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INVITED REVIEW ARTICLE

Current Diagnosis and Management of Female Genital Tuberculosis

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Abstract Female genital tuberculosis (FGTB) is an important cause of significant morbidity, short- and long-term sequelae especially infertility whose incidence varies from 3 to 16 % cases in India. Mycobacterium tuberculosis is the etiological agent for tuberculosis. The fallopian tubes are involved in 90–100 % cases, endometrium is involved in 50–80 % cases, ovaries are involved in 20–30 % cases, and cervix is involved in 5–15 % cases of genital TB. Tuberculosis of vagina and vulva is rare (1–2 %). The diagnosis is made by detection of acid-fast bacilli on microscopy or culture on endometrial biopsy or on histopathological detection of epithelioid granuloma on biopsy. Polymerase chain reaction may be false positive and alone is not sufficient to make the diagnosis. Laparoscopy and hysteroscopy can diagnose genital tuberculosis by various findings. Treatment is by giving daily therapy of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) for 2 months followed by daily 4 month therapy of rifampicin (R) and isoniazid (H). Alternatively 2 months intensive phase of RHZE can be daily followed by alternate day combination phase (RH) of 4 months. Three weekly dosing throughout therapy (RHZE thrice weekly for 2 months followed by RH thrice weekly for 4 months) can be given as directly observed treatment short-course. Surgery is rarely required only as drainage of abscesses. There is a role of in vitro fertilization and embryo transfer in women whose fallopian tubes are damaged but endometrium is healthy. Surrogacy or adoption is needed for women whose endometrium is also damaged.

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Introduction

Tuberculosis continues to be a major health problem throughout the world affecting about 9.4 million people annually with about two million deaths [1, 2]. Over 95 % of new TB cases and deaths occur in developing countries with India and China together accounting for 40 % of the world's TB burden. Co-infection with human immunodeficiency virus (HIV), more liberal immigration from high risk to low risk areas due to globalization has been responsible for increased incidence all over the world. Multidrug resistant (MDR) and extreme-drug resistant TB (XDR), usually caused by poor case management, are a cause of serious concern [1, 2].

World Health Organization (WHO) in a drastic step declared TB a global emergency in 1993 and promoted a new effective TB control called Directly Observed Treatment Short-course (DOTS) strategy with 70 % case detection rate and 85 % successfully treatment rates [3]. The Revised National Tuberculosis Control Programme (RNTCP) of India incorporating DOTS strategy has achieved 100 % geographical coverage with 71 % case detection rate and 87 % treatment success rate with a sevenfold decrease in death rate (from 29 to 4 %) in the year of 2010 [4].

Apart from commonest and the most infectious pulmonary TB, extra pulmonary TB (EPTB) is being increasingly encountered throughout the world [5]. Female genital TB (FGTB) is an important cause of significant morbidity, short- and long-term sequelae especially infertility [5–8]. Timely diagnosis and prompt appropriate treatment may prevent infertility and other sequelae of the disease.

Epidemiology

The incidence of FGTB varies in different countries from 1 % in infertility clinics of USA, 6.15–21.1 % in South Africa and 1–19 % in various parts of India [7, 9–13]. In infertility patients, incidence of FGTB varies from 3 to 16 % in India with higher incidence being from apex institutes like All India Institute of Medical Sciences (AIIMS), New Delhi, where prevalence of FGTB in women of infertility was 26 % and incidence of infertility in FGTB to be 42.5 %, which may be due to referral of difficult and intractable cases to this apex hospital from all over India, especially from states like Bihar where prevalence of TB is very high [8, 13]. Similarly incidence of FGTB is also very high in women seeking assisted reproduction being 24.5 % overall but as high as 48.5 % with tubal factor infertility [14]. The FGTB is present in younger age (20–40 years) as compared to premenopausal age in developed countries [6, 8–15]. It may be due to younger age at marriage and child bearing in developing countries as compared to western world [8]. There has been fivefold increase in overall incidence of TB in countries with high prevalence of HIV due to impaired immunity in them [16].

