**Female genital Tuberculosis in infertile women: a practical paradigm for management based on reproductive outcome on retrospective analysis of various subfertility therapies following anti-tubercular therapy**

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# ABSTRACT

Objectives

To determine fertility outcomes after diagnosing genital tuberculosis followed by anti-tubercular therapy (ATT) and response to different subfertility treatment modalities. Hysteroscopy and laparoscopy data were also analysed to determine whether or not starting ATT early on in the course of tuberculosis treatment was more effective.

Study design

Among the infertile women, presented in department Reproductive Medicine in Bansal Hospital, Bhopal from Feb 2014 to June 2022, who underwent diagnostic hysteroscopy and laparoscopy, 1083 women having positive finding(s) suggestive of tuberculosis were received anti-tubercular therapy for at least six months. Retrospectively, we analysed the pregnancy outcome of these women after receiving anti-tubercular therapy followed by different subfertility treatments.

Results

In vitro fertilization (IVF) was a primary modality of treatment. 551(55.88%) women undergoing IVF with their oocytes resulted in 348(63.15%) clinical pregnancies, 264(47.91%) ongoing pregnancies, 84(15.24%) first-trimester miscarriages, and live birth in 246(44.64%) women. Clinical pregnancy rate, ongoing pregnancy rate, and live birth rate all show a statistically significant (P = 0.039) improvement when illness is diagnosed early through hystero-laparoscopy and treated with ATT, followed by fertility therapy.

Conclusions

Diagnostic hysteroscopy and laparoscopy may be performed to examine high-risk infertile individuals by analysing the reproductive system, including tubal factor. This helps choose a treatment strategy and forecast its success. This study shows that if ATT initiated at early stage as suggested by endoscopy findings IVF reproductive outcomes equivalent to the background population. Late-stage ATT results are often quite dismal, despite the fact that IVF and other adjuvant therapy may improve fertility.

## Key words

Hysteroscopy, Laparoscopy, Female genital tuberculosis, Female infertility, Anti-tubercular therapy, IVF/ICSI outcome, Pregnancy

# Tweetable abstract

"Early diagnosis of genital tuberculosis through hysteroscopy and laparoscopy, followed by anti-tubercular therapy (ATT) and fertility treatment, significantly improves reproductive outcomes in infertile women suffering from genital tuberculosis. After completion of ATT, IVF yields similar clinical pregnancies, ongoing pregnancies, and live births if disease detected in early stage. Timely intervention is crucial for successful fertility outcomes. #GenitalTuberculosis #FertilityTreatment"

# INTRODUCTION

To have children and to produce offspring is a fundamental human motivation. Not becoming a parent is one of life's greatest disappointments. Genital tuberculosis is a common cause of infertility in developing countries. Since the time of Hippocrates, who thought that pregnancy had a beneficial effect on TB and women's reproductive health, the problem of tuberculosis in infertile women and pregnancy has been a source of worry and dispute. (1) However, due to its evasive nature, the condition is challenging to diagnose; moreover, even if it is diagnosed, the treatment and its effect on the pregnancy result are still up for debate, even in the era of assisted reproductive conception.

Female genital tuberculosis (FGTB) is a common cause of infertility in India, Africa, and other developing countries, although it is often misdiagnosed because of paucibacillary illness. A systemic review showed that overall, primary and secondary infertility prevalence among the FGTB population was 88%, 66%, and 34%, respectively. (2) Fifty percent of Extra-pulmonary tuberculosis (EPTB) cases in India were detected in HIV-positive individuals, with the remaining 15 to 20 percent occurring in immune-competent patients. (3,4). Among these, 9% are FGTB in women's reproductive age group, adversely affecting their reproductive health. (3,4) The morphological and pathophysiological distortions caused by FGTB have a major impact on a woman's ability to conceive a child. (5–7) Due to high emigration rates to the United States and European countries also struggling in recent years with infertile women with tuberculosis.(8) There is neither an algorithm nor evidence-based guidance for people with latent tuberculosis or female genital tuberculosis who are seeking treatment at fertility clinics.(9,10) On histopathology, the presence of typical caseous granuloma, with or without Langerhans giant cells, is diagnostic of genital TB. (11) The presence of epithelioid cell granulomas in various phases, as well as multinucleated giant cells of both Langhans and foreign body type and lymphoid aggregation, is a critical histologic finding for diagnosing endometrial TB. (12,13) The study that has been published in relation to FGTB makes reference to a number of observations that were made during hysteroscopy and laparoscopy. (11,14–16) There is a paucity of research available about the likelihood of conception and pregnancy outcomes in infertile women who have had anti-tubercular treatment (ATT), particularly following in vitro fertilization (IVF).

