https://jrhm.org/

Journal of
Reproductive Healthcare
and Medicine

Indian Society for the
Study of Reproduction &
Fertility

Invited Article

Genital tuberculosis: A silent contributor to infertility and adverse pregnancy outcomes

Mudra Sikenis[1], Bhavna Prajapati[1], Ashutosh Kumar Singh[1], Karmveer Yadav[1], Akhlaqur Rahman[1], Megha Katare Pandey[2], Ram Kumar Nema[1]

[1]Division of Environmental Biotechnology Genetics and Molecular Biology, ICMR – National Institute for Research in Environmental Health, [2]Translational Medicine Centre, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India.

***Corresponding author:**
Ram Kumar Nema,
Division of Environmental Biotechnology Genetics and Molecular Biology, ICMR – National Institute for Research in Environmental Health, Bhopal, Madhya Pradesh, India.

ramkumar.nema@icmr.gov.in

Received: 14 October 2024
Accepted: 04 December 2024
Published: 31 December 2024

DOI
10.25259/JRHM_25_2024

Quick Response Code:

ABSTRACT

Genital tuberculosis (GTB) is a significant yet often unnoticed reason for infertility, disproportionately affecting women in areas with a high burden of tuberculosis (TB). Notwithstanding its considerable effect on reproductive health, GTB remains underdiagnosed due to its inconspicuous clinical presentation and the limits of existing diagnostic tools. This review gives a top-to-bottom examination of the epidemiological patterns and physiological impacts of GTB, featuring the intricate interchange between illness and infertility. The discussion envelops the complex difficulties in diagnosing GTB-associated infertility, which incorporate the nonspecific symptoms, the absence of delicate and explicit diagnostic tests, and the potential for misdiagnosis with other gynecological conditions. Furthermore, we investigate the ongoing pharmacological medications used to treat GTB, focusing on their efficacy, limitations, and the emergence of drug-resistant TB strains that complicate treatment outcomes.

Keywords: Genital tuberculosis, Infertility, Reproductive health, Genital tuberculosis-associated infertility

INTRODUCTION

Genital tuberculosis (GTB) is a considerable, however frequently under recognized reason for infertility, especially in geological regions where tuberculosis (TB) is endemic.[1] Despite its significant impact on reproductive health, GTB is still greatly underdiagnosed and underreported in clinical and public health settings.[2] This lack of detection is partly due to the obscure and often asymptomatic nature of the disease. It can progress silently and cause irreversible damage to the reproductive system before it is detected.[3]

Infertility presents as a multifaceted condition that has a global impact, affecting millions of individuals and exerting far-reaching implications for both individuals and societies.[4] In regions where TB is prevalent, the presence of GTB exacerbates the burden of infertility, yet it is often disregarded in clinical and public health discussions. According to the World Health Organization, TB affects almost a quarter[5] of the global populace, with a considerable number of instances occurring in developing nations. However, the accurate magnitude of GTB among women of reproductive age remains inadequately studied, leading to a gap in understanding its full impact on infertility.

GTB dominatingly influences the fallopian tubes, endometrium, and intermittently the ovaries and cervix, prompting conditions such as tubal blockage, endometrial dysfunction, and adhesions

that completely compromise fertility.[6] The disorder includes complex immunological interactions, including the formation of granulomas, to cause tissue scarring, which disturbs normal reproductive function.[7] The clinical manifestation of GTB is often dubious, mirroring other gynecological problems,[8] which complicates its diagnosis and defers fitting treatment. In spite of the known correlation between GTB and infertility, research on this topic remains restricted.[9] Epidemiological examinations are diminished, and the reliable prevalence of GTB-related infertility is not deep-rooted, especially in high-risk populations.[10] The analytical intricacies are additionally intensified by the limits of current methods, for example, histopathology, culture, and polymerase chain reaction (PCR).[11] These methods, while effective, frequently neglect to identify the illness in its initial phases or in conditions where the bacterial burden is low.

The treatment of GTB is regularly based on the standard anti-TB regimens utilized for pneumonic TB.[12] However, the adequacy of these medicines in altering infertility related to GTB is unsure.[13] This implies that structural and functional damage caused by the infection may persist even after successful eradication of the bacteria, underlining the need for new treatment approaches that specifically address the reproductive consequences of GTB.

This review contemplates a thorough examination of the epidemiological and physiological parts of GTB-related infertility, with an emphasis on classifying research gaps and investigating expected pharmacological mediations. By revealing insight into these areas, we plan to underline the significance of further developing awareness, upgrading diagnostic abilities, and developing more viable treatment procedures. Such advancement is critical to decreasing the burden of infertility related with GTB, especially in TB-endemic regions.

EPIDEMIOLOGICAL INSIGHTS

Over the past few years, female GTB (FGTB) was diagnosed in 0.94% of 12,971 biopsy samples examined across multiple hospitals. A total of 122 FGTB cases were identified, with the prevalence varying by year and institution. The highest prevalence rate (1.8%) occurred in 2013, while the lowest (0.32%) was in 2019. This year-to-year variation suggests that factors such as diagnostic practices, public health initiatives, or changes in disease transmission may have influenced detection rates over time.[14]

The prevalence of GTB exhibits significant variability across different regions, reflecting the broader epidemiological trends of TB and the associated socioeconomic and healthcare conditions.[15] A recent systematic review published in 2024 on GTB in women highlights a significant burden of the disease in low socioeconomic settings, particularly among poorer populations. The study found that half of the cases involved the vulva, while the endometrium, cervix, and fallopian tubes were less frequently affected. In some instances, multiple organs were involved. The study also revealed a concerning connection between GTB and infertility, with 12.5% of the women facing infertility. Among these, most struggled with primary infertility, and one case involved secondary infertility.[16]

Risk factors

The risk factors for GTB are closely entwined with those related to pulmonary TB.[17] However, certain factors connected with reproductive health and overall health status explicitly increment susceptibility to GTB.[18] Understanding these risk factors is critical for recognizing high-risk populations and carrying out intervention mediations to diminish the burden of this disease.

