RESEARCH PAPER

Diagnosis of Genital Tuberculosis in Infertile Women: A Comparative Study from a Tertiary Care.

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ABSTRACT
Background: Female genital tuberculosis (FGTB) is a well-recognized but frequently overlooked cause of infertility in regions with high tuberculosis prevalence. The absence of specific symptoms and the low bacillary load often lead to delayed or missed diagnosis when single diagnostic tests are used.
Objective: To assess and compare the diagnostic performance of immunological, molecular, histopathological, and endoscopic modalities for FGTB using a composite reference standard (CRS) in infertile women.
Methods: A retrospective analysis was conducted at a tertiary care hospital in Srinagar between 2021 and 2022. Twenty-five infertile women with clinical suspicion of FGTB underwent evaluation with interferon-gamma release assay (IGRA), endometrial GeneXpert MTB/RIF, MPT64-PCR, histopathology, mycobacterial culture, and pelvic imaging including laparoscopy where indicated. Diagnostic indices were calculated against CRS.
Results: The mean participant age was 30.2 years; three-fourths had primary infertility. IGRA demonstrated the highest sensitivity (80%) and specificity (95%). Laparoscopy revealed tubercular features in 80% of patients. Molecular tests showed moderate sensitivity, with GeneXpert detecting 60% of cases. Combining modalities increased the overall diagnostic yield to 85%.
Conclusion: Reliance on a single test is insufficient for diagnosing FGTB. A multimodal diagnostic strategy significantly enhances detection and may allow earlier intervention to improve reproductive outcomes in endemic areas.
Keywords: Female genital tuberculosis, infertility, IGRA, GeneXpert, laparoscopy, composite reference standard.
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INTRODUCTION

Tuberculosis continues to impose a significant disease burden in India, with extrapulmonary forms accounting for a substantial proportion of cases among women. Female genital tuberculosis (FGTB) is a notable yet under-recognised cause of infertility, particularly in regions where tuberculosis (TB) is endemic.(1)

- Female genital tuberculosis (FGTB) represents one of the most important extrapulmonary manifestations, particularly in women of reproductive age, where it contributes to infertility through irreversible anatomical and functional damage to the reproductive tract.
- The prevalence of FGTB among infertile women varies widely across India, ranging from 3% to 16%. Studies from northern India, including Kashmir, have reported higher prevalence, likely reflecting increased background TB exposure. Studies in Kashmir showed a prevalence of 37.31 per 100,000 people in 2020, and the prevalence rates ranging from 6.37% to 8.80% in infertile females.(2*)
- These rates highlight the pressing need for more effective diagnostic strategies in high-prevalence settings.(3,4)
- Despite this, FGTB remains underdiagnosed due to its indolent course and nonspecific clinical presentation. Menstrual disturbances, pelvic pain, or mild constitutional symptoms may occur, but up to half of affected women remain asymptomatic until infertility is investigated.
- Diagnosis is further complicated by the paucibacillary nature of genital TB. Conventional microbiological techniques, such as culture, have limited sensitivity and require prolonged incubation. Histopathology may fail to demonstrate classical granulomas in early disease. Molecular tests offer rapid detection but are dependent on adequate tissue sampling. Immunological tests, including IGRA, identify TB

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infection but cannot reliably distinguish latent infection from active genital disease.

• Given these limitations, recent approaches emphasize the use of a composite reference standard (CRS), integrating clinical, laboratory, and imaging findings. The use of a composite reference standard (CRS), which combines multiple diagnostic methods, may improve diagnostic accuracy and detection rates in FGTB. CRS can include techniques like culture, GeneXpert, PCR, histology, and imaging, enhancing the reliability of diagnosis.(5–7)

This study was undertaken to evaluate the diagnostic utility of commonly used tests for FGTB when interpreted against CRS in infertile women from a TB-endemic region.

