Original Article

Hysterosalpingography Observations in Female Genital Tuberculosis with Infertility

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Abstract

Background: Hysterosalpingography (HSG) is radiographic evaluation of uterine cavity and tubal patency. **Aims:** The aim of this study was to evaluate the safety and utilisation of HSG in female genital tuberculosis (FGTB) with infertility. **Settings and Design:** The study was conducted in a tertiary referral centre of North India. **Materials and Methods:** It was a prospective study on 87 cases of FGTB with infertility. Diagnosis of FGTB was made by composite reference standard using the presence of acid-fast bacilli on microscopy/culture or positive GeneXpert, positive polymerase chain reaction or epithelioid granuloma on endometrial biopsy or definitive or probable findings on laparoscopy or hysteroscopy. **Statistical Analysis Used:** Suitable statistical methods were used with STATA software version 12.0. **Results:** HSG findings were normal in 49 (56.32%) cases. There were filling defects in 14 (16.09%), short and shrunken cavity in 4 (4.49%), intrauterine synechiae in 14 (16.09%), T-shaped cavity in 3 (3.44%) and deformed uterine cavity in 5 (5.74%) cases. Fallopian tube findings were hydrosalpinx in 12 (13.79%) and 11 (12.64%) cases, beading of tube in 4 (4.59%) and 2 (2.29%) cases, pipestem appearance in 2 (2.29%) cases each and Maltese cross appearance in 3 (3.44%) and 2 (2.29%) cases, respectively. Tubal blockage was seen in 69 (79.31%) and 67 (77.01%) cases being cornual block in 28 (32.18%) and 26 (29.88%) cases, mid-tubal block in 16 (18.39%) and 15 (17.24%) cases, multiple blocks in 10 (11.49%) and 12 (13.79%) cases and fimbrial block in 15 (17.24%) and 14 (16.09%) cases. None of the cases had flare-up of the disease after HSG in the current study. **Conclusion:** HSG is a useful modality in FGTB with infertility.

Keywords: *Extrapulmonary tuberculosis, female genital tuberculosis, hysterosalpingography, infertility*

Introduction

Infertility affects 10%–15% of couples causing serious social and psychological issues and financial burden.[1,2] Various causes of infertility include hypothalamic, pituitary, ovarian, tubal and endometrial causes.[1-5] Tubal factors are responsible for up to 30%–40% of cases in some studies.[3] Fallopian tubes are vulnerable to infections such as acute and chronic pelvic inflammatory diseases including tuberculosis (TB), endometriosis and past surgeries.[1] Tubal patency is an important test for subfertility which can be assessed by hysterosalpingography (HSG), sonosalpingography and laparoscopic dye test.[1,3-7] HSG includes instillation of oil-based or water-based contrast medium into endometrial cavity followed by radiography to evaluate uterine cavity and tubal patency.[8,9] There is a therapeutic effect of HSG contrast medium in subfertile women

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with an increase in pregnancy rate which is considerably more with oil-based contrast medium than water-based contrast medium.[8] However, recent studies indicate that much safer water-based contrast medium-based HSG is also associated with increased pregnancy rate.[9,10] Female genital TB (FGTB) can cause subfertility through tubal blockage, endometrial atrophy and synechiae (Asherman's syndrome) and ovarian causes.[11,12]

The present study was conducted to evaluate the role of HSG in FGTB to detect endometrial and tubal disease.

Materials and Methods

It was a prospective cohort study conducted on 87 patients out of 167 women with infertility diagnosed to have FGTB on composite reference standard (CRS) as per Appendix 1 over a 4-year study period (January 2015–March 2019) in whom HSG was done before suspicion of TB as infertility protocol. The Ethical clearance was taken from the Institute Ethical Committee, Vide No: Z-28015/44/2015. The study setting was in a tertiary referral centre. The study was carried out in compliance with the ethical principles of the Declaration of Helsinki. No sample size calculation was performed.

