Female genitourinary tuberculosis: A clinico epidemiological and diagnostic study

Dr. Sandhyasri Panda, Dr. Apurva Ganeshprakash Gupta, Dr. P Prabhakar Varma and Dr. T Venkateswara Rao

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Abstract

Introduction: Increasing number of genital tuberculosis (GTB) were reported post COVID pandemic, in year 2022. This study aims to estimate the incidence, presentations, diagnostic modalities and treatment plan adopted in our tertiary care centre for Female GTB.

Methods: This is a study between 2014 to 2022 from DEPT of OBGYN all cases of FGTB were analysed, supplementary data were collected from departments of Pulmonary medicine, general medicine, DVL, General surgery, Urology and TB core committee meetings. Data analysis was done in proportion and percentages.

Results: Ten out of 1342 were FGTB, making an incidence of 0.74%. In GUTB, men: women was 1:5. In 2022 (Post COVID pandemic) 30% of FGTB were reported. Ninety percent were low SE class; mean age was 30.6 years; common presenting symptoms were pain abdomen, menstrual disorder, TO mass each being 60%; infertility being 20% and pregnancy with urogenital TB 10%; 30% presented with concomitant PTB. Diagnosis was established by bacteriology in 40%, histopathology in 40% including a case of endometrial osseous metaplasia, imaging in 20%. Overall, imaging was supportive in diagnosis in 90%. Menstrual abnormality noted were either hypomenorrhea (66%) or ammenorhea (34%).

Conclusion: Although menstrual abnormalities, TO pathology, and infertility are common presentations, GUTB should be considered as a diagnosis in pregnant women with sterile pyuria. Normal menstruation returns ~four weeks of ATT among patients of PTB and 6 months those with endometrial involvement. The choice of treatment for TO mass in FGTB is ATT and broad spectrum antibiotics.

Keywords: Female Genital TB, endometrial osseous metaplasia, TB in Pre and Post COVID pandemic

Introduction

Numerous human tissues and organs are impacted by Mycobacterium tuberculosis, which can result in a variety of pathologies, including inflammation, exudation, ulceration, necrosis, fibrosis, calcification, and more.

The Global TB Report 2021 states that the incidence of all types of tuberculosis in India was estimated to be 188 per 100,000 people in 2020 (129-257 per 100,000 people). The state of Andhra Pradesh reported the incidence of pulmonary tuberculosis as 75% and that of EPTB as 25% [1].

Although TB is more common in men in India, the disease has a significant impact on women as well, particularly those in the reproductive age range (15-49 years). Additionally, diagnosing TB in pregnant women is challenging because both the illness and pregnancy share nonspecific symptoms [1,2].

It is hard to determine the precise incidence of Female Genital TB (FGTB), which is less than 1% in developed nations and more than 1% in developing nations [1]. FGTB occurs in 10-20% of adolescent patients with pulmonary tuberculosis. GTB represents 15-20% of EPTB in men and women inclusive [3]. Furthermore, FGTB occurs concurrently in 10% of pulmonary TB (PTB) patients and accounts for 9% of EPTB cases, which is typically a disease of young women [4]. According to tertiary care facilities and centres that register for assisted reproduction, the reported incidence from infertility clinics varies from 1% to 48% [5].

Corresponding Author:
Dr. Sandhyasri Panda
MD, FICOG, Department of Obstetrics and Gynecology, Maharajah’s Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India
Female Genital Tuberculosis (FGTB) may present as an enigmatic disorder. FGTB is frequently a secondary symptom of a primary infection that originates in the lungs or bowel through haematogenous, lymphatic, directly from an adjacent affected organ, or, less frequently, as a primary lesion in the lower genital tract that results from a direct microbial contract or from sexually transmitting the disease from an infected partner [7]. It is difficult to establish the diagnosis by a single test or by a combination of tests because of the paucibacillary nature of the lesions and the atypical presentation of FGTB. As a result, even when a variety of supportive tests are provided via an algorithm [8], it is occasionally a diagnosis of exclusion, or a clinical diagnosis, and is then subjected to a therapeutic trial using antitubercular medications. Other times, the lesions are simple, and a single test-bacteriology, histology, imaging, immunology, or a combination of these-along with a strong clinical history is enough to make a confirmed diagnosis [9].