Immunosuppressive States and GTB: Immunosuppressive conditions and therapies increase the risk of GTB by reactivating latent *Mycobacterium tuberculosis* infections. Treatments for autoimmune diseases, organ transplants, and cancer, with factors associated with human immunodeficiency virus (HIV) infection and chronic alcoholism, compromise the immune defense, creating a suitable condition for TB progression. Key risk factors, such as HIV, depletes the CD4+ T-cells, which are essential for immune function. Resulting patients with low counts of CD4 below 200 cells/uL increase the potential risk of TB, including extrapulmonary forms like GTB.[19]

HIV co-infection

One of the main risk factors for having GTB is co-infection with HIV. The immunosuppression achieved by HIV enhances and improves the risk of TB, including its extrapulmonary form, like GTB.[20] HIV debilitates the immune system, making it more convenient for *M. tuberculosis* to spread from the lungs to different parts of the body, including the genital tract.[21] This spread happens through the circulatory system or lymphatic system and is facilitated by the reduced ability of the immune system to contain the infection.[22] In areas with high HIV prevalence, for example, sub-Saharan Africa, the cross-over of TB and HIV plagues adds to an expanded frequency of GTB, especially among women of reproductive age.[23] This co-infection additionally muddles the clinical administration of TB, as patients with both HIV and TB frequently present with abnormal side effects and are bound to have dispersed and drug-safe types of TB.[24]

Socioeconomic determinants

Socioeconomic factors are crucial in determining the factors of developing GTB. Poverty, overcrowding, malnutrition,

and limited access to medical services are irrefutable risk factors for TB, and these factors likewise impact the frequency of GTB.[25] Women living in low-resource settings are especially susceptible due to a combination of socioeconomic disadvantages and deficient admittance to reproductive health services.[26] In such settings, the absence of resources frequently prompts delayed or missed diagnoses of both pulmonary and genital TB.[27] Overcrowded living conditions and malnutrition further compound the risk by advancing the transmission of TB and debilitating the immune system, respectively.[28] Moreover, the lack of access to healthcare implies that women in these settings are less inclined to early and accurate diagnoses, prompting a higher risk of developing progressed and complicated types of GTB.[29]

PHYSIOLOGICAL IMPACT OF GTB ON REPRODUCTIVE HEALTH

GTB affects reproductive health. The infection focuses on the reproductive organs, leading to a cascade of pathological changes that can severely impede fertility.[30] Understanding the pathophysiology of GTB-related infertility is fundamental for creating powerful symptomatic and treatment methodologies. Recent studies have shown that *M. tuberculosis* in GTB disrupts reproductive function through granuloma formation and chronic inflammation. Granulomas release cytokines such as tumor necrosis factor-alpha and interleukin-1 beta, driving fibrosis, adhesions, and scarring in the fallopian tubes and endometrium, impairing embryo implantation and increasing miscarriage risk. Hormonal imbalance further disrupts ovarian reserve and uterine receptivity.[31]

Pathophysiology of GTB-related infertility in women

Genitourinary tuberculosis (GTB) can cause damage to several parts of the reproductive system, which can lead to a range of issues that adversely influence fertility.

Fallopian tubes

The fallopian tubes are the most often impacted site in GTB, with involvement reported in up to 90% of cases.[32] The infection prompts granulomatous irritation, which prompts scarring, fibrosis, and eventually tubal impediment.[33] This tubal damage is the essential cause of tubal factor infertility, the most common manifestation sign of GTB-related infertility.[34] Hydrosalpinx, a condition described by the gathering of liquid inside a blocked fallopian tube, is a frequent consequence of this scarring process.[35] The presence of hydrosalpinx blocks the entry of the ovum as well as establishes an unfriendly climate for sperm, further exacerbating infertility.[36]

Endometrium

Endometrial involvement is observed in approximately 50–60% of GTB cases.[37] The infection prompts endometrial thinning, fibrosis, and the formation of intrauterine adhesions, collectively alluded to as Asherman's syndrome.[38] These pathological changes result in a hostile uterine environment, impeding embryo implantation and increasing the risk of recurrent miscarriages.[39] The endometrium's failure to recover and support a pregnancy is a critical factor in GTB-related infertility,[40] making it a significant objective for remedial mediation.

Ovaries

Although less commonly involved, with an occurrence of around 10–30%, ovarian TB can have huge ramifications for fertility.[41] Tuberculous granulomas may form inside the ovaries, prompting tissue harm and a decrease in ovarian reserve.[42] The reduction in feasible ovarian follicles can adversely affect the achievement success rates of assisted reproductive technologies such as *in vitro* fertilization, where the amount and nature of oocytes are significant determinants of the result.[43] Ovarian TB may likewise disturb typical hormonal capability, further disrupting fertility treatment.[44]

Cervix and vagina

Association of the cervix and vagina in GTB is uncommon; however, it can contribute to fertility issues.[45] Cervical TB might appear as ongoing cervicitis, described by persistent inflammation and potential cervical stenosis.[46] Cervical stenosis, or narrowing of the cervical canal, can impede the entry of sperm, preventing fertilization.[47] Vaginal TB is even more uncommon; however, when present, it can cause nearby ulceration and scarring,[48] which might influence sexual capability and reproductive well-being.

Role of Hormonal Patterns in Female Susceptibility to GTB: Hormonal changes have proven to have a significant impact on women affected by GTB, which can, in turn, harm their reproductive health. Women suffering from TB often experience imbalances in their hormones, such as higher levels of testosterone and lower levels of prolactin, which can disrupt menstrual cycle and, impair fertility. These changes can lead to issues with menstrual cycles and infertility. While menstrual abnormalities are prevalent in GTB, they can also be observed in the case of pulmonary TB and extra-pulmonary TB, emphasizing association with the hormonal system. Infertility, however, is more specific to GTB due to its direct impact on reproductive organs. Furthermore, the stigma surrounding TB and reproductive health often delays diagnosis and treatment, worsening the hormonal and reproductive health outcomes. Therefore, it becomes essential for healthcare workers to provide comprehensive

care to patients, including gynecologists and psychologists, to tackle these challenges. This approach paves the road to early treatment and prevents long-term problems. Raising awareness and improving the management of TB is crucial step in reducing it's prevalence, preventing complications, and enhancing early detection.[2]

Pathophysiology of GTB-related infertility in men

In men, GTB ordinarily gives non-specific symptoms that can be effectively mistaken for other urological conditions, leading to delays in diagnosis and treatment.[49] The involvement of male reproductive organs by GTB is less common than in women yet can still result in significant fertility issues.

Epididymis and testes

The epididymis is the most commonly impacted site in men, with epididymal TB presenting as excruciating scrotal swelling and, in some cases, as a substantial mass.[50] If the infection spreads to the testes, it can cause testicular enlargement, pain, and, in severe cases, the formation of testicular abscesses.[51] Chronic infection of the epididymis and testicles can prompt fibrosis and scarring, which might obstruct the vas deferens.[52] This impediment results in obstructive azoospermia, a condition where no sperm are available in the ejaculate, prompting infertility.[53]

Prostate and seminal vesicles

GTB can also involve the prostate and seminal vesicles, causing chronic prostatitis characterized by pelvic pain and dysuria.[54] The inflammation and subsequent scarring of these organs can hinder the structure of seminal fluid, decreasing its capacity to help sperm viability and motility.[55] This can further compromise male fertility by diminishing the possibilities of successful treatment.

