**Research Article** 

**Al-Rafidain J Med Sci. 2024;7(1):57-63. DOI:** https://doi.org/10.54133/ajms.v7i1.1016 Hystro-laparoscopy in infertilty



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# Predictors for Successful Pregnancy Following Hystro-Laparoscopic Intervention among Infertile Females: A Cohort Study

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#### Abstract

Background: Infertility is a major medical and sociopsychological problem that impacts a couple's life. Investigations help guide therapeutic intervention by exploring underlying causes. Hysteroscopy can identify and treat intrauterine pathologies such as adhesion, septum, and endometrial polyps. Laparoscopy has a diagnostic and therapeutic role in the pelvic cavity, including tubal blockage, pelvic adhesions, endometriosis, and polycystic ovaries. *Objective*: To evaluate the value of combined hystro-laparoscopic interventions in managing female infertility and to explore predictors for a successful pregnancy. Methods: A retrospective cohort study enrolled (142) eligible females who underwent hystro-laparoscopy. Participants' demographic criteria were recorded. Additionally, intraoperative interventions (hysteroscopic removal of polyp and septum) and laparoscopic removal of pelvic adhesions, removal of chocolate cyst, ovarian drilling and laparoscopic chromotubation). All patients were followed up for six months. Logistic regression and odd ratio were used to assess the intervention's reliability in predicting pregnancy. *Results*: Clinical pregnancy was reported in 48/142, with a success rate of 33.8%. Pregnant women had significantly lower ages and lived in urban areas. Laparoscopic adhesion removal and tubal block correction reliably predicted clinical pregnancy, with adjusted odds ratios (AOR) of 0.25; 95% CI (0.08–0.78) and 0.40; 95% CI (0.16-0.98), respectively. None of the hysteroscopic interventions was statistically significant. Conclusions: Because hysterolaparoscopic procedures improve the chances of getting pregnant and are minimally invasive, they are an important part of fertility workups and can be used to diagnose and treat fertility problems.

Keywords: Adhesion, Clinical pregnancy, Hystro-laparoscopy, Infertility, Ovarian drilling, Tubal block.

المنبئات للحمل الناجح بعد التدخل بالمنظار بين الإناث المصابات بالعقم: دراسة أترابية

#### الخلاصة

الخلفية: العقم هو مشكلة طبية واجتماعية نفسية رئيسية تؤثر على حياة الزوجين. تساعد التحقيقات في توجيه التدخل العلاجي من خلال استكشاف الأسباب الكامنة. يمكن لتنظير الرحم تحديد و علاج الأمراض داخل الرحم مثل الالتصاق والحاجز والأورام الحميدة في بطانة الرحم. تنظير البطن له دور تشخيصي و علاجي في تجويف الحوض، بما في ذلك انسداد البوق، التصاقات الحوض، بطانة الرحم، وتكيس المبايض. الهدف: تقييم قيمة التدخلات المركبة بالمنظار في معالجة الأمراض داخل الرحم مثل الالتصاق والحاجز والأورام الحميدة في بطانة الرحم. تنظير البطن له دور تشخيصي و علاجي في ذلك انسداد البوق، التصاقات الحوض، بطانة الرحم، وتكيس المبايض. الهدف: تقييم قيمة التدخلات المركبة بالمنظار في معالجة العقر بعد النساء و استكشاف المنبئات بالحمل الناجح. الطريقة: سجلت در اسة أتر ابية بأثر رجعي (142) أنثى مؤهلة خضعن لتنظير الرحم. تم مع معالجة العقم عند النساء و استكشاف المنبئات بالحمل الناجح. الطريقة: سجلت در اسة أتر ابية بأثر رجعي (142) أنثى مؤهلة خضعن لتنظير الرحم. تم و إز الة النتوءات من جدار الرحم بالمنظار) و إز الة التصاقات الحوض، و إز الة التوءات من جدار الرحم بلائمار) و إز الة التصاقات الحوض، و إز الة التتوءات من جدار الرحم بالمنظار) و إز الة التصاقات الحوض، و إز الة التكيسات شبيهة الشوكولاته، وحفر المبيض و مالمنطن و المالمان إلى الماحي و الماحمل. النتائج: تم الإبلاغ عن الحمل السريري في لها معرفي معرفيقية النودار اللوحمن و والنسبة الفردية لتقيم موثوقية التدخل في التنبؤ بالحمل. النتائج: تم الإبلاغ عن الحمل السريري في 142/4، معدل نجاح 3.8%. النساء و الموامل لديهن أعمار أقل بكثير ويعشن في المناطق الحضرية. أدى إز الة الالتصاق بالمنظار و تصحيح كتلة البوق بشكل موثوق للتنبؤ بالحمل السريري، الحوامل لديهن أعمار أقل بكثير ويعش في المناطق الحضرية. أدى إز الة الالتصاق بالمنظار و محميح كتلة البوق بشكل موثوق للتنبؤ بالحمل السريري، الوامل لديهن أعمار أقل بكثير ويعش في المناطق الحضرية. أدى إز الة الالتصاق بالمنظار و تصحيح كتلة البوق بشكل موثوق للتنبؤ بالحمل السريري، معن معار أقل بكثير ويعش في الماطق الحضرية. أدى إز الة الالتصاق بالمنظار وتصحيح كتلة البوق بشكل موثوق للتنبؤ بالحمل السريري، مع نسب الأر جحية المعدلة من 20.5 ؟ 20.5 (20.5 -20.5 (20.5 -20.5 )) اكن معن معان مار موى مان مل

