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Original research article

Hospital Based Assessment The HSG Findings of Genital TB in Infertile Women: An Observational Study

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Abstract

Aim: The aim of the present study was to determine the HSG findings of genital TB in infertile women.

Methods: The present study was conducted in the Department of obstetrics and Gynecology, Advanced Maternity Fertility Centre Janm IVF, Bhagalpur, Bihar, India of 100 women who had a proven genital TB.

Results: The mean age was 26.6 ± 4.4 years, mean body mass index was 24.8 kg/m2, and mean duration of infertility was 6.08 years. Primary infertility was seen in 33 (66%) women, while secondary infertility was seen in 17 (34%) women. Normal cycles were seen in 50 women, menorrhagia in 10, hypomenorrhea in 30, oligomenorrhea in 5, primary amenorrhea in 3 and secondary amenorrhea in 2 women. There was no difference in the serum FSH concentration levels. However AMH and AFC were significantly lower.

Conclusion: Both laparoscopy and molecular tests are complementary tests and together can effectively confirm the diagnosis of Genital TB. Very often, it is the HSG finding that alerts the clinician as to the presence of GTB. Though imaging findings may be highly suggestive of TB, some of the features such as tubal block and hydrosalpinx are not specific for TB and may be seen in other infective causes of tubal damage also.

Keywords: Tuberculosis, Female genital, Hysterosalpingography, Infertility, Fallopian tube diseases

Introduction

Female genital tuberculosis (FGTB) is an important variety of extrapulmonary tuberculosis (TB) causing significant morbidity in women such as menstrual dysfunction, infertility, ectopic pregnancy, and tubo-ovarian mass.[1-4] The prevalence of FGTB in infertile women ranges from 7% to 15% in developing countries rising to 26% in tertiary referral hospitals and up to 48% in tubal factor infertility.[3,5] The infection spreads to genital organs normally by hematogenous route with the frequency of involvement of fallopian tubes (90%), endometrium (50–80%), ovaries (20–30%), cervix (5–10%), and rarely vulva and vagina.[1] FGTB is an important cause of intrauterine adhesions (Asherman's syndrome), pelvic adhesions, and perihepatic adhesions (Fitz–Hugh–Curtis syndrome).[6,7]

Diagnosis of FGTB is usually made by endometrial sampling for acid-fast bacilli (AFB) microscopy, culture, histopathological epithelioid granuloma, positive polymerase chain reaction, diagnostic hysteroscopy, and/or laparoscopy for various TB findings.[8,9] Imaging

modalities such as ultrasound, computerized axial tomography, magnetic resonance imaging (MRI), and positron-emission tomography (PET) have also been found to be useful in women with tubo-ovarian masses with FGTB.[10,11]

HSG is the choice imaging method for evaluation the abnormalities of the fallopian tubes in patients with genital TB. HSG is a helpful imaging modality for evaluating the internal architecture of the female genital tract and is the most invaluable procedure in the assessment of tubal factor infertility in developing countries. The two imaging techniques useful in the diagnosis of FGTB are hysterosalpingography (HSG) and ultrasonography (USG). HSG evaluates the internal structure of the female genital tract and tubal patency, whereas USG allows simultaneous evaluation of ovarian, uterine, and extra pelvic involvement.

The laparoscopic findings suggestive of genital TB may vary from normal appearance to tubercles on the surface, fimbrial block, fimbrial phimosis, tubal beading, peritubal adhesions,
periovarian adhesions, tubo-ovarian mass, hydrosalpinx, and rigid tubes. The aim of this study was to determine the HSG findings of genital TB in infertile women.

MATERIALS AND METHODS

The present study was conducted in the Department of obstetrics and Gynecology, Advanced Maternity Fertility Centre Janm IVF, Bhagalpur, Bihar, India of 100 women who had a proven genital TB for 2 years. The medical records of patients were reviewed for data collection.

Inclusion criteria

All participants were women with complaints of infertility to whom FGTB was suspected as a cause of infertility or women with infertility of unknown etiology.

Exclusion criteria

- Women who had other explainable causes of infertility such as anatomical and endocrinal.
- Acute PID.

Methodology

All women underwent HSG as an initial investigation for primary and secondary infertility. The type and duration of the infertility, personal history, and clinical symptoms (including menstrual irregularities, abdominal and pelvic pain, fever and general symptoms) were recorded for all women. The HSG was performed between the 8th and 11th day of the menstrual cycle. Water soluble contrast medium was introduced using a canola placed in the cervical canal under aseptic condition. Films were taken with the woman in supine anteroposterior projection and oblique views were done when necessary.

