

Effect of the decision to perform hysteroscopy on asymptomatic patients before undergoing assisted reproduction technologies—a systematic review and meta-analysis



Greg J. Marchand, MD, FACS, FICS, FACOG; Ahmed Taher Masoud, MD; Hollie Ulibarri, BS; Julia Parise, BS; Amanda Arroyo, BS; Catherine Coriell, BS; Sydnee Goetz, BS; Carmen Moir, BS; Atley Moberly, BS

OBJECTIVE: Routine hysteroscopic evaluation before assisted reproductive technology treatment is a novel approach with the potential to reduce assisted reproductive technology failure even in the absence of evidence of uterine pathology. Following the publication of several relatively high-quality trials on this topic, we sought to determine if this practice is beneficial.

DATA SOURCES: We searched Web of Science, MEDLINE, PubMed, Scopus, Cochrane Library, and ClinicalTrials.gov from each database's inception until May 31, 2022 with our search strategy, attempting to locate all randomized controlled trials assessing the use of hysteroscopy in otherwise asymptomatic women undergoing assisted reproductive technology.

STUDY ELIGIBILITY CRITERIA: We included only randomized controlled trials that included at least one of our selected outcomes, and we excluded any studies with suspicion of pathology before the time of hysteroscopy, other than knowledge of the patient's infertility. We included all the aforementioned studies regardless of procedures or modifications performed as a result of hysteroscopic findings. Our initial search yielded 1802 results, which were reduced to 1421 after removal of duplicates. Ultimately, 11 studies were found to meet our criteria and were included in our quantitative synthesis.

METHODS: We used ReviewManager software, version 5.4.1 to analyze the data, which we imported after manually gathering from the 11 studies. Continuous and dichotomous outcomes were imported as standard deviations. Pooled analysis was described as a mean difference, relative to 95 % confidence interval in cases of continuous data. Dichotomous outcomes were analyzed using risk ratios and 95% confidence intervals. In homogeneous outcomes, we used a fixed-effects model, and in heterogeneous outcomes we used a random-effects model.

RESULTS: Our results showed that hysteroscopy was associated with significant improvement in the clinical pregnancy rate (risk ratio, 1.27 [1.11–1.45]; $P<.001$). We found no differences between the hysteroscopy group and the control group in live birth rate (risk ratio, 1.26 [0.99–1.59]; $P=.06$), miscarriage rate (risk ratio, 0.99 [0.81–1.19]; $P=.88$), fertilization rate (risk ratio, 1.01 [0.93–1.09]; $P=.88$), incidence of multiple gestations (risk ratio, 1.29 [0.98–1.71]; $P=.07$), number of embryos transferred (mean difference, 0.04 [–0.18 to 0.26]; $P=.73$), chemical pregnancy rate (risk ratio, 1.01 [0.86–1.17]; $P=.93$), and number of oocytes retrieved (mean difference, 0.44 [–0.11 to 0.98]; $P=.11$).

CONCLUSION: We observed an improvement in the clinical pregnancy rate, but no significant improvement in the live birth rate with routine hysteroscopy before assisted reproductive technology treatment. We believe this does not represent sufficient evidence to recommend routine hysteroscopy for otherwise asymptomatic patients before assisted reproductive technology treatment at this time.

Key words: assisted reproductive technology, hysteroscopy, infertility, in vitro fertilization

From the Faculty of Medicine, Marchand Institute for Minimally Invasive Surgery, Mesa, AZ (Drs Marchand and Masoud, Mses Ulibarri, Parise, and Arroyo, Ms Coriell, and Mses Goetz, Moir, and Moberly); and Faculty of Medicine, Fayoum University, Fayoum, Egypt (Dr Masoud).

The authors report no conflict of interest.

The authors report no funding for this study.

This study was exempt from institutional review board (IRB) review by the Marchand Institute for Minimally Invasive Surgery IRB (January 2022), and was exempt from consent requirements because it is a systematic review, retrospectively examining previously published data.

Although we were influenced by the questions of our patients to theorize this analysis, no patients or members of the public were involved in the study, and the protocols described in the Cochrane Manual and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analysis Of Observational Studies in Epidemiology) checklists were meticulously followed.

The Marchand Institute for Minimally Invasive Surgery remains committed to diversity and tolerance in its research and actively maintains a workplace free of racism and sexism. More than half of the authors for this study are female, and many represent diverse backgrounds and underrepresented ethnic groups.

The study was registered on the International Prospective Register of Systematic Reviews (registration number: CRD42022309631).

Corresponding author: Greg J. Marchand, MD, FACS, FACOG, FICS. gm@marchandinstitute.org

2666-5778/\$36.00

© 2023 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

<http://dx.doi.org/10.1016/j.xagr.2023.100178>

AJOG Global Reports at a Glance

Why was this study conducted?

A: Despite no widely accepted guideline, our researchers noticed the publication of many studies where reproductive endocrinologists would routinely perform hysteroscopy prior to assisted reproduction technologies, such as in vitro fertilization, on asymptomatic patients with no identified pathology. As a result we sought out to find if evidence existed of a benefit to this practice.

Key findings

A: The decision to perform hysteroscopy prior to assisted reproduction technologies seems to be associated with a higher clinical pregnancy rate, but no difference was seen in the rates of live birth, the miscarriages rate, the incidence of multiple gestations or the chemical pregnancy rate.

What does this add to what is known?

This study does not definitively show benefit to the routine practice of hysteroscopy prior to assisted reproduction technologies, but adds to the body of evidence suggesting that there may be some improvement with this practice, as evidenced by the increased rate in clinical pregnancies.

