

Unexplained Infertility with Normal Hysterosalpingography Report: Is Laparoscopy the Next Rational Step?

Maruf Siddiqui¹, Nusrat Ghafoor², Rusmila Shamim Abdullah³,
Fahmida Naznine³, T A Chowdhury⁴

Abstract

Study Objective: To evaluate the role of laparoscopy in patients with unexplained infertility with normal Hysterosalpingography (HSG) reports.

Study design and setting: This prospective interventional study was carried out at the Department of Infertility & Reproductive Medicine, Anwer Khan Modern Medical College, Dhaka, Bangladesh in between January 2015 to September 2019.

Materials & Methods: A total of 220 patients with unexplained infertility were recruited as the study population. Inclusion criteria included a normal uterus and adnexa on transvaginal ultrasonography (TVS), an evidence of ovulation by a serum day 21 progesterone in a natural cycle, a normal semen parameter of the husband, a normal thyroid stimulating hormone (TSH) level, a normal blood sugar profile and a normal findings in Hysterosalpingography (HSG). All patients were recruited for a diagnostic laparoscopy. However, interventions were done where necessary to enhance the fertility potential of those patients.

Results: Findings were normal in 47 patients (23.5%). (Table I) Endometriosis was diagnosed in as high as 123 patients (61.5%). 27 patients (13.5%) were found to have peritubal and/or perifimbrial adhesions. Flimsy adhesions and distorted tubo-ovarian relationships were found in 14 patients (6.36%) in which possible diagnosis was Pelvic Inflammatory Disease (PID). Interestingly, 9 patients (4.09%) had unilateral tubal block though their previous Hysterosalpingography (HSG) reports showed patent tubes with free spillage in the pelvis. Following laparoscopy, a total of 159 patients (72.27%) were advised for a timed intercourse, ovulation induction with letrozole, ovulation induction with letrozole and Gonadotropins and Intrauterine Inseminations (IUI). However, still a significant number of 61 patients (27.73%) were advised or recruited for Assisted Reproductive Technology (ART) following the laparoscopy. Following Laparoscopic surgery, a total of 102 patients (46.36%) conceived within the next one year.

Conclusion & Recommendation: Laparoscopy should be performed in patients with unexplained infertility and normal HSG reports because of its diagnostic and therapeutic values specially in younger age group of patients or in patients who cannot afford to proceed for repeated cycles of ART.

Key Words: Unexplained Infertility, Hysterosalpingography, Laparoscopy

Introduction

The patient is labelled as a case of unexplained infertility when no possible cause is found with currently available diagnostic facilities. Unexplained infertility generally accounts to 15-20% of total causes of Infertility throughout the world. The first steps are usually the assessment of a healthy uterus, a normal semen parameter and an evidence of ovulation in a natural cycle. Timed intercourse around

ovulation time is advised in many of the centers to increase the pregnancy rates. If the couple fails to conceive naturally, then controlled ovarian stimulation (COH) or superovulation along with measurement of follicles and endometrial thickness assessment is considered as the next step. The conventional drugs used for COH include clomiphene citrate, letrozole or even gonadotropins. Many of the RCTs demonstrated a higher pregnancy rate following a COH because it increases the quality of follicle

1. Professor & Head, Dept. of Infertility & Reproductive Medicine, Anwer Khan Modern Medical College, Dhaka, Bangladesh
2. Associate Professor & Consultant, Dept. of Radiology & Imaging, Ibrahim Cardiac Hospital & Research Institute (ICHRI), Dhaka
3. Assistant Registrar, Dept. of Infertility & Reproductive Medicine, Anwer Khan Modern Medical College, Dhaka
4. Honorary Chief Consultant and Professor of Obstetrics & Gynecology, Ibrahim Medical College & BIRDEM Hospital, Dhaka, Bangladesh

Corresponding Author: Prof. Dr. Maruf Siddiqui, Dept. of Infertility & Reproductive Medicine, Anwer Khan Modern Medical College, Block F, House 20, Road 8, Dhanmondi, Dhaka, Bangladesh. E-mail: drmaruf2000@yahoo.com.