The inclusion criteria were cases of FGTB diagnosed on CRS who had HSG done for their infertility for tubal patency. The exclusion criteria were frank TB diagnosed before HSG or patient refused for HSG. Informed written consent was taken from all subjects. History taking, clinical examination and baseline investigations were performed. Endometrial sampling was taken in all patients in secretory phase (days 21–23) with no. 4 Karman's cannula for acid-fast bacilli (AFB) on microscopy, culture, polymerase chain reaction (and in-house DNA PCR in which a 240-bp region of the mpt64 gene was amplified by PCR) and GeneXpert and for histological type of endometrium and for any epithelioid granulomatous endometritis. Diagnostic laparoscopy with or without hysteroscopy was performed in majority of the cases for findings of FGTB which included definite findings such as beaded tubes, caseous nodules, tubercles, abdominal and pelvic adhesions, hydrosalpinx, pyosalpinx, shaggy areas and probable findings such as convoluted tubes, hyperaemic tubes and straw-coloured fluid. HSG was not routinely done in cases of FGTB for fear of flare-up of the disease but was done in 87 cases before diagnosis of FGTB as part of infertility protocol and its findings in endometrial cavity and tubes were observed in all cases. All subjects of FGTB were treated free of cost in directly observed treatment short-course centres daily.

Statistical analysis

Data analysis was carried out using STATA software version 12.0 STATA Corp 2011, Texas, USA Continuous variables were tested using Kolmogorov–Smirnov test and comparison of two groups means were tested using Student's 't' independent test. Percentage values and comparison were tested using Chi-square/Fisher's exact test. Diagnostic accuracy between CRS and the tests such as GeneXpert and PCR, sensitivity, specificity, positive predictive value, negative predictive value, LR (+) and LR (−) were calculated using 95% confidence intervals.

Results

The characteristics of women in the study are shown in Table 1. The mean age, body mass index and parity were 27.2 ± 4.6 years, 22.5 ± 2.35 kg/m^2 and 0.31, respectively. Family history and past history of TB were seen in 19 (21.8%) and 24 (27.58%), cases respectively. Infertility was primary in 68 (78.18%) and secondary in 19 (21.83%), with a mean duration of infertility being 2.5 ± 1.5 years. Menstrual dysfunction was

Table 1: Characteristics and symptomatology of patients (*n*=87)

Characteristics	*n* (%)
Age (years)	
Range	21-39
Mean±SD	27.2±4.6
Body mass index (kg/m^2)	
Range	18.1-31.5
Mean±SD	22.5±2.35
Parity	
Range	0-3
Mean	0.31
Family history of TB	19 (21.83)
Past history of TB or anti-tubercular therapy	24 (27.58)
Type of infertility	
Primary	68 (78.16)
Secondary	19 (21.83)
Duration of infertility (years)	
Range	1.5-6
Mean±SD	2.5±1.5
Menstrual symptoms	
Normal menstruation	35 (40.22)
Heavy menstrual bleeding	2 (2.29)
Hypomenorrhoea	22 (25.28)
Oligomenorrhoea	25 (28.73)
Secondary amenorrhoea	3 (3.44)
Anorexia	12 (13.79)
Weight loss	13 (14.94)
Pyrexia	10 (11.49)
Abdominal or pelvic pain	16 (18.39)
Abdominal or pelvic lump	11 (12.64)
Unhealthy vaginal discharge	27 (31.03)

TB=Tuberculosis, SD=Standard deviation

common being heavy menstrual bleeding in 2 (2.29%), oligomenorrhoea in 25 (28.73%), hypomenorrhoea in 22 (25.28%) and secondary amenorrhoea in 3 (3.44%) cases, respectively. Other symptoms were pyrexia (11.49%), loss of appetite (13.79%), weight loss (14.94%), abdominal or pelvic pain (18.39%), unhealthy discharge (31.03%) and abdominal or pelvic lump (12.64%).

Table 2 shows the examination and general investigations. Various signs were fever (9.19%), lymphadenopathy (6.89%), pallor (39.08%), jaundice (2.29%), chest crepitations (8.04%), abdominal lump on palpitation (4.59%), unhealthy vaginal discharge demonstrated on speculum examination (40.22%), uterine enlargement on bimanual examination (4.59%), adnexal mass on bimanual examination (22.98%) and being unilateral in 13.79% and bilateral in 9.19% of cases. The mean haemoglobin was 10.8 ± 0.85, with anaemia being seen in 22 (25.28%) cases, while the mean erythrocyte sedimentation rate was 29.1 ± 11.8 in 1st h. The mean random blood sugar was 91.5 ± 4.8 mg/dl while the mean leucocyte count was 6125 ± 248/mm^3. Positive Mantoux test was seen in 36.78% of cases while abnormal chest X-ray was seen in 8 (9.19%) cases showing old healed lesions.

