Unveiling Genital Tuberculosis: India's Hidden Infertility Epidemic

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A B S T R A C T

Genital tuberculosis (GTB) is a significant yet underrecognized cause of infertility, particularly in high-burden countries like India. It often presents asymptomatically or mimics other reproductive disorders, leading to delayed diagnosis and treatment. GTB primarily affects women of reproductive age but can also impact men, contributing to infertility through various pathophysiological mechanisms. Despite its prevalence, GTB remains a hidden epidemic due to limited awareness, diagnostic challenges, and systemic healthcare gaps. This narrative review explores the epidemiology, pathophysiology, clinical presentation, and impact of GTB on infertility in India. It also highlights diagnostic and management challenges while proposing strategies to address this critical public health issue.

GTB contributes to 15-20% of infertility cases in India, with the highest burden among women aged 20-40 years. Hematogenous spread of *Mycobacterium tuberculosis* leads to chronic inflammation, fibrosis, and scarring of reproductive organs, resulting in irreversible damage. Traditional methods like microscopy and culture are inadequate for GTB detection. Advanced techniques, though more accurate, remain inaccessible to many due to cost and resource constraints. While antitubercular therapy (ATT) can control infection, restoring fertility often requires surgical intervention or assisted reproductive technologies, which are financially prohibitive for most patients. GTB is a silent epidemic with profound implications for reproductive health and social well-being in India. Addressing GTB requires enhanced awareness, integration of infertility screening into TB programs, improved access to advanced diagnostics and treatments, and targeted public health policies. Bridging these gaps can mitigate the burden of infertility and improve quality of life for affected individuals.

Keywords: Genital tuberculosis, infertility, India, antitubercular therapy, public health challenges, assisted reproduction

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INTRODUCTION

Tuberculosis (TB), caused by Mycobacterium tuberculosis, is one of the most persistent infectious diseases globally, and India bears the brunt of its burden. Despite advancements in diagnosis and treatment, India accounts for over 25% of the world's TB cases, making it a significant public health concern. While pulmonary TB, the most common manifestation, has garnered much attention, extrapulmonary TB (EPTB) remains a lesser-known but equally severe form of the disease. Among EPTB presentations, genital tuberculosis (GTB) poses a unique challenge due to its subtle presentation and profound implications on reproductive health, particularly infertility. GTB refers to the infection of the reproductive organs, often secondary to a primary focus in the lungs or gastrointestinal tract.¹ It predominantly affects women in their reproductive years and is one of the leading causes of tubal factor infertility in India. Studies suggest that GTB is responsible for 15-20% of infertility cases in high-prevalence areas, yet it remains underdiagnosed due to vague symptoms and limited awareness among healthcare providers. For men, GTB can lead to infertility through conditions like epididymitis and prostatitis, further compounding its impact on couples struggling with childlessness.²

The burden of infertility in India is significant, with estimates suggesting that around 10-15% of couples face difficulties conceiving. Infertility, while a medical condition, has deep social and cultural ramifications in India. Childbearing is often seen as a cornerstone of marital life, and the inability to conceive can result in emotional distress, marital discord, and even ostracism, particularly for women. In this context, GTB's role as a silent yet impactful contributor to infertility warrants urgent attention. Despite its significant implications, GTB is often termed a "hidden" cause of infertility. This is due to several factors, including the asymptomatic nature of early disease, the overlap of its clinical presentation with other reproductive conditions, and the lack of reliable diagnostic tools in resource-constrained settings. Consequently, many cases go unrecognized until irreversible damage to the reproductive organs has occurred. This delay not only hampers effective treatment but also severely diminishes the chances of conception, even with advanced reproductive technologies.³

The diagnosis and management of GTB are fraught with challenges. Traditional diagnostic methods like microscopy and culture have limited sensitivity, particularly in genital specimens. While newer techniques such as polymerase chain reaction (PCR) and laparoscopy offer better accuracy, they remain inaccessible to many due to their high cost and limited availability. Treatment with antitubercular therapy (ATT) can eradicate the infection, but restoring fertility often requires additional interventions, including surgery or assisted reproductive technologies (ART).⁴ These treatments are financially and emotionally taxing, especially for individuals in low- and middle-income settings. Given the interplay of biological, social, and systemic factors, addressing GTB as a cause of infertility requires a multifaceted approach. This narrative review aims to shed light on the epidemiology, pathophysiology, and clinical presentation of GTB in India, highlighting its impact on infertility. It will also explore the challenges in diagnosis and management, discuss the public health implications, and propose strategies for improved prevention, detection, and treatment. By bridging gaps in knowledge and practice, this review seeks to contribute to a more comprehensive response to this hidden yet critical public health challenge.⁵