# OBJECTIVE

To investigate the reproductive outcomes of various subfertility treatment methods after diagnosing genital tuberculosis in infertile female based on the findings of diagnostic hysteroscopy and laparoscopy and then treating them with anti-tuberculous therapy (ATT). Hysteroscopy and laparoscopy data were also analysed to determine whether or not starting ATT early on in the course of tuberculosis treatment was more effective.

# MATERIALS AND METHODS

This is a retrospective study where 16784 sub-fertile women undergone diagnostic Hystero-laparoscopy from Feb 2014 to June 2022 among which 1083 women had findings corresponding to abdominopelvic tuberculosis and these women were given anti-tubercular therapy (ATT).(Table 1) Upon completion of the course of ATT according to the infertile couple profile (e.g. age, duration of infertility, history of previous conception or miscarriage etc.) and based on the investigations ( condition of fallopian tubes on laparoscopy, endometrium on hysteroscopy, serum anti-Mullerian hormone(AMH), semen analysis report etc.) different treatment options ( natural method, timed intercourse with ovulation induction, ovulation induction with IUI, in-vitro fertilization etc.) were given. Couple with otherwise normal findings after treatment with ATT were allowed to try naturally or with ovulation induction and timed intercourse and IUI were offered only depending on male factor. Couples with long duration of infertility (more than 3 years, tubal factor, decrease ovarian reserve, severe male factor) offered in-vitro fertilization (IVF) directly. IVF with donor oocyte offered only to those with advance maternal age (over 42 years) and with decrease ovarian reserve evident by low AMH and antral follicular count (AFC). Embryo donation were only to those with sever male factor (azoospermia) along with severe female factor or very advanced couple age (over 49 years for both partner). Those who did not conceived without assisted reproduction in 12 months were offered IVF. Some women with poor endometrium on ultrasound (endometrial thickness<4 mm, endometrial volume < 1 cc, low blood flow) after completion of ATT were treated with hysteroscopic sub-endometrial activated platelet rich plasma injection for 3 cycle or until adequate endometrial thickness could achieve. Every patient undergone frozen embryo transfer (FET) in IVF cycle with hormonal preparation and ERA (endometrial receptivity analysis) was done those had two failed transfers. We traced their conception rate through different treatment and in conceived cases clinical pregnancy rate, ongoing pregnancy rate, ectopic pregnancy, first and second trimester miscarriage rate, preterm delivery and finally live birth rate. We further looked at the hysteroscopy and laparoscopy findings to know at what tubercular stage of the disease (early or late stage) anti tubercular therapy (ATT) was started and whether initiation of ATT at early stage beneficial or not?