Table 3 shows various diagnostic modalities used for diagnosis of FGTB with some patients having more than one finding. Pre-menstrual endometrial biopsy was done in all the cases while peritoneal biopsy was done in only 15 cases. Positive AFB on microscopy and culture of endometrium biopsy was seen in 1 (1.14%) and 3 (3.44%) cases, respectively, while in only 1 (1.14%) in peritoneal biopsy group. Positive GeneXpert was seen in 4 (4.59%) and 0 case, respectively. Positive PCR was seen in 65 (74.71%) cases of endometrial biopsy. Positive epithelioid granuloma or granulomatous endometritis was seen in 14 (16.09%) cases in endometrial biopsy and 2 (2.29%) cases of peritoneal biopsy. Definite findings of FGTB (beaded tubes, caseous nodules or tubercles) were seen in 42 (48.27%) cases while probable findings were seen in 45 (51.72%) cases while positive findings of FGTB were seen in 38 (43.67%) cases on hysteroscopy.

Table 4 shows endometrial findings on HSG [Figures 1-7]. Normal endometrial cavity was seen in 49 (56.32%) cases. A total of 2 (2.29%) cases each showed inability to perform HSG due to constricted cervix and non-visualisation of endometrial cavity. There was irregularity of endometrium in 15 (17.24%), filling defects in 14 (16.09%) [Figures 1, 5 and 7], short and shrunken cavity in 4 (4.59%) [Figure 6], intrauterine synechiae in 14 (16.09%), T-shaped cavity in 3 (3.44%) and deformed uterine cavity in 5 (5.74%) cases.

Table 2: Examination and baseline investigations (*n*=87)

Characteristics	*n* (%)
Fever	8 (9.19)
Lymphadenopathy	6 (6.89)
Pallor	34 (39.08)
Jaundice	2 (2.29)
Crepitations on chest auscultation	7 (8.04)
Abdominal lump on palpation	4 (4.59)
Unhealthy discharge on per speculum examination	35 (40.22)
Uterine enlargement on bimanual examination	4 (4.59)
Adnexal mass on bimanual examination	20 (22.98)
Unilateral	12 (13.79)
Bilateral	8 (9.19)
Haemoglobin	11 (33.33)
Range	9.1–13.8
Mean±SD	10.8±0.85
Anaemia	22 (25.28)
ESR in mm first hour	
Range	14-63
Mean±SD	29.1±11.8
Random blood sugar	
Range	80.1–104
Mean±SD	91.5±4.8
Leucocyte count, mean±SD	6125±248
Infectious Mantoux test (>10 mm)	32 (36.78)
Abnormal chest X-ray (old healed lesions)	8 (9.19)

ESR=Erythrocyte sedimentation rate, SD=Standard deviation

Table 3: Diagnostic modalities used (*n*=87)

Diagnostic method	*n* (%)
Endometrial biopsy	87 (100)
Positive AFB on microscopy	1 (1.14)
Positive AFB on culture	3 (3.44)
Positive GeneXpert	4 (4.59)
Positive PCR	65 (74.71)
Epithelioid granulomas or granulomatous endometrium	14 (16.09)
Peritoneal biopsy (done in only 15 cases)	
Positive AFB on microscopy or culture	1 (1.14)
Positive GeneXpert	0
Epithelioid granulomas or granulomatous endometrium	2 (2.29)
Definite findings of FGTB on laparoscopy	42 (48.27)
Probable findings of FGTB on laparoscopy	45 (51.72)
Positive findings of TB on hysteroscopy	38 (43.67)

Some patients had more than one finding. AFB=Acid-fast bacilli, FGTB=Female genital TB, TB=Tuberculosis, PCR=Polymerase chain reaction

Incidental findings were unicornuate uterus in 1 (1.14%) case, arcuate uterus in 1 (1.14%) and submucosal fibroid in 1 (1.14%) case. Some patients had more than one finding.