Systemic symptoms

In both men and women, GTB may present with systemic symptoms such as low-grade fever, night sweats, and weight loss.[8] However, these fewer common symptoms are frequently overshadowed by the predominant reproductive symptoms. Given the systemic nature of TB, the existence of these general symptoms can serve as valuable diagnostic indicators, particularly in instances where reproductive symptoms are nonspecific or mild.[56]

DIAGNOSTIC CHALLENGES AND MODALITIES

Diagnosing GTB presents a huge challenge due to its asymptomatic presentation and the limitations of current diagnostic methods.[14] For a precise diagnosis, a diverse methodology is required that combines clinical evaluation, imaging procedures, microbiological testing, and histopathological assessment.

Clinical history and examination

Detailed clinical history

A detailed clinical history is essential to the diagnosis of GTB.[57] Individuals who reside in TB-endemic regions, have a history of pulmonary TB[58], or have been exposed to TB should be constantly evaluated for GTB, particularly if they have symptoms associated with chronic pelvic pain, infertility, or other related conditions.[59] However, the constantly asymptomatic and non-specific nature of GTB makes diagnosis difficult and increases the risk that the illness will go undiagnosed for extended periods.[60]

Physical examination

Important insights can be obtained through physical examination, although the non-specificity of the results frequently imposes restrictions on it.[61] Adnexal discomfort, pelvic masses, or adhesions are indications of chronic pelvic inflammation in women.[62] Physical examination in men may show nodules in the epididymis or scrotal enlargement; however, these findings are similar to those of other illnesses, such as bacterial epididymitis.[63] Additional diagnostic testing is frequently required to confirm GTB when there are no distinguishing physical indications.

Imaging techniques

Ultrasound

In cases where women are initially suspected of having GTB, transvaginal ultrasound is often used as part of the assessment process.[64] It is capable of detecting anomalies such as intrauterine adhesions, endometrial thickening, and hydrosalpinx.[65] Ultrasound is used extensively, although its specificity for GTB is limited because the abnormalities it detects can also be linked to other pelvic disorders.[66]

Hysterosalpingography (HSG)

A key radiography method for assessing tubal patency is HSG. A contrast agent is injected into the fallopian tubes and uterus so that HSG can see tubal occlusions, which are a defining feature of GTB.[67] A beaded look or numerous strictures along the fallopian tubes, which are symptomatic of tuberculous salpingitis, are characteristic features in GTB.[45] HSG results must be confirmed by other diagnostic techniques as it is unable to conclusively identify GTB on its own.[68]

Magnetic resonance imaging (MRI)

When other imaging modalities are unable to yield definitive results in difficult cases, MRI can provide superior imaging information on pelvic tissues.[69] It can determine the degree of illness involvement and identify minor pathological alterations in the reproductive organs.[70] However, MRI is not often used as a diagnostic tool for GTB due to its high cost and restricted availability, especially in settings with minimal resources.

Microbiological and molecular tests

Endometrial biopsy and culture

Diagnosing GTB can be achieved most directly using endometrial biopsy. Biopsy-derived tissue samples are analyzed histopathologically and cultivated to check for *M. tuberculosis*.[71] However, the sensitivity of endometrial biopsy varies, and the paucibacillary characteristic of GTB frequently causes false-negative results in the diagnosis.[72] Biopsy continues to be an essential part of the diagnostic procedure in spite of these drawbacks.

PCR

The ability to detect TB deoxyribonucleic acid (DNA) in tissue samples or bodily fluids with great sensitivity and specificity has transformed the diagnosis of GTB.[73] When low bacterial populations prevent traditional culture methods from identifying the infection, PCR is especially helpful.[74] In addition, PCR is highly susceptible to contamination, which can result in false positives as even trace amounts of non-target DNA may be amplified, producing misleading results. Diagnosing FGTB becomes complicated by atypical tissue reactions and bacteriologically silent infections, which conventional methods often fail to detect.[75] However, in many low-resource situations, PCR is not as accessible, and the risk of false positives from contamination needs to be carefully controlled.[76]

Mycobacterial culture

Mycobacterial culture is still the gold standard for diagnosing TB; however, in the context of GTB, its reliability is reduced due to the generally low bacterial load seen in genital tissues.[77] Treatment delays might also come from the culture technique' lengthy turnaround time, which frequently takes several weeks to produce findings.[78] Mycobacterial cultures have poor sensitivity and require a long turnaround time; therefore, they should be used in conjunction with faster and more sensitive diagnostic techniques such as PCR.[79]

Histopathology and laparoscopy

Histopathology

Histopathology plays a critical role in diagnosing GTB and differentiating it from other granulomatous diseases, such as sarcoidosis. The hallmark findings of caseating granulomas with necrosis on histopathological examination are a key feature of TB but can sometimes overlap with the non-caseating granulomas seen in sarcoidosis or fungal infections.[80,81] Consequently, histological findings may not be definitive; to confirm GTB, histology should be read in conjunction with microbiological tests such as PCR or mycobacterium culture and molecular investigations.

Laparoscopy

In GTB, laparoscopy is used as a diagnostic and therapeutic tool.[73] Direct pelvic organ viewing made possible by this minimally invasive method makes it possible to identify common GTB abnormalities such as adhesions, caseous nodules, and beaded fallopian tubes.[72] Biopsy sample collection for histological and microbiological investigation is also made possible through laparoscopy.[82] However, the procedure's invasiveness and restricted availability in places with minimal resources could prevent it from being widely used.

PHARMACOLOGICAL INTERVENTIONS

Anti-tubercular therapy (ATT) is the mainstay of the pharmacological management of GTB (GBT), and it is comparable to the treatment regimens for pulmonary TB.[83] To guarantee effective treatment and reduce consequences to reproductive health, however, specific treatments are required due to the particular obstacles presented by GTB, such as the localized and frequently latent form of the infection.[49]

Standard ATT

First-line drugs

The use of first-line anti-tubercular medications, such as isoniazid, rifampicin, ethambutol, and pyrazinamide, is the cornerstone of treatment for GTB.[84] The treatment for pulmonary TB usually involves the administration of these drugs in combination over 6–9 months.[85] The objectives of this combination therapy are to eradicate the *M. tuberculosis* infection, stop medication resistance from emerging, and lower the chance of relapse.[86] The response in GTB patients can be slower and less predictable despite the regimen's general effectiveness.[87] This is mostly because the infection tends to become localized and latent within the reproductive organs.