# RESULTS

Table 2 and Figure 1-3 describes the various hysteroscopic and laparoscopic findings that were corresponds to female genital tuberculosis (FGTB) and on the basis of the findings 1083 women were given ATT at least for 6 months. Around 78% of women presented with primary infertility whereas 22% presented with secondary infertility and among them 19% had miscarriage with no living issue probably due to poor invasion of trophoblast in tubercular endometrium. Most of the women (39%) were over 35 years of age with overall mean age 33.0+2.3 years. Among the 1083 women only 384 individuals had endometrial tuberculosis verified via histopathological examination having epithelioid cell granulomas, multinucleated giant cells of both Langhans and foreign body type, and lymphoid aggregate; demonstration of AFB; culture positive for Tuberculosis (Lowenstein-Jensen (LJ) culture, BACTEC culture) and GeneXpert MTB/RIF assay suggesting poor reliability of these methods. Only 8.49% (92/1083) patients offered for spontaneous conception after completion of ATT within 12 months. 8.49% (92/1083) patients were offered ovulation induction with timed intercourse and 14.87% (161/1083) women were given ovulation induction with IUI (when semen analysis showed moderate abnormality). Among the patients underwent ovulation induction with timed intercourse clinical pregnancy, ongoing pregnancy, first trimester miscarriage and live birth rate were 53/92, 35/92, 42/92 and 34/92 respectively (P value 0.000). Among the women undergone at least 3 to 6 cycle IUI with ovarian stimulation clinical pregnancy, ongoing pregnancy, first trimester miscarriage and live birth rate were 103/161, 69/161,45/161 and 66/161 respectively (P value 0.000). Majority of women offered invitro fertilization (self IVF 55.88% (551/1083) mostly due to considering long duration of infertility, donor oocyte IVF 10.80% (117/1083) and embryo donation 13.39% (145/1083)). Women underwent IVF with their own oocyte clinical pregnancy, ongoing pregnancy, first trimester miscarriage, second trimester miscarriage and live birth rate were 63.15% (348/551), 47.91% (264/551), 15.24% (84/551), 3.08% (17/551) and 44.64% (246/551) respectively (P value 0.000). Women underwent IVF with donor oocyte clinical pregnancy, ongoing pregnancy, first trimester miscarriage, second trimester miscarriage and live birth rate were 67.52% (79/117), 36.75% (43/117), 21.36% (25/117), 2.56% (3/117) and 49.57% (58/117) respectively (P value 0.000). (Table 3) Women underwent IVF with donor embryo clinical pregnancy, ongoing pregnancy, first trimester miscarriage, second trimester miscarriage and live birth rate were 46.89% (68/145), 40.68% (59/145), 13.79% (20/145), 0.68% (1/145) and 27.58% (40/145) respectively (P value 0.000). Even after undergoing intensive ATT and relook hysteroscopy PRP therapy, the endometrium and uterus of 17 women was so severely damaged that adoption or surrogacy was presented as an only alternative. Overall clinical pregnancy, ongoing pregnancy, ectopic pregnancy, first trimester miscarriage, second trimester miscarriage and live birth rate were 64.63% (700/1083), 44.32% (480/1083), 3.04% (33/1083), 17.26% (187/1083), 2.4% (26/1083) and 41.73% (452/1083) respectively.

We had attempted to establish the tuberculosis illness stage using hystero-laproscopic findings (Table 4), which indicated that 66,4% of subjects were in the early inflammatory stage and 33.5% were in the late fibrotic stage. Most of patient belongs to the late-stage disease has undergone in vitro fertilization as often they had long duration of infertility, non-restorable tubal destruction (Tubal factor), tuberculosis-oophoritis, tubo-ovarian mass and endometrial abnormality. There was no latent or dormant subject in our study included. If we consider reproductive outcome in terms of clinical pregnancy rate, ongoing pregnancy rate and live birth rate in early stage versus late stage of disease (562/720 vs 138/363, 413/720 vs 104/363, 388/720 vs 56/363 respectively) clearly significant better (P value 0.039) reproductive outcome seen when disease was detected in early stage via hystero-laparoscopy and treated with ATT followed by fertility treatment.

