

Findings in diagnostic laparoscopy in patients with unexplained infertility

Shilpa Bhandari, Aparna Singh, Pallavi Agrawal¹, Ishita Ganguli

Departments of Reproductive and Fetal Medicine and ¹Obstetrics and Gynaecology, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India

ABSTRACT

Objective: Infertility is a growing concern of the society. In many cases the exact cause of infertility may not be elucidated, whether it is the tubal factor, male factor, uterine factor, or a combination. This adds to the emotional trauma of the couple. Many previous reports have tried to decipher the cause and the best line of management for these cases of unexplained infertility. The choice often lies between a diagnostic approach favoring laparoscopic evaluation and a therapeutic approach favoring the use of assisted reproductive techniques. This paper aims to understand the role of diagnostic hysterolaparoscopy in cases of unexplained infertility, the optimum time to perform it, and its role in changing the future management plan. **Design:** This was a retrospective study. **Patients and Methods:** Data of the identified patients were collected from patient case records and they included factors such as age, duration and type of infertility, clinical examination findings, and gynecological ultrasound. Previous treatment history included details of ovulation stimulation, intrauterine insemination (IUI), and other treatment. Intraoperative findings such as presence of peritubal adhesions, endometriosis, tubal pathology, perihepatic adhesions, and hysteroscopic findings were recorded. **Results:** Our study shows that performing diagnostic hysterolaparoscopy in cases of unexplained infertility is of advantage, especially in patients who have had two or more failed IUI in the past. **Conclusion:** Performing diagnostic hysterolaparoscopy prior to ovulation induction/IUI has not shown any significant advantage.

Keywords: Diagnostic hysterolaparoscopy, intrauterine insemination (IUI), unexplained infertility

INTRODUCTION

Infertility is a growing concern of the society. It is estimated that 10-15% of couples in India are infertile. Identifying the cause of infertility is complex and after a standard evaluation

20-30% of couples will have no clearly identifiable cause of their infertility.^[1,2] However, these estimates include couples in which the female partner may not have been thoroughly evaluated with laparoscopy for pelvic pathology (such as endometriosis). It has been estimated that using laparoscopy as a standard test have tubal function would reduce the apparent incidence of unexplained infertility from 10% to 3.5%.^[3]

Diagnostic laparoscopy is the final step in determining the cause of infertility and is also frequently performed as a standard procedure in diagnosing infertility.^[4]

Address for correspondence:

Dr. Shipla Bhandari,
Department of Reproductive and Fetal Medicine,
Sri Aurobindo Medical College and PG Institute, Indore,
Ujjain State Highway, Near MR 10 Crossing, Indore - 453 555,
Madhya Pradesh, India.
E-mail: drshilpa.b@gmail.com

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However, the role of laparoscopy as a standard approach to the management of infertility remains controversial for several reasons. Although women with infertility have an increased prevalence of endometriosis (estimated at greater than 30%), it is difficult to predict which patients are likely to benefit from surgery.^[5,6] Modern fertility treatments, especially *in vitro* fertilization (IVF), result in marked improvements in fecundity; it is unclear whether these treatments are compromised by unrecognized endometriosis. Consequently, patients increasingly forgo surgery, particularly if they are otherwise asymptomatic and their initial diagnostic studies [i.e., hysterosalpingogram (HSG)] are normal.^[7,8]

Theoretically, there are potential benefits to routinely performing laparoscopy in infertile women. First, it is possible to avoid fertility treatments and their direct as well as indirect financial and social costs, such as multiple gestation pregnancy.^[5,9] Second, intraoperative findings can guide postsurgical management, circumventing treatments that are of low benefit and costly.^[10] Third, surgically correcting endometriosis may enhance response to fertility treatments or mitigate the effects of comorbidities such as pelvic pain.^[11]

Diagnostic laparoscopy is thus essential in determining the optimal management plan.^[4]

Similarly, visualizing the uterine cavity and identifying the possible pathology has made hysteroscopy an equally important tool in infertility evaluation. Combining hysteroscopy with laparoscopy has become a standard tool of evaluation though the absolute role of hysteroscopy in unexplained infertility is yet to be elucidated.^[12-15]

This study aims to understand the role of diagnostic hysterolaparoscopy in cases of unexplained infertility, the optimum time to perform it, and its role in changing the future management plan.