Treatment duration

ATT for GTB typically lasts 2 months, with an initial intensive phase that includes the administration of all four first-line medications.[88] This is followed by a continuation phase that lasts 4–7 months but uses a modified drug regimen. Typically, therapy lasts between 6 and 9 months; however,

in situations where there is a sluggish clinical response, widespread disease, or the existence of comorbidities such as drug resistance, this can be extended.[89] The clinical response, microbiological data, and imaging results should all be taken into consideration when deciding how long to continue treatment. Prolonged therapy, however, carries hazards that need to be carefully handled, including drug toxicity and patient non-compliance.[90]

Challenges in treatment

One of the significant challenges in managing GTB is the potential for drug resistance, particularly in regions with high rates of multidrug-resistant TB (MDR-TB).[91] The emergence of drug-resistant strains necessitates the use of second-line drugs, which are often less effective, more toxic, and require longer treatment durations.[92] In addition, the presence of fibrotic tissue and granulomas in the reproductive organs can hinder drug penetration, leading to suboptimal drug levels at the site of infection.[93] This reduced efficacy may contribute to persistent infection and ongoing reproductive tract damage despite adherence to ATT.

Novel pharmacological interventions

New anti-tubercular agents

Drug-resistant TB, including MDR-TB, may be better managed in the future thanks to the development of novel anti-tubercular drugs.[94] Two other recent medications that have demonstrated success in treating MDR-TB are bedaquiline and delamanid.[95] while delamanid, a nitroimidazole derivative, prevents the formation of mycolic acid, bedaquiline, a diarylquinoline, targets the adenosine triphosphate (ATP) synthase of *M. tuberculosis*.[96] Although these medications are now part of MDR-TB treatment plans, it is unclear how well they work in the specific treatment of GTB.[96] The safety, effectiveness, and best way to take these medications in the setting of GTB need further investigation; in particular, the way they affect fertility and reproductive health will need to be clarified.

Adjunctive therapies

In an effort to lessen the negative consequences of the condition on reproductive health and increase the efficacy of standard ATT, adjunctive therapies have been investigated.[97] For example, corticosteroids have been used to lessen inflammation and stop adhesions and scarring from forming inside the reproductive organs.[98] The potential of immunomodulatory drugs, like thalidomide, to alter the immune response and enhance therapeutic results has also been studied.[99] With uncertainties regarding long-term results and adverse effects, the evidence for the use of these supplementary therapies in GTB is, nevertheless, sparse and inconsistent. More thorough clinical trials are required to prove their safety and efficacy, as their use is still debatable.

Fertility preservation

Given the profound impact of GTB on fertility, there is a growing interest in strategies aimed at preserving ovarian function and overall reproductive potential during and after treatment.[61] Hormonal therapy, such as gonadotropin-releasing hormone agonists, is one strategy that has been studied for safeguarding the ovarian reserve during ATT.[100] These medications function by momentarily inhibiting ovarian function, which lowers the possibility of fibrosis or inflammation-related ovarian damage. Large-scale clinical trials are necessary to confirm the effectiveness of these therapies in preventing infertility and improving reproductive outcomes in women with GTB, despite the encouraging results of early research.[101]

PUBLIC HEALTH IMPLICATIONS AND STRATEGIES

GTB has far-reaching public health concerns, particularly in areas where TB is prevalent.[102] To address the issues posed by GTB, an integrated approach is required, including raising awareness, enhancing diagnostic skills, strengthening treatment and follow-up, and tackling the disease's socioeconomic factors.

Increasing awareness

Raising awareness among healthcare providers

One of the most effective techniques for reducing GTB is to raise awareness among healthcare providers, particularly those working in reproductive health.[37] GTB frequently presents with nonspecific symptoms, causing diagnostic and therapeutic delays.[57] To address this, specialized educational programs and training workshops should be designed to provide clinicians with the knowledge necessary to detect the early indications of GTB.[103] These programs should emphasize the importance of GTB in the differential diagnosis of infertility and persistent pelvic discomfort, especially in areas where TB is prevalent.[100]

Public education campaigns

Public health activities should also include campaigns to raise awareness of GTB among the general public. These programs have the potential to educate communities on the risks of TB, particularly its extrapulmonary variants, as well as the significance of getting timely medical advice for reproductive health issues. Public education should also

address the stigma associated with TB and infertility, which frequently discourages people from seeking treatment.[104]

Improving diagnostic capabilities

Enhancing diagnostic infrastructure

Improving diagnostic infrastructure at primary and secondary healthcare levels is critical for early diagnosis of GTB. This necessitates the investment in molecular diagnostic methods such as PCR testing, which detects *M. tuberculosis* quickly and accurately. Furthermore, increasing the availability of imaging tools such as ultrasound and MRI in resource-constrained settings can aid in the diagnosis of GTB, especially in complex cases.[105]

Training healthcare providers

Training healthcare personnel in the use and interpretation of diagnostic tests is critical to improve the accuracy and reliability of GTB diagnosis.[106] This includes ensuring that healthcare staff can perform and interpret endometrial biopsies, HSG, and other diagnostic techniques required to evaluate GTB.[107] Furthermore, incorporating TB testing services within reproductive health clinics can speed up the diagnosis process and allow for earlier detection of GTB infections.

Strengthening treatment and follow-up

Access to effective ATT

Ensuring that patients have access to appropriate ATT is critical for attaining successful treatment results in GTB.[108] Healthcare systems must create clear criteria for GTB management, including the proper use of first- and second-line medications.[109] Regular follow-up care is also essential for monitoring treatment progress, managing side effects, and avoiding relapse.

Addressing treatment adherence

Barriers to treatment adherence, including financial restraints, transportation issues, and limited access to healthcare facilities, must be addressed to ensure that patients complete the entire course of ATT. To overcome these barriers, healthcare systems should provide support services such as patient counseling, financial aid, and transportation subsidies. Furthermore, directly observed therapy can be an effective technique for increasing adherence and improving treatment outcomes.[110]

Addressing socioeconomic determinants

Improving living conditions and access to healthcare

Poverty, overcrowding, malnutrition, and a lack of access to health care are all important socioeconomic drivers of TB transmission.[111] Public health strategies must prioritize initiatives that address these root causes. This includes improving living circumstances, increasing access to nutritious food, and making reproductive health treatments available and affordable to all women, particularly those from vulnerable areas.[112]

Education and community engagement

Education and community participation are critical components of a comprehensive public health approach for combating GTB.[113] Educational initiatives should concentrate on TB prevention, emphasizing the need for early detection and treatment of both pulmonary and extrapulmonary TB.[114] Community involvement programs can assist in mobilizing local resources and create a supportive atmosphere for persons afflicted by GTB, lowering stigma and encouraging more people to seek treatment.