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### **INTRODUCTION**

Defining the underlying cause of infertility has a critical role in its management. When a couple fails to achieve pregnancy after one year of regular, unprotected sex, those couples are called infertile couples. Infertility sheds its shadow on couples' psychological, social, and mental well-being as well as their families [1]. Many investigations are used to explore the causes of female infertility, which is responsible for around 33% of all cases. While malerelated infertility accounts for 32%, as for the rest, there seems to be no cause, and thus, it is deemed to be unexplained infertility [2]. Hormonal, structural, and congenital anomalies of the female genital tract are all probable causes [3]. The gold standard for evaluating female fertility is laparoscopy, which can diagnose pelvic adhesion and blocked tubes [4]. Furthermore, it can resolve them through adhesion lysis, cautery, and restoring the patency of blocked tubes. Correcting and restoring the normal pelvic anatomy, along with the mini-invasive nature of the surgery, makes laparoscopy an efficient tool for subfertile couples [5]. Endometriosis happens when the endometrial gland and stroma grow outside the endometrium, thus impairing female fertility in more than one way. First, endometriosis affects hormonal profiling, leading to dysfunctional hormones that negatively impact ovarian function, particularly in endometriomas. Second, it can create an inflammatory, hostile environment, causing toxic effects on the sperm and fertilized ova. Finally, adhesion distorts the pelvic cavity, causing interference with ovarian pick-up and transfer. [6]. Laparoscopy is critical for releasing endometriosiscaused adhesion, removing endometriosis tissues, and removing ovarian endometrioma (also known as chocolate cysts) [7]. Polycystic ovarian syndrome (PCOS) lies on top of ovulatory disorders that were successfully treated by life style changes, ditery modification, insuline sensitizers and ovulation induction. However, when medical therapy fails, PCOS cases are referred for laparoscopic ovarian drilling (LOD) [8]. For a long time, doctors have used hysteroscopy to check the integrity of the uterine cavity because it allows them to directly see and evaluate the endometrium and ostea of the tubes. It can also detect problems that hysterosalpingography (HSG) missed, such as polyps or septums, and show adhesion [9]. By getting rid of the mechanical blockage and repairing the hormonal and structural integrity of the uterine cavity, hysteroscopic polypectomy and septoplasty may help restoring fertility [10]. This makes the uterine cavity a favorable environment for fertilization and implantation. Adding both tests to hysteroscopy and laparoscopic surgery is not a new idea; it has the added benefits of both tests in a cost-effective way that lets operated cases get both diagnosis and treatment at the same time [11]. The mini-invasive nature of hystrolaparoscopical tests, added to their high accuracy in unveiling infertility causes, allows for choosing the right therapy, guiding the clinical decision for higher pregnancy rates. All of that made the intervention

worth implementing in practice [12]. While many studies evaluated the validity of hysteroscopic laparoscopic surgery, none were conducted in our country [13–15]. The current study aims to evaluate the effectiveness of the surgery in improving the overall clinical pregnancy rates, explore which surgical intervention (whether laparoscopic or hysteroscopic) has led to higher rates, and define which intervention reliably predicts a positive outcome.

### **METHODS**

#### Study design and setting

A retrospective cohort study was conducted at Al-Razzi Private Hospital/Infertility Center from October 2018 until May 2023. The hospital lies in the center of Anbar Province, Iraq and is considered a tertiary center for the province and its nearby areas. Referred cases suffering from infertility were invited to participate after the study goals were explained. Informed consent was obtained from all participants before enrolling in the study.

### Ethical consideration

Approval of the study protocol was obtained from the Ethics Approval Committee of the University of Anbar Number 76 (dated 21/4/2018).

### Inclusion criteria

The study included all females experiencing infertility, whether primary or secondary, who had a normal hormonal profile, including ovarian hormones, prolactin, and thyroid, and had normal male partners. If they had polycystic ovarian syndrome, were not responding to medical treatment, had a history of previous hystero-salpingography (HSG) showing abnormal tubal patency, refused to undergo HSG, or had an endometrial polyp, septum, or endometrioma, we included them.

#### Exclusion criteria

We excluded couples with male factor infertility, females with abnormal thyroid and prolactin levels, and those with chronic illnesses like diabetes, asthma, or steroids. Cases with incomplete data were omitted.