AIM OF THE STUDY

- This study aims to evaluate and compare the effectiveness of individual diagnostic techniques in detecting FGTB in women with infertility.
- By analyzing sensitivity, specificity, and predictive values, the study seeks to establish a more reliable diagnostic framework for FGTB, which may lead to earlier detection and timely treatment, ultimately improving reproductive outcomes for affected women.

Materials and Methods

Study Design and Setting

This retrospective observational study was conducted in the Department of Obstetrics and Gynaecology at Government Medical College, Srinagar, a tertiary referral centre catering to a high TB-burden population.

Study Period

January 2021 to December 2022.

Study Population

Twenty-five women presenting with primary or secondary infertility and clinical suspicion of FGTB were included.

Inclusion Criteria

Women aged 18–45 years
Unexplained infertility or infertility with suggestive clinical/imaging features
No prior anti-tubercular therapy

Exclusion Criteria

Current or past pulmonary tuberculosis
Previous anti-TB treatment
HIV infection
Endometriosis, pelvic malignancy, or known endocrine causes of infertility
Ethical approval obtained from institutional review board.

Diagnostic Work-up

Immunological Testing
Interferon-gamma release assay (IGRA)
Endometrial Sampling
Endometrial biopsy was obtained during the premenstrual phase (days 20–25) and divided for:
GeneXpert MTB/RIF
MPT64-based PCR
Histopathological examination
Mycobacterial culture (where feasible)
Imaging and Endoscopy
Transvaginal ultrasonography
Hysterosalpingography
Diagnostic hysteroscopy
Diagnostic laparoscopy (in selected cases)
Composite Reference Standard
FGTB diagnosis was established when at least two diagnostic parameters (microbiological, molecular, histopathological,
immunological, or laparoscopic) were positive.

Statistical Analysis

Data were analyzed using SPSS version 25. Sensitivity, specificity, PPV, and NPV were calculated for each modality against CRS. Agreement was assessed using Cohen's kappa coefficient. Statistical significance was set at $p < 0.05$.

Results

Demographics and Clinical Characteristics

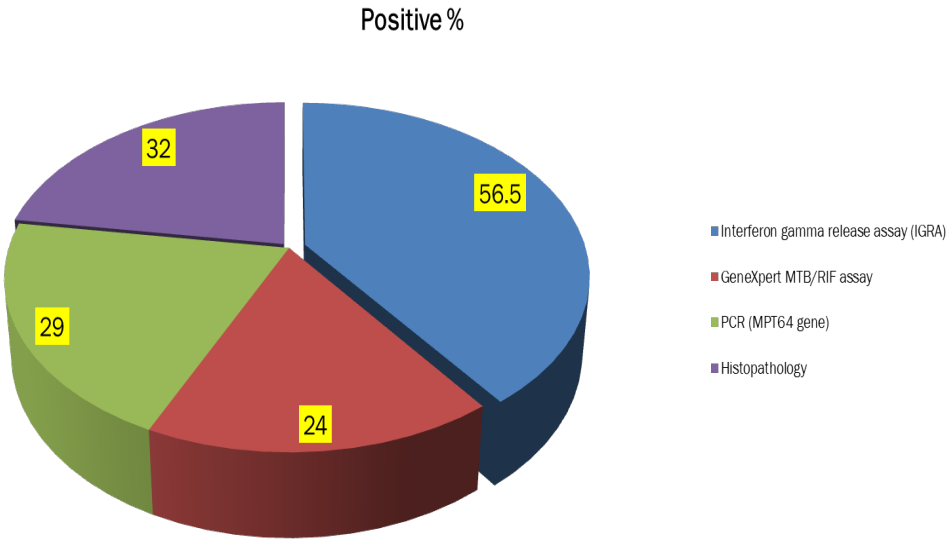
variable	Infertile group
Mean age(years)	30.2
Primary infertility	75%
Secondary infertility	25%
Asymptomatic	40%
Symptomatic	60%
Menstrual irregularities	45%
Chronic pelvic pain	35%
Vaginal discharge	5%