FUTURE PERSPECTIVES

Future research in GTB should focus on the wide array to address the gaps in understanding and dealing with the disease successfully.

- Epidemiological Research: There is a requirement for more strong epidemiological investigations to measure the burden of GTB-related infertility and to recognize explicit risk factors. This examination ought to incorporate population-based surveys and case-control studies to acquire an extensive comprehension of GTB's effect on reproductive health.
- Diagnostic Innovations: Advances in analytic techniques are significant for early and accurate detection of GTB. Future research should focus on developing more sensitive and specific diagnostic tests, particularly molecular diagnostics such as next-generation sequencing and advanced PCR techniques. Examination of biomarkers to recognize inert and dynamic GTB is also important to work on analytic accuracy.
- Pharmacological Research: Developing novel pharmacological mediations is fundamental to further improve GTB treatment results. Research should focus on new anti-tubercular drugs with better efficacy and fewer side effects. Furthermore, studies on the adequacy of adjunctive therapies to deal with GTB's reproductive complications are expected to improve treatment protocol.
- Long-Term Reproductive Outcomes: Understanding the long-term reproductive outcomes of women treated for GTB is indispensable. Research should investigate the effect of anti-tubercular treatment on ovarian capability, pregnancy results, and the potential for fertility rebuilding. Longitudinal investigations that follow patients over a while post-treatment will give important experiences into the long-term impacts of GTB on reproductive well-being.

These diagnostic assessments play a pivotal role in advancing the diagnosis, treatment, and management of GTB, thereby optimizing reproductive health outcomes for affected individuals.

CONCLUSION

GTB is a critical, yet much of the time neglected, etiological factor in infertility, especially in areas with a high predominance of TB. The frequently asymptomatic nature of GTB, combined with non-specific clinical presentations, presents huge diagnostic difficulties, prompting delayed diagnosis and irreversible reproductive sequelae. While molecular diagnostic procedures, like PCR, have enhanced the detection of *M. tuberculosis*, the fluctuation in their sensitivity and particularity requires dependence on traditional methods such as culture and histopathology for definitive findings. Early and precise recognition stays significant in saving reproductive potential and preventing long-term infertility.

Epidemiological patterns feature the dire requirement for comprehensive public health intercessions, especially focusing on women of reproductive age, to moderate the double burden of TB and infertility. Upgrading diagnostic protocols, extending the comprehension of GTB's pathophysiology, and creating targeted treatment techniques should be key areas of future exploration. In addition, improving clinical awareness and training among healthcare professionals, particularly in high-risk districts, is fundamental to guaranteeing timely intervention and diminishing the worldwide effect of GTB on infertility results.

Acknowledgments

The authors are thankful to the Director, Indian Council of Medical Research – National Institute for Research in Environmental Health (ICMR-NIREH), Bhopal, India.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Sharma SK, Upadhyay V. Epidemiology, diagnosis & treatment of non-tuberculous mycobacterial diseases. Indian J Med Res 2020;152:185-226.
2. Garg K, Saini V, Kaur J, Goel P, Agarwal P, Singh I. Hormonal changes and reproductive health issues in females with tuberculosis. Indian J Tuberc 2020;67:3-7.
3. Gupta S, Gupta P. Etiopathogenesis, challenges and remedies associated with female genital tuberculosis: Potential role of nuclear receptors. Front Immunol 2020;11:02161.
4. Inhorn MC. Quest for conception: Gender, infertility, and Egyptian medical traditions; 1994. p. 441. Available from: https://www.google.co.in/books/edition/Quest_for_Conception/LE3kkvpLCLUC?hl=en&gbpv=1&dq=Quest+for+conception%E2%80%AF:+gender,+infertility,+and+Egyptian+medical+traditions&pg=PR9&printsec=frontcover [Last accessed on 2024 Aug 14].
5. Türkmen IC, Başsüllü N, Comunoğlu C, Bağcı P, Aydın O, Comunoğlu N, *et al.* Female genital system tuberculosis: A retrospective clinicopathological study of 1,548 cases in Turkish women. Arch Gynecol Obstet 2012;286:379-84.
6. Deshmukh S, Deshmukh S. Tuberculosis and Hysteroscopy. Bangladesh J 2022;2:92-7.
7. Lemish NY, Korchynska OO. Diseases of the female reproductive system. Part II. Ukraine: Uzhgorod national University; 2015.
8. Kulchavenya E. Urogenital tuberculosis: Epidemiology, diagnosis, therapy. Berlin: Springer; 2014. p. 1-137.
9. Jirge PR. Effect of genital tuberculosis on ovarian reserve. US Endocrinol 2020;16:104-8.
10. Tzvetkov D, Tzvetkova P. Tuberculosis of male genital system--myth or reality in 21st century. Arch Androl 2006;52:375-81.
11. Dahiya B, Kamra E, Alam D, Chauhan M, Mehta PK. Insight into diagnosis of female genital tuberculosis. Expert Rev Mol Diagn 2022;22:625-42.
12. Vasava MS, Bhoi MN, Rathwa SK, Borad MA, Nair SG, Patel HD. Drug development against tuberculosis: Past, present and future. Indian J Tuberc 2017;64:252-75.
13. The selection and use of essential medicines Report of the WHO expert committee, 2017 (including the 20th WHO model list of essential medicines and the 6th Model List of essential medicines for children).
14. Melkamu K, Damie A, Ashenafi S, Sori M, Girma S, Yimam S, *et al.* Histopathologic patterns of female genital tuberculosis with clinical correlation: A 10-year (2013-2022) retrospective cross-sectional study. BMC Womens Health 2024;24:370.
15. Hassan I, Khan AR, Samreen Z, Baloch K, Zahir A. Clinical characteristics and outcome of genitourinary tuberculosis in Balochistan: An observational study. Prof Med J 2024;31:326-