# DISCUSSION

# A literature review of the diagnostic dilemma in infertile women-the problem

Worldwide, a startlingly high percentage of infertile women have Female genital tuberculosis (FGTB). Low-income countries bear the brunt of the disease's effects, followed by middle-income nations and then those with high per capita incomes. FGTB is a chronic illness that causes mild symptoms. In almost all cases of FGTB, the fallopian tubes are damaged, leading to infertility alongside endometrial involvement. (17) The pooled prevalence of FGTB was 20% (95 percent confidence interval: 15-25 percent, I2 = 99.94%), and the prevalence of overall infertility, primary infertility, and secondary infertility among FGTB population were 88%, 66.3%, and 34.3%, respectively, according to a recent systematic review of 42 studies involving 30,918 infertile women.(2) Almost always, the fallopian tubes are implicated in a case of FGTB. This condition is frequently bilateral, resulting in both exo- and endo-salpingitis and tubal obstruction. Endometrial receptivity is altered by tuberculosis because of endometrial injury and the development of intrauterine synechiae. Latent FGTB can cause implantation failure. Microscopical identification of acid-fast bacilli, culture of endometrial biopsy tissue, or histological analysis of biopsy tissue from an epithelioid granuloma are common diagnostic methods for FGTB. Histopathological detection of epithelioid granuloma or granulomatous illness from an endometrial (or peritoneal) biopsy material has a nearly perfect specificity but a relatively low sensitivity.(11,18,19) As the endometrium is removed during menstruation, typical caseation, granuloma and other features is uncommon in FGTB. Till date there is no proper evaluation method for detecting FGTB. Diagnosing female genital tuberculosis (FGTB) accurately typically involves a combination of clinical evaluation, medical history, Tuberculin skin test (TST), blood tests like QuantiFERON-TB Gold or T-SPOT, genital tract sampling (endometrial biopsy, fluid aspiration, cervical and vaginal swab), culture and molecular tests. A composite reference standard also has been developed but it is often not of much value(20,21) when considering infertile population. Accurately diagnosing female genital tuberculosis (FGTB) might be difficult for a number of reasons. (I) Minimal bacterial load: The bacterium responsible for tuberculosis (TB), Mycobacterium tuberculosis, may be present in the genital tract, although in very low levels. Regular laboratory methods, such as microscopy or culture, need a large number of germs to get good findings, making it challenging to discover the bacteria. Constraints imposed by sample size. (II) It is not usually easy to collect samples from the female vagina and cervix for diagnostic testing. It might be difficult to get a representative sample if the germs are concentrated in one area or are dispersed unevenly. Endometrial biopsies and fluid aspirations are examples of invasive procedures that may be necessary but are not always practical or acceptable to patients. (III) Symptoms of FGTB, such as pelvic discomfort, irregular menstrual flow, or infertility, often overlap with those of other gynaecological disorders, such as pelvic inflammatory disease (PID) and endometriosis. As a result, FGTB may go undiagnosed or be diagnosed too late. (IV) The absence of a single, highly accurate test for FGTB is a problem, as is the difficulty of obtaining such a test. The presence of the bacterium or an immunological response to TB is the basis for diagnostic diagnostics, although these tests may not be sensitive enough or specific enough for FGTB. (V) It might be challenging and time consuming to grow Mycobacterium TB from samples taken from the vaginal tract. In addition, specialist knowledge and high-tech equipment are needed for bacterial identification in culture.

A prospective study conducted in the United States used QuantiFERON-TB Gold to detect FGTB in infertile women. The researchers concluded that all high-risk women seeking infertility care in the United States should be screened for tuberculosis; those who test positive should have an endometrial biopsy performed, which would then be analysed using histology, polymerase chain reaction, and culture for Mycobacterium tuberculosis before initiating fertility treatment.(22) But in this study only 7.7% of at risk population were positive among all at risk patients which makes it not good screening tool. A prospective study to assess diagnostic value of polymerase chain reaction (PCR) in endometrial aspirates (EAs) in comparison with conventional tests showed conventional tests were positive in 2% patients and PCR was positive in 58.1% of endometrial samples, with sensitivity of 62.5% (95% confidence interval [CI], 24.49-91.48), specificity of 41.91% (95% CI, 36.88-47.07), positive predictive value of 2.23% (95% CI, 1.31-3.78), negative predictive value of 98.14% (95% CI, 95.53-99.24), and a diagnostic accuracy of 42.34% (95% CI, 37.35-47.45) with conventional tests.(23)  Only 9.1% of patients with negative PCR results had no laparoscopic findings indicative of TB, while 39.3% of those with positive PCR results had such findings. The kappa value was 0.25, which indicates that PCR and laparoscopy are roughly on the same level of accuracy. (23) In a European retrospective study where 2653 endometrial specimens were analysed and pathological evaluation was positive for tuberculosis in 19 cases (0.72%) in infertile women indicating that need for diagnostic hystro-laparoscoy in such sub-fertile women to detect tuberculosis at early stage.(24)