The Cartridge Based Nucleic Acid Amplification Test (CBNAAT), also known as the Gene Xpert, is a rapid molecular test that is currently used to diagnose FGTB. It is considered to be highly specific but less sensitive, making it a good rule-in test but a poor rule-out test [5, 6, 10]. Standard laboratory tests, such as histopathology and bacteriological investigation (Smear/culture), produce poor sensitivity. Interferon-γ release assays (IGRAs), imaging, laparoscopy, histology, and clinical suspicion are the mainstays of the FGTB diagnosis process. A good diagnostic efficacy that could lead to the development of a point-of-care (POC) test can be obtained by using NAATs to detect MTB circulating free DNA (cfDNA) in readily accessible samples, such as the urine or plasma of FGTB cases [5].

According to an article in PMC, male genitourinary tuberculosis (GUTB) is the second most prevalent extrapulmonary manifestation of tuberculosis (EPTB) in developing nations, accounting for 20-40% of cases. In 5-30% of these cases, there is isolated genital organ involvement [11]. Prior to the COVID-19 pandemic, tuberculosis (TB) surpassed HIV/AIDS as the most common infectious agent-related cause of death, particularly in developing nations. The SDGs’ global TB targets called for TB epidemics to be eradicated by 2030. The goal of the WHO End TB Strategy was to reduce tuberculosis (TB) incidence rate by 90% (new and recurrence cases per 100,000 people annually) by 2035. This goal had been steadily approached until the COVID-19 pandemic had a drastic impact on the provision of tuberculosis care; there was a significant decrease in the number of new cases of TB reported globally in 2020, from 7.1 million to 5.8 million, an 18% decrease from 2019. Consequently, the number of tuberculosis deaths had gone up in 2020. 2021 was predicted to have the largest impact on TB deaths, while 2022 was predicted to have the largest impact on TB incidence [12].

In 2021 (19, 33, 381), there were 19% more incident TB patients (new and recurrence) reported than in 2020 (16, 28, 161). The Global TB Report 2021 reported that 3.06 lakh children aged 0 to 14 contract TB annually, accounting for approximately 11% of all estimated TB cases [12].

Objective
1. To study the incidence of female and male genital TB
2. To study the spectrums of FGTB
3. To study different diagnostic tests applied for their diagnosis
4. Their treatment options and response to therapy

Methodology
Data from prospectively collected FGTB cases were reviewed, and the types of samples and tests offered to obtain the diagnosis were noted. The following tests are used to ascertain the diagnosis: Mantoux test, microscopy for AFB, Culture and sensitivity, endometrial biopsy, HP study for granulomatous lesion, serum CA 125, testing for ADA levels in serum or ascitic fluid, body fluids and sputum for CBNAAT. Where appropriate and practical, ultrasound, X-rays, and CT scans studies were conducted. Additional information was gathered from the TB core committee meetings as well as the departments of pulmonary medicine, general medicine, DVL, general surgery, and urology. The data was analyzed using proportions and percentages.

Results
A total of 1342 TB cases were reported from our institute between June 2014 and December 2022. Of these, 703 (52.38%) were cases of pulmonary TB; and 639 (47.62%) were cases of EPTB, which included 12 cases of genitourinary TB (two male and ten female). Thus, the overall incidence of FGTB is 0.74% (10/1342) and among EPTB accounting for 1.6% (10/639). The age range of the ten subjects in the series was 14 to 50 years, with a mean age of 30.6 years. There were nine out of ten from low SES. In 3/10, h/o smoking was elicited. None had diabetes, alcoholism, or HIV AIDS.
### Table 1: Clinico-epidemiology and methods of diagnosis of cases