A detailed history of the symptoms, menstrual history (amenorrhea, oligomenorrhea, menorrhagia; duration of cycles, amount of menstrual blood flow, with or without associated dysmenorrhea) was taken. The endometrial aspirate was taken in premenstrual phase and sent in saline for AFB microscopy, culture, PCR for M. tuberculosis, and in formaline for histopathological evidence of epithelioid granuloma.
A cycle Day 2–4 hormone profile including serum follicular stimulating hormone (FSH), leutinizing hormone (LH) and AMH was performed. Serum FSH and LH were measured using automated electrochemiluminiscence assays (Roche Diagnostics e411, Boehringer

Mannheim, Germany), while 2 ml of blood was collected from the subjects and serum was frozen at −40°C for the AMH assay. AMH was measured in batches with Gen II enzyme-linked immunosorbent assay (Beckman Coulter Inc., USA). The inter-assay co-efficient of variation for AMH was 3.8–11.0% and the intra-assay co-efficient of variation was 5.1–10.1%.

Follow-up and treatment

All women in Group I were evaluated by a pulmonologist (A.K. or S.K.). They were counselled and prescribed standard ATT. They received verbal and written information regarding the need for compliance and possible side effects and were asked to report in the event of experiencing any recognized side effects of ATT. They were followed up every 15 days for the first 2 months. Fertility treatment was initiated subsequently as governed by the clinical indication, while ensuring compliance with ATT. IVF, when deemed necessary, was performed after ATT completion.

Age, duration and aetiology of infertility, ovarian reserve and previous treatment guided further management. A short duration of ovulation induction and timed intercourse or up to two cycles of IUI or IVF/ICSI were advised as appropriate. Individualized ovarian stimulation protocols were used for IVF based on serum AMH values. A maximum of two embryos were transferred on Days 3 or 5. Transfer of three embryos was considered in women who were above 35 years of age or poor ovarian responders or women with previous IVF failures. Those who conceived were followed up for further nine months to document the pregnancy outcome.

Statistical analysis

Descriptive statistics such as mean, median, standard deviation, and range were calculated for study characteristics age, weight, and duration of infertility. Assumptions of normality for continuous primary outcome variables were tested using Kolmogrov-Smirnov-tests. Changes in outcome variables (continuous variables) were compared using student's t-test paired test from baseline to posttest. Similarly, changes in qualitative variables were compared using McNemar's chi-square test. Frequency variables across categories were compared using chi-square test or Fischer's exact test as appropriate. A probability level $P < 0.05$ was considered for statistical significance. All data analysis was carried out using the SPSS software version 9.0, IBM Inc., USA).

RESULTS

Table 1: Characteristics and menstrual pattern of women

Characteristic	**Range**	**Mean**
Age (years)	20–38	26.6
Body mass index (kg/m²)	18.6–32.8	24.8
Parity	0–4	0.9
Duration of infertility (years)	2–14	6.08±2.6
Type of infertility (%)		
Primary	70 women (70%)	
Secondary	30 women (30%)	
Menstrual pattern		
Normal cycle	50	
Hypomenorrhea	30	
Menorrhagia	10	
Oligomenorrhea	5	

Primary amenorrhea	3
Secondary amenorrhea	2

The mean age was 26.6 ± 4.4 years, mean body mass index was 24.8 kg/m2, and mean duration of infertility was 6.08 years. Primary infertility was seen in 33 (66%) women, while secondary infertility was seen in 17 (34%) women. Normal cycles were seen in 50 women, menorrhagia in 10, hypomenorrhea in 30, oligomenorrhea in 5, primary amenorrhea in 3 and secondary amenorrhea in 2 women. There was no difference in the serum FSH concentration levels. However AMH and AFC were significantly lower.

A normal uterine cavity was observed in 55 women, an irregular cavity in 10 women, an Irregular intrauterine filling defect in 10, T-Shaped cavity in 5 women, a small shrunken cavity in 10 women and synechiae in 15 women. Five women with uterine abnormality had more than one abnormal finding at HSG. The most common tubal abnormalities were tubal occlusion and hydrosalpinx which were more common on the right fallopian tube. Complete tubal occlusion was observed in 60 patients and hydrosalpinx in 30 patients. Hydrosalpinx was associated with complete tubal blockage in 5 cases and in 10 patients there was incomplete blockage with a mild peritoneal spillage of contrast medium. Ovarian calcification was seen in one patient and we did not observe tubal calcification in any patients. HSG demonstrated venous and lymphatic intravasation of contrast media in the pelvic vessels in 5 patients.

Table 2: Diagnosis of female genital tuberculosis

Diagnostic method	**N %**
Positive acid-fast bacilli on endometrial aspirate	4 (4%)
Tuberculous granuloma on histopathology of endometrial tissue	5 (5%)
Tuberculous granuloma on histopathology of biopsy from peritoneal tubercles	10 (10%)
Positive DNA polymerase chain reaction on endometrial aspirate	95 (95%)
Definite findings of tuberculosis on laparoscopy	85 (85%)

The method of diagnosis of FGTB is shown in Table 2. There was positive endometrial aspirate, AFB culture in 4%, epithelioid tuberculous granuloma on endometrial aspirate in 10%, TB granuloma on histopathology of biopsy from peritoneal tubercle in 10, and positive PCR in 95% cases.