#### Interventions and outcome measurements

During the interview, couples who consented to participate provided all their demographic information, including age, occupation, residency, duration, and type of infertility. We then measured the patient's weight and height to determine their body mass index (BMI), using the following formulas: Weight in kg over the height in (m<sup>2</sup>). An explanation was made of the nature of the operation and its possible advantages and side effects. For each operated case, a record was made for the intra-

### Murshid et al

operative interventions, which include laparoscopic interventions (laparoscopic release of adhesion, laparoscopic removal of endometriosis, laparoscopic ovarian drilling, and laparoscopic corrections of the blocked tube) and hysteroscopic interventions (hysteroscopic polypectomy and hysteroscopic removal of the uterine septum). The hystrolaparoscopic procedure was performed under general anesthesia. The whole procedure lasted between 25 and 60 minutes, depending on the intervention done. We first performed the hysteroscopy using a 5 mm Bertucci/KaRL (STORZ hysteroscope, Tuttlingen, Germany). During the procedure, polypectomy, removal of the uterine septum (according to respective findings), and visualization of the ostia were done for all. (Figure 1).



**Figure 1:** Hysteroscopic intervention, showing A) polypectomy, and B) septum removal.

After that, we proceeded to laparoscopy with a 5 mm or 10 mm, 36 cm-long KaRL STORZ laparoscop according to the type of intervention, diagnostic or therapeutic, respectively. During laparoscopy, pelvic adhesions could be removed by cautery or ligaSure, depending on the patient's symptoms and the findings of the laparoscopy (Figure 2).



Figure 2: Laparoscopic adhesion-lysis procedure.

This released the adhesions around the fallopian tubes and made them more mobile, restoring the normal anatomy of the pelvis. If endometriosis was encountered, removal was performed either by excision or by ablation. We performed laparoscopic ovarian drilling when we encountered polycystic ovaries (Figure 3A) that were not responding to medical treatment. The tubal patency was checked by injecting methylene-blue dye through the cervix and observing the dye passing from the fimbria ends of the tubes through chromotubation (Figure 3B). During the postoperative period, patients remained for 4-8 hours until full recovery and were discharged home. We advised them to return for a checkup ten days after the operation. In addition, patients who had a septum or large polyp removed were advised to take estrofem and progesterone for one month to enhance endometrial healing. All patients were followed for up to 6 months.



**Figure 3**: (A) Laparoscopic ovarian drilling, and (B) a positive tubal patency test with free spillage of dye.

Six months post-surgery, we followed the cases; we regarded the outcome as positive for those who had positive pregnancies and negative for those who failed to get pregnant (Figure 4).



Figure 4: The study flowchart.

### Sampling power

We calculated the sample size based on the WHO guidelines, taking into account the 10-15% prevalence of infertility [2] and using the software Epi-Info version 7.0 [16] with a 95% confidence interval. A sample size of 138 was representative; our study recruited 142 cases.

### Statistical analysis

The data were subjected to statistical analysis using SPSS 22.0 software (IBM, New York, USA). The collected data, including demographic characteristics, were given as the mean  $\pm$  standard deviation or number and percentage for continuous data and categorical data, respectively. The data were analyzed using the Chi-square test and/or the student's t-test, depending on appropriateness. The study employed multiple logistic regression to examine the impact of surgical interventions on the patient's pregnancy outcome. Statistical significance was set for results with a *p*-value less than 0.05.

# RESULTS

A retrospective cohort study included all referred cases to our infertility center who were eligible for the inclusion criteria. The cases who achieved clinical pregnancy were (48/142) vs. (94/142) who failed to get pregnant, with a success rate of 33.8% in Table 1.

Table 1: Distribution of sample study according to demographic criteria in Pregnant and Non-pregnant groups

	Variables (n=142)		Pregnant (n=48)	Non-pregnant (n=94)	<i>p</i> -value
Age (year)			29.31±0.79	32.77±0.66	0.002 ¶
BMI (kg/m <sup>2</sup> )			30.03±0.60	32.49±1.56	0.270 ¶
Occupation		Housev	wife 32(66.67)	62(65.96)	0.002
		Employ	yed 16(33.33)	32(34.04)	0.002
Residency		Urban	33(68.75)	64(68.09)	0.002
		Rural	15(31.25)	30(31.91)	0.002
Infertility type		Primar	y 21(43.75)	44(46.81)	0.37
		Second	lary 27(56.25)	50(53.19)	0.57
Infertility duration (year)			5.25±0.57	5.98±0.36	0.256 ¶
		None	22(45.83)	44(46.81)	
Delivery mode for secondary	/ infertility	Vagina	1 18(37.50)	19(20.21)	0.27
		CS	4(8.33)	19(20.21)	0.27
		Combi	ned 4(8.33)	12(12.77)	

Values are expressed as frequencies, percentages, and mean $\pm$ SD. Chi-Square compared all parameters except those marked with ¶ where comparison is done using *t*-test; BMI: body mass index, CS: cesarian section.