<table>
<thead>
<tr>
<th>S. N.</th>
<th>Symptomatology</th>
<th>Clinical Presentation</th>
<th>Age (Yr)</th>
<th>Menstrual abnormality</th>
<th>Imaging</th>
<th>Microscopy</th>
<th>Histology</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Abdominal pain</td>
<td>Pregnancy with recurrent UTI with sterile pyuria</td>
<td>20</td>
<td>N/A</td>
<td>Normal</td>
<td>Urine AFB +ve</td>
<td>-</td>
<td>Started on ATT post LSCS; neonate on prophylactic INH.</td>
</tr>
<tr>
<td>2.</td>
<td>Abdominal pain</td>
<td>Post hysterectomy, right adnexal mass with fornical tenderness</td>
<td>43</td>
<td>N/A</td>
<td>TO mass</td>
<td>-</td>
<td>-</td>
<td>Lost to F/U</td>
</tr>
<tr>
<td>3.</td>
<td>Abdominal pain</td>
<td>Postmenopause</td>
<td>49</td>
<td>N/A</td>
<td>TO mass</td>
<td>CBNAAT +ve</td>
<td>-</td>
<td>Lost to F/U</td>
</tr>
<tr>
<td>4.</td>
<td>Abdominal pain</td>
<td>Postmenopause, 20 weeks mass P/A, ↑CA125, ↑ADA</td>
<td>50</td>
<td>N/A</td>
<td>TO mass</td>
<td>-</td>
<td>Granulomatous lesion +</td>
<td>Improvement in general wellbeing, appetite and bowel function at 1m visit, abdominal mass resolved</td>
</tr>
<tr>
<td>5.</td>
<td>Disseminated TB</td>
<td>Concomitant pulmonary TB</td>
<td>14</td>
<td>Amenorrhoea</td>
<td>TO mass</td>
<td>CBNAAT +ve</td>
<td>-</td>
<td>Resumed regular menses after 40 days of ATT, first cycle was progesterone withdrawl bleeding</td>
</tr>
<tr>
<td>6.</td>
<td>Miliary TB</td>
<td>Miliary TB</td>
<td>15</td>
<td>HYPMENORRH ghéA</td>
<td>TO mass</td>
<td>CBNAAT -ve</td>
<td>-</td>
<td>Resumed regular menses after 2months of ATT, Left ovary cystic changes with solid components → Spontaneous resolution</td>
</tr>
<tr>
<td>7.</td>
<td>Pulmonary TB</td>
<td>Hypomenorrhoea F/B Amenorrhoe</td>
<td>22</td>
<td>Lung consolidation + upper lobe cavity + bronchiectatic changes</td>
<td>CBNAAT +ve</td>
<td>-</td>
<td>-</td>
<td>Resumed regular menses after 24days of ATT</td>
</tr>
<tr>
<td>8.</td>
<td>Persistent white discharge</td>
<td>Ulcerative growth on cervix</td>
<td>30</td>
<td>AMENORRHŒA 6yrs duration</td>
<td>TO mass</td>
<td>-</td>
<td>Granuloma</td>
<td>Healthy looking cervix after 6m ATT</td>
</tr>
<tr>
<td>9.</td>
<td>Primary infertility</td>
<td>Primary infertility</td>
<td>36</td>
<td>Hypomenorrhoea F/B Amenorrhoe</td>
<td>TO mass</td>
<td>-</td>
<td>Granulomatous endometrium</td>
<td>Resumed menstruation after 6m ATT and subjected to laparotomy; adhesiolysis, RSO with left ovarian cystectomy performed.</td>
</tr>
<tr>
<td>10.</td>
<td>Primary infertility</td>
<td>Primary infertility</td>
<td>27</td>
<td>Hypomenorrhoea</td>
<td>Calcification of endo myometrium</td>
<td>Osseous metaplasia of endometrium</td>
<td>-</td>
<td>Resumed menstruation after 6m ATT</td>
</tr>
</tbody>
</table>

NB: Subjects are rearranged based on common symptomatology; N/A- Not applicable; F/B- Followed by; RSO-Right salphingo-oopherectomy
Abdominal pain and abnormal menstruation were the two most common presenting symptoms in 6/10 (60%) each. Six out of ten (60%) women had an ovary, tube, or both involved, with an adnexal lesion being the most common USG and/or clinical finding. Infertility was a presenting symptom in 20% of subjects, and pregnancy with Urogenital TB was the symptom in 10%.