DISCUSSION

TB remains the most common cause of mortality from infectious disease. Every year around 7 million people worldwide develop TB; of these 2 million will die, with 90% of death occurring in low-income countries.[12] There is direct relationship between prevalence of genital TB and pulmonary TB. About 75% of cases with active genital TB have a normal chest x-ray, so a normal chest x-ray cannot exclude the diagnosis of genital TB.[13]

The primary focus of genital TB is the fallopian tubes, which are usually affected bilaterally but not symmetrically.[14] The fallopian tubes are the most common affected genital organs, followed by endometrium, ovary and cervix.[13,15] HSG is a safe, simple, inexpensive and rapid imaging test which can show the internal surface of uterine cavity and fallopian tubes. Some authors have substituted laparoscopy for HSG due to the higher false positive results in the diagnosis of tubal block and its failure to detect mild to moderate peritoneal adhesions.[14]
When TB affects the genital organs, infertility results as a result tubal obstruction and dysfunction, destruction of the endometrium resulting in intra-uterine adhesions and in

advanced stages, by causing ovulatory failure. When the tubercle bacilli reach the tube, infection begins in the mucosa and then spreads through the tubal wall to the peritoneal surface. In a small number of cases secondary to an abdominal lesion, the tubes, ovaries and the uterine serosa are involved initially and then spread towards the mucosa takes place.[16] As a part of infertility work up, HSG is the initial investigation frequently is performed to evaluate tubal patency in those women who do not have morbidities such as pelvic inflammatory disease (PID), previous ectopic pregnancy, previous surgical procedures and endometriosis. In developing countries, HSG continues to be the preliminary investigation to detect the abnormalities of the uterus and fallopian tubes and their patency. It is a reliable test for ruling out tubal occlusion, and it is less invasive and less expensive.[17]

Tubal occlusion in TB is considered the most common finding seen on HSG and occurs most commonly at the junction between the isthmus and ampulla. The tuberculous granulomas can also get calcified in the tubes, endometrial cavities and in the ovaries. The presence calcified lymph nodes or calcified areas in the course of fallopian tubes suggest the diagnosis of the TB. Tubal calcification are usually seen in the form of small linear streaks or tiny nodules in the course of the tubes. Plain films of the pelvis may show such calcifications which must be differentiated from other causes of calcifications such as calcified pelvic nodes, calcified uterine myomas, urinary calculi, pelvic phleboliths and calcification in an ovarian dermoid.
The various abnormalities on HSG depend on the site of the involvement and the severity of the disease. The presence of caseous ulceration of the mucosa of the fallopian tube, irregular tubal contour and diverticular out pouching around the tube may cause a tufted appearance Isthmic diverticula may resemble salpingitis isthmica nodosa but in tubal TB, diverticular out pouching are larger, asymmetric, and are not usually restricted to the isthmic portion of the tube as compared with those of classic salpingitis isthmica nodosa.[18]

Adequate follicular development in response to gonadotrophins is dependent on the ovarian reserve at that period of time. Various tests of ovarian reserve such as AMH, FSH, and AFC have become a part of the routine diagnostic procedure for infertility patients. Recent studies have shown decreased ovarian reserve in FGTB patients.[19-21] Poor ovarian blood flow has also been observed in infertile women with FGTB undergoing assisted reproduction.[22] In the present study, performed in FGTB patients without obvious ovarian involvement diagnosed by endometrial aspiration studies showing evidence of AFB on culture or microscopy, histopathological evidence of epithelioid granuloma, positive PCR along with findings on laparoscopy and/or hysteroscopy, and ovarian function was assessed at enrolment. AMH has been observed to be a superior marker for predicting both oocyte number and quality.[23,24] In the present study, we observed decrease in AMH levels and no change was observed in FSH levels. M. tuberculosis has an antigonadotropic effect.

CONCLUSION

Both laparoscopy and molecular tests are complementary tests and together can effectively confirm the diagnosis of Genital TB. There is direct relationship between prevalence of genital TB and pulmonary TB. About 75% of cases with active genital TB have a normal chest x-ray, so a normal chest x-ray cannot exclude the diagnosis of genital TB. Very often, it is the HSG finding that alerts the clinician as to the presence of GTB. Though imaging findings may be highly suggestive of TB, some of the features such as tubal block and hydrosalpinx are not specific for TB and may be seen in other infective causes of tubal damage also. Therefore, if the treatment for TB is started as early as possible then the TB can be prevented.

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