Table 5 shows fallopian tube findings on HSG in right and left tubes, respectively, being normal tubes on the

Table 4: Endometrial findings in female genital tuberculosis on hysterosalpingography (*n*=87)

HSG findings	*n* (%)
Normal endometrium cavity	49 (56.32)
Inability to perform HSG due to constricted cervix	2 (2.29)
Non-visualisation of endometrial cavity	2 (2.29)
Irregularity of endometrium	15 (17.24)
Filling defects	14 (16.09)
Short and shrunken endometrial cavity	4 (4.59)
Intrauterine synechiae	14 (16.09)
T-shaped cavity	3 (3.44)
Deformed uterine cavity	5 (5.74)
Incidental findings	
Unicornuate uterus	1 (1.14)
Submucous myoma	1 (1.14)
Arcuate uterus	1 (1.14)

Some patients had more than one finding.
HSG=Hysterosalpingography

right and left sides in 18 (20.68%) and 20 (22.98%) cases, tubes not visualised in 28 (32.18%) and 26 (29.88%) cases, hydrosalpinx in 12 (13.79%) [Figures 1-3] and 11 (12.64%) cases, beading of tube in 4 (4.59%) and 2 (2.29%) cases, pipestem appearance [Figure 4] and salpingitis isthmica nodosa in 2 (2.29%) cases each, respectively, Maltese cross appearance was seen in 3 (3.44%) and 2 (2.29%) cases, while calcification was seen in 1 (1.14%) cases each. Intravasation of dye into lymphatics and vessels in 13 (14.94%) and 12 (13.79%) cases, respectively [Figures 2 and 7]. There was no significant difference in findings in two tubes. Tubal patency was seen in 18 (20.68%) and 20 (22.98%) cases on right and left sides, respectively, while tubal blockage was seen in 69 (79.31%) and 67 (77.01%) cases being cornual block in 28 (32.18%) and 26 (29.88%) cases [Figures 3 and 5], mid-tubal block in 16 (18.39%) and 15 (17.24%) cases [Figures 4 and 6], multiple blocks in 10 (11.49%) and 12 (13.79%) cases and fimbrial block in 15 (17.24%) and 14 (16.09%) cases [Figure 7], respectively. Many patients had more than one finding. None of the patients had flare-up of TB following HSG in the present study.

All patients were given anti-tubercular therapy for 6 months, and poor prognosis of fertility was explained to them.

A total of 4 (4.59%) patients had exacerbation of TB after HSG with fever, malaise, lower abdominal and pelvic pain and excessive vaginal discharge with pelvic tenderness on bimanual examination. They were admitted for 1–2 days and were given conservative management in terms of intravenous fluids and broad-spectrum antibiotics and analgesics. All of them recovered in 2–3 days and were discharged home.

Figure 1: HSG showing right-sided beaded tube (single arrow) and left-sided hydrosalpinx (double arrow) in case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

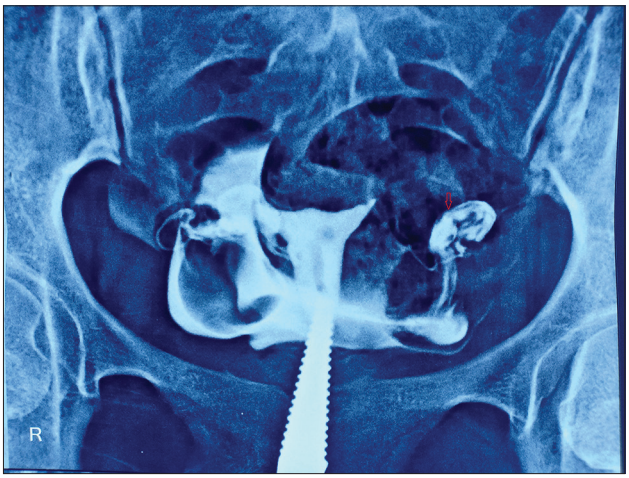

Figure 2: HSG showing left-sided distal hydrosalpinx (arrow) with delayed spill with venous and lymphatic intravasation in case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