Introduction

Infertility, defined as the inability to achieve pregnancy after 1 year of unprotected, timed intercourse, can result in severe psychological, mental, and even medical disease for patients.^{1,2} It affects approximately 37% of couples worldwide, and originates from the male factor in 57% of cases, from the female factor in 35%, and from both in the remaining 8%.³ The most common causes of female-factor infertility include tubal blockage, ovulatory disorders, endometriosis, tubal abnormalities, uterine abnormalities, and hormonal disorders.⁴ A basic workup for infertility may include assessment of semen, ovarian reserve and function, the uterine cavity, the patency of the fallopian tubes, and endocrinology.⁵ Regarding the assessment of the uterine cavity, several options exist, including ultrasonography, hysterosalpingography, and hysteroscopy.⁶ Some clinicians may also choose to forgo the assessment in asymptomatic women.⁶ Although invasive, hysteroscopy provides the surgeon the possibility of immediate surgical repair of discovered pathology, which may include endometrial polyps, leiomyomas, septums, or other intra-uterine pathology.^{7–9} In the recent months, we noticed several relatively high-quality randomized controlled trials (RCTs) published on the topic of performing hysteroscopy before assisted

reproductive technology (ART) treatment in otherwise asymptomatic women. Thus, in this meta-analysis we sought to estimate the efficacy of performing hysteroscopy before ART application in improving the outcomes of the different ART techniques in infertile patients, and any resulting treatments or treatment plan modifications made as a result of the findings of that hysteroscopy.

Methods**Search strategy**

This study was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.¹⁰ We conducted our search in electronic databases, including Web of Science, MEDLINE, PubMed, Scopus, Cochrane Library, and ClinicalTrials.gov, from the inception of each database until May 31, 2022 using the following strategy: (Infertility OR Sterility OR Subfertility OR Sub-Fertility) AND (Hysteroscop* OR “Uterine Endoscopy” OR ureteroscopy) AND (“live birth” OR “pregnancy rate” OR miscarriage).

Study selection

Two authors performed title and abstract screening followed by full-text screening. This process was performed according to the following eligibility criteria:

- Population: infertile women undergoing any ART technique.
- Intervention: hysteroscopy in otherwise asymptomatic women.
- Comparator: control group.
- Outcomes: clinical pregnancy rate (defined as ultrasound and serologic confirmation of intrauterine pregnancy), live birth rate per cycle, miscarriage rate, fertilization rate, multiple pregnancies, number of transferred embryos, chemical pregnancy rate, and number of oocytes retrieved.
- Study design: we included RCTs only and excluded all other study designs, meta-analyses, and reviews.

Quality assessment

We evaluated the risk of bias of the included RCTs according to the Cochrane Handbook for Systematic Reviews of Interventions.¹¹ We assessed 7 domains in each study: (1) random sequence generation; (2) selective reporting; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) allocation concealment; and (7) other biases.

Data extraction

Data were retrieved manually from the included studies and placed into spreadsheets. We extracted baseline data such as the demographic data of patients, the number of patients with primary infertility, the number of patients with secondary infertility, the duration of infertility, and the causes of infertility. Then, we extracted the following outcomes: clinical pregnancy rate, live birth rate per cycle, miscarriage rate, fertilization rate, multiple pregnancies, number of transferred embryos, chemical pregnancy rate, and number of oocytes retrieved. We also extracted additional data that were required to complete our quality assessment of the included studies.

Statistical analysis

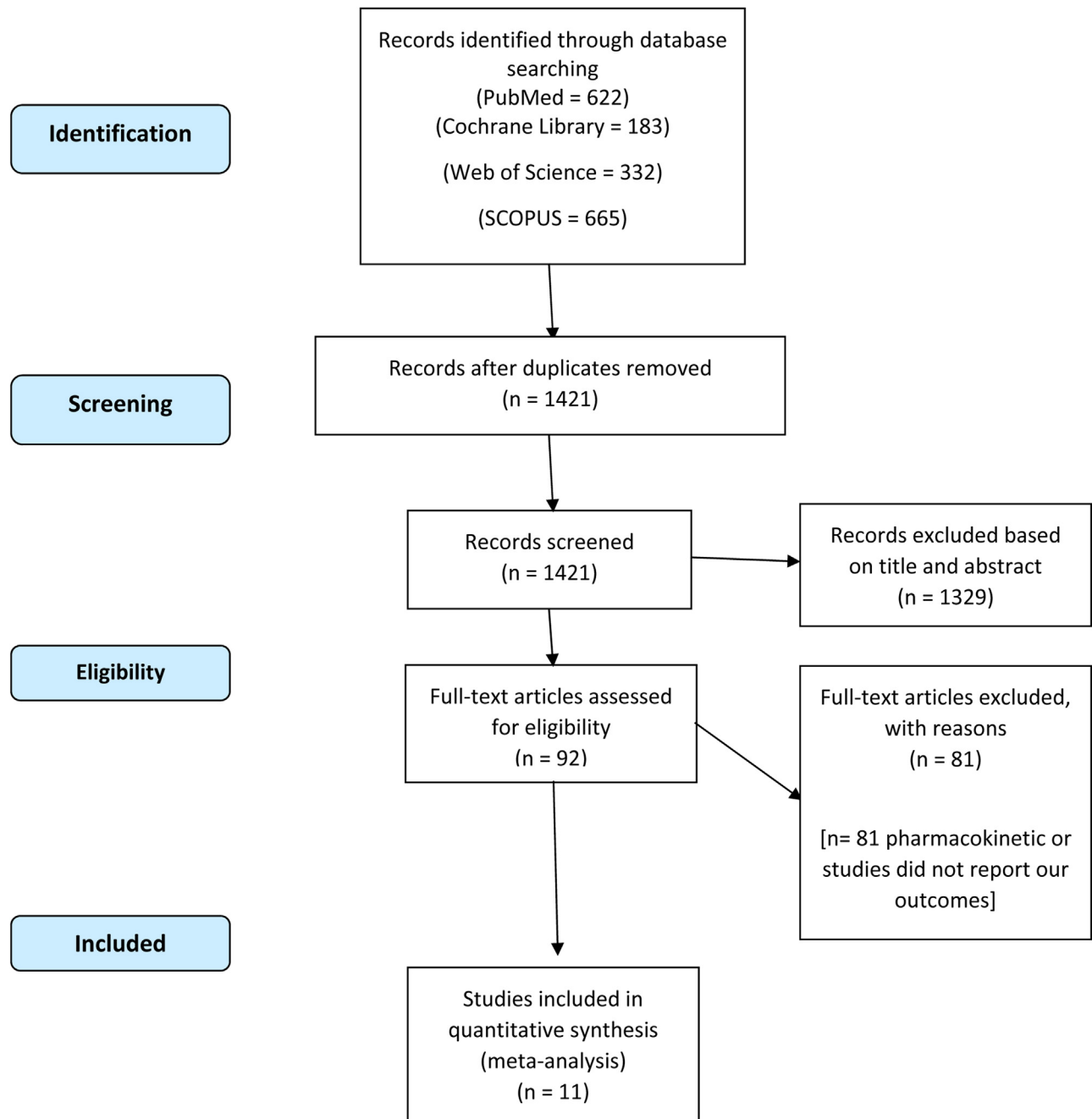
We used ReviewManager (RevMan) software, version 5.4.1 (Cochrane, London, United Kingdom) to analyze the data. Continuous and dichotomous