Surgery is considered for more advanced cases of FGTB, but a multidrug anti-TB regimen consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol is the mainstay of treatment.(11,18,25,26) Medication used to combat tuberculosis (TB) infection has been linked to negative side effects in the domain of reproductive health, including its ability to cause birth defects in the foetus.(27) Early anti-tuberculosis treatment in women with no evidence of tubal or endometrial damage who tested positive for the disease using an endometrial TB-PCR test significantly increased the likelihood of spontaneous pregnancy.(28) But in clinical practise, PCR is not utilised to diagnose FGTB or to initiate anti-tubercular therapy due to its high false positivity and potential false negative rates.(29) Instead, it is used as a tool to examine further for FGTB utilising endoscopic procedures.(19,30–32) Based on our experience and available literature laparo-hysteroscopy not only improves diagnostic yield (11,14,23) for FGTB also provides a comprehensive assessment of reproductive organ including tubal factor and also help to decide fertility treatment modality and prognosis of fertility treatment. When looking for tuberculosis lesions, it is important to take a thorough examination of the pelvic organs (uterus, ovaries, tubes) and the entire peritoneal cavity, which includes the upper abdomen.(18,25,33) In one study, laparoscopy revealed definitive GTB in 9.1% of women and probable GTB in 37.4% of women, who were then given ATT; of these women, 74.1% had a positive endometrial aspiration PCR and 59.3% had a positive laparoscopy finding.(34) Treatment of FGTB is similar to pulmonary TB and is given for total 6 months. It consists of four drugs regimen with rifampicin (r), isoniazid (h) pyrazinamide (z) and ethambutol (E) daily orally for first 2 months of intensive phase.(3,35) In the continuation phase, three-drug regimen (unlike 2 drugs in past) is given using rifampicin (R), isoniazid (I) and ethambutol (E) orally daily for next 4 months.

# Our study: the interpretation

In light of the existing literature, it is clear that there is a huge discrepancy in our ability to accurately identify FGTB worldwide, and this is particularly true in the infertile subpopulation, when there is a narrow window of opportunity to do so. Moreover, delaying diagnosing not only increases patient anxiety and time to conceive also it will have devastating impact of endometrium and ovarian reserve. We perform diagnostic laparoscopy and hysteroscopy at the outset to diagnose the illness stage (early or late) and if required, afterwards after the patient has completed full ant-tubercular therapy to prognosticate the patient and arrange additional treatment for infertility. Initiation of ATT at early (inflammatory) stage of disease and after completion of ATT subfertility treatment should be offered. If ATT cloud be started at early-stage endometrium is often salvageable and after IVF outcome of ATT treated early-stage genital tuberculosis is similar to background population. Whereas if endoscopy findings were suggestive of late (fibrotic) stage of the disease reproductive outcome is often poor even after IVF. As during this phase endometrium is effected severely (intrauterine adhesions) and also losses its regenerative ability and also drastic change in endometrial receptivity may occur.(36–39) Tubercular endometrium at this stage has reduced receptivity markers(LIF, LIFR, and pSTAT3) and aberrant LIF-STAT3 signalling.(40) Even after IVF/ICSI (Self or Donor oocyte) this group of patients have poor reproductive outcome. Additionally, diagnostic hystero-laparoscopy not only provides a concept of the tuberculosis diagnosis and stage, but also provides a very excellent image on what reproductive organs are implicated and how much, giving clinicians an assumption of fertility prognosis and help couples to council and provide treatment options. If the hysteroscope and laparoscopy reveal a healthy endometrium and patent fallopian tubes, the couple can attempt natural conception or use ovulation induction medicines and IUI. IVF ET (in vitro fertilisation and embryo transfer) is undertaken if there is an enough receptive endometrium accessible as seen on hysteroscopy despite a blocked or damaged tubercular tubes. When diagnostic endoscopy suggests disease is in late stage after completion of anti-tubercular therapy often in vitro fertilization is chosen as treatment option as other fertility treatment modalities are not be useful in these patients and most often tubes are often grossly involved and endometrium abnormality are also often present. Re-look hysteroscopic adhesiolysis followed by adjuvant therapies such as platelet rich plasma sub endometrial injection under hysteroscopic guidance, GM-CSF installation, a small dose of estrogen, and a cyclical regimen of progesterone are preferred if the tubes are blocked and the endometrium is not receptive and adhesions are present (late stage). After ATT if the adhesions cannot be surgically treated or the surgery fails, the best option is to offer gestational surrogacy using the intended parents' own egg. If the ovaries are injured, an egg donation programme should be made available regardless of tubal status, assuming sufficient endometrium is present. Couples who have been trying to conceive for a long time and are well into advanced age group should seriously consider participating in an embryo donation programme. Adoption is recommended if a woman has clogged tubes, an unreceptive endometrium, and damaged ovaries.