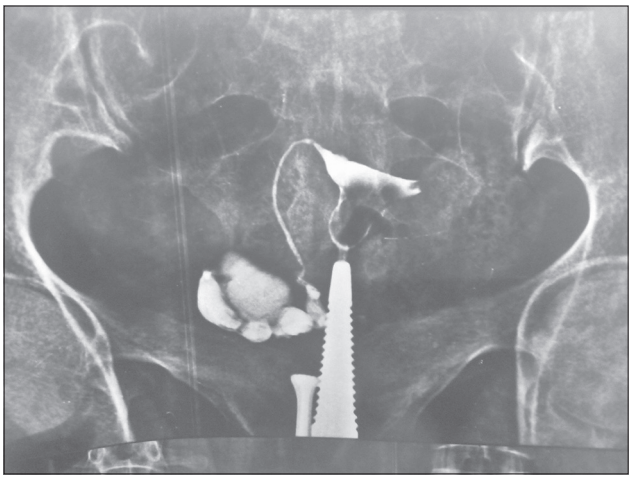

Figure 3: HSG showing right fimbrial dilatation (terminal hydrosalpinx) with loculated spill and left tubal cornual block with filling defect in the case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

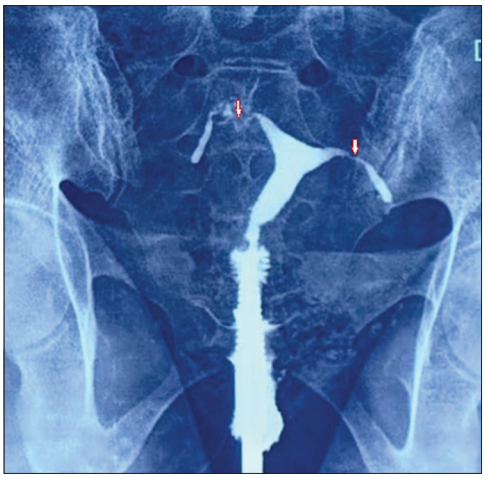

Figure 4: HSG showing bilateral mid-tubal block with pipestem rigidity (arrow) in case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

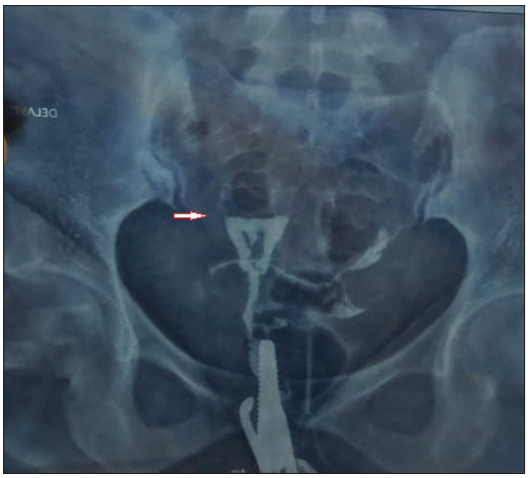

Figure 5: HSG showing filling defect in uterine cavity with right-sided cornual block (arrow) in a case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

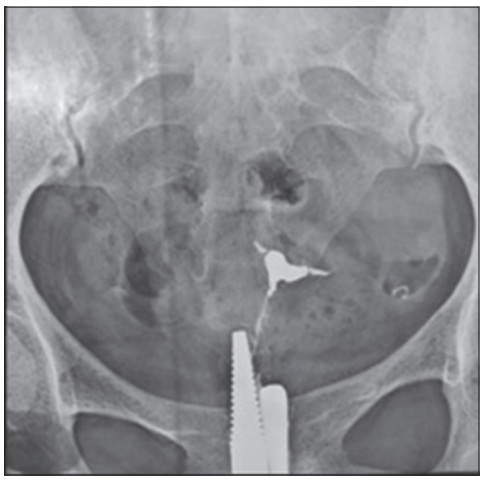

Figure 6: HSG showing small shrunken cavity with bilateral isthmic block in case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

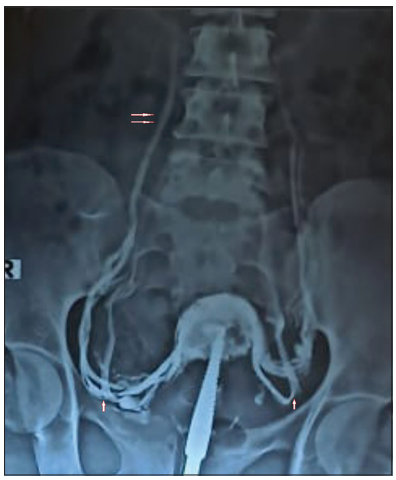

Figure 7: HSG showing small filling defect in uterine cavity with bilateral fimbrial block (single arrow) with intravasation of dye in both ovarian veins up to abdomen (double arrow) in a case of FGTB. HSG = Hysterosalpingography, FGTB = Female genital tuberculosis

None of the patients required any laparoscopy or laparotomy.