outcomes were imported from the spreadsheet into the RevMan software as mean±standard deviation and percentage and total, respectively. Pooled analysis was described as mean difference (MD), relative to 95% confidence

interval (CI) in cases of continuous data, and dichotomous data were analyzed using risk ratio (RR) and 95% CI. In homogeneous outcomes, we used a fixed-effects model, whereas heterogeneous outcomes were analyzed under

the random-effects model. We measured heterogeneity among studies using I-squared (Higgins I^2). Outcomes with $I^2 > 50\%$ or $P < .1$ in the pooled analysis were considered heterogeneous.^{12,13}

FIGURE 1
PRISMA flow diagram of our literature search



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. *Am J Obstet Gynecol Glob Rep* 2023.

TABLE 1
Demographic data of included patients

Study ID	Sample size		Age, y, mean (SD)		BMI, mean (SD)	
	Hysteroscopy	Control	Hysteroscopy	Control	Hysteroscopy	Control
Alleyassin et al, ¹⁴ 2017	110	110	29.5 (3.8)	29.1 (4.3)	25.47 (3.71)	25.6 (3.7)
Ben Abid et al, ¹⁶ 2021	84	87	32.3 (4.4)	32.3 (5.1)	NR	NR
Demiroglu and Gurgan, ¹⁵ 2004	211	211	35.8 (0.4)	34.3 (0.8)	NR	NR
El-nashar and Nasr, ¹⁷ 2011	62	62	NR	NR	NR	NR
Elsetohy et al, ¹⁸ 2015	102	101	31.1 (5.8)	29.9 (4.8)	29.1 (5.0)	29.5 (5.8)
El-Toukhy et al, ¹⁹ 2016	350	352	33 (0.685)	33 (0.686)	22.875 (1)	22.85 (0.8)
Ghasemi et al, ²⁰ 2022	123	125	29.9 (3.8)	30.5 (4.2)	24.19 (2.8)	23.9 (3.5)
Kilic et al, ²¹ 2013	100	398	31.9 (3.4)	31.4 (3.2)	NR	NR
Moramezi et al, ²² 2012	55	33	28.8 (3)	29.8 (3)	23.99 (0.59)	24 (0.69)
Rama Raju et al, ²³ 2006	255	265	28.2 (0.76)	26.7 (0.5)	22.9 (0.56)	26.7 (0.1)
Smit et al, ²⁴ 2016	369	373	33 (4.4)	33 (4.5)	25 (4.2)	24 (4.3)

BMI, body mass index; NR, not reported; SD, standard deviation.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

Results

Summary of the included studies

The PRISMA flow diagram of our search is shown in Figure 1. We analyzed 3938 infertile women from 11 included RCTs^{14–24}; 1821 patients underwent hysteroscopy, whereas 2117 patients were allocated to the control group. The

2 groups were found to be similar in sample size, age, and body mass index. The demographic data of patients, the number of patients with primary infertility, the number of patients with secondary infertility, the duration of infertility, and the causes of infertility are described in Tables 1–3.

Results of the quality assessment

The quality assessment of the included trials yielded an overall moderate risk of bias. Concerning the randomization domain, all studies reported proper randomization, so they were categorized as having low risk of bias except Kilic et al,²¹ which was categorized as at high

TABLE 2
Patients with primary and secondary infertility, and the duration of infertility

Study ID	Primary infertility, n (%)		Secondary infertility, n (%)		Duration of infertility, y, mean (SD)	
	Hysteroscopy	Control	Hysteroscopy	Control	Hysteroscopy	Control
Alleyassin et al, ¹⁴ 2017	NR	NR	NR	NR	4.74 (3.44)	4.59 (3.25)
Ben Abid et al, ¹⁶ 2021	77 (91.7)	76 (87.4)	7 (8.3)	11 (12.6)	4.28 (2.99)	4.75 (3.43)
Demiroglu and Gurgan, ¹⁵ 2004	NR	NR	NR	NR	6.1 (0.4)	6.2 (0.3)
El-nashar and Nasr, ¹⁷ 2011	NR	NR	NR	NR	NR	NR
Elsetohy et al, ¹⁸ 2015	58 (59.8)	65 (67.7)	39 (40.2)	31 (32.3)	5.9 (3.7)	5.7 (3.4)
El-Toukhy et al, ¹⁹ 2016	NR	NR	NR	NR	4 (0.34)	3.75 (0.5)
Ghasemi et al, ²⁰ 2022	NR	NR	NR	NR	NR	NR
Kilic et al, ²¹ 2013	NR	NR	NR	NR	7	6
Moramezi et al, ²² 2012	NR	NR	NR	NR	3.7 (0.49)	4.4 (0.57)
Rama Raju et al, ²³ 2006	NR	NR	NR	NR	7.03 (0.62)	7.01 (0.10)
Smit et al, ²⁴ 2016	NR	NR	NR	NR	2.6 (1.9)	2.1 (2.7)

NR, not reported; SD, standard deviation.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