Menstrual abnormality noted were either hypomenorrhea (66%) and/or amenorrhea (34%). Median time to resume regular menses was shorter among subjects with concomittant PTB than those who presented with genital TB and/or infertility. The former due to early diagnosis and treatment for PTB than those with FGTB.

The pregnant woman was diagnosed with renal tuberculosis at term and was delivered by cesarean section and started on ATT; the neonate was put on prophylactic ATT with INH.

A postmenopausal women with suspicious malignant lesion underwent laparotomy and was diagnosed with frozen pelvis; biopsy taken from same and it showed granulomatous lesion.

One patient who presented with infertility and a pelvic mass underwent a review USG after 6months ATT and eventually required a laparotomy for persistent pelvic pain during which adhesiolysis, RSO with left ovarian cystectomy was performed as fertility preserving surgery. Five other subjects with TO mass were managed conservatively.

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One of the subjects who had primary infertility with hypomenorrhoea showed endometriometrial calcification on USG Pelvis, and osseous metaplasia of the endometrium on HP study [13].

Menstrual abnormalities returned to normal after continuing ATT for a median of 4 weeks in 5/6 subjects (83%), 3 young girls, one with osseous metaplasia of the endometrium and one with ulcerative cervical growth.

**Table 2: Percentage distribution of primary diagnostic modality among FGTB**

<table>
<thead>
<tr>
<th>Diagnostic modality</th>
<th>Bacteriology</th>
<th>Histology</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Percentage</td>
<td>40%</td>
<td>40%</td>
<td>20%</td>
</tr>
</tbody>
</table>

In our study 40% subjects were diagnosed based on bacteriology, 40% on histology and 20% on imaging.

**Table 3: Proportion of different diagnostic tests among PTB, EPTB and FGTB**

<table>
<thead>
<tr>
<th>Total (1342)</th>
<th>Bacteriology +</th>
<th>Clinical + histology</th>
<th>Imaging (Chest Xray, chest CT, USG abdomen, pelvis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTB</td>
<td>703(52.38%)</td>
<td>542(77.09%)</td>
<td>161(22.9%)</td>
</tr>
<tr>
<td>EPTB</td>
<td>639(47.61%)</td>
<td>48(7.52%)</td>
<td>591(92.48%)</td>
</tr>
<tr>
<td>FGTB</td>
<td>10(0.74%)</td>
<td>4(40%)</td>
<td>4(40%)</td>
</tr>
</tbody>
</table>

Table 3 shows that 7.5% of EPTB and 40% of FGTB were bacteriology +ve, the latter due to concomittant PTB in three subjects. Although imaging was the primary diagnostic modality in two of the subjects of FGTB, it was a supportive tool in 9 out of 10 subjects with significant findings.

**Graph 1:** No. of cases prior to and following COVID 19

Graph 1 highlights the falling and rising trends of TB in pre and post COVID era and the higher number of EPTB as reported from our institute.

It also shows that three out of ten (30%) cases are reported in the 2022, reflecting a resurgence of tuberculosis post-COVID as predicted by WHO [12]. The total number of TB cases in adolescence during 2022 was 10. As a result, there is a 20% concomittant affection of genital organs in adolescent.