37.
16. NematiShahri F, Pouresmaeil O, Sharifi A, Mardani F, Mardaneh J. Genital tuberculosis in women; a systematic review. J Clin Care Skills 2024;5:49-54.
17. Chatterjee S, Bishista B, Abira D. Changing trends of tubercular assault on reproduction. Med Res Arch 2024;12:6.
18. Shende P, Valecha SM, Gandhewar M, Dhingra D. Genital tuberculosis and infertility. Int J Reprod Contracept Obstet Gynecol 2017;6:3514-8.
19. Ilmer M, Bergauer F, Friese K, Mylonas I. Genital tuberculosis as the cause of tuboovarian abscess in an immunosuppressed patient. Infect Dis Obstet Gynecol 2009;2009:745060.
20. Fatima Z, Hameed S, Saibabu V, Sharma S, Hans S. Diagnosis and management of tuberculosis: Propagation beyond lungs diagnosis & management of tuberculosis. Available from: https://www.openaccessebooks.com [Last accessed on 2024 Aug 25].
21. Pasternak MS, Rubin RH. Urinary tract tuberculosis. Diseases of the kidney and urinary tract. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2001. p. 1017-37.
22. Liao S, von der Weid PY. Lymphatic system: An active pathway for immune protection. Semin Cell Dev Biol 2015;38:83-9.
23. Van Rensburg D, Janse van Rensburg-Bonthuyzen E, Heunis C, Meulemans H. Tuberculosis control in South Africa: Reasons for persistent failure. Acta Acad 2005;2005 Suppl-1:1-55.
24. Pawlowski A, Jansson M, Sköld M, Rottenberg ME, Källenius G. Tuberculosis and HIV co-infection. PLoS Pathog 2012;8:e1002464.
25. Murray JF. A century of tuberculosis. Am J Respir Crit Care Med 2012;169:1181-6.
26. Bou-Karroum L, Iaia DG, El-Jardali F, Abou Samra C, Salameh S, Sleem Z, *et al.* Financing for equity for women's, children's and adolescents' health in low- and middle-income countries: A scoping review. PLoS Glob Public Health 2024;4:e0003573.
27. Castellanos Reynosa ME, Caal ME, Mercado D, Medina N, Pérez JC, Emeto TI, *et al.* Clinical characteristics, diagnosis, treatment and outcomes of patients living with HIV and co-infected with tuberculosis and histoplasmosis: A 5-y retrospective case series. Trans R Soc Trop Med Hyg 2024;118:391-8.
28. Yuliyanti S. Beyond clinical outcomes: Exploring the psychosocial and physical dimensions of quality of life in tuberculosis patients receiving outpatient care. Open Access Indones J Med Rev 2024;4:738-53.
29. Fatima Z, Hameed S, Saibabu V, Sharma S, Hans S. Diagnosis and management of tuberculosis: Propagation beyond lungs diagnosis & management of tuberculosis. Available from: https://www.openaccessebooks.com [Last accessed on 2024 Sep 16].
30. Deshmukh, S. TBC and hysteroscopy. In: Tinelli A, Alonso Pacheco L, Haimovich S, editors. Hysteroscopy. Cham: Springer; 2018.
31. Bayoumi RR, Boivin J, Fatemi HM, Hurt L, Serour GI, Poel SV, *et al.* Looking beyond the obvious: A critical systematic review and meta-analyses of risk factors for fertility problems in a globalized world. medRxiv [Preprint]; 2021.
32. Kochar Kaur K, Allahbadia G, Singh M, Kaur KK. Advances in diagnosis and management of female genital tuberculosis-a comprehensive review. Acta Sci Microbiol 2019;2:2581-3226.
33. Shetty N, Tang JW, Andrews J. Infectious disease : Pathogenesis, prevention, and case studies. Chichester, UK: Wiley-Blackwell; 2009. p. 674.
34. Gai X, Chi H, Li R, Sun Y. Tuberculosis in infertility and *in vitro* fertilization-embryo transfer. Chin Med J (Engl) 2024;137:2404-11.
35. Liang B, Wei C, Kolin DL, Howitt B. Benign lesions of the fallopian tube. In: Gynecologic and obstetric pathology. Singapore: Springer Nature Singapore; 2024. p. 1-20.
36. Muralinath E, Guru Prasad M, Sony S. Clinical review articles in physio pharmacology. Maharashtra: Laxmi Book Publication; 2024.
37. Cao W, Fu X, Li H, Bei J, Li L, Wang L. Tuberculosis in pregnancy and assisted reproductive technology. Drug Discov Ther 2024;18:80-8.
38. Gargett CE, Schwab KE, Deane JA. Endometrial stem/progenitor cells: The first 10 years. Hum Reprod Update 2016;22:137-63.
39. Lin M, Xu H, Qiu J. Inflammation in recurrent miscarriage - a comprehensive perspective from uterine microenvironment and immune cell imbalance to therapeutic strategies. Ginekol Pol 2024;95:266-75.
40. Subramani E, Jothiramajayam M, Dutta M, Chakravorty D, Joshi M, Srivastava S, *et al.* NMR-based metabonomics for understanding the influence of dormant female genital tuberculosis on metabolism of the human endometrium. Hum Reprod 2016;31:854-65.
41. Jirge PR, Chougule SM, Keni A, Kumar S, Modi D. Latent genital tuberculosis adversely affects the ovarian reserve in infertile women. Hum Reprod 2018;33:1262-9.
42. Sharma JB, Sharma S, Sharma E, Dharmendra S, Singh S. Immune disturbances in female genital tuberculosis and latent genital tuberculosis. Am J Reprod Immunol 2023;89:e13632.
43. Bhandari HM, Choudhary MK, Stewart JA. Complications of assisted reproductive technology treatment and the factors influencing reproductive outcome. Obstet Gynaecol 2018;20:177-86.
44. Wang Z, Zhang X, Dai B, Li D, Chen X. Analysis of the potential regulatory mechanisms of female and latent genital tuberculosis affecting ovarian reserve function using untargeted metabolomics. Sci Rep 2024;14:9519.
45. Gita GM, Gautam K, Basu S. Practical guide in infertility. New Delhi: Jaypee Brothers; 2018. p. 498.
46. Polson A. Infectious diseases of the male and female urogenital tract: A review of the histology of selected entities. Diagn Histopathol 2024;30:546-53.
47. Vitale SG, De Angelis MC, Della Corte L, Saponara S, Carugno J, Laganà AS, *et al.* Uterine cervical stenosis: From classification to advances in management. Overcoming the obstacles to access the uterine cavity. Arch Gynecol Obstet 2024;309:755-64.
48. Dundr P, Němejcová K, Bártů M. Benign Lesions of the Vagina. In: Gynecologic and obstetric pathology. Singapore: Springer Nature Singapore; 2024. p. 1-43.
49. Kulchavenya E. Current therapy and surgery for urogenital tuberculosis. In: Current therapy and surgery for urogenital tuberculosis. Berlin: Springer; 2016. p. 1-97.
50. Mehboob K, Madani TA. Isolated tuberculous orchitis presented as epididymo-orchitis: An unusual presentation of