Etiopathogenesis

Mycobacterium tuberculosis is the etiological agent for tuberculosis. Predisposing factors for TB include factors reducing personal immunity like poverty, overcrowding with improper ventilation, inadequate access to health care, malnutrition, diabetes mellitus, smoking, alcohol and drug abuse, end stage renal disease cancer treatment hemodialysis patients and patient with HIV infection [1–3, 5–8, 16]. Genital TB generally occurs secondary to pulmonary (commonest) or extra pulmonary TB like gastro-intestinal tract, kidneys, skeletal system, meninges and miliary TB [5–8] through hematogenous and lymphatic route. However, primary genital TB can rarely occur in women whose male partners have active genitourinary TB (e.g., tuberculosis epididymitis) by transmission through infected semen [5, 8]. The site of involvement in primary genital TB can be cervix, vagina or vulva [5, 8]. Direct contiguous spread from nearby abdominal organs like intestines or abdominal lymph nodes can also cause genital TB. The fallopian tubes are involved in 90–100 % cases with congestion, military tubercles, hydrosalpinx, pyosalpinx and tubo-ovarian masses [5, 8]. Endometrium is involved in 50–80 % cases with caseation and ulceration causing intrauterine adhesions (Asherman's syndrome) [17]. Ovaries are involved in 20–30 % cases with tubo-ovarian masses [5, 8]. Cervical TB may be seen in 5–15 % cases of genital TB and may masquerade cervical cancer necessitating biopsy for confirmation of diagnosis with granulomatous lesion [18]. Tuberculosis of vagina and vulva is rare (1–2 %) with a hypertrophic lesion or a nonhealing ulcer mimicking malignancy needing biopsy and histopathological examination to confirm the diagnosis. Rarely TB of the vagina can cause involvement of Bartholin's glands, vesicovaginal and rectovaginal fistula formation [19]. Peritoneal TB can be a disseminated form of TB with tubercles all over the peritoneum, intestines and omentum and may cause ascites and abdominal mass. It may masquerade as ovarian cancer as even CA 125 levels are raised in peritoneal TB with CT scan and MRI also

giving similar picture and diagnosis may be made only on laparotomy done for suspected ovarian cancer [20, 21]. Ascitic fluid tapping for bio-chemical analysis (elevated adenosine deaminase level in ascitic fluid in peritoneal TB) is useful in diagnosis [22]. Laparoscopic biopsy with frozen section evaluation has also been suggested to avoid laparotomy in such cases [21, 22]. Positron emission tomography with 18 F-fluorodeoxy glucose (FDG-PET) has been successfully used for the preoperative diagnosis of peritoneal tuberculosis and tuberculous tubo-ovarian masses [23, 24]. Varying grades of pelvic and abdominal adhesions including perihepatic adhesions (Fitz-Hugh–Curtis syndrome) are common in genital and peritoneal tuberculosis [25, 26]. Rarely genital TB may be associated with other gynecological pathologies like ovarian cancer, genital prolapse and fibroid uterus [5–8].

Clinical Features

The clinical presentation of genital TB depends upon the site of involvement of genital organs and is shown in Table 1 [5, 8, 11, 27]. Up to 11 % of women with genital TB may be asymptomatic [8, 13]. The age of presentation in 80 % of women is 20–40 years age group especially in developing countries. Infertility is the commonest presentation of genital TB due to the involvement of fallopian tubes (blocked and damaged tubes), endometrium (non-reception and damaged endometrium with Asherman's syndrome) and ovarian damage with poor ovarian reserve and volume [6–8, 17, 28].

The various signs of FGTB depend on the site of involvement of genital organs and are shown in Table 1 [5, 6, 8, 18–21, 28].

Differential Diagnosis

As genital TB may manifest in different ways with no characteristic symptoms and signs, the differential diagnosis depends upon the clinical presentation and is shown in Table 2 [5, 6, 8, 18–20].