EPIDEMIOLOGY AND PATHOPHYSIOLOGY OF GENITAL TUBERCULOSIS

Studies estimate that GTB accounts for 15-20% of infertility cases in high-burden regions, with prevalence rates among infertile women ranging from 18% to as high as 30% in some urban areas.^{6,7} However, the true burden is likely underreported due to diagnostic challenges and asymptomatic presentations.⁸ The high prevalence of GTB in India can be attributed to several factors. Poverty, malnutrition, and overcrowding create conditions conducive to TB transmission. Women in rural areas face additional risks due to limited healthcare access and delayed diagnosis. HIV co-infection, another significant risk factor, has further fuelled the TB epidemic in India. Poor awareness and social stigma surrounding infertility often prevent individuals from seeking timely medical intervention, exacerbating the problem.³ GTB disproportionately affects women of reproductive age, with the majority of cases occurring between 20-40 years. This demographic vulnerability is particularly concerning given the critical importance of this age group for fertility. For men, although less common, GTB can manifest in conditions like epididymitis and prostatitis, leading to oligospermia or azoospermia, which further contribute to infertility.⁵

GTB typically results from hematogenous spread of *Mycobacterium tuberculosis* from a primary site, such as the lungs or lymph nodes. In rare cases, direct spread from adjacent organs or ascending infection from the lower genital tract can occur. The infection primarily involves the female reproductive organs but can also affect the male genital tract. Female genital TB primarily involves the fallopian tubes (90-100% of cases), followed by the endometrium, ovaries, cervix, and vagina. The fallopian tubes' rich blood supply predisposes them to hematogenous infection. Tubercle bacilli invade the tubal mucosa, causing granulomatous inflammation characterized by epithelioid cells, Langhans giant cells, and caseation necrosis. This leads to tubal obstruction, hydrosalpinx, or pyosalpinx, often resulting in infertility. The endometrium is the second most common site. Endometrial TB manifests as caseating or noncaseating granulomas, leading to uterine adhesions (Asherman's syndrome).⁹ The ovaries may become infected via contiguous spread, forming tubo-ovarian masses or abscesses. Cervical and vaginal TB are rare and often result from direct spread.¹⁰

In men, genital TB predominantly involves the epididymis (epididymal TB) due to its dense blood supply. Infection leads to caseating granulomas, which may result in abscesses or fistulas. Testicular involvement is usually secondary to epididymal TB, presenting as scrotal swelling or masses. The prostate can be infected, causing prostatitis, calcifications, or abscesses. Seminal vesicles and vas deferens involvement may lead to fibrosis, obstruction, and infertility.¹⁰ In both sexes, chronic inflammation induces fibrosis, scarring, and calcification, impairing reproductive function. The latent nature of TB means symptoms are often nonspecific, delaying diagnosis. Early detection and treatment with antitubercular therapy are crucial to prevent complications like infertility or pelvic organ damage.¹¹

CLINICAL PRESENTATION AND CHALLENGES IN DIAGNOSIS

Genital tuberculosis (TB) is a form of extrapulmonary TB affecting the reproductive organs. Its clinical presentation is often nonspecific, leading to delayed diagnosis. The disease poses a significant challenge due to its subtle symptoms, lack of specific diagnostic criteria, and varied manifestations between men and women. In women, genital TB predominantly affects the fallopian tubes, followed by the endometrium, ovaries, cervix, and vagina. Common symptoms include:¹²

- a) Infertility: This is the most frequent presentation, with up to 70-80% of affected women seeking medical attention due to difficulty conceiving. Tubal obstruction, endometrial adhesions, or ovarian involvement contribute to infertility.
- b) Menstrual Irregularities: These may include oligomenorrhea, amenorrhea, or menorrhagia. These irregularities result from endometrial destruction and scarring.
- c) Pelvic Pain: Chronic pelvic pain, often nonspecific, is common due to inflammation and adhesions.
- d) General Symptoms: Constitutional symptoms like low-grade fever, weight loss, and malaise are sometimes present but not specific.