Conception rates are low among infertile women with genital TB even after multidrug therapy for TB, and the risk of complications such as ectopic pregnancy and miscarriage is high. (17,26) According to a study the conception rate was low to 19.2%, the live birth rate being still low 7.2%.(41) Females with genital TB have lower peak E2 levels, fewer oocytes, and fewer embryos after controlled ovarian hyperstimulation, and higher basal FSH levels.(42,43) In a study by Dai et al (36) observed that endometrial thickness, the proportion of high-quality embryos, the proportion of embryos that implant, and the cumulative pregnancy rate in endometrial tuberculosis were all considerably lower than in tubal tuberculosis patients or in controls.(36)  Moreover IVF/ICSI pregnancy outcomes in patients with tubal tuberculosis showed no difference as compared with controls.(36) FGTB appear to represent a less favourable subset within other tubal factor patients when treated with IVF.(17,43,44) Multiple inflammatory signalling pathways, including mitogen-activated protein kinase (MAPK), natural killer (NK) cells, nuclear factor kappa-B (NF-KB), tumour necrosis factor (TNF), and toll-like receptor (TLR) signalling, are dysregulated in FGTB, resulting in immune disturbances that impede implantation. Endometrial biopsies may be able to detect these atypical immune factors and pathways at an early stage of disease, before any irreparable damage has been done.(38)

As evident by data in this study if we are able to start ATT in early stage as evident on hysteroscopy and laparoscopy reproductive outcomes are comparable after IVF to background population. Whereas if ATT was started in late stage of disease even after IVF and variety of adjuvant treatment reproductive outcome is often very poor. As there is no good enough diagnostic tool for this sub fertile population to detect FGTB and start ATT; although hysteroscopy and laparoscopy is invasive and not without risk, we chose this method as it helps to detect the FGTB and not only prognosticate according to stage of disease also gives idea to choose treatment option according to tubercular involvement of reproductive organ and moreover it helps in counselling the couple. To the very best of our knowledge if no evidence-based recommendation available for management of infertile woman suffering with female genital tuberculosis for such patients offering microscopy diagnostic hystero-laparoscopy will be definitely be beneficial and will provide a clear framework of management. It is quite evident that past literature most often stays that conception rates hey infertile woman with female genital tuberculosis are often low but this is due to the fact they are often diagnosed in the late stage the reason behind this is most of the diagnostic tests used such as microbiological tests on endometrial sampling which have low sensitivity and the abnormalities that could be found in radiological imaging such as in HSG or ultrasound or MRI are often found in the late stage of disease. Since the goal is to detect the disease at an early stage where it is possible to restore the tubal and endometrial function with antitubercular therapy, diagnostic hysteroscopy and laparoscopy are the best modality of diagnosis for infertile women suffering from female genital tuberculosis, as evident by the study and our two decades of experience. Our proposed management plan can be found in Figure 4.