The pregnant group had significantly lower maternal age (p=0.002), while the BMI and infertility duration showed no statistical significance among the two groups. The occupation and residency show statistical differences between the two groups; pregnant cases were mostly housewives (66.67%) and lived in urban areas (68.75%) compared to non-pregnant cases. There are no significant differences between the two groups in terms of the types of infertility (primary or secondary) or the delivery mode among secondary

infertility cases. Table 2 presents the intraoperative findings of the study participants, based on the laparoscopic and hysteroscopic interventions performed in the two groups. The pregnant group had a significantly lower incidence of adhesion (12.5%), endometriosis (4.17%), and tubal blockage (18.75%) *vs.* non-pregnant cases, with p=0.0007, 0.0001, and 0.0097, respectively. Diagnosing PCOS by laparoscopy was significantly lower (45.83%) among pregnant cases (p=0.009).

Table 2: Distribution of sample study according to laparoscopic and hysteroscopic intervention in pregnant and non-pres	gnant
groups	

Variables total (n=142)		Pregnant (n=48)	Non-pregnant (n=94)	<i>p</i> -value Chi-square	
Laparoscopic intervention					
Adhesion lucis	Yes	6(12.50)	46(48.94)	0.0007	
Adhesion-tysis	No	42(87.50)	48(51.06)	0.0007	
Pamoual of andomatricais	Yes	2(4.17)	14(14.89)	0.0001	
Removal of endometriosis	No	46(95.83)	80(85.11)	0.0001	
Ovarian drilling of polycystic ovarias	Yes	22(45.83)	17(18.09)	0.009	
Ovarian unning of polycystic ovaries	No	26(54.17)	77(81.91)		
Correction of tubal block	Yes	9(18.75)	47(50.0)	0.0097	
Correction of tubar block	No	39(81.25)	47(50.0)		
Hysteroscopic intervention					
Polypectomy	Yes	17(35.42)	24(25.53)	0.002	
rorypectomy	No	31(64.58)	70(74.47)	0.002	
Peroval of centum	Yes	6(12.50)	11(11.70)	0.0001	
Removal of septum	No	42(87.50)	83(88.30)		

Values are expressed as frequencies and percentages.

As for the hysteroscopic intervention, pregnant cases had a higher incidence of uterine polyp (35.42%) and septum (12.50%) vs. non-pregnant cases p=0.0001. The adjusted odds ratio was calculated in Table 3 to explore predictors that led to a successful pregnancy. It was found that laparoscopic removal of the adhesion and correction of the tubal block were the most reliable predictors for clinical pregnancy, with an adjusted odds ratio (AOR) of 0.25 (95% CI (0.08 to 0.78); p=0.017 and an AOR of 0.40 (95% CI (0.16 to 0.98); p=0.45 respectively. Notably, the AOR for laparoscopic ovarian drilling in PCOS cases was 3.53, with a *p*-value of 0.052, which was not significant.

**Table 3.** The adjusted odd ratio (for BMI and duration of infertility) for having a positive pregnancy according to the intervention sub-type

Intervention	Wald	Adjusted-Odds ratio	95% CI	<i>p</i> -value
Laparoscopic-adhesion lysis	5.68	0.25	0.08 to 0.78	0.017
	Reference group			
Laparoscopic-removal of endometriosis	0.005	1.07	0.18 to 6.31	0.94
	Reference group			
Laparoscopic-ovarian drilling of polycystic ovaries	3.53	2.30	0.86 to 5.39	0.052
	Reference group			
Laparoscopic-correction of tubal block	4.02	0.40	0.16 to 0.98	0.045
	Reference group			
Hysteroscopic-polypectomy	0.004	1.03	0.42 to 2.52	0.95
	Reference group			
Hysteroscopic-removal of septum	0.19	1.33	0.38 to 4.59	0.66

Hysteroscopic removal of the polyp and septum, when with laparoscopic removal combined of endometriosis, did not result in a significant difference. Finally, a sub-group analysis was done to shed light on which type of intervention led to positive outcomes among the pregnant cases, as shown in Figure 5. It was found that laparoscopic intervention led to the highest number of positive cases (22/48), followed by laparoscopic-hysteroscopic (11/48). Interestingly, 84% of cases get pregnant without any interventions, i.e., only a diagnostic procedure was done. Finally, 6/48 cases become pregnant after undergoing a hysteroscopic procedure. The difference was highly significant across the sub-groups, with p=0.0006. It is worth mentioning that no major complications were encountered through all operations, no perforation was reported, and no cases of ectopic pregnancies were found. Minor bleeding, when it occurred, was successfully stopped by cauterization.