In men, genital TB primarily involves the epididymis, testis, prostate, and seminal vesicles. Common symptoms include:¹³

- a) Scrotal Swelling: Epididymal TB presents as painless or painful swelling, often mimicking other scrotal conditions like bacterial epididymo-orchitis.
- b) Infertility: Obstruction of the vas deferens and seminal vesicles due to fibrosis leads to azoo-spermia or oligospermia.
- c) Dysuria and Perineal Pain: Prostate TB may manifest as painful urination or vague discomfort in the perineum.
- d) Abscess Formation: Chronic inflammation may lead to abscesses or fistulas, presenting as non-healing sinuses.

The flowchart given below outlines the step-by-step approach to diagnosing genital TB in patients, typically those presenting with infertility or reproductive health symptoms (figure 1).^{14,15}



Figure 1: Diagnostic pathway for Genital tuberculosis

Table 1: Factors complicating the diagnosis of Genital TB

Factor	Delay in diagnosis	
Subclinical Presentation	Many patients remain asymptomatic or present with vague complaints, delaying clinical suspicion.	
Lack of Specific Biomarkers	Routine blood tests and imaging lack specificity. Elevated ESR or CRP may suggest infec- tion but are not diagnostic.	
Overlap with Other Condi- tions	Conditions like pelvic inflammatory disease (PID), endometriosis, and bacterial epidid- ymo-orchitis mimic genital TB, often leading to misdiagnosis.	
Low Sensitivity of Tests	 Microscopy and Culture: Acid-fast bacilli (AFB) detection has low sensitivity in genital TB. Culture of endometrial or epididymal tissue is time-consuming and has variable yield. Histopathology: Granulomas with caseation are suggestive but not always present. Molecular Tests: Polymerase chain reaction (PCR) offers high sensitivity but can produce false positives due to cross-contamination. 	
Imaging Limitations	Ultrasound, CT, or MRI may reveal findings like tubal thickening or abscesses but are not specific.	
Invasive Procedures	Laparoscopy and biopsy are often required for definitive diagnosis, but these are inva- sive and may not always be feasible.	
Need for Advanced Techniques	PCR, histopathological examination, and laparoscopy are more accurate but are not widely available in resource-limited settings.	
Economic Barriers	Advanced diagnostic tools are often prohibitively expensive for patients in low-income settings.	

However, diagnosing genital TB is difficult due to its non-specific symptoms, insidious onset, and overlap with other reproductive or pelvic diseases. Several factors complicate the diagnostic process (Table 1):¹⁶

CLINICAL MANAGEMENT AND REPRODUCTIVE INTERVENTIONS

Antitubercular therapy (ATT), including first-line drugs like isoniazid, rifampicin, pyrazinamide, and ethambutol, remains the cornerstone of treatment. While effective in eradicating the infection, ATT alone often fails to restore fertility due to the irreversible damage caused by the disease. For women, restoring fertility after ATT requires a multidisciplinary approach. Surgical intervention is considered when complications like tubal obstruction, abscess formation, or severe pelvic adhesions persist despite ATT.¹⁷ Laparoscopy is a diagnostic and therapeutic tool for identifying tubal damage, pelvic adhesions, or endometrial scarring. Minimal corrective surgery may improve reproductive outcomes in selected cases. For mild tubal blockages, surgical procedures like salpingostomy or adhesiolysis may restore patency. However, the success rate is low in advanced TB cases due to extensive scarring. For uterine involvement, hysteroscopy can help manage intrauterine adhesions (Asherman's syndrome) through adhesiolysis. Repeated surgeries may be necessary for severe cases. In cases of extensive damage, surgical correction may not restore fertility, necessitating the use of ART.18

ART is often the only viable option for infertility in patients with genital TB, especially when reproduc-

tive organ damage is irreversible. The stigma associated with infertility and TB can cause significant emotional distress. Psychological counselling plays a crucial role in helping patients cope with the diagnosis and treatment process. Couples should be educated about the nature of the disease, its implications on fertility, and the available treatment options.¹⁹

• In Vitro Fertilization (IVF):20

IVF bypasses damaged fallopian tubes by directly fertilizing the egg outside the body and transferring the embryo into the uterus.

A properly treated uterine cavity is essential for implantation. In cases with severe endometrial scarring, surrogacy may be the only option.

- Intracytoplasmic Sperm Injection (ICSI):²¹For male infertility caused by genital TB, ICSI may be employed to inject a single sperm directly into the egg, especially in cases of low sperm count or azoospermia due to TB-related obstruction.
- Egg or Sperm Donation: In cases of ovarian or testicular damage, donor eggs or sperm may be used for conception.
- **Gestational Surrogacy**: In women with severe uterine scarring, gestational surrogacy provides a viable option for parenthood.