**Discussion**

FGTB is more common in younger (20-40 years) women in South East Asia and Africa and in older (Premenopausal) women in Europe and the United States, possibly due to early child bearing in developing countries [8, 14-16]. The average age in our series is 30.6 years. In a series of 13 cases, Boubacar Efared et al. reported a mean age of 39.92 years (Range: 18-74 years) [17]. The majority of patients were of reproductive age, and four were postmenopausal (40%) vs (30.76%) [17], which is similar to the current series,
where 3/10 (30%) were postmenopausal. However, Aslan G et al. [18] reported GTB is uncommon in postmenopausal women, accounting for only about 1% of postmenopausal bleeding. According to the same author, Genital TB (GTB) is a type of extrapulmonary TB that is more common in women [18]. Bhavna D et al. and Kamra E et al. reported urogenital tuberculosis (UGTB) a common manifestation of extrapulmonary tuberculosis (EPTB), which affects men and women in a 2:1 ratio [5, 20]. During our study, two male patients were positive for Urine AFB. Thus, men: women ratio is 1:5.

In the current study, the prevalence of FGTB is 0.74%. According to Kaya A et al., FGTB has a 1% incidence in developed countries and a >1% incidence in developing countries; due to its subtle presentation, many cases are overlooked and diagnosed incidentally. As a result, the true prevalence of FG-TB is unknown [3]. We found FGTB to be 1.6% of EPTB, whereas other studies have found it to be 15-20% [4] and 9% [9], which could be explained by specialty treatment being addressed in those settings. According to JB Sharma et al., the incidence ranges from 1% to 48% depending on the tertiary care facilities and the centres registering for assisted reproduction [6].

In our study, there is a 20% concomitant affection of genital organs in adolescent PTB, compared to 10% in Bhavna D et al. [9] and 10-20% according to Ahmed S et al. [4].

In the current study prevalence of infertility is 20%, abdominal pain is 60% and menstrual abnormality was 60% whereas Kaya et al. [3] reported it as 100%; 20% and 20% respectively in a series of 5 patients. Similarly, Aslan G et al. [18] reported 44% infertility, 25% pain abdomen, 18% vaginal bleeding, 5% amenorrhea, and 4% vaginal discharge. In our series, vaginal discharge is reported at 10%.

One subject (10%) vs. 53.84% [17] among TO masses, who presented with ascites, neoplastic ovarian mass/pyometra with elevated CA125 value, underwent laparotomy; and procedure was limited to only biopsy due to a frozen pelvis. Patients with tuboovarian TB who have peritoneal involvement (ascites) and a high level of serum CA-125 are frequently misdiagnosed as having ovarian carcinoma and undergo unnecessary and aggressive surgery [17, 19, 21].

In the present study, ATT resumed normal menstruation in 83% (5/6) of patients; Tiwari M et al. reported it as 81% in a case control study involving 200 patients [22], the median time to resume menses was 4 week among patients with concomitant PTB and it was 6months among patients who presented with infertility.

We report a case of osseous metaplasia who presented with primary infertility and hypomenorrhoea, Anupam Kaur et al. reported a similar case study, both subjects were diagnosed as presumptive TB and put on ATT [13].

Fig 1: Ulcerative lesion on cervix

![Ulcerative lesion on cervix](image1)

Fig 2: Inflamed Right and Left Ovary with heterogeneous collection with thickened Fallopian tubes.

![Inflamed Right and Left Ovary](image2)

Fig 3: Post 6 months of ATT: USG Pelvis showing normal Right Ovary and cystic Left Ovary with concretions

![Post 6 months of ATT: USG Pelvis showing normal Right Ovary and cystic Left Ovary with concretions](image3)
Fig 4: Endometrial curetting showed osseous metaplasia on HP study

Conclusion
Poverty poses a risk. Although menstrual abnormalities, TO pathology, and infertility are common presentations, GUTB should be considered as a diagnosis in pregnant women with sterile pyuria. Concurrent PTB, rapid molecular tests, and imaging aid in diagnosis. Normal menstruation returns after a median of four weeks of ATT among patients of PTB but it takes longer for those with endometrial involvement. The choice of treatment for TO mass in FGTB is ATT and broad spectrum antibiotics.

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Conflict of interest: None.

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1. India TB Report 2022