**Figure 5:** The distribution of positive pregnancy cases based on the intervention type.

# DISCUSSION

The analysis showed that the pregnancy rate following hystro-laprosopy was 33.8%; cases that got pregnant were significantly younger, housewives and lived in urban areas. The type and duration of infertility have no statistical impact on pregnancy rates. Those who got pregnant had meaningfully lower pelvic adhesion, tubal blockage, endometriosis, and polycystic ovaries. Laparoscopic removal of the adhesion and correction of the tubal block were the most successful predictors of clinical pregnancy; however, none of the hysteroscopic interventions predicted successful outcomes. The most frequent abnormalities seen in the hysteroscopy were polyps, followed by a uterine septum with a total frequency of 60.95% and 24.2%, respectively. In an Egyptian study enrolling unexplained infertility cases [17], uterine polyps were found in 30% of cases, endometritis in 13%, fibroids in 9%, and uterine septum in 3%. Another study by Makled et al. examined unexplained infertility cases and found that 31% of cases suffered from uterine polyps [18]. Hysteroscopy is a valuable tool for direct visualization correction of and intrauterine abnormalities [9]. It reveals hidden abnormalities, especially when transvaginal ultrasound is normal. Hysteroscopy had higher accuracy in assessing the uterus compared to transvaginal ultrasound, saline infusion sonography, and hysterosalpingography [19,20]. The current study found that removing the

polyp and septum through hysteroscopy did not significantly improve the chance of a positive pregnancy, with odds ratios (AOR) of 1.03 and 1.33 for each. This aligns with previous studies that explored pregnancy after hysteroscopic correction [21]. Many interventions were used to enhance endometrial recovery and reduce fibrosis for a higher clinical pregnancy, including dry amnion grafts, bone marrow stem cell scaffolds, and granulocyte colonystimulating factors. More research is currently needed to evaluate the efficacy of these interventions [22,23]. Out of the 48 women who tested positive for pregnancy, only 6 had hysteroscopy intervention, while 11 had both hysteroscopy and laparoscopic intervention. This may be why hysteroscopy intervention alone was not a good predictor. Different inclusion criteria could be another reason for the lower odds, as most earlier studies included unexplained infertility in women [24]. The use of laparoscopic surgery in endometriosis-related subfertility (minimal and mild cases) to increase pregnancy and live birth rates [25]. However, the recommendation was not extended to severe endometriosis cases [26]. Most of the included cases had moderate-to-severe endometriosis, which may explain why the intervention did not increase pregnancy odds. Earlier studies recommended combining hysteroscopy with operative laparoscopy to remove endometriosisrelated adhesions. It was found that they suffered a higher incidence of endometrial polyps, which, when removed, increased the pregnancy odds [27.28]. Polycystic ovaries are one of the most frequent causes of female infertility [8]. Laparoscopic ovarian drilling (LOD) was used to improve the pregnancy odds in the included cases; however, it failed to reach statistical significance. This was in accordance with Eftekhar and Seow et al., who agreed that the improvement in fertility potential following LOD was transient (for six months in most cases). Moreover, cases that underwent IVF did not show higher pregnancy rates compared to those who had no LOD. Still, the intervention was beneficial in reducing ovarian hyperstimulation syndrome, a critical side effect of inducing the ovaries among PCOS cases [29,30]. We have to acknowledge the long-term side effects of LOD in terms of reducing ovarian reserve and the risk of premature menopause [8]. In the literature, laparoscopic adhesion-lysis had a controversial impact on fertility. In a comparative study where the pregnancy rate was 47% vs. 56%; P>0.05, respectively, after six-month follow-ups, some participants discussed that laparoscopic adhesionlysis had no role in improving fertility compared to expectant management [31]. Other studies have reported a favorable effect on pregnancy odds [5,32]. One of the benefits of laparoscopic adhesion-lysis is the restoration of the normal pelvic cavity anatomy, which increases the likelihood of a natural pregnancy, in addition to the advantages of the mini-invasive surgery of laparoscopy. However, laparoscopy does carry some disadvantages. Some surgeons in 2nd-look surgery reported adhesion re-formation following its use, as with any surgery that could trigger peritoneal adhesion. Other laparoscopic complications, including internal organ perforation and anesthetic complications, are also a concern [11]. Researchers postulated that the type of adhesion (thin and filmy are least likely to recure) and the time of operation significantly influence the success of adhesion lysis and the likelihood of adhesion re-formation [5,33]. The tubal block corrected by laparoscopy resulted in 18.75% positive pregnancy cases; none of them was an ectopic pregnancy [34]. Other studies scored higher pregnancy rates: 26.1% for Kasia et al., 33.3% for Canis et al., and 27.4% for Dubuisson et al. [35,36]. The difference can be attributed to the severity of tubal damage and to the site affected, which may be proximal or distal. Zhang et al. studied independent risk factors for predicting positive pregnancy among cases with tubal block. The results showed that the best predictors were a mother's age less than 35 years, a tubal function score of 2.44, and a history of no tubal ectopic pregnancy, all with a P-value of less than 0.001 [37]. It was shown that the intervention that led to the highest pregnancy in the current work was laparoscopy, followed by laparoscopic-hysteroscopic (22/48 vs. 11/48), while hysteroscopy was the last (6/48; p=0.0006). Laparoscopy is gaining more and more attention in infertility workup, and it continues to advance and take important roles both as a diagnostic and therapeutic tool in infertile cases. Moreover, it can be integrated into assisted reproductive techniques with the advantage of being minimally invasive [11]. Notably, 8/48% of pregnant cases underwent only diagnostic hystro-laparoscopic procedures since both exams were normal and no intervention was needed. One possible cause is the psychological effect and reassurance that come from knowing that everything is fine. This placebo effect may correct minor problems in the ovarian or tubal function, leading to natural conception [38]. Secondly, the diagnostic procedure alone, without any intervention, has the potential to resolve tubal spasms and undetected minor obstacles. The "clean-up act" could be a reason for improved tubal or endometrial responsiveness [11]. Finally, the in-depth counseling that infertile couples receive upon visiting specialized fertility centers could improve their odds by educating them about the best intercourse timing and other related issues.