Date of Submission: 07-09-2020 | Date of Acceptance: 15-12-2020

and improves the state of endometrium. Many centers prefer to go for Hysterosalpingography (HSG) after that and if the findings are normal, they prefer to proceed for 3-4 cycles of Intrauterine Insemination (IUI). In case when the patient remains childless in spite of performing IUIs with COH, the options are proceeding for Assisted Reproductive Technology (ART) or Laparoscopy. A significant number of centers and fertility specialists now a days have been avoiding laparoscopies and straightly going for ART cycles until the patient conceives. But ART generally does not have a very promising outcome and may need repeated trials. Moreover, a substantial portion of patients in a developing country like Bangladesh cannot afford to proceed for ART. On the other hand, diagnostic laparoscopy is helpful to find out several causes in unexplained infertility and can help the physician to establish a diagnosis for that patient. Diagnostic laparoscopies were effective to find out the exact pathology in 21% to as high as 68% patients in unexplained infertility (Corson et al.2000¹, Badawi et al.1999², Cundiff et al.1995³). Endometriosis and different types of tubal diseases are the prime findings in those studies. Laparoscopy also gives the opportunity not only to diagnose, but also to perform necessary interventions depending on the precise pathology. COH and IUIs are repeated again when there are normal laparoscopic findings or when mild problems are corrected during the procedure. The patients are referred for ART when there are extensive adhesions in the pelvic cavity or in case of moderate to extensive tubal damages. Fertility specialists throughout the world are increasingly deviated to proceeding for ART in unexplained infertility bypassing the laparoscopy. It is still a controversial issue whether diagnostic laparoscopies should be performed in unexplained infertility with normal HSG findings. But that is not a practical approach for many of the infertile patients in Bangladesh as ART is expensive and may need repeated trials. This prospective study was therefore done to evaluate the role of laparoscopy in patients with unexplained infertility and a normal HSG report.

Materials and Methods

This prospective interventional study was carried out in a total of 220 patients with unexplained infertility and a normal Hysterosalpingography (HSG) report in between January 2015 to December 2019 at the department of infertility & reproductive Medicine, Anwer Khan Modern Medical College, Dhaka, Bangladesh.

Inclusion criteria included

1. A transvaginal ultrasonography (TVS) showing normal uterus and adnexa,
2. Evidence of ovulation by a serum day 21 progesterone in a natural cycle
3. A normal semen parameter of the husband
4. A normal thyroid stimulating hormone (TSH) level
5. A normal blood sugar profile and
6. A normal Hysterosalpingography (HSG) finding.

HSG finding was considered as normal by

1. Visualization of a bilateral tubal spillage
2. Absence of any hydrosalpinx and
3. Absence of any uterine abnormalities.

The mean age of the patient was 29.9±3.2 years.

All patients were recruited for a diagnostic laparoscopy. All normal and abnormal findings were documented. However, interventions were done where necessary to enhance the fertility potential of those patients. Following laparoscopy, patients were advised for a timed intercourse, ovulation induction with letrozole, ovulation induction with letrozole and Gonadotropins and Intrauterine Inseminations (IUI). Some of the patients were advised or recruited for ART following the laparoscopies due to their indication in laparoscopy findings. All the patients were followed up for the next one year following laparoscopies to find out the fertility outcome.