Discussion

HSG is radiographic visualisation of uterine cavity and fallopian tubes after injecting a radio-opaque contrasting medium into uterine cavity through the cervix.[9] It is usually the first investigation for tubal patency being easily available even at small centres and remote places and is very economical and does not need anaesthesia.[1,6] Laparoscopy and dye test, though gives direct depiction of the peritoneal cavity, requires general anaesthesia, expensive equipment and expertise and is available only at bigger hospitals and is usually used after tubal blockage is detected on HSG.[13-15] HSG, especially with the use of oil-based contrast medium, has some therapeutic roles in increasing pregnancy rates.[8-10]

HSG is generally avoided in suspected FGTB, especially active disease to avoid flare-up of the disease, but is often preferred as part of infertility protocol in unsuspected indolent cases of FGTB and can detect uterine and tubal disease.[6,11,12] In endometrial findings, HSG detected filling defects and intrauterine synechiae in 16.09% of cases, T-shaped cavity in 3.44% of cases and deformed uterine cavity in 5.74% of cases in the present study. These results were similar to the findings of Chavhan *et al*.[6] who observed filling defects and intra-uterine synechiae, distorted and T-shaped cavity in their study.[6]

Various tubal findings in the present study were hydrosalpinx, beaded tubes, pipestem appearance, Maltese cross appearance, intravasation of dye and tubal blocks. Chavhan *et al*.[6] observed tubal

Table 5: Fallopian tube findings in female genital tuberculosis on hysterosalpingography (*n*=87)

HSG finding	Right tube, *n* (%)	Left tube, *n* (%)	*P*	Significant (NS)
Normal	18 (20.68)	20 (22.98)	0.25	NS
Tubes not visualised	28 (32.18)	26 (29.88)	0.26	NS
Hydrosalpinx	12 (13.79)	11 (12.64)	0.24	NS
Beading of tubes	4 (4.59)	2 (2.29)	0.10	NS
Pipestem appearance	2 (2.29)	2 (2.29)	0	NS
Salpingitis isthmica nodosa	2 (2.29)	2 (2.29)	0.26	NS
Maltese cross appearance	3 (3.44)	2 (2.29)	0.26	NS
Calcification of tube	1 (1.14)	1 (1.14)	0	NS
Intravasation of dye into veins or lymphatics	13 (14.94)	12 (13.7)	0.10	NS
Tubal patency				
Patent tubes with dye spill	18 (20.68)	20 (22.98)	0.58	NS
Tubal blockage	69 (79.31)	67 (77.01)	0.25	NS
Cornual block	28 (32.18)	26 (29.88)	0.26	NS
Mid-tubal block	16 (18.39)	15 (17.24)	0.54	NS
Multiple block	10 (11.49)	12 (13.79)	0.25	NS
Fimbrial block	15 (17.24)	14 (16.09)	0.54	NS

Some patients had more than one finding. NS = Non-significant

calcification, beading, salpingitis isthmica nodosa, rigid pipestem appearance, cornual, mid-tubal and fimbrial blocks on HSG in FGTB.[6] Eng *et al*.[16] and Kumar *et al*.[17] described calcific lymph nodes, tubal obstruction, ragged tubes, stem pipe tubes, golf club appearance, rosette tubes, leopard skin appearance and tobacco pouch appearance on HSG in FGTB.[16,17] Farrokh *et al*.[18] detected irregular cavity, filling defects, T-shaped cavity, small shrunken cavity and synechiae on HSG in FGTB in their study.[18] In a study of HSG in FGTB from Iran, Ahmadi *et al*.[19] observed beaded tubes, golf club tube, pipestem tube, cobblestone tube, T-shaped cavity, pseudo-unicornuate uterus and collar stud abscess.[19] Shah *et al*.[20] also detected calcified tubes, Asherman's syndrome, irregular endometrial cavity, pseudo-unicornuate uterus and intravasation of dye in their study from Mumbai.[20] Aggarwal *et al*.[21] also reviewed the role of HSG and ultrasound in FGTB and observed them to be the best to detect tubercular changes in fallopian tubes and uterus.[21] Thangappah *et al*.[22] observed classification, distorted uterine cavity, beaded tubes, blocked tubes using intravasation of dye and hydrosalpinx in their recent study on HSG in FGTB.[22] However, HSG has its limitations as certain finding such as hydrosalpinx and hydrosalpinx are non-specific and can occur in other infectious diseases necessitating other tests such as endometrial biopsy and CRS for diagnosis of FGTB.