Diagnosis

Being a paucibacillary disease, demonstration of mycobacterium tuberculosis is not possible in all the cases. A high index of suspicion is required. The diagnostic dilemma arises due to varied clinical presentation, diverse results on imaging and endoscopy and availability of battery of bacteriological, serological and histopathological tests which are often required to get a collective evidence

Table 1 Symptoms and signs in FGTB

(A) Symptoms in genital TB [5, 6, 8, 11, 27]
Asymptomatic (up to 11 %)
General systemic symptoms
Pyrexia with night sweats
Loss of appetite
Weight loss
Poor general condition
Menstrual dysfunction
Puberty menorrhagia
Menorrhagia
Postmenopausal bleeding
Oligomenorrhea
Hypomenorrhea
Amenorrhea (primary and secondary)
Dysmenorrhea
Infertility (primary and secondary)
Abdominal lump
Abdominal pain (may be flared up after HSG or D&C)
Chronic pelvic pain (may be flared up after HSG or D&C)
Acute abdomen (in rupture of tubo-ovarian abscess or flaring up of TB after HSG, D&C, coitus, exercise, menstruation)
Abnormal vaginal discharge
Unusual symptoms
Vaginal or vulva ulcers
Labial swelling
Retention urinary
Urinary incontinence
Fecal incontinence
(B) Signs in genital TB [5, 6, 8, 18–21]
No physical sign (common)
Systemic examination
Fever
Lymphadenopathy (in lymphnodes TB)
Crepitations on chest auscultation (PTB)
Other systemic signs depending on site of EPTB
Abdominal examination
Doughy feel of abdomen
Ascites
Mass abdomen (vague or definite)
Vaginal examination
Uterine enlargement (pyometra)
Adnexal tenderness and induration
Adnexal masses and tubo-ovarian mass
Fullness and tenderness in pouch of Douglas
Rare signs
Hypertrophic lesions in cervix, vagina or vulva (may masquerade malignancy)
Ulcerative lesions in cervix, vagina or vulva (may masquerade, venereal diseases or malignancy)
Labial mass (Bartholin swelling)

Table 1 continued

Vesicovaginal fistula
Rectovaginal fistula
Tubovesical fistula
Tuboperitoneal fistula
Tubointestinal fistula
Uterocutaneous fistula

Table 2 Differential diagnosis (DD) of genital TB [5, 6, 8, 18–20]

The differential diagnosis depends on the clinical presentation
For women presenting with pain and adnexal mass following possibilities should be considered
Acute and chronic pelvic infections
Ectopic pregnancy
Endometriosis
Ovarian cancer
Appendicitis
For granulomatous lesions in the pelvis
Syphilis
Actinomycosis
Granuloma inguinale venereum
Filariasis
Crohn's diseases
Schistosomiasis
Silicosis
Brucellosis
Histoplasmosis
Leprosy
Ulcerative or hypertrophic lesions
Vaginal cyst
Vulval and vaginal warts
Condyloma lata
Condyloma acuminata
Bartholin abscess
Vulval cancer
Vaginal cancer
Cervical cancer

of the diagnosis of genital TB [8, 11]. The diagnostic approach used is family history of TB or history of anti-tuberculous therapy (ATT) in a close family member or a past history of TB or ATT in the patient may show recrudescence of TB in the genital region. History of HIV positivity is also important. Detailed general physical examination for any lymphadenopathy and any evidence of TB at any other site in body (bones, joints, skin, etc.), chest examination (PTB), abdominal examination (abdominal TB), examination of external genitalia (vulvar or vaginal TB), speculum examination (cervical TB), bimanual examination (endometrial or fallopian tube TB) help in the diagnosis of genital TB [5, 6, 8, 18].

All tests are not required for every single case of genital TB. The tests will depend upon the site of TB and its clinical presentation. The various tests are shown in Table 3 [29–33].

