemans MJC, et al. Hysteroscopy before in-vitro fertilisation (inSIGHT): a multicentre, randomised controlled trial. Lancet. 2016; 387: 2622-9.
18. El-Toukhy T, Campo R, Khalaf Y, et al. Hysteroscopy in recurrent in-vitro fertilisation failure (TROPHY): a multicentre, randomised controlled trial. Lancet. 2016; 387: 2614-21.