Conclusion

HSG appears to be a useful modality in detection of FGTB as it gives useful information about uterine and tubal findings without any adverse effects.

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Conflicts of interest

There are no conflicts of interest.

Data availability statement

The data sets in this study are available with the author upon reasonable request.

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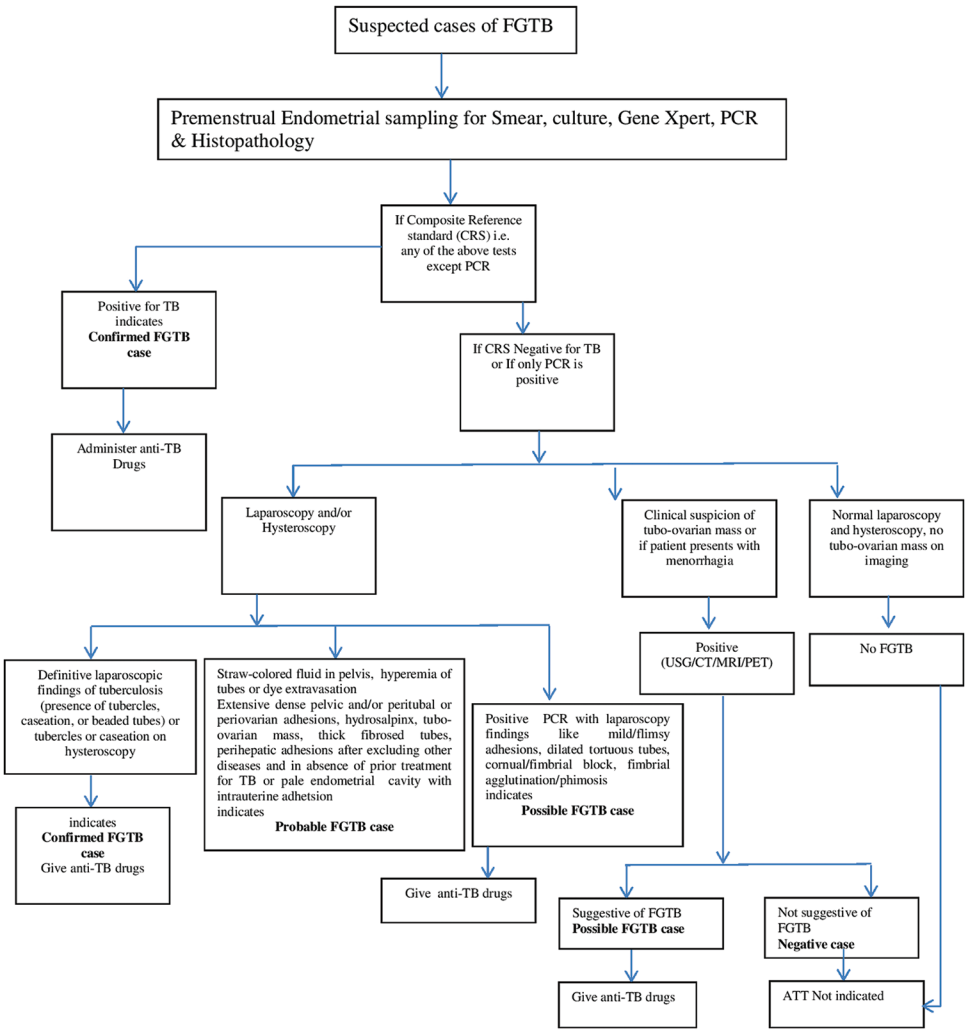

Appendix 1: Flowchart algorithm using composite reference standard for diagnosis of female genital TB. TB: Tuberculosis, FGTB: Female genital tuberculosis, PCR: Polymerase chain reaction, CRS: Composite reference standard, USG: Ultrasound, CT: Computerised tomography, MRI: Magnetic resonance imaging, PET: Positron emission tomography, ATT: Anti-tubercular therapy