TABLE 3
Causes of infertility in included patients

Study ID	Cause of infertility, %							
	Male factor		Ovulatory disorder		Tubal/peritoneal factor		Unexplained	
	Hysteroscopy	Control	Hysteroscopy	Control	Hysteroscopy	Control	Hysteroscopy	Control
Alleyassin et al, ¹⁴ 2017	37 (33.6)	32 (29.1)	33 (30)	35 (32.1)	22 (20.1)	26 (23.5)	18 (16.3)	17 (15.3)
Ben Abid et al, ¹⁶ 2021	70 (83.33)	75 (86.2)	NR	NR	7 (8.33)	2 (2.29)	2 (2.38)	4 (4.59)
Demiroglu and Gurgan, ¹⁵ 2004	62 (29)	50 (24)	66 (31)	74 (35)	NR	NR	40	87 (41)
El-nashar and Nasr, ¹⁷ 2011	NR	NR	NR	NR	NR	NR	NR	NR
Elsetohy et al, ¹⁸ 2015	48 (49.5)	51 (53.1)	15 (15.5)	17 (17.7)	27 (27.8)	25 (26)	21 (21.6)	19 (19.8)
El-Toukhy et al, ¹⁹ 2016	157 (45%)	159 (45%)	21 (6%)	26 (7%)	61 (17%)	53 (15%)	52 (15%)	62 (18%)
Ghasemi et al, ²⁰ 2022	NR	NR	NR	NR	NR	NR	NR	NR
Kilic et al, ²¹ 2013	43 (43%)	173 (43%)	6 (6%)	31 (8%)	7 (7%)	37 (9%)	44 (44%)	157 (40%)
Moramezi et al, ²² 2012	45 (80%)	36 (69.1%)	NR	NR	NR	NR	8 (14.8%)	15 (27.3%)
Rama Raju et al, ²³ 2006	NR	NR	NR	NR	NR	NR	NR	NR
Smit- et al, ²⁴ 2016	209 (57%)	193 (52%)	NR	NR	32 (9%)	40 (11%)	112 (30%)	104 (28%)

NR, not reported.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

risk of bias. Regarding attrition and reporting bias, all studies were categorized as having low risk of bias. The full results of our assessment of quality are illustrated in Figure 2.

Analysis of outcomes

Clinical pregnancy rate. Most studies reported this outcome^{14–20,22–24}; 8 RCTs were conducted in 1 center and were allocated to the first subgroup (unicenter subgroup). The overall RR showed that hysteroscopy significantly increased the clinical pregnancy rate compared with the control group (RR, 1.41 [1.26–1.59]; $P<.001$). Data were homogeneous ($P=.57$; $I^2=0\%$) (Figure 3, A).

Regarding the multicenter subgroup, data from 2 trials were analyzed. The combined RR did not show any difference between the hysteroscopy and the control group (RR, 1.04 [0.93–1.16]; $P=.53$). Pooled analysis was homogeneous ($P=.68$; $I^2=0\%$) (Figure 3, B).

The combined analysis of all trials from both subgroups favored the hysteroscopy group over the control group (RR, 1.27 [1.11–1.45]; $P<.001$) (Figure 3, C).

Live birth rate per cycle. Five studies reported the live birth rate as an

outcome.^{16,19–21,23} The overall RR showed no significant difference between the 2 groups (RR, 1.26 [0.99–1.59]; $P=.06$). Data were heterogeneous ($P=.06$; $I^2=56\%$) (Figure 4, A). We were able to solve the heterogeneity by excluding Raju et al²³ ($P=0.27$; $I^2=23\%$). The combined analysis after solving the heterogeneity also showed similar live birth rates between the 2 groups (RR, 1.13 [0.93–1.38]; $P=.22$) (Figure 4, B).

Miscarriage rate. Data on the miscarriage rate were retrieved from 5 studies.^{14–16,23,24} We found no significant difference between the hysteroscopy and the control group (RR, 0.99 [0.81–1.19]; $P=.88$). Pooled analysis was homogeneous ($P=.48$; $I^2=0\%$) (Figure 5).

Fertilization rate. Three studies reported the fertilization rate.^{14,15,18} The overall RR showed a similar fertilization rate in both groups (RR, 1.01 [0.93–1.09]; $P=.88$). The overall analysis was homogeneous ($P=.78$; $I^2=0\%$) (Figure 6).

Multiple pregnancy. Four studies^{14,16,23,24} reported the outcome of multiple

pregnancy. The combined analysis showed no difference between the hysteroscopy and the control group (RR, 1.29 [0.98–1.71]; $P=.07$). Data were homogeneous ($P=.60$; $I^2=0\%$) (Figure 7).

Number of transferred embryos. Four studies reported data on the number of transferred embryos. We found no variation between the 2 groups (MD, 0.04 [–0.18 to 0.26]; $P=.73$). The overall MD was initially heterogeneous ($P=.002$; $I^2=80\%$) (Figure 8, A). To solve the heterogeneity among studies, we excluded Alleyassin et al¹⁴ ($P=.68$; $I^2=0\%$). The combined MD after solving the heterogeneity also showed a similar number of transferred embryos in both groups (MD, –0.06 [–0.19 to 0.06]; $P=.31$) (Figure 8, B).

Chemical pregnancy rate. This outcome was reported by 2 studies.^{19,20} Pooled analysis showed no significant variation between the 2 groups (RR, 1.01 [0.86–1.17]; $P=.93$). The overall RR was homogeneous ($P=.18$; $I^2=44\%$) (Figure 9).

Number of oocytes retrieved. The number of oocytes retrieved from patients

FIGURE 2
Full results of our quality assessments of the included studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Alleyassin 2016	+	+	?	+	+	+	+
Benabid 2021	+	-	-	?	+	+	+
Demiroglu 2004	+	-	?	+	+	+	+
El-nashar 2011	+	?	?	?	+	+	+
Elsetohy 2014	+	+	?	-	+	+	+
El-toukhy 2016	+	+	-	+	+	+	+
Ghasemi 2022	+	-	-	?	+	+	+
Kilic 2012	-	?	-	-	+	+	+
Moramezi 2012	+	?	?	?	+	+	+
Rama Raju 2006	+	?	?	?	+	+	+
Smit 2016	+	+	-	-	+	+	+

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. *Am J Obstet Gynecol Glob Rep* 2023.

was similar in both groups (MD, 0.44 [-0.11 to 0.98]; $P=.11$). Pooled data were homogeneous ($P=.57$; $I^2=0\%$) (Figure 10).