# Strength and limitations

The major limitation of our study is it is a retrospective single centre study where data quality and confounding variables always be questioned. The results may not apply to other populations or other historical periods since this research depends on data from a select group of people or a particular time period. There is a risk that the findings are not generalizable since the research sample is not representative of the larger population of interest. However, it must be recognised that FGTB is a significant cause of subfertility in underdeveloped countries and that there is a dearth of high-quality studies focusing on infertility. While this research was conducted at a central location, a substantial sample size was employed, and to the best of our knowledge it is the first of its kind to examine the effects of tuberculosis diagnosis at early and late stage and impact on the fertility of infertile women.

# CONCLUSIONS

When a young woman encounters infertility, it is very heart-breaking. In order to prevent irreversible damage to the tubes, it is essential to detect and treat instances of genital TB as soon as possible. The occurrence of GTB cannot be determined by a single test.(18,20,34,45) The detection rate can be improved by using a battery of tests; but certainly, diagnostic hysteroscopy and laparoscopy can be considered as tool(14,18,23,42) to evaluate infertile patient at high risk of having FGTB since it allows for a thorough analysis of the reproductive system, tubal factor included, and aids in selecting an appropriate treatment plan and predicting the outcome of said plan. Relook endoscopy can be considered in some patients after anti-tuberculous therapy for the purpose of evaluating the uterine cavity, which is especially important when contemplating in-vitro conception. When endoscopic findings reveal tuberculosis, it is vital to begin antitubercular therapy (ATT) as soon as possible.(12,37,46) ATT is more effective when started early in the inflammatory phase rather than late in the fibrotic phase. If the patient received ATT during the early inflammatory phase of the condition, the reproductive outcomes following IVF are comparable to background sub-fertile population. If endoscopic findings imply a late fibrotic phase of illness, reproductive outcomes are up-setter even with ATT. Following early endoscopic diagnosis, treatment with anti-tubercular drugs is favourable for fertility when tubal and endometrial damage is minimal; not only with assisted reproduction but also with spontaneous and ovulation induction after consider all other fertility parameters. Even with in-vitro fertilisation and donor gamete or embryo, the outcome is dismal in cases where the organs (i.e., endometrium) are more significantly damaged. Reproductive results following IVF are similar to the background population if ATT is started at an early stage, as shown by hysteroscopy and laparoscopy in this research and also in our two decades of experience. While IVF and other forms of adjuvant therapy may improve fertility, if ATT is started at a late stage of illness, the results are frequently extremely poor. In Figure 4 we proposed our management algorithm for infertile women with FGTB.

# AUTHORS CONTRIBUTIONS

R.M. was responsible for all aspects of the research project, including data collection and analysis, article design, literature evaluation, table/figure creation, paper writing, and conclusion drawing. P.B. performed surgeries on patients, helped in article design, data analysis and reviewed the manuscript. The manuscript was revised and organised by N.J.

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# Consent

It is our institutional policy to take written consent from each patient undergoing any procedure and a part of it may reproduce or publish only for academic purpose. Written informed consent was obtained from each patient for publication of images without disclosing their personal details. It is retrospective study and all patient had consent for the same.

# Ethical approval

The study received ethical approvals from Bansal Hospital Institutional Human Ethics Committee on 20/3/21.

# Funding

No funding is associated with this study.

# Data availability Statement

The data that support the findings of the study are available from the corresponding author upon reasonable request also submitted as supplementary file. Also unstructured data available in Bansal hospital database.

# Conflict of interest

We do not have any conflicts of interest to declare and also no competing interests.

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Figure 1. Major hysteroscopic findings in female genital tuberculosis

Figure 2. Major laparoscopic findings in women with female genital tuberculosis

Figure 3. Various tubal abnormality can be found in women with female genital tuberculosis

Figure 4. A practical paradigm approach in infertile women with female genital tuberculosis

Table 1. Consort flowchart of the study.

Table 2. Hysteroscopic and laparoscopic findings seen in study population

Table 3. comparison between different subfertility treatment and reproductive outcome

Table 4. Hysteroscopic and laparoscopic findings suggestive of different stages of tuberculosis