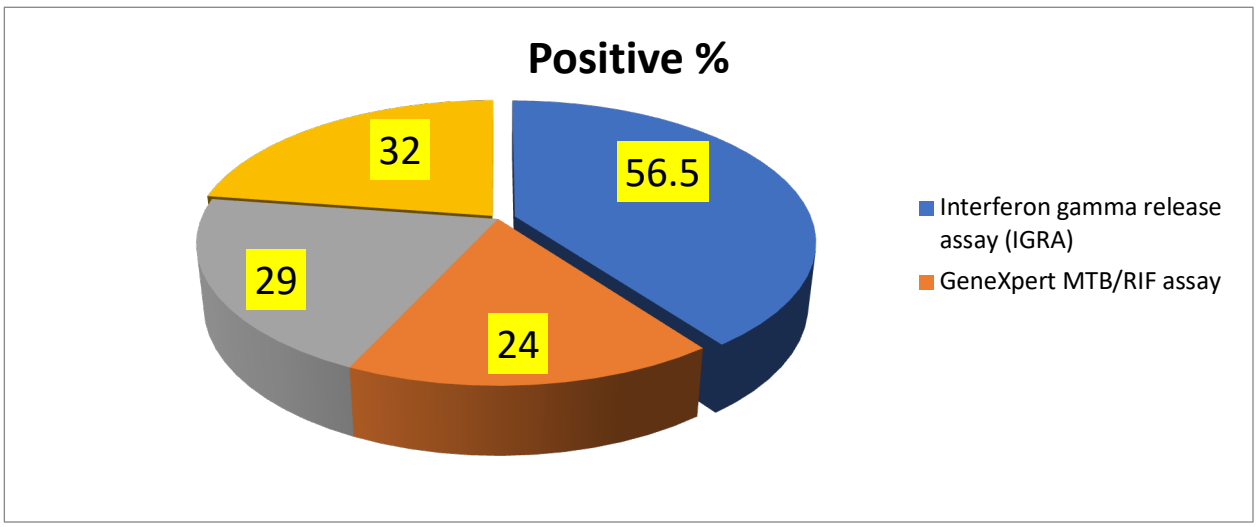
Mean age: 30.2 ± 4.1 years

Imaging and Laparoscopic Findings

Diagnostic test	Positive findings	% positive (infertile patient)
Ultrasonography	9	36
Hystero-salphingography (HSG)	12	48
Laparoscopic findings	20	80

Ultrasonography suggestive of TB: 36%
Abnormal HSG findings: 48%
Hysteroscopic abnormalities: 52%
Laparoscopic evidence of TB: 80%
Laboratory Diagnostic Test Results





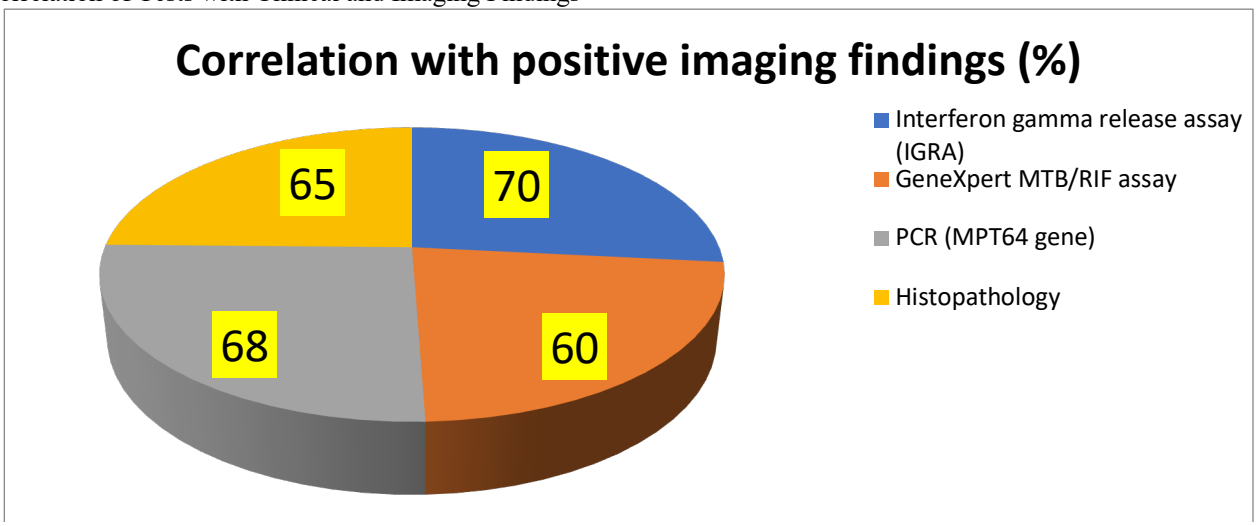
IGRA positivity: 85%
PCR positivity: 72%
Histopathology suggestive of TB: 70%