Discussion

In this meta-analysis, we sought to determine whether hysteroscopy could increase the success rates of ARTs such

as in vitro fertilization (IVF), intracytoplasmic sperm injection, and intrauterine insemination. Our analysis demonstrated that performing hysteroscopy before the different assisted conception techniques could increase the clinical pregnancy rate significantly. However, hysteroscopy did not improve the live birth rate, miscarriage rate,

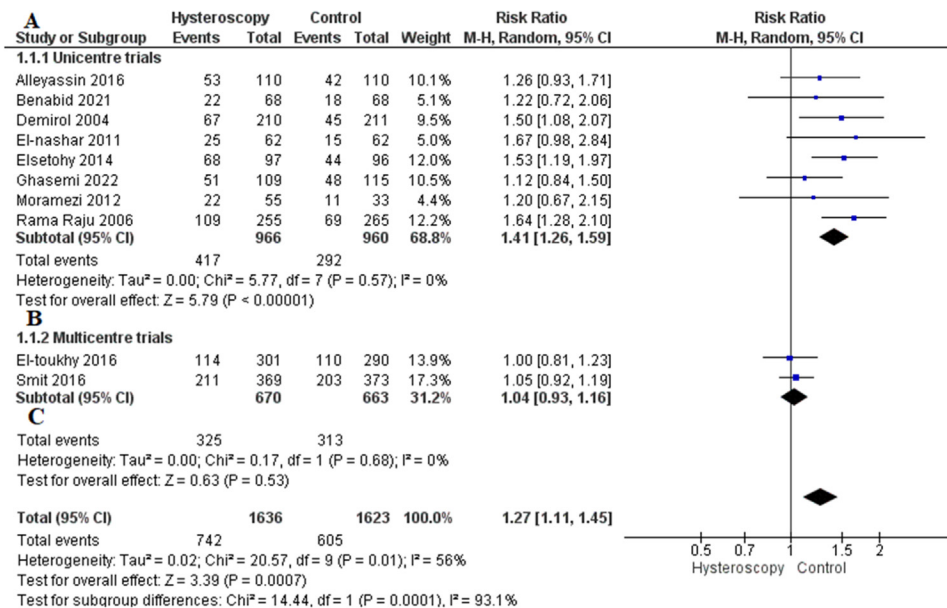
fertilization rate, chemical pregnancy rate, multiple pregnancy, number of transferred embryos, or number of oocytes retrieved.

It is notable that a statistically significant difference in the clinical pregnancy rate was observed when performing hysteroscopy before ART, but this did not result in a statistically significant difference in the live birth rate, a result that the authors cannot completely explain. Multiple conditions were diagnosed and treated in the study arms that included hysteroscopy before ART. These treatments included hysteroscopic polypectomy, hysteroscopic myomectomy, lysis of adhesions, and medical treatment for endometritis diagnosed at time of hysteroscopy. One possible explanation for this phenomenon would be the persistence of pathology that would have otherwise prevented implantation later resulting in miscarriage as a result of the inability of our current treatments to truly resolve the condition. Statistically speaking, if this was true for even one of the pathologies, it would explain the lack of significance in the clinical pregnancy data. Another possible explanation is that many patients suffer from >1 pathology, and that after treating a cause found on hysteroscopy (polyps, fibroids, adhesions, endometritis), a second pathology (eg, genetic) then results in miscarriage.

Many previous analyses have found similar results. In 2008, El-Toukhy et al²⁵ conducted a meta-analysis that was limited to office hysteroscopy but otherwise considered similar outcomes, and found improvements in almost all outcomes with routine hysteroscopy. They attributed this beneficial role to the ability of hysteroscopy to visualize and treat intrauterine abnormalities including polyps, fibroids, endometritis, and intrauterine adhesions. In researching the percentage of female patients suffering from hysteroscopically correctable uterine pathology, we found several authors estimating that such pathologies are found at the time of hysteroscopy in approximately 50%.^{26–28}

Endometritis in particular was of interest in many of these studies because many authors have previously referenced the increased sensitivity of hysteroscopic

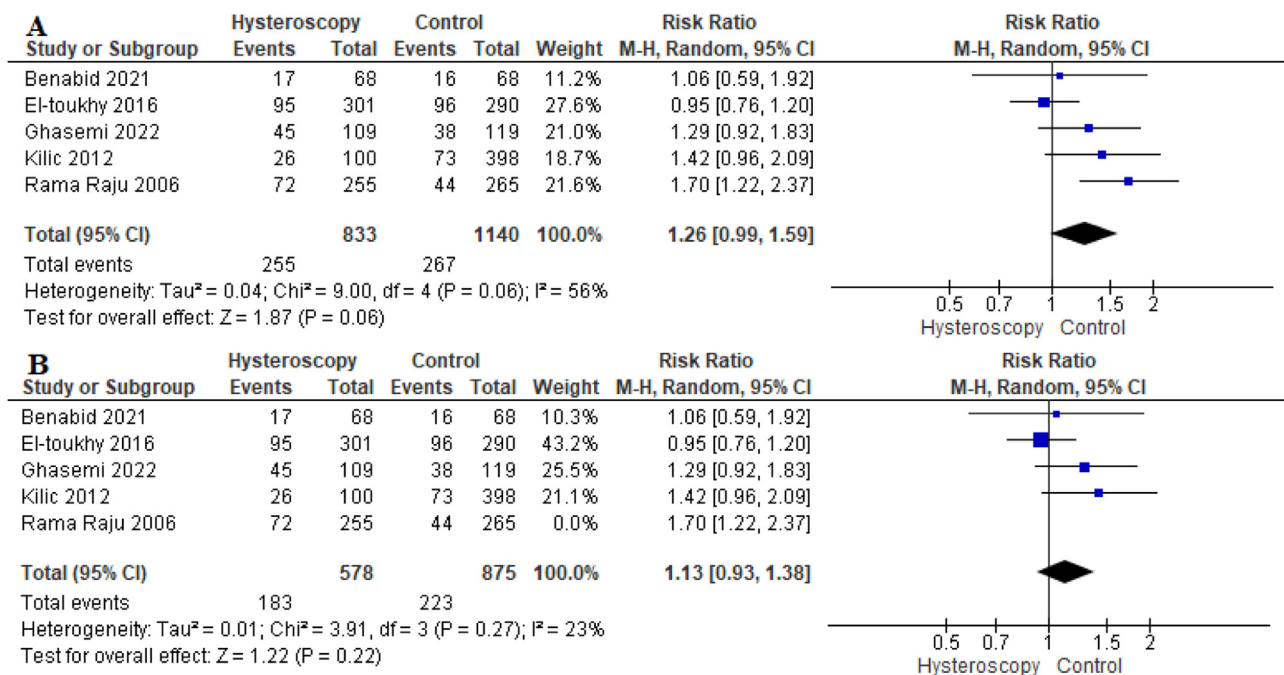
FIGURE 3
Forest plot of the outcome of rate of clinical pregnancy



CI, confidence interval; M-H, Mantel-Haenszel.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

FIGURE 4
Forest plot of the live birth rate per cycle



CI, confidence interval; M-H, Mantel-Haenszel.