PATIENTS AND METHODS

This is a retrospective analysis of all patients who underwent diagnostic laparoscopy at Sri Aurobindo Institute of Medical Sciences, Indore, MP, India from January 2013 to December 2013. Patients with infertility of duration >3 years, regular cycles, and normal HSG were considered for the study. Patients with history of abdominal surgery, suspected Koch's abdomen or ultrasonography suggestive of fibroid, adenomyosis, chocolate cyst, or tubo-ovarian mass were excluded from the evaluation. Hormonal abnormalities known to cause anovulation such as thyroid dysfunction, hyperprolactinemia, and polycystic ovarian syndrome were excluded. Couples with abnormal semen analysis were also not included in this study. Between January 2013 and December 2013, a total of 546 patients underwent hysterolaparoscopy. Of them, 198 patients had normal HSG findings, normal ultrasonography, and regular ovulating periods. In this study, the criteria for normal HSG were^[1] absence of intrauterine adhesions^[2] and visualization of bilateral tubal spill of contrast media without the presence of hydrosalpinx.

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of infertility, clinical examination findings, and gynecological ultrasound. Previous treatment history included details of ovulation stimulation, intrauterine insemination (IUI) and other treatment. Intraoperative findings such as presence of peritubal adhesions, endometriosis, tubal pathology, perihepatic adhesions, and hysteroscopic findings were recorded.

Because this was a retrospective cohort study, informed consent by the patients was not needed. Specific approval was obtained from the institutional review board before starting the study.

RESULTS

A total of 198 patients fulfilled the criteria. The demographic parameters of the group are given in Table 1. Out of 198 women, 109 (55.1%) had primary and 89 (44.9%) had secondary infertility.

In the secondary infertility group hysteroscopic abnormalities were more common, while in the primary infertility group laparoscopic abnormalities were seen more frequently. Patients undergoing laparoscopy after previous failed IUI were more likely to have abnormalities in both laparoscopy and hysteroscopy.

Endometriosis and adnexal adhesions were the most common abnormalities detected in laparoscopy in the primary and secondary infertility groups, respectively. The most common intrauterine pathology in both the groups was periosteal adhesions.

Of the 198 patients included in the study, 103 (52%) had pathological findings at laparoscopy [Table 2]. Whereas only 46 patients had pathological findings by hysteroscopy [Table 3].

Out of 198 patients, findings at laparoscopy led to a change of treatment planned for 42. Of these patients, 19 were advised direct IVF, whereas 23 patients were advised further IUI [Table 4].

DISCUSSION

The position of diagnostic laparoscopy in current fertility practice is still under debate. Until recently, laparoscopy was the final diagnostic procedure of female fertility exploration, as outlined by the American Fertility Society in 1992 and by the World Health Organization guidelines.^[16] In 1997, Glatstein *et al.* reported that 89% of all reproductive endocrinologists in the USA routinely performed a laparoscopy in the diagnostic work-up of infertility.^[17] However, some investigators showed that diagnostic laparoscopy did not reveal any pathology or only minimal and

Table 1: Demographic profile of patients

| Parameter | Total | Normal finding (%) | Pelvic pathology (%) |
|---------------------------|------------------------|--------------------|----------------------|
| Age (*) | 29.8 years | | |
| BMI (*) | 26.9 kg/m ² | | |
| Marital life (*) | 5.6 years | | |
| Primary infertility (#) | 109 | 39 (35.8) | 70 (64.2) |
| Secondary infertility (#) | 89 | 56 (62.9) | 33 (37.1) |
| Previous IUI done (#) | 76 | 16 (21.1) | 60 (78.9) |

(*)Values presented as mean, (#)Values presented as percentage, BMI = Body mass index