Role of Endoscopy in FGTB

Hysteroscopy

Endoscopic visualization of the uterine cavity in genital TB may show a normal cavity (if no endometrial TB or early stage TB) with bilateral open ostia. More often, however, the endometrium is pale looking, and the cavity is partially or completely obliterated by adhesions of varying grade (grade 1 to grade 4) often involving ostia as observed by us (Fig. 2) [34]. There may be a small shrunken cavity. In our study on hysteroscopy in genital TB, we observed increased difficulty to distend the cavity and to do the procedure and increased chances of complications like excessive bleeding, perforation and flare-up of genital TB [35]. Hence, hysteroscopy in a patient with genital TB should be done by an experienced person preferably under laparoscopic guidance to avoid false passage formation and injury to the pelvic organs.

Laparoscopy (Figs. 3, 4)

A laparoscopy and dye hydrotubation (lap and dye test) is the most reliable tool to diagnose genital TB, especially for tubal, ovarian and peritoneal disease [8, 36]. The test can be combined with hysteroscopy for more information as follows [8, 34, 36].

1. In subacute stage, there may be congestion, edema and adhesions in pelvic organs with multiple fluid-filled pockets. There are miliary tubercles, white yellow and opaque plaques over the fallopian tubes and uterus.
2. In chronic stage, there may be following abnormalities.
   a. Yellow small nodules on tubes (nodular salpingitis).
   b. Short and swollen tubes with agglutinated fimbriae (patchy salpingitis.
   c. Unilateral or bilateral hydrosalpinx with retort-shaped tubes due to agglutination of fimbriae.
   d. Pyosalpinx or caseosalpinx: The tube usually bilateral is distended with caseous material with ovoid white yellow distension of ampulla with poor vascularization.
   e. Caseous nodules may be seen (Fig. 4).

Table 3 Investigations in genital TB [5–8, 15, 28–33]

Blood tests
Anemia, leucocytosis with lymphocytosis and raised ESR; nonspecific
Serological tests like ELISA are not very sensitive and specific
Moderate rise in levels of CA 125 in genital TB
Mantoux (tuberculin) test and interferon gamma release assays; poor sensitivity and specificity
Chest X-ray
For pulmonary TB
Imaging methods
Ultrasonography (USG)
Computerized axial tomography (CT scan)
Magnetic resonance imaging (MRI) [29]: useful for tubo-ovarian masses
Positron emission tomography (PET scan) [24]: tubercular tubo-ovarian masses (Fig. 1)
Hysterosalpingography (HSG) [30]: Endometrial TB can cause synechiae formation, a distorted, obliterated or T-shaped cavity and venous and lymphatic intravasation
Endometrial biopsy, curettage or aspirate
Histopathology Demonstration of epithelioid granuloma
Mycobacterial smear and culture Using Lowenstein–Jensen (LJ) medium or BACTEC 460 or mycobacteria growth inhibitor tube (MGIT) and specific gene probes can help in rapid identification and diagnosis [15]
Polymerase chain reaction (PCR) Rapid (1–2 days), sensitive and specific method for detecting mycobacterial DNA (mpt 64 gene) with high pickup rate but can be false negative due to contamination or false positive as it can pick up even single mycobacterium tuberculosis and may not be able to differentiate between infection and disease [31, 32]. Hence ATT should not be started just on the basis of positive PCR unless there is some other evidence of FGTB on clinical examination or on investigations like the presence of tubercles or other stigmata of TB on laparoscopy. However, Jindal et al. [33] observed high pregnancy rate for treating infertility with positive PCR alone with ATT

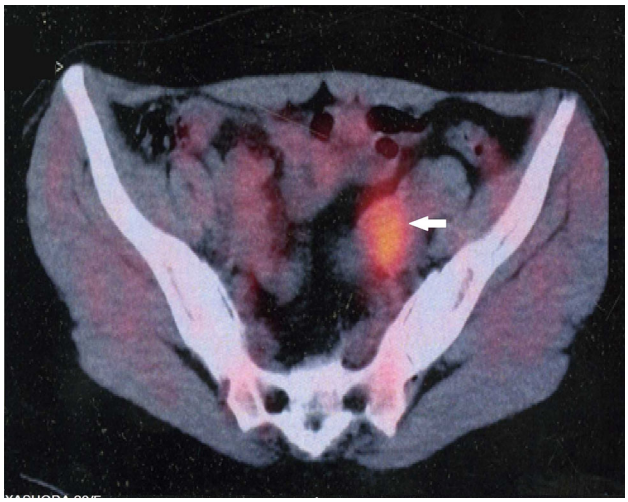

Fig. 1 PET scan showing *left* tubo-ovarian mass (*arrow*) with increase FDG uptake in FGTB case