CHALLENGES IN DIAGNOSIS AND PUBLIC HEALTH INTERVENTIONS

India's healthcare system struggles to meet the demands of early screening and treatment for GTB. Primary healthcare centers often lack the resources and expertise needed for accurate diagnosis and management. Stigma and lack of awareness about GTB and its link to infertility prevent many individuals from seeking timely care. Educational campaigns targeting both healthcare providers and the general public are urgently needed.²⁰ While India's National TB Elimination Program (NTEP) has made strides in combating pulmonary TB, it has yet to adequately address extrapulmonary forms like GTB. Infertility affects approximately 10-15% of couples in India, with tubal factor infertility being one of the most common causes. Among these cases, GTB accounts for 15-20%, highlighting its significant role in the infertility landscape.²²

Delayed Diagnosis and Underreporting

One of the foremost challenges in managing infertility caused by genital TB is delayed diagnosis. Genital TB is often asymptomatic in its early stages or presents with non-specific symptoms such as pelvic pain, menstrual irregularities, or vague discomfort, making it difficult to detect. Furthermore, patients may not seek medical attention until infertility becomes apparent, which can take years after the initial infection. There are no standardized screening programs for genital TB, particularly for women with infertility, in most countries. This results in underreporting and delayed treatment. Current diagnostic methods, such as polymerase chain reaction (PCR), histopathology, and imaging, have limitations in sensitivity and specificity. Additionally, access to advanced diagnostic techniques is restricted in rural and resource-limited settings.¹⁰

Stigma and Social Taboo

Infertility, particularly in developing countries, is deeply stigmatized. Women are often blamed for the inability to conceive, even when the underlying cause lies with male partners or other factors such as TB.²³ The societal stigma associated with infertility prevents many individuals from seeking timely medical help. Women bear a disproportionate burden of blame for infertility. In patriarchal societies, infertility can lead to emotional abuse, marital discord, or even abandonment. Despite its prevalence, genital TB as a cause of infertility remains poorly discussed in public health dialogues, perpetuating ignorance and stigma.²⁴ Infertility caused by genital TB has profound psychosocial effects, including depression, anxiety, and social isolation. Public health systems often lack the resources to address the mental health needs of affected individuals, compounding their suffering.25

Healthcare Infrastructure and Access

Resource-constrained healthcare systems struggle to provide adequate care for patients with genital TB and associated infertility.²⁶ Challenges include:

• Limited Access to Specialists: Infertility caused by genital TB often requires a multidisciplinary ap-

proach involving gynecologists, urologists, infectious disease specialists, and reproductive endocrinologists.¹⁷ However, such expertise is often unavailable in rural and underserved areas.

- Inadequate Facilities: Laparoscopy, hysteroscopy, and advanced imaging required for diagnosis and treatment are unavailable or unaffordable for many.²⁷
- Insufficient Primary Healthcare: Primary healthcare providers may lack awareness or training to identify and refer cases of genital TB effectively.

Economic Barriers

Infertility treatments, especially those involving assisted reproductive technologies (ART) such as in vitro fertilization (IVF), are prohibitively expensive for most patients in low- and middle-income countries (LMICs). Patients with genital TB face additional financial challenges. Advanced diagnostic tools (e.g., PCR tests, laparoscopies) and prolonged antitubercular therapy (ATT) regimens can be costly, deterring patients from seeking care. For patients with irreversible damage to reproductive organs, ART is often the only option, but its cost is beyond the reach of most in LMICs.³ Table 2 summarizes the various diagnostic tests in terms of their sensitivity, specificity and costs.²⁸⁻³¹

Table 2: Comparison of sensitivity, specificity, and cost for various diagnostic methods used for genital TB

Diagnostic	Sensitivity	Specificity	Average
modality	(%)	(%)	Cost (INR)
Histopathology	40	80	2000
PCR for M. Tuberculo-	80	95	4000
sis DNA			
Laparoscopy	90	90	15000
Hysteroscopy	85	88	14000
Pelvic MRI	70	75	10000
Culture (Lowenstein	30	85	3000
Jensen medium)			

Lack of Awareness and Education

Public awareness about genital TB and its link to infertility is limited, even in TB-endemic regions. This lack of awareness leads to several public health challenges.³²

- Ignorance of Symptoms: Many individuals fail to recognize the symptoms of genital TB or seek treatment only when infertility becomes evident.
- Misconceptions: Infertility is often attributed to supernatural causes or lifestyle factors, overshad-owing preventable medical conditions like genital TB.
- Inadequate Health Education: Public health campaigns rarely address the reproductive consequences of TB, leaving a critical gap in knowledge.³³

Multidrug-Resistant Tuberculosis (MDR-TB)

The rising prevalence of multidrug-resistant tuberculosis (MDR-TB) poses another significant challenge. MDR-TB is more difficult and expensive to treat and requires prolonged therapy with secondline drugs.³⁴ For genital TB patients, MDR-TB exacerbates organ damage and further reduces the likelihood of restoring fertility.