### **Study limitations**

This was a single-center experience, so we are unable to globalize our results. Being a retrospective study is another limitation. Although we enrolled males with normal semen analysis, paternal age was another confounder that was not considered in the analysis [39]. The most recent guidelines recommended following endometriosis cases for 1 year to see the impact of surgery, while we followed for 6 months [27]. We did not perform second-look surgery to check the adhesion recurrence rate following laparoscopic adhesion lysis. Interventions following hysteroscopy can improve the pregnancy rate, but this was not the case here. Lastly, transvaginal ultrasound (TVUS) is a great way to check the integrity of the uterine cavity and rule out malformations without the risk of radiation or allergy contrast that comes with HSG [40–41]. We didn't discuss all patients because their TVUS reports lacked complete data.

### Study strength

This was, to the best of our knowledge, the first long study from Anbar Province that comprehensively analyzed, examined, and followed referee cases for our fertility center in 5 years. The analysis showed a pregnancy rate of 33.8% among infertile couples; other interventions, such as intrauterine insemination, had 10-15% success, while in vitro fertilization had a success of 30-50%, keeping in mind the effect of maternal age on the outcome, so hystro-laprosopy did improve the fertility odds for enrolled cases [42]. In addition, exploring determinants for a positive pregnancy can have many advantages, such as determining interventions most strongly associated with a positive pregnancy and creating prediction models and risk stratification methods to tailor therapeutic strategies. We believe these findings can potentially shape clinical decision-making and aid in resource allocation to improve pregnancy outcomes.

#### Conclusion

The hystro-laparoscopy offers a safe and comprehensive evaluation of the pelvic and endometrium cavities. Moreover, it simultaneously adds to the benefits of therapeutic interventions at no extra cost. Laparoscopic adhesion-lysis and correction of blocked tubes were the most successful predictors for clinical pregnancy. We recommend a prospective longitudinal study with a one-year follow-up to explore further beneficial impacts on female fertility.

#### **Conflict of interests**

No conflict of interests was declared by the authors.

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The authors did not receive any source of fund.

#### Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

#### REFERENCES

- Liang S, Chen Y, Wang Q, Chen H, Cui C, Xu X, et al. Prevalence and associated factors of infertility among 20-49 year old women in Henan Province, China. *Reprod Health*. 2021;18(1):254. doi: 10.1186/s12978-021-01298-2.
- Thable A, Duff E, Dika C. Infertility management in primary care. Nurse Pract. 2020;45(5):48-54. doi: 10.1097/01.NPR.0000660356.18430.0a.
- Anonymous. Infertility Workup for the Women's Health Specialist: ACOG Committee Opinion, Number 781. Obstet Gynecol. 2019;133(6):e377-e384. doi: 10.1097/AOG.00000000003271.
- Arab W. Diagnostic laparoscopy for unexplained subfertility: a comprehensive review. *JBRA Assist Reprod*. 2022;26(1):145-152. doi: 10.5935/1518-0557.20210084.
- Ghobrial S, Ott J, Parry JP. An overview of postoperative intraabdominal adhesions and their role on female infertility: a narrative review. J Clin Med. 2023;12(6):2263.