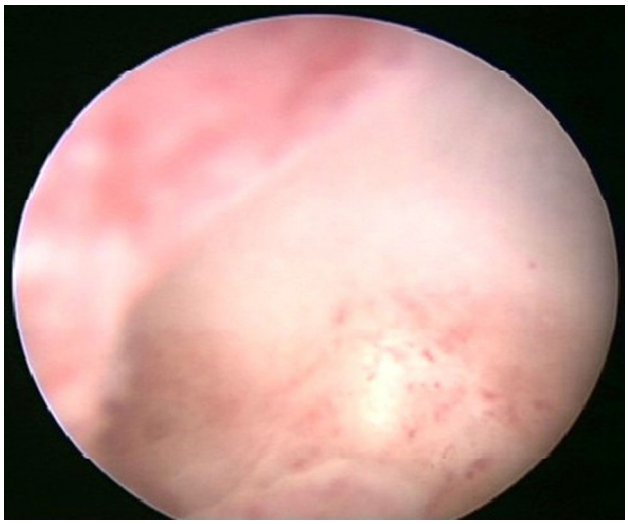

Fig. 2 Hysteroscopy showing grade 2 adhesions and pale endometrium in a FGTB case

Adhesions

Various types of adhesions may be present in genital TB covering genital organs with or without omentum and intestines. There is very high prevalence (48 %) of perihepatic adhesions on laparoscopy in FGTB cases (Fig. 3) [25, 26]. In a laparoscopic study on 85 women with FGTB, we observed tubercles on peritoneum (15.9 % cases), tubo-ovarian masses (26 %), caseous nodules (7.2 %), encysted ascites (8.7 %), various grades of pelvic adhesions (65.8 %), hydrosalpinx (21.7 %), pyosalpinx (2.9 %), beaded tubes (10 %), tobacco pouch appearance (2.9 %) and inability to see tubes due to adhesions (14.2 %) [36]. We also observed increased complications on laparoscopy for FGTB as compared to laparoscopy performed for non-tuberculous patients (31 vs 4 %) like inability to see pelvis (10.3 vs 1.3 %), excessive bleeding (2.3 vs 0 %),

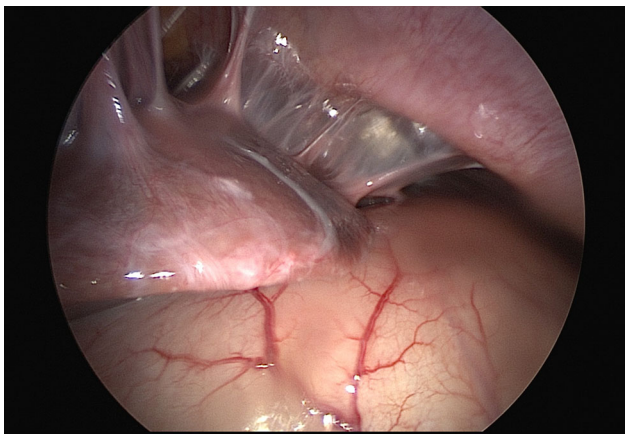

Fig. 3 Laparoscopic findings showing Fitz-Hugh–Curtis syndrome in FGTB case

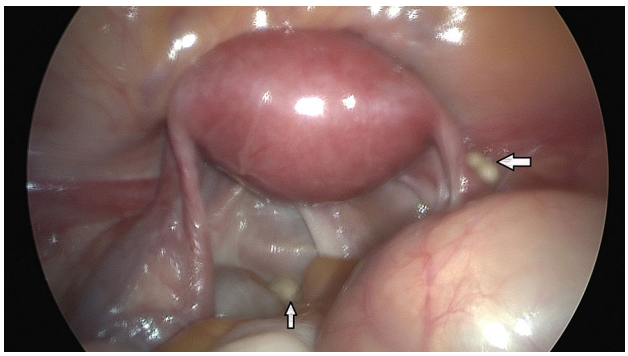

Fig. 4 Laparoscopic findings showing tubercles and caseous nodules (*arrows*) in FGTB case