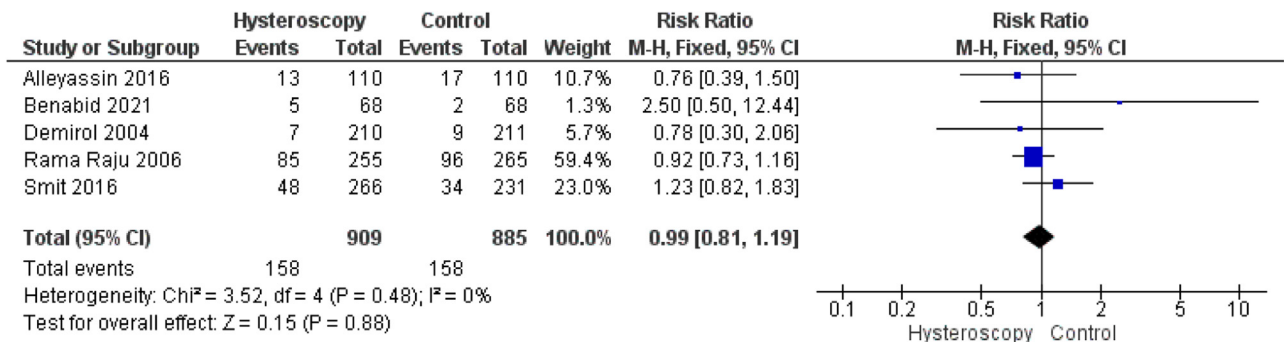
Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

visualization over ultrasound in the diagnosis of chronic endometritis, with some sources citing a >33% increase in sensitivity.^{29,30} This would lead to greater

opportunity for the use of antimicrobial treatments for chronic endometritis in infertile patients given that chronic endometritis is estimated to be a cause in

up to 40% of women suffering from infertility worldwide.³⁰

Another previous meta-analysis by Chung et al³¹ from 2006 concluded that

FIGURE 5
Forest plot of the miscarriage rate

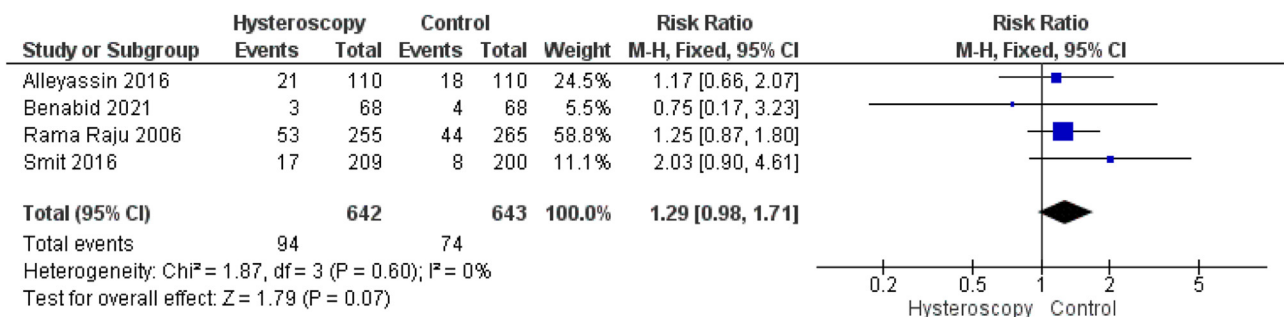
CI, confidence interval; M-H, Mantel-Haenszel.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

FIGURE 6
Forest plot of the fertilization rate

CI, confidence interval; M-H, Mantel-Haenszel.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

FIGURE 7
Forest plot of the rate of multiple pregnancy

CI, confidence interval; M-H, Mantel-Haenszel.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

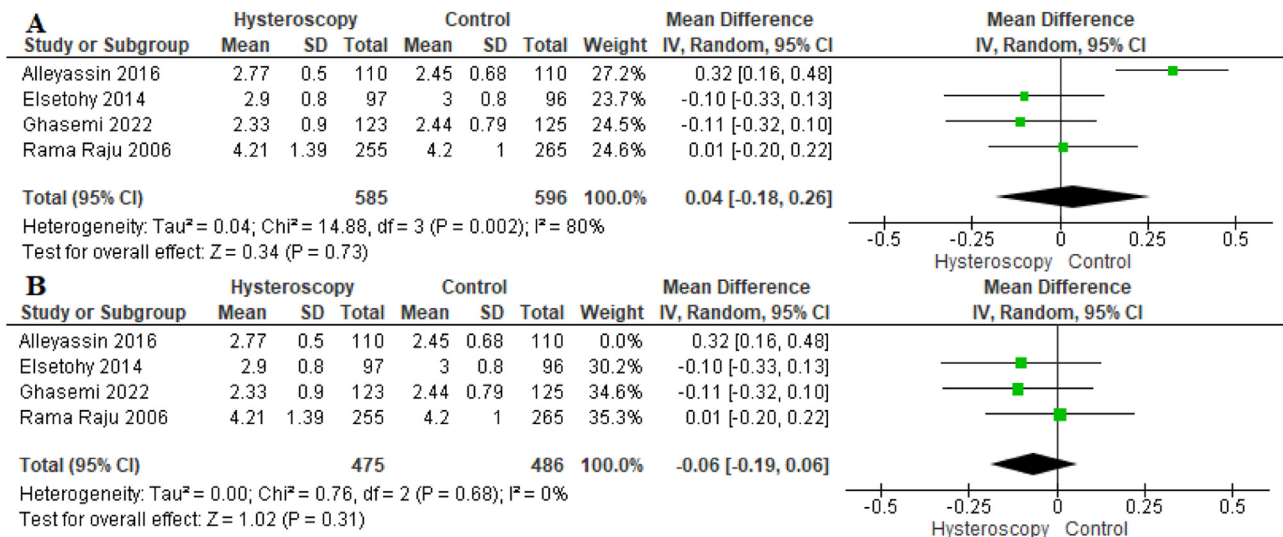
hysteroscopy could improve IVF outcomes in patients regardless of the presence of hysteroscopic uterine abnormalities. This study, however, was limited to patients who had repeated failures of ARTs as opposed to the routine practice of hysteroscopy.