Lack of Integrated Public Health Programs

TB control programs typically focus on pulmonary TB, with limited attention to extrapulmonary forms such as genital TB.³⁵ Public health initiatives often fail to integrate infertility management into TB control programs, resulting in a fragmented approach.

PUBLIC HEALTH INTERVENTIONS TO OVERCOME CHALLENGES

Addressing infertility caused by genital TB presents unique public health challenges, including delayed diagnosis, stigma, economic barriers, and inadequate healthcare infrastructure. A coordinated, multi-level response involving awareness, affordable treatment, and integration of infertility care into TB control programs is essential to mitigate the impact of genital TB on reproductive health (Figure 2). By overcoming these challenges, public health systems can improve the quality of life for affected individuals and reduce the burden of infertility worldwide.³⁶

Awareness Campaigns and Screening programs: India's Revised National TB Control Programme (RNTCP), now part of the National Tuberculosis Elimination Programme (NTEP), provides a strong foundation for tackling TB. Incorporating genital TB awareness into these programs can address this often-overlooked form of extrapulmonary TB. Public health campaigns should educate communities about genital TB, its link to infertility, and the importance of early diagnosis and treatment. Routine screening for genital TB in women presenting with infertility, especially in TB-endemic regions, should be integrated into national TB programs.

Affordable Treatment and subsidization of diagnostic tests: Governments and healthcare providers must work to subsidize the costs of diagnostic tests, ATT, and infertility treatments, including ART, to make them accessible to all. The cost of diagnosing genital TB, often requiring advanced techniques like polymerase chain reaction (PCR), histopathology, or imaging, is a major barrier for patients in India. Subsidizing these tests can significantly improve early detection. Tiered payment system can be planned and implemented where diagnostic costs are adjusted based on the patient's socioeconomic status, ensuring affordability for low-income individuals.

Training Healthcare Workers: Healthcare providers, particularly at the primary care level, play a crucial role in early detection. Training programs should focus on equipping doctors, nurses, and allied health workers to identify and manage genital TB. Other strategies include updating medical and nursing school syllabi to include detailed modules on recognizing and managing genital TB, establishing telemedicine platforms where primary care providers can consult specialists for guidance on suspected genital TB cases and organizing regular workshops and training sessions for healthcare providers, focusing on common symptoms of genital TB, diagnostic pathways, including when to refer patients for advanced care.



Figure 2: Multipronged approach strategy to combat public health challenges in addressing GTB associated infertility

Research and Innovation: Investment in research for better diagnostic tools and treatment options for genital TB is essential. Developing precise, costeffective, and widely accessible diagnostic methods for genital TB is crucial to reduce delays in diagnosis and improve patient outcomes. Research should focus on developing rapid, point-of-care diagnostic tools, similar to GeneXpert for pulmonary TB, tailored to detect genital TB specifically. Portable devices that can be used in rural and resource-limited settings should be prioritized.

Mental Health Support: Counselling services should be made available to support patients dealing with the emotional impact of infertility. Joint counselling sessions for couples can help to address marital stress related to infertility, fostering mutual understanding and support. Establishment of patient support groups allow individuals to share experiences, reduce feelings of isolation, and build resilience.

CONCLUSION

Genital tuberculosis is a silent yet devastating cause of infertility in India. Its asymptomatic nature, diagnostic challenges, and profound social and economic implications make it a critical public health issue. Addressing GTB requires a coordinated effort involving awareness, improved diagnostics, and access to affordable treatments. By prioritizing this hidden epidemic, India can not only improve reproductive health outcomes but also alleviate the social and emotional burdens associated with infertility. The management of genital TB in infertile patients is challenging due to the irreversible damage it causes to reproductive organs. Early diagnosis, effective ATT, and appropriate use of surgical and ART interventions can help affected patients achieve parenthood. A holistic approach, combining medical, surgical and psychological care, is essential to address both the physical and emotional aspects of infertility caused by genital TB.

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