tuberculosis. Urol Ann 2022;14:189-95.
51. Ramachandran A, Das CJ, Razik A. Male genital tract tuberculosis: A comprehensive review of imaging findings and differential diagnosis. Abdom Radiol (NY) 2021;46:1677-86.
52. Carroll M. Clinical reproductive science. United States: Wiley; 2019. p. 410.
53. Jarvi K, Lo K, Grober E, Mak V, Fischer A, Grantmyre J, *et al.* The workup and management of azoospermic males. Can Urol Assoc J 2015;9:229-35.
54. Nepal P, Ojili V, Kumar S, Kumar D, Nagar A. Imaging spectrum of common and rare infections affecting the lower genitourinary tract. Abdom Radiol (NY) 2021;46:2665-82.
55. Dutta S, Sengupta P, Slama P, Roychoudhury S. Oxidative stress, testicular inflammatory pathways, and male reproduction. Int J Mol Sci 2021;22:10043.
56. Bartolomeu-Gonçalves G, Marinho De Souza J, Fernandes BT, Spoladori LF, Correia GF, de Castro IM, *et al*. Tuberculosis diagnosis: Current, ongoing, and future approaches. Diseases 2024;12:202.
57. Kudu E, Danış F. Recognizing and addressing the challenges of gastrointestinal tuberculosis. World J Clin Cases 2024;12: 3648-53.
58. Kiwanuka N, Quach T, Kakaire R, Zalwango S, Castellanos M, Sekandi J, *et al.* Incidence of tuberculous infection in a TB-endemic city. Int J Tuberc Lung Dis 2024;28:266-72.
59. Bayoumi RR, Hurt L, Zhang N, Law YJ, Venetis C, Fatem HM, *et al.* A critical systematic review and meta-analyses of risk factors for fertility problems in a globalized world. Reprod Biomed Online 2024;48:103217.
60. World Health Organization. Digital adaptation kit for tuberculosis: Operational requirements for implementing WHO recommendations in digital systems. Switzerland: World Health Organization; 2024.
61. Lukinovic N, Malovrh EP, Takac I, Sobocan M, Knez J. Advances in diagnostics and management of gestational trophoblastic disease. Radiol Oncol 2022;56:430-9.
62. Biggs WS, Marks ST. Diagnosis and management of adnexal masses. Am Fam Physician 2016;93:676-81.
63. Mcconaghy JR, Panchal B. Epididymitis: An overview. Am Fam Physician. 2016;94:723-6.
64. Aslan G, Ulger M, Ulger ST, Durukan H, Yazici FG, Emekdas G. Female genital tuberculosis cases with distinct clinical symptoms: Four case reports. Int J Reprod Biomed 2018;16:57-60.
65. Campbell S. Ultrasound evaluation in female infertility: Part 2, the uterus and implantation of the embryo. Obstet Gynecol Clin North Am 2019;46:697-713.
66. Kulchavenya E. Urogenital tuberculosis: Definition and classification. Ther Adv Infect Dis 2014;2:117-22.
67. Gejji SF. Prevalence of genital tract tuberculosis in infertile female patients. MS Thesis. Rajiv Gandhi University of Health Sciences (India), 2016 ProQuest Dissertations and Theses; 2016. p. 30587454.
68. Kumari G, Goel D, Mishra S. Comparison of conventional and modern biomedical tools used for diagnosis of genital tract tuberculosis: An overview. IOSR J Pharm Biol Sci 2013;7:19-24.
69. Tong A, Cope AG, Waters TL, McDonald JS, VanBuren WM. Best practices: Ultrasound versus MRI in the assessment of pelvic endometriosis. Am J Roentgenol 2024;1-16. Doi: 10.2214/ajr.24.31085.
70. Shibuki S, Saida T, Hoshiai S, Ishiguro T, Sakai M, Amano T, *et al.* Imaging findings in inflammatory disease of the genital organs. Jpn J Radiol 2024;42:331-46.
71. Kochar Kaur K. How to maximize the utility of nonsurgical modalities for diagnosing early-stage endometriosis without surgery; 2024. Available from: https://www.researchgate.net/publication/382887984 [Last accessed on 2024 Sep 16].
72. Advisor AM. Laboratory diagnosis of genital tuberculosis: A narrative review. Bangladesh J Infect Dis 2023;10:92-100.
73. Panda S, Ganeshprakash Gupta A, Prabhakar Varma P, Venkateswara Rao T. Female genitourinary tuberculosis: A clinico epidemiological and diagnostic study. Int J Gynaecol Sci 2024;6:4-9.
74. Matys J, Kensy J, Gedrange T, Zawiślak I, Grzech-Leśniak K, Dobrzyński M. A molecular approach for detecting bacteria and fungi in healthcare environment aerosols: A systematic review. Int J Mol Sci 2024;25:4154.
75. Bhanothu V, Venkatesan V. Conventional polymerase chain reaction and amplification refractory mutation system-multi-gene/multi-primer PCR in the diagnosis of female genital tuberculosis. Arch Microbiol 2019;201:267-81.
76. Chidzwondo F, Mutapi F. Challenge of diagnosing acute infections in poor resource settings in Africa. Open Res Afr 2024;4:28.
77. Sethi A, Bajaj B, Nair D, Pachauri D, Gupta M, Mahajan A. Comparison of conventional methods with newer diagnostic modalities to detect genital tuberculosis in infertile women. J Obstet Gynaecol India 2022;72:426-32.
78. Downie DL, Rao P, David-Ferdon C, Courtney S, Lee JS, Kugley S, *et al*. Literature review of pathogen agnostic molecular testing of clinical specimens from difficult-to-diagnose patients: Implications for Public Health. Health Secur 2024;22:93-107.
79. Mugenyi N, Ssewante N, Baruch Baluku J, Bongomin F, Irene MM, Andama A, *et al.* Innovative laboratory methods for improved tuberculosis diagnosis and drug-susceptibility testing. Front Tuberc 2024;1:1295979.
80. Zlatar L, Knopf J, Singh J, Wang H, Muñoz-Becerra M, Herrmann I, *et al*. Neutrophil extracellular traps characterize caseating granulomas. Cell Death Dis 2024;15:548.
81. Neves FS, Pereira IA, Sztajnbok F, Neto NS. Sarcoidosis: A general overview. Adv Rheumatol 2024;64:57.
82. Mohamed AA, Bhat NA, Abukhater M, Riaz MM. The role of laparoscopy in diagnosis of abdominal tuberculosis. Int Surg J 2016;3:1557-63.
83. Sharma JB, Sneha J, Singh UB, Kumar S, Roy KK, Singh N, *et al.* Effect of antitubercular treatment on ovarian function in female genital tuberculosis with infertility. J Hum Reprod Sci 2016;9:145-50.
84. Davies PD, Yew WW. Recent developments in the treatment of tuberculosis. Expert Opin Investig Drugs 2003;12:1297-312.
85. Holger DJ, Althubyani A, Morrisette T, Rebold N, Tailor M. Updates in pulmonary drug-resistant tuberculosis pharmacotherapy: A focus on BPaL and BPaLM. Pharmacotherapy 2024;44:268-82.
86. Dheda K, Mirzayev F, Cirillo DM, Udwadia Z, Dooley KE,