- Smolarz B, Szyłło K, Romanowicz H. Endometriosis: epidemiology, classification, pathogenesis, treatment and genetics (review of literature). *Int J Mol Sci.* 2021;22(19):10554.
- Bhat RG, Dhulked S, Ramachandran A, Bhaktha R, Vasudeva A, Kumar P, et al. Laparoscopic cystectomy of endometrioma: Good surgical technique does not adversely affect ovarian reserve. J Hum Reprod Sci. 2014;7(2):125-129. doi: 10.4103/0974-1208.138871.
- Ali AI, Hassan WN, Alrawi S. A copeptin as a predictor marker for insulin resistance among women with polycystic ovary syndrome. *Curr Womens Health Rev.* 2022;18(4):67-72.
- American College of Obstetricians and Gynecologists. The use of hysteroscopy for the diagnosis and treatment of intrauterine pathology: ACOG Committee Opinion, Number 800. Obstet Gynecol. 2020;135:e138-e148. doi: 10.1097/AOG.000000000003712.
- Al-Husban N, Odeh O, AlRamahi M, Qadri S, Al-Husban H. Fertility-enhancing hysteroscopic surgery; multi-center retrospective cohort study of reproductive outcome. *BMC Womens Health.* 2023;23(1):459. doi: 10.1186/s12905-023-02562-2.
- Kabadi Y, Harsha B. Hysterolaparoscopy in the evaluation and management of female infertility. J Obstet Gynaecol India. 2016;66:478-481. doi: 10.1007/s13224-016-0863-5.
- Puri S, Jain D, Puri S, Kaushal S, Deol SK. Laparohysteroscopy in female infertility: a diagnostic cum therapeutic tool in Indian setting. *Int J Appl Basic Med Res.* 2015;5(1):46-48. doi: 10.4103/2229-516X.149240.
- Gad MS, Dawood RM, Antar MS, Ali SE. Role of hysteroscopy and laparoscopy in evaluation of unexplained infertility. *Menoufia Med J.* 2019;32(4):1401. doi: 10.4103/mmj.mmj\_387\_18.
- Mishra S, Sudhir S. Diagnostic hysterolaparoscopy in evaluation of female infertility in a Rural Medical College. *Indian J Obstet Gynecol Res.* 2016;3(3):196-198. doi: 10.5958/2394-2754.2016.00044.8.
- Ugboaja JO, Oguejiofor CB, Ogelle OM. Hysterolaparoscopy (pan-endoscopy) in the management of female infertility in Nigeria: A report of 230 cases. *Niger J Gen Pract*. 2020;18(2):53-58. doi: 10.4103/NJGP.NJGP\_9\_20.
- Community Medicine4all. How to calculate sample size with Epi Info 7 [Internet]. 2018 [cited 2024 May 22]. Available at: <u>https://communitymedicine4all.com/2018/06/23/how-tocalculate-sample-size-with-epi-info-7/</u>
- Mohamed MA, Elmazzaly SM. Role of diagnostic hysteroscopy in cases with unexplained infertility. *Al-Azhar Int Med* J. 2022;3(9):88-95. doi: 10.21608/aimj.2022.128782.1882.
- Makled AK, Farghali MM, Shenouda DS. Role of hysteroscopy and endometrial biopsy in women with unexplained infertility. *Arch Gynecol Obstet*. 2014;289:187-192. doi: 10.1007/s00404-013-2931-8.
- Khan F, Jamaat S, Al-Jaroudi D. Saline infusion sonohysterography versus hysteroscopy for uterine cavity evaluation. *Ann Saudi Med.* 2011;31(4):387-392. doi: 10.4103/0256-4947.83213.
- 20. Vitale SG, Carugno J, Riemma G, Török P, Cianci S, De Franciscis P, et al. Hysteroscopy for assessing fallopian tubal obstruction: A systematic review and diagnostic test accuracy meta-analysis. *J Minim Invasive Gynecol*. 2021;28(4):769-778. doi: 10.1016/j.jmig.2020.11.013.
- Lin LJ, Qiao XY, Chen XP, Xu LZ, Chen H. Efficacy of reducing recurrence of intrauterine adhesions and improving pregnancy outcome after hysteroscopic adhesiolysis: A systematic review and network meta-analysis of randomized controlled trials. *Clin Exp Obstet Gynecol*. 2024;51(4):102. doi: 10.31083/j.ceog5104102.
- 22. Gan L, Duan H, Xu Q, Tang YQ, Li JJ, Sun FQ, et al. Human amniotic mesenchymal stromal cell transplantation improves endometrial regeneration in rodent models of intrauterine adhesions. *Cytotherapy*. 2017;19(5):603-616. doi: 10.1016/j.jcyt.2017.02.003.
- Han Q, Du Y. Advances in the application of biomimetic endometrium interfaces for uterine bioengineering in female infertility. *Front Bioeng Biotechnol.* 2020;8:153. doi: 10.3389/fbioe.2020.00153.
- 24. National Collaborating Centre for Women's and Children's Health. Fertility: assessment and treatment for people with

fertility problems. London: Royal College of Obstetricians & Gynaecologists; 2013.