In more recent reviews, Pundir et al³² in 2014 performed a meta-analysis of 6 studies evaluating the efficacy of routine hysteroscopy before the first IVF cycle in infertile women. They concluded that hysteroscopy could significantly increase the clinical pregnancy rate (RR,

1.44; $P=.01$). Although consistent with our findings, this study was limited by significant heterogeneity in all outcomes. In addition, only 1 of the 6 included studies was randomized.

Before this study, the most recent analysis by Mao et al³³ in 2019 included

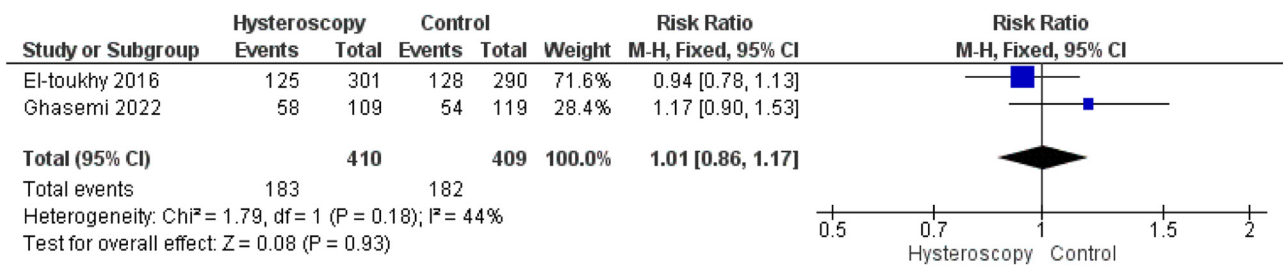
FIGURE 8
Forest plot of the number of embryos transferred



CI, confidence interval; IV, inverse variance; SD, standard deviation.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

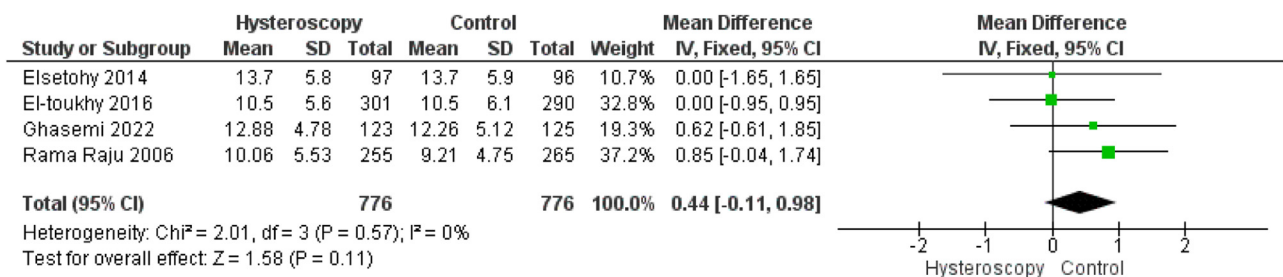
FIGURE 9
Forest plot of the chemical pregnancy rate



CI, confidence interval; M-H, Mantel-Haenszel.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

FIGURE 10
Forest plot of the number of oocytes retrieved



CI, confidence interval; IV, inverse variance; SD, standard deviation.

Marchand. Effect of the decision to perform hysteroscopy on asymptomatic patients. Am J Obstet Gynecol Glob Rep 2023.

3932 patients and showed that hysteroscopy was associated with a better clinical pregnancy rate ($P < .001$) and

implantation rate ($P = .025$) compared with the control group. As in our study, they found no significant difference

between the hysteroscopy group and the control group in terms of live birth rate and miscarriage rate. This analysis

included only 8 studies, only 3 of which were RCTs.

Although our findings were largely consistent with previous analyses, the exact mechanism of improving the clinical pregnancy rate after hysteroscopy is still unclear. Raju et al²³ suggested that hysteroscopy may treat small intrauterine lesions to increase the pregnancy rate. Shohayeb et al³⁴ reported that it was likely that endometrial “scratching” or performing a biopsy could change the features of the endometrium, facilitating embryo implantation. We do not believe that there is any clear consensus on the mechanism of action at this time.

Strengths and limitations

This was a large meta-analysis that had sufficient evidence to include only RCTs because of the newly published studies since the last analysis. With regard to limitations, 3 of the 8 outcomes were heterogeneous. Although heterogeneity decreases the certainty of evidence according to GRADE (Grading of Recommendations, Assessment, Development and Evaluations) guidelines, we were able to solve the heterogeneity in all cases. This was accomplished by subgroup analysis and the “leave-one-out method,” as described in the Cochrane handbook.¹²

Conclusion

We found that hysteroscopy performed before different ART procedures could improve the clinical pregnancy rate. A trend was observed toward an increased live birth rate in the hysteroscopy group, but statistical significance was not reached. We did not observe an increase in the miscarriage rate, fertilization rate, chemical pregnancy rate, multiple pregnancy, number of transferred embryos, or number of oocytes retrieved. Thus, we consider that the beneficial role of hysteroscopy should be assessed in further RCTs with more high-quality evidence before considering it a routine procedure in infertile women. Analysis of the cost-effectiveness of routine hysteroscopy before ART treatment would also provide valuable data.

ACKNOWLEDGMENTS

The Marchand Institute for Minimally Invasive Surgery would like to acknowledge the efforts of all of the students, researchers, residents, and fellows at the institute who put their time and effort into these projects without compensation, only for the betterment of women's health. We firmly assure them that the future of medicine belongs to them.