peritonitis (8 vs 1.8 %) [37]. The adhesions are typically vascular, and adhesiolysis can increase the risk of bleeding and flare-up of the disease [8, 36, 37].

Combination of Tests (Algorithm)

The final diagnosis is made from good history taking, careful systemic and gynecological examination and judicious use of diagnostic modalities like endometrial biopsy in conjunction with imaging methods and endoscopic visualization especially with laparoscopy. Some authors have developed an algorithm for accurate diagnosis of FGTB by combining history taking, examination and investigations [11, 38].

Treatment

Medical Treatment

Multiple drug therapy in adequate doses and for sufficient duration is the main stay in the treatment of TB including FGTB. In olden days before rifampicin, the antituberculous therapy (ATT) was given for 18–24 months with significant side effects and poor compliance. Short-course chemotherapy for 6–9 months has been found to be effective for medical treatment of FGTB [39]. In a study funded by Central TB Division, Ministry of Health, Govt. of India, we observed 6-month intermittent DOTS therapy to be equally effective to 9-month therapy.

DOTS (Directly Observed Treatment Short-Course) Strategy Treatment

American Thoracic Society [40] and British Thoracic Society and NICE (National Institute of Clinical Excellence) Guidelines (2006) [41] recommend that first choice of treatment should be the 'standard recommended regimen' using a daily dosing schedule using combination tablets and does not consider DOTS necessary in management of most cases of TB in developed countries who can adhere to treatment. DOTS is favored by WHO to prevent MDR and for better results. WHO in its recent guidelines has removed category 3 and recommended daily therapy of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) for 2 months followed by daily 4-month therapy of rifampicin (R) and isoniazid (H). Alternatively 2 months intensive phase of RHZE can be daily followed by alternate day combination phase (RH) of 4 months. Three weekly dosing throughout therapy (2RHZE, 4HR) can be given as DOTS provided every dose is directly observed and the patient is not HIV positive or living in an HIV prevalent setting [2].

The patient is first categorized to one of the treatment categories and is then given treatment as per guidelines for national programmes by WHO (Table 4). Genital TB is classified under category 1 being seriously ill extra pulmonary disease. To ensure quality-assured drugs in adequate doses, a full 6-month course pack box is booked for an individual patient in the DOTS center with fixed drug combipacks (FDC) of isoniazid, rifampicin, pyrazinamide and ethambutol thrice a week for first 2 months (intensive phase) under direct observation followed by combination blister pack of isoniazid and rifampicin thrice a week for next 4 months (continuation phase).

Rarely FGTB cases can have relapse or failure categorizing them into category II (Table 4), which includes 2 months intramuscular injections of streptomycin thrice weekly along with other four drugs (SRHZE) of category I under direct supervision of DOTS center health worker for first 2 months followed by four drugs (RHZE) thrice a week for another month (intensive phase) followed by continuation phase with three drugs isoniazid (H), rifampicin (R) and ethambutol (E) thrice a week for another 5 months.

Table 4 Category-wise treatment regimens for tuberculosis including FGTB [2, 4, 5, 8]