Chang KC, *et al.* Multidrug-resistant tuberculosis. Nat Rev Dis Primers 2024;10:22.
87. Johnson TM, Rivera CG, Lee G, Zeuli JD. Pharmacology of emerging drugs for the treatment of multi-drug resistant tuberculosis. J Clin Tuberc Other Mycobact Dis 2024;37:100470.
88. Raja BY, Ganachari MS. Identification and evaluation of drug related problems to first line therapy of antitubercular drugs among the pulmonary tuberculosis patients in a tertiary care hospital- A Randomised controlled study. Int J Pharm Sci Drug Res 2024;16:142-8.
89. Mahajan N, Naidu P, Kaur SD. Insight into the diagnosis and management of subclinical genital tuberculosis in women with infertility. J Hum Reprod Sci 2016;9:135-44.
90. Veldsman C. The prevalence of isoniazid and rifampicin resistance of *Mycobacterium tuberculosis*. University of Pretoria (South Africa), 2009 ProQuest Dissertations and Theses; 2009. p. 30715454.
91. Drug-resistant tuberculosis: What is the situation, what are the needs to roll it back. AMR Control. Available from: https://resistancecontrol.info/2017/drug-resistant-tuberculosis-what-is-the-situation-what-are-the-needs-to-roll-it-back-2 [Last accessed on 2024 Sep 18].
92. Terreni M, Taccani M, Pregnolato M. New antibiotics for multidrug-resistant bacterial strains: Latest research developments and future perspectives. Molecules 2021;26:2671.
93. Datta M. Overcoming transport barriers in *tuberculosis granulomas* to improve Drug Delivery. [Doctoral Dissertation, Tufts University] ProQuest Dissertations and Theses; 2018. p. 10811011.
94. Ahmad S, Mokaddas E. Current status and future trends in the diagnosis and treatment of drug-susceptible and multidrug-resistant tuberculosis. J Infect Public Health 2014;7:75-91.
95. Li Y, Sun F, Zhang W. Bedaquiline and delamanid in the treatment of multidrug-resistant tuberculosis: Promising but challenging. Drug Dev Res 2019;80:98-105.
96. Bahuguna A, Rawat DS. An overview of new antitubercular drugs, drug candidates, and their targets. Med Res Rev 2020;40:263-92.
97. Sharma SK, Katoch K, Sarin R, Balambal R, Kumar Jain N, Patel N, *et al.* Efficacy and Safety of *Mycobacterium indicus* pranii as an adjunct therapy in category II pulmonary tuberculosis in a randomized trial. Sci Rep 2017;7:3354.
98. Pados G, Venetis CA, Almaloglou K, Tarlatzis BC. Prevention of intra-peritoneal adhesions in gynaecological surgery: Theory and evidence. Reprod Biomed Online 2010;21:290-303.
99. Abdallah AE, Eissa IH, Mehany AB, Sakr H, Sakr TM, Metwaly KH, *et al.* Immunomodulation and anticancer evaluation of quinazoline-based thalidomide analogs: Design, synthesis, docking, and dynamic simulation. J Mol Struct 2024;1317:139082.
100. Sathe S, Hinduja R. Abrnomalities of the pelvis. Foreword. New Delhi: Jaypee Brothers; 2018.
101. Fernandes GF, Thompson AM, Castagnolo D, Denny WA, Dos Santos JL. Tuberculosis drug discovery: Challenges and new horizons. J Med Chem 2022;65:7489-531.
102. Zahoor D, Manzoor Bhat M, Kanth F, Farhana A. Prevalence of genital tuberculosis in infertile women; a study from a tertiary care center in North India. Int J Contemp Med Res 2019;6:F1-3.
103. Khatri GR. National tuberculosis control programme. Indian Med Assoc 1996;94:372-5, 384.
104. Tadesse S. Stigma against tuberculosis patients in Addis Ababa, Ethiopia. PLoS One 2016;11:e0152900.
105. Moumtzoglou PK, Bandyopadhyay A, Hoque A, Kumar MS, Saavedra NS. Indian digital health information systems: Initiatives and opportunities with socio-economic perspective. Econ Affairs 2024;69:1175-89.
106. WHO. Operational handbook on tuberculosis. Module 3 diagnosis - rapid diagnostics for tuberculosis detection. 3rd ed. Geneva: WHO; 2024.
107. Sulbha A. Arora S, Rubina Merchant GN, editor. Reproductive medicine: Challenges, solutions and breakthroughs; 2014. p. 668. Available from: https://books.google.com.bd/books?id=wbAiAwAAQBAJ&pg=PA120&dq=mechanism+of+action+of+Letrozole&hl=en&sa=X&redir_esc=y#v=onepage&q=mechanism%20of%20action%20of%20Letrozole&f=false [Last accessed on 2024 Sep 19].
108. Jindal UN, Verma S, Bala Y. Favorable infertility outcomes following anti-tubercular treatment prescribed on the sole basis of a positive polymerase chain reaction test for endometrial tuberculosis. Hum Reprod 2012;27:1368-74.
109. World Health Organization. Guidelines for treatment of drug-susceptible tuberculosis and patient care. Switzerland: World Health Organization; 2017.
110. Garfein RS, Doshi RP. Synchronous and asynchronous video observed therapy (VOT) for tuberculosis treatment adherence monitoring and support. J Clin Tuberc Other Mycobact Dis 2019;17:100098.
111. Srivastava K, Kant S, Verma A. Role of environmental factors in transmission of tuberculosis. Hum Health 2015;2:12.
112. Narasimhan M, Hargreaves JR, Logie CH, Abdool-Karim Q, Aujla M, Hopkins J, *et al.* Self-care interventions for women's health and well-being. Nat Med 2024;30:660-9.
113. World Health Organization. Guidance on engagement of communities and civil society to end tuberculosis. Geneva: World Health Organization; 2023. p. 1-36.
114. Al-Worafi YM. Tuberculosis management in developing countries. Handbook of medical and health sciences in developing countries. Cham: Springer; 2024. p. 1-40.

How to cite this article: Sikenis M, Prajapati B, Singh AK, Yadav K, Rahman A, Pandey MK, *et al.* Genital tuberculosis: A silent contributor to infertility and adverse pregnancy outcomes. J Reprod Healthc Med. 2024;5:17. doi: 10.25259/JRHM_25_2024