- Jin X, Beguerie JR. Laparoscopic surgery for subfertility related to endometriosis: a meta-analysis. *Taiwan J Obstet Gynecol*. 2014;53(3):303-308. doi: 10.1016/j.tjog.2013.02.004.
- European Society of Human Reproduction and Embryology. ESHRE guideline: Endometriosis. *Hum Reprod Open*. 2022;2022(2). doi: 10.1093/hropen/hoac009.
- Luo B, Pei T, Huang X, Huang W. A new nomogram to predict spontaneous pregnancy after laparoscopy combining hysteroscopy in women with minimal to mild endometriosisassociated infertility. *Clin Exp Obstet Gynecol.* 2024;51(4):98. doi: 10.31083/j.ecog5104098.
- Zhang YN, Zhang YS, Yu Q, Guo ZZ, Ma JL, Yan L. Higher prevalence of endometrial polyps in infertile patients with endometriosis. *Gynecol Obstet Invest*. 2018;83(6):558-563. doi: 10.1159/000487946.
- Eftekhar M, Firoozabadi RD, Khani P, Bideh EZ, Forghani H. Effect of laparoscopic ovarian drilling on outcomes of in vitro fertilization in clomiphene-resistant women with polycystic ovary syndrome. *Int J Fertil Steril.* 2016;10(1):42. doi: 10.22074/ijfs.2016.4767.
- Seow KM, Chang YW, Chen KH, Juan CC, Huang CY, Lin LT, et al. Molecular mechanisms of laparoscopic ovarian drilling and its therapeutic effects in polycystic ovary syndrome. *Int J Mol Sci.* 2020;21(21):8147. doi: 10.3390/ijms21218147.
- Gürgan T, Ürman B, Aksu T, Yarali H, Develioglu O, Kisnisci HA. The effect of short-interval laparoscopic lysis of adhesions on pregnancy rates following Nd-YAG laser photocoagulation of polycystic ovaries. *Obstet Gynecol.* 1992;80(1):45-47. PMID: 1534881.
- 32. Maruyama M, Osuga Y, Momoeda M, Yano T, Tsutsumi O, Taketani Y. Pregnancy rates after laparoscopic treatment. Differences related to tubal status and presence of endometriosis. J Reprod Med. 2000;45(2):89-93. PMID: 10710736
- Tabibian N, Swehli E, Boyd A, Umbreen A, Tabibian J. Abdominal adhesions: A practical review of an often overlooked entity. *Ann Med Surg.* 2017;15:9-13. doi: 10.1016/j.amsu.2017.01.021.
- 34. Kasia JM, Ngowa JD, Mimboe YS, Toukam M, Ngassam A, Noa CC, et al. Laparoscopic fimbrioplasty and neosalpingostomy in female infertility: A review of 402 cases at the gynecological endoscopic surgery and human reproductive teaching hospital in yaoundé-cameroon. J Reprod Infertil. 2016;17(2):104-109. PMID: 27141465.
- Canis M, Mage G, Pouly JL, Manhes H, Wattiez A, Bruhat MA. Laparoscopic distal tuboplasty: report of 87 cases and a 4-year experience. *Fertil Steril.* 1991;56(4):616-621. doi: 10.1016/s0015-0282(16)54589-0.
- Dubuisson JB, de Jolinière JB, Aubriot FX, Daraï E, Foulot H, Mandelbrot L. Terminal tuboplasties by laparoscopy: 65 consecutive cases. *Fertil Steril*. 1990;54(3):401-403. doi: 10.1016/s0015-0282(16)53751-0.
- 37. Zhang L, Jiang F, Qi R, Fu W, Wang Y, Gui D. Pregnancy outcomes in patients with tubal infertility following laparoscopic treatment: a multivariate predictive study. *Ann Palliat Med.* 2021;10(1):46262-46462. doi: 10.21037/apm-20-2347.
- Wager TD, Atlas LY. The neuroscience of placebo effects: connecting context, learning and health. *Nat Rev Neurosci*. 2015;16(7):403-418. doi: 10.1038/nrn3976.
- Nori W, Helmi ZR. Can follicular fluid 8-oxo-2'deoxyguanosine predict the clinical outcomes in ICSI cycle among couples with normospermia male? *Obstet Gynecol Sci.* 2023;66(5):430. doi: 10.5468/ogs.22170.
- Thaker N, Dhande R, Parihar P. Role of transvaginal sonography in the diagnosis of female infertility: A comprehensive review. *Cureus*. 2023;15(12):e50048. doi: 10.7759/cureus.50048.
- Abdulqader Shaymaa, Nori W, Akram NN, Al-Kinani M. Radiological modalities for the assessment of fetal growth restriction: A comprehensive review. *AL-Kindy Coll Med J.* 2024;20(1):4-13. doi: 10.47723/nz221421.
- 42. Mendieta MA, Aranda AS, López JFM, Sánchez AMR, Mondragón EC, Monterrosas LÁD, et al. Comparative analysis of the pregnancy rate via *in vitro* fertilization vs. previous artificial insemination in patients with unexplained infertility. *JBRA Assist Reprod*. 2022;26(1):22-27. doi: 10.5935/1518-0557.20210038.