TB diagnostic category	TB patients	TB treatment regimens		
		Initial phase (daily or 3 times weekly)	Continuation phase (daily or 3 times weekly)	
I	New smear-positive patients. New smear-negative pulmonary TB with extensive parenchymal involvement. Severe concomitant HIV disease or severe forms of extra-pulmonary TB (FGTB included)	2HRZE Dose INH 600 mg Rifampicin 450 (600 mg if >50kg) Pyrazinamide 1500 mg Ethambutol 1200 mg for 2 months	4HR INH 600 mg Rifampicin 450 (600 mg if >50kg) for 4 months	
II	Previously treated sputum smear-positive pulmonary TB: Relapse (FGTB included) Treatment after default (FGTB included) Treatment failure (FGTB included)	2 HRZES/IHRZE Dose RHZE as in category I above. Injection streptomycin 0.75 gm daily or thrice weekly (DOTS) for 2 months followed by 1 month of RHZE	5HRE Dose INH 600 mg Rifampicin 450 (600 mg if >50kg) Ethambutol 1200 mg for 5 months	
IV	Chronic and MDR-TB cases (still sputum-positive after supervised re-treatment/ or culture positive or histopathologically proven FGTB).	Drug	Dose (mg) if weight < 45 kg	Dose (mg) if weight > 45 kg
		Kanamycin (IM)	500	750
		Ofloxacin (O)	600	800
		Ethionamide (O)	500	750
		Pyrazinamide (O)	1250	1500
		Ethambutol (O)	800	1000
		Cycloserine (O)	500	750
		Ofloxacin (O)	600	800
		Ethionamide (O)	500	750
		Ethambutol (O)	800	1000
		Cycloserine (O)	500	750

6 to 9 months intensive phase

18 months continuation phase

IM intramuscular, *O* oral

Non-DOTS Treatment

Patients not opting for DOTS treatment must take daily therapy of RHZE for 2 months (intensive phase) followed by RH for 4 months (continuation phase). Convenient and economic combipacks are available in market.

Treatment of Chronic Cases, Drug Resistant and Multidrug Resistant (MDR) FGTB

It is same as for pulmonary MDR with second-line drugs and is shown in Table 4 and is needed for long duration (18–24 months).

Monitoring

The women should be counseled about the importance of taking ATT regularly and consumption of good and nutritious diet and should report in case of any side effects of the drugs. Liver function test is no longer done regularly unless there are symptoms of hepatic toxicity. Similarly pyridoxine is not routinely prescribed with ATT unless there are symptoms of peripheral neuropathy with isoniazid. Rarely hepatitis can be caused by isoniazid, rifampicin and pyrazinamide, optic neuritis by ethambutol and auditory and vestibular toxicity by streptomycin in which case the opinion of an expert should be sought for restarting the ATT in a modified form.

Treatment of FGTB in HIV-Positive Women

HIV has had a disastrous impact on attempts to control as TB is a leading cause of HIV-related morbidity and mortality, while HIV is the most important factor for fuelling the TB epidemic in high HIV prevalence populations. In India, RNTCP and National AIDS Control Organization (NACO) have joined hands for better management of this dual epidemic. Possible options for antiretroviral therapy in TB patients include:

- Defer antiretroviral therapy until TB treatment is completed
- Defer antiretroviral therapy until the end of the initial phase of treatment and use ethambutol and isoniazid in the continuation phase
- Treat TB with a rifampicin-containing regimen and use efavirenz + 2 NRTIs (nucleoside reverse transcriptase inhibitors)
- Treat TB with a rifampicin-containing regimen and use 2 NRTIs and then change to a maximally suppressive HAART regimen on completion of TB treatment.

Surgical Treatment

The medical therapy, especially the modern short-course chemotherapy consisting of rifampicin and other drugs, is highly effective for the treatment of FGTB with rare need of surgery [8]. However, limited surgery like drainage from residual large pelvic or tubo-ovarian abscesses or pyosalpinx can be performed followed by ATT for better results as recommended by American Thoracic Society [8, 40].

There are much higher chances of complications during surgery in women with genital TB in hysteroscopy, laparoscopy, vaginal hysterectomy and laparotomy [35, 37, 42, 43]. There is excessive hemorrhage and nonavailability of surgical planes at time of laparotomy with higher risks of injury to the bowel and other pelvic and abdominal organs. In a case of abdomino-pelvic TB, bowel loops may be matted together with no plane between them and uterus and adnexa may be buried underneath the plastic adhesions and bowel loops and are inapproachable. Even trying to perform a diagnostic laparoscopy or laparotomy in such cases can cause injury to bowel necessitating a very difficult laparotomy and resection of injured bowel. It is better to take biopsies from the representative areas and close the abdomen without pelvic clearance in cases of laparotomy done for suspected pelvic tumors but found to be tubercular at laparotomy followed by full medical treatment.