REFERENCES

- Practice Committee of the American Society for Reproductive Medicine, Practice Committee of the Society for Assisted Reproductive Technology. Role of assisted hatching in in vitro fertilization: a guideline. *Fertil Steril* 2014;102:348–51.
- Guttmacher AF. Factors affecting normal expectancy of conception. *J Am Med Assoc* 1956; 161.
- Recent advances in medically assisted conception. Report of a WHO scientific group. *World Health Organ Tech Rep Ser* 1992;820:1–111.
- Kuohung W, Hornstein MD, Barbieri RL. Causes of female infertility. U: UpToDate [Internet]. Eckler, K: UpToDate. 2017.
- Sadeghi MR. Low success rate of ART, an illusion, a reality or simply a too high expectation? *J Reprod Infertil* 2012;13:123.
- Seshadri S, El-Toukhy T, Douiri A, Jayaprakasan K, Khalaf Y. Diagnostic accuracy of saline infusion sonography in the evaluation of uterine cavity abnormalities prior to assisted reproductive techniques: a systematic review and meta-analyses. *Hum Reprod Update* 2015;21:262–74.
- Umrani S, Clark TJ, Saridogan E, et al. BSGE/ESGE guideline on management of fluid distension media in operative hysteroscopy. *Gynecol Surg* 2016;13:289–303.
- Yen CF, Chou HH, Wu HM, Lee CL, Chang TC. Effectiveness and appropriateness in the application of office hysteroscopy. *J Formos Med Assoc* 2019;118:1480–7.
- Gambadauro P, Navaratnarajah R, Carli V. Anxiety at outpatient hysteroscopy. *Gynecol Surg* 2015;12:189–96.
- Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *Ann Intern Med* 2009;151:264–9.
- Higgins JP. Cochrane handbook for systematic reviews of interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011 www.cochrane-handbook.org.
- Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane handbook for systematic reviews of interventions. John Wiley & Sons; 2019 Sep 23.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J* 2003;327:557–60.
- Alleyassin A, Abiri A, Agha-Hosseini M, Sarvi F. The value of routine hysteroscopy before the first intracytoplasmic sperm injection treatment cycle. *Gynecol Obstet Invest* 2017;82:125–30.
- Demiroglu A, Gurgan T. Effect of treatment of intrauterine pathologies with office hysteroscopy in patients with recurrent IVF failure. *Reprod Biomed Online* 2004;8:590–4.
- Ben Abid H, Fekih M, Fathallah K, Chachia S, Bibi M, Khairi H. Office hysteroscopy before first in vitro fertilization. A randomized controlled trial. *J Gynecol Obstet Hum Reprod* 2021;50:102109.
- El-nashar IH, Nasr A. The role of hysteroscopy before intracytoplasmic sperm injection (ICSI): a randomized controlled trial. *Fertil Steril* 2011;96:S266.
- Elsetohy KAAA, Askalany AH, Hassan M, Dawood Z. Routine office hysteroscopy prior to ICSI vs. ICSI alone in patients with normal transvaginal ultrasound: a randomized controlled trial. *Arch Gynecol Obstet* 2015;291:193–9.
- 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.
- Ghasemi M, Aleyasin A, Fatemi HM, Ghaemdoost F, Shahrakipour M. Uterine cavity irrigation with office hysteroscopy during ovarian stimulation for IVF: a randomized controlled trial. *Front Endocrinol (Lausanne)* 2022;13:778988.
- Kilic Y, Bastu E, Ergun B. Validity and efficacy of office hysteroscopy before in vitro fertilization treatment. *Arch Gynecol Obstet* 2013;287:577–81.
- Moramezi F, Barati M, Mohammadjafari R, Barati S, Hemadi M. Effect of hysteroscopy before intra uterine insemination on fertility in infertile couples. *Pak J Biol Sci* 2012;15:942–6.
- Rama Raju GA, Shashi Kumari G, Krishna KM, Prakash GJ, Madan K. Assessment of uterine cavity by hysteroscopy in assisted reproduction programme and its influence on pregnancy outcome. *Arch Gynecol Obstet* 2006;274:160–4.
- Smit JG, Kasius JC, Eijkemans MJC, et al. Hysteroscopy before in-vitro fertilisation (inSIGHT): a multicentre, randomised controlled trial. *Lancet* 2016;387:2622–9.
- 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.
- Makris N, Xygakis A, Michalas S, Dachlythras M, Prevedourakis C. Day clinic diagnostic hysteroscopy in a state hospital. *Clin Exp Obstet Gynecol* 1999;26:91–2.
- Levi Setti PE, Colombo GV, Savasi V, Bulletti C, Albani E, Ferrazzi E. Implantation failure in assisted reproduction technology and a critical approach to treatment. *Ann N Y Acad Sci* 2004;1034:184–99.

- 28.** Cunha-Filho JSL, De Souza CAB, Salazar CC, Facin AC, Freitas FM, Passos EP. Accuracy of hysterosalpingography and hysteroscopy for diagnosis of intrauterine lesions in infertile patients in an assisted fertilization programme. *Gynaecol Endosc* 2001;10:45–8.
- 29.** Singh N, Sethi A. Endometritis-Diagnosis, Treatment and its impact on fertility-A Scoping Review. *JBRA Assisted Reproduction* 2022;26:538.
- 30.** Louis F, Lulla CP. Hysteroscopy is superior to 3D ultrasound in gynecological diagnosis. *J Obstet Gynaecol India* 2020;70:447–61.
- 31.** Chung Y, Suh C, Choi Y, Kim J, Moon S, Kim S. Effects of endometrial evaluation with office hysteroscopy in IVF-ET patients with repeated failures. *Fertil Steril* 2006;86:S152.
- 32.** 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.
- 33.** Mao X, Wu L, Chen Q, Kuang Y, Zhang S. Effect of hysteroscopy before starting in-vitro fertilization for women with recurrent implantation failure: a meta-analysis and systematic review. *Medicine (Baltimore)* 2019;98:e14075.
- 34.** Shohayeb A, El-Khayat W. Does a single endometrial biopsy regimen (S-EBR) improve ICSI outcome in patients with repeated implantation failure? A randomised controlled trial. *Eur J Obstet Gynecol Reprod Biol* 2012;164:176–9.