Table 2: Findings at laparoscopy

| Type of pathology | Ochoa <i>et al.</i> ^[19] (%) | Tanahatoo <i>et al.</i> ^[20] (%) | Tsuji <i>et al.</i> ^[25] (%) | Bonneau <i>et al.</i> ^[26] (%) | Drake <i>et al.</i> ^[9] (%) | Jayakumari <i>et al.</i> ^[15] (%) | Present study (%) |
|------------------------|---|---|---|---|--|--|-------------------|
| Normal | 33/92 (35.9) | 33/64 (51.6) | 11/57 (19.3) | 19/114 (16.7) | 6/24 (25) | 16/127 (12.6) | 95/198 (47.9) |
| Minimal endometriosis | 21/92 (22.8) | 28/64 (43.8) | 14/57 (24.6) | 72/114 (63.2) | 11/24 (45.9) | 48/127 (37.8) | 48 (24.2) |
| Mild endometriosis | 6/92 (6.5) | | 7/57 (12.3) | | | 42/127 (33.1) | 41 (20.7) |
| Moderate endometriosis | 8/92 (8.7) | | 8/57 (14) | | | 8/127 (6.3) | 7 (3.5) |
| Severe endometriosis | 2/92 (2.2) | | 7/57 (12.3) | | | | |
| Endometriotic cyst | 8/92 (8.7) | | | | | | |
| Adhesions | 30/92 (32.6) | 3/64 (4.7) | 5/57 (8.8) | 5/57 (8.8) | 5/57 (8.8) | 4/127 (3.1) | 35 (17.8) |
| Tubal pathology | 1/92 (1.1) | 0/64 | 3/57 (5.3) | 24/114 (21.1) | | 22/127 (17.3) | 42 (21.2) |
| Perihepatic adhesions | | | | | | | 33 (16.9) |
| Tubercular granuloma | | | | | | | 2 (1.2) |

Table 3: Findings at hysteroscopy

| Type of pathology | Makled <i>et al.</i> ^[13] | Jayakrishnan ^[14] | Present study (%) |
|----------------------------------|--------------------------------------|------------------------------|-------------------|
| Normal | 14 | 127/127 | 152 (76.8) |
| Periosteal adhesions | | | 13 (6.6) |
| Polyyps | 31/93 | | 9 (4.5) |
| Stenosis of internal os | 6 | | 3 (1.5) |
| Deep-seated ostia — small cavity | | | 4 (2) |
| Septum | | | 1 (0.5) |
| Fundal adhesions | 7 | | 6 (3) |
| Endometritis | 14/93 | | 6 (3) |
| Endometrial hyperplasia | 15 | | 4 (2) |

mild endometriosis in 40-70% of all cases.^[4]

The available evidence on the role of laparoscopy before ovulation induction merely focuses on the comparison between HSG and laparoscopy findings for the diagnosis of tubal pathology, the diagnosis and treatment of adhesions, and the treatment of minimal and mild endometriosis. This study also takes into consideration the role of laparoscopy in patients who have previously failed IUI as against those who have never undergone any treatment.

The most common pelvic pathology in our study was minimal endometriosis, whereas tubal pathology was observed in 21% cases despite a normal HSG [Table 2]. In a cohort study, Lessey *et al.* also found a high prevalence of endometriosis in patients with unexplained infertility.^[12] In a similar study, Poncelet *et al.* found that laparoscopy revealed pelvic pathology in 95 out of 114 patients. Of those, 72 had endometriosis, 46 pelvic adhesions, and 24 tubal disease.^[18]

In a retrospective study, Capelo *et al.*^[19] performed diagnostic laparoscopy in 92 patients after four failed cycles of ovulation induction treatment with clomiphene citrate. Laparoscopic findings were strictly normal in only 36% of cases (as against 48% in our study), whereas endometriosis and/or pelvic adhesions were observed in 50% and 33%, respectively. The authors concluded that laparoscopy continues to be a useful tool in the work-up of an infertile couple but regrettably did not present any pregnancy rates following laparoscopic surgery.^[19] These results are comparable to that obtained in our study. The slightly higher percentage of normal findings in our study is because of a higher number of patients who have not been treated previously. Tubal pathology is significantly higher in our study, perhaps because of the higher incidence of tuberculosis in India.

In the retrospective study done by Tanahatoo *et al.*,^[20] diagnostic laparoscopy changed the intended treatment in 124 of 495 patients (25%). This is comparable to our study where the treatment was changed *post* laparoscopy in 42 patients (21.1%). Excluding the presence of minimal and mild endometriosis as pelvic pathology without therapeutic implications, the additional value of diagnostic laparoscopy is limited to only 9 of 198 patients (8%), which is similar to previous reports.^[20] This coincides with previous studies done by Tanahatoo *et al.*,^[10] who also concluded that diagnostic laparoscopy is a reliable procedure in detecting abnormalities and in contributing to the management plan.