Results

A total of 220 patients met the inclusion criteria and was recruited for a diagnostic laparoscopy. However, interventions were done where necessary to enhance the fertility potential of those patients. Findings were normal in 47 patients (21.36%). (Table I) Endometriosis was diagnosed in as high as 123 patients (61.5%). 27 patients (13.5%) were found to have peritubal and/or perifimbrial adhesions. Flimsy adhesions and distorted tubo-ovarian relationships were found in 14 patients (6.36%) in which possible diagnosis was Pelvic Inflammatory Disease (PID). Interestingly, 9 patients (4.09%) had unilateral tubal block though their previous Hysterosalpingography (HSG) reports showed patent tubes with free spillage in the pelvis. (Table II)

Table I. Laparoscopic findings in study population

Type of findings at laparoscopy	Total 220 pts N(%)
Normal findings	47(21.36%)
Pathologies detected	173(78.64%)

Table 1. Among 220 patients, findings were normal in 47 patients (21.36%).

The different treatment modalities used during the laparoscopy were as follows: Endometriosis was treated by fulguration/bipolar coagulation, adhesiolysis was done in peritubal/fimbrial adhesions and also in cases of distorted anatomy due to suspected pelvic inflammatory disease to restore the normal tube ovarian relationship, and hysteroscopic cannulation was performed in blocked tubes with subsequent observation of free spillage of dye through laparoscopy. Small subserous myomas were observed in a few cases but they were not documented in this study or treated as they were not considered to be the etiological factor for infertility.

Following laparoscopy, a total of 159 patients (72.27%) were advised for a timed intercourse, ovulation induction with letrozole, ovulation induction with letrozole and

Table II

Type of pathological findings at laparoscopy	Total 173 pts N(%)
Endometriosis	123(61.5%)
Grade I -----	57(25.9%)
Grade II -----	27(12.27%)
Grade III -----	22(10%)
Grade IV -----	17(7.27%)
Peritubal/fimbrial adhesions	27(13.5%)
Distorted anatomy	14(6.36%)
Tubal block	09(4.09%)

Table II. A total number of 173 patients were detected with pathology or abnormal findings at laparoscopy. Endometriosis was diagnosed in 123 patients (61.5%). 27 patients (13.5%) were found to have peritubal and/or perifimbrial adhesions. Flimsy adhesions and distorted tubo-ovarian relationships were found in 14 patients (6.36%) and 9 patients (4.09%) had unilateral tubal block.

However, still a significant number of 61 patients (27.73%) were advised or recruited for Assisted Reproductive Technology (ART) following the laparoscopy. So, laparoscopy definitely helped us in this study to identify which patients to refer for ART and who are those in whom other type of treatment modalities can be offered again.

Table III. Patterns of treatment resulting in pregnancy following laparoscopy

Type of treatment	N=102
Timed Intercourse	23
Letrozole	37
Letrozole + Gonadotropins	14
OI + IUI	17
ART	11

Following Laparoscopic surgery, a total of 102 patients (46.36%) conceived within the next one year. The pattern of treatment is illustrated in table III. 23 patients conceived simply by maintaining a timed intercourse, a large number of 37 patients got pregnant by ovulation induction or superovulation by letrozole up to 7.5 mg, 14 patients conceived with Gonadotropins along with letrozole and 17 patients got pregnant through Intrauterine Inseminations (IUI). 11 patients got pregnant after going through ART. Unfortunately, many of the patients referred for ART could not afford it and we lost tracking some of the patients.

Discussion

HSG is widely used for assessment of tubal patency worldwide. However, the exact assessment of tubal patency and status can only be possible by laparoscopy which allows for direct visualization. Many RCTs (Swart et al. 1995, Rice et al. 1986) demonstrated the sensitivity of HSG in detecting peritubal adhesions ranging from as low as 34% to as high as 83%. But a number of studies (Corson et al. 2000¹, Badawi et al. 1999², Belisle et al. 1996⁴, Cundiff et al. 1995³) reported to diagnose pathologies in 21% to 68% cases in laparoscopies for infertile patients with normal HSG findings. Tsuji et al. 2009⁵ reported a normal finding in laparoscopy in only 19.3% patients who had a normal HSG and were labelled as a case of unexplained infertility. In our study, 47 patients (21.36%) only had normal findings in laparoscopy and a definite pathology was detected in a large number of 173 patients (78.64%). In patients with unexplained infertility with normal HSG, diagnostic laparoscopy can assist us to directly visualize the pelvic cavity including endometriosis, tubal adhesions and tubal diseases.