Sometimes even after a full 6-month course of ATT, women with genital TB with infertility do not conceive when laparoscopy and hysteroscopy may be repeated to see any remaining disease. Outcome for fertility in FGTB is only good when ATT is started in early disease. However, cases of advanced TB with extensive adhesions in pelvis and uterus are usually untreatable with very poor prognosis for fertility. Tuboplasty performed after ATT does not help much with chances of flare-up of the disease and risk of ectopic pregnancy, should the women conceive [10, 44].

In Vitro Fertilization (IVF)

Most women with genital TB present with infertility and have poor prognosis for fertility in spite of ATT. The conception rate is low (19.2 %) with live birth rate being still low (7 %) in Tripathy and Tripathy series [10]. Parikh et al. [12] found IVF with ET to be the only hope for some of these women whose endometrium was not damaged with pregnancy rate of 16.6 % per transfer. Jindal [11] observed IVF–ET to be most successful out of all ART modalities in genital TB patients with 17.3 % conception rate in contrast to only 4.3 % with fertility enhancing surgery. Dam et al. [45] found latent genital TB responsible for repeated IVF failure in young Indian patients in Kolkata presenting with unexplained infertility with apparently normal pelvis and non-endometrial tubal factors. If after ATT their tubes are still damaged but their endometrium is receptive (no adhesions or mild adhesions which can be hysteroscopically resected), IVF–ET is recommended [8, 46]. However, if they have endometrial TB causing damage to the endometrium with shrunken small uterine cavity with Asherman's syndrome, adoption or gestational surrogacy is advised to them [47].

New TB Research

There has been a renewed interest in research in TB at global level. New and improved BCG vaccines are being developed. New drugs, effective against strains that are resistant to conventional drugs and requiring a shorter treatment regimen, are being developed. Newer shorter (4–5 months) regime of ATT is being developed and studied [48]. By controlling TB, FGTB can also be kept at bay and treated early to prevent the development of short-term and long-term sequelae of this menace [8].

Key Points for Clinical Practice

1. FGTB prevalence varies in different countries being much more common in developing countries, especially Africa and Asia, and is usually a secondary infection from lungs and other sites like abdomen.
2. FGTB is responsible for up to 16 % cases of infertility in developing countries, while infertility is seen in up to 40–50 % cases of genital TB. Other main symptoms

are menstrual dysfunction, especially oligomenorrhea, amenorrhea, chronic pelvic pain and vaginal discharge.
3. High index of suspicion is required as many cases can be asymptomatic in early stages when it can be treated without causing significant damage to genital organs as untreated FGTB can cause permanent sterility through tubal damage and endometrial destruction (Asherman's syndrome)
4. Diagnosis is by good history taking, thorough clinical examination and judicious use of investigations, especially endometrial sampling for AFB culture, PCR and histopathological testing. Laparoscopy and hysteroscopy may be helpful in early diagnosis and to see the severity of disease for prognostication for fertility
5. Medical treatment using DOTS strategy under direct observation and using quality-assured drugs in appropriate dosage and for adequate time is the main stay of treatment.
6. Prognosis for fertility is poor. However, for tubal disease in the absence of endometrial disease, ART especially IVF–ET, may give some results. In cases of endometrial disease with shrunken cavity, prognosis for fertility is very poor even with IVF ET.
7. Surgical treatment is rarely required and should only be done in exceptional circumstances and should be in the form of limited surgery like laparoscopy, hysteroscopy and drainage of abscess as surgery in genital and peritoneal TB can be difficult and hazardous.
8. Treatment of TB in HIV-positive woman is same as in HIV-negative woman in consultation with experts in the field.

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Compliance with Ethical Standards

Conflict of interest There is no conflict of interest.

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