Some of the previous studies show relatively low impact of laparoscopy on overall pregnancy rates. This has led to a movement from “diagnostic work-up” to a “prognosis-oriented approach” in the investigation and treatment of the infertile couple. Therefore, many found it logical to offer patients with a normal HSG a treatment by combined gonadotropins and IUI for 3-6 months, switching to assisted reproductive technology (ART) if such a treatment failed.^[21] Goldman *et al.* found that in the absence of findings during an unexplained infertility evaluation, routine laparoscopy was not necessary. The majority of patients who proceed to treatment will become pregnant. However, this study compared pregnancy outcomes in women with unexplained infertility rather than findings at laparoscopy.^[22] Shimizu *et al.* concluded that diagnostic laparoscopy should be offered as an option for younger patients who desire spontaneous pregnancy because no significant difference was found in the cumulative pregnancy rate between patients proceeding to direct IVF and those doing so after laparoscopy. In the latter, however, the chance of spontaneous conceptions was higher.^[23]

However, in our study, significant pelvic pathologies were seen in patients who have undergone 2-3 cycles of failed IUI. In our study, out of the 76 patients with previous failed IUI, 60 had positive findings on laparoscopy. One may, by extrapolation, expect a higher pregnancy rate after laparoscopic treatment after several failed IUI cycles. Whether laparoscopy should be performed after or before IUI was studied in a retrospective study designed by Tanahatoo *et al.*^[10]

Few reports in the available literature on imaging modalities in unexplained infertility focus on hysteroscopic findings along with laparoscopy. In many previous studies, no significant finding had been found on hysteroscopy. This is not surprising, as other authors have also demonstrated that a regular myometrial-endometrial interface and homogeneous endometrial structure

Table 4: Postlaparoscopy treatment plan

| Treatment plan | Lavy <i>et al.</i> ^[27] | Tsuji <i>et al.</i> ^[28] | Jayakrishnan <i>et al.</i> ^[15] | Present study |
|--------------------|------------------------------------|-------------------------------------|--|----------------|
| Fertile period/IUI | 60/63 (95.2%) | 49/57 (86%) | 151/172 (87.8%) | 179/198(90.4%) |
| Direct IVF | 3/63 (4.8%) | 8/57 (14%) | 21/172 (12.2%) | 19/198 (9.6%) |

on transvaginal sonography indicated a normal endometrium and precluded the need for diagnostic hysteroscopy.^[13]

In our study, 77% patients had normal findings [Table 3]. The most common pathology seen on hysteroscopy was periosteal adhesions, whose clinical significance is debatable. Nine cases showed the presence of polyps not previously seen on ultrasonography. Hysteroscopic findings of asymptomatic endometrial polyps have been reported to be 10-32%. The role of endometrial polyps in infertility has not been clearly defined, though a prospective study of 224 infertile women who underwent hysteroscopy observed a 50% pregnancy rate after polypectomy.^[24]

Demonstration of the effectiveness of laparoscopy would be inadequate without it being cost-effective. Unfortunately, there are insufficient studies to enable us to assess the cost-benefit ratio of laparoscopy in unexplained infertility. The Practice Committee of the American Society of Reproductive Medicine suggests that laparoscopy should be seriously considered before applying aggressive empirical treatments involving significant cost and/or potential risks.^[2] Moayeri *et al.* found that laparoscopy followed by expectant management after surgical correction of endometriosis was cost-effective. They determined that the dropout rate had the largest impact on the incremental cost-effectiveness ratio and that therefore it was the most important factor for determining when laparoscopy was the optimum choice specifically, when dropout from fertility treatments exceeded 9%.^[24]

The timing of laparoscopy, too, has been a matter of debate. Although laparoscopy prior to initiating treatment looks attractive, the cost of this surgical procedure is high, especially when patients have to pay for the costs. Many clinicians thus prefer to treat couples with unexplained infertility with a few cycles of ovulation stimulation with IUI before proceeding to laparoscopy.

In our study, performing a laparoscopy after at least three cycles of ovulation stimulation with IUI should have logically led to a reduction in the number of negative laparoscopies, which is evident by the comparatively higher detection of pelvic pathology in this study (78.9%). These cases are those where laparoscopy would have led to either increased fertility or a change in the treatment modality.

CONCLUSION

In conclusion, laparoscopy has been found to be an effective component of infertility management, especially when patients have failed three or more cycles of IUI. Even though the outcome in terms of clinical pregnancy may not be significant as per previous studies, laparoscopy may help prevent unnecessary treatment wherein success rates are low. Further well-controlled prospective randomized trials are required to compare the roles of laparoscopy and IUI in patients of unexplained infertility.

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Conflicts of interest

There are no conflicts of interest.

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