In our study, endometriosis was detected in 61.5% patients, peritubal or perifimbrial adhesions in 13.5% cases and blocked tubes in 4.09% cases. Isao et al in a Japanese study reported the incidence of endometriosis in 63.2% cases, peritubal adhesions in 8.8% cases and tubal occlusion in 5.3 % cases which are more or less similar with our study. However, we detected 6.36% patients with distorted anatomy and flimsy adhesions in addition to the peritubal adhesions may be attributed to the high prevalence of pelvic inflammatory disease in Indian subcontinent region.

In unexplained infertility with normal HSG findings, Fatum et al. 2002⁶ suggested to treat the patients with 3 to 6 cycles of combined gonadotropins and IUI, and then switching them to ART. They recommended that diagnostic laparoscopy should be omitted in such group of patients. Due to development of ART procedures worldwide, many fertility specialists are planning to bypass laparoscopy and proceeding for ovulation induction with IUI and finally ART.

Nakagawa et al. 2007⁷ performed diagnostic laparoscopy for unexplained infertility and the compared the pregnancy rate following laparoscopy with that following ART performed in the same center. They reported a significantly higher pregnancy rate following laparoscopy compared to ART especially in younger age group.

Olarinoye AO et al 2014⁸ al in their study recommended HSG as a simple and nearly non invasive method to assess tubal patency and uterine anomalies with low complication rate, but they also recommended to proceed for a laparoscopic evaluation in cases of persisting infertility with a normal HSG report.

Bosteels Jan et 2007⁹ al in their study commented that the routine use of diagnostic laparoscopy for the evaluation of all cases of female infertility is currently under debate. However, diagnostic laparoscopy after several failed cycles of ovulation induction enables the detection of a significant proportion of pelvic pathology amenable to treatment according to data published in retrospective non-controlled studies.

Merviel et al 2011¹⁰ tried to assess the value of systematic laparoscopy in infertility assessment in their study. They concluded that laparoscopy is of course indicated in unexplained infertility even though the HSG seems to be normal.

In our study, a total of 102 patients (46.36%) got pregnant within the next 1 year following laparoscopy which is very encouraging. Tsuji et al. 2009 reported a similar pregnancy rate of 50.9% following laparoscopy in their study. Laparoscopy helped us not only to identify the definite pathology, but also to proceed for necessary interventions in the same setting to increase the pregnancy rate.

Conclusion

Many fertility specialists nowadays prefer to omit laparoscopy in patients with unexplained infertility and normal HSG reports. A significant number of patients remain childless after going through IUI and ART procedures. ART is expensive and usually require repeated trials. Many patients of Bangladesh are not affluent enough to go through it. On the other hand, laparoscopy is also relatively expensive and require general anesthesia. It has got a distinctive advantage of directly visualizing the pelvic cavity and for making interventions as required, moreover the patients can again be recruited for natural trial, ovulation induction or IUI again. Our study demonstrated a significant pregnancy rate following one year of laparoscopy. Laparoscopy definitely can be helpful to identify which patients are required to refer for ART and who are those patients in which other type of treatment modalities can be offered. We therefore recommend that laparoscopy should be performed in patients with unexplained infertility and normal HSG reports because of its diagnostic and therapeutic values especially in younger age group of patients or in patients who cannot afford to proceed for repeated cycles of ART.

Source of Fund: Nil

Conflict of Interest: None

How to cite this article: Siddiqui M, Ghafoor N, Abdullah RS et al. Unexplained Infertility with Normal Hysterosalpingography Reports: Is Laparoscopy the next rational step? *Bangladesh J Fertil Steril*; 2021;1(2): 80-83

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