GeneXpert positivity: 60%

Diagnostic Accuracy Comparison

Test	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV)(%)	Negative predictive value (PPV)(%)
Interferon gamma release assay (IGRA)	80	95	92	88
GeneXpert MTB/RIF assay	60	100	100	85
PCR (MPT64 gene)	72	100	100	89
Histopathology	70	100	100	88

Overall diagnostic yield using CRS was 85%.
Correlation of Tests with Clinical and Imaging Findings



Discussion

- Our study reported a mean age of 30.2 years among participants, with a predominant prevalence of primary infertility (75%), corroborating findings from previous studies that identify GTB as a significant, yet often underdiagnosed, cause of infertility in young women. (8)
- The observation that 40% of patients exhibited clinical symptoms such as menstrual irregularities (45%) aligns with literature. (8)
- 60% of asymptomatic women underscores the critical need for comprehensive screening strategies for GTB, as highlighted in a study by Sethi et al. (9)

a. In our findings, HSG revealed abnormal tubal findings in 48% of cases. This is consistent with previous literature that emphasises the importance of HSG in diagnosing GTB.(8,10)

b. Furthermore, laparoscopic evaluations identified intra-abdominal manifestations in 80% of women which corroborates the findings of Chavan et al.(8)

➢ Our study indicated that IGRA exhibited the highest sensitivity (80%) and specificity (95%), aligning with findings from studies that regard IGRA as a robust tool for diagnosing TB in various forms, including GTB.

➢ The positive predictive value of 92% further underscores its utility as a valuable screening tool in this context, reinforcing the work of Sethi et al., who similarly found IGRA to be a reliable indicator of TB presence. (9)

- In contrast, GeneXpert demonstrated a lower detection rate (24%) but with exceptional
- specificity (100%). it provides high accuracy for confirmed cases. (6,7)

- The reliance on PCR, targeting the MPT64 gene, yielded a sensitivity of 72% and a specificity of 100%. This confirms previous studies suggesting that PCR can be an effective adjunct in diagnosing GTB. (5,6)
- Histopathological examination confirmed GTB in 32% of cases with a sensitivity of 70%. This aligns with the literature that recognises histopathology as the gold standard for diagnosing TB.(8,10)
- The composite analysis indicated that integrating IGRA, GeneXpert, and histopathological findings achieved a diagnostic yield of 85%. This finding supports the notion that a multimodal approach significantly enhances diagnostic accuracy, as seen in the study by Afzali et al., and Chavan et.al. (8,10)
- This study highlights the limitations of relying on individual diagnostic tests for FGTB and underscores the value of an integrated diagnostic strategy. The high rate of asymptomatic presentation observed reinforces the need for heightened clinical suspicion in infertile women from TB-endemic regions.
- IGRA demonstrated excellent sensitivity and specificity in this cohort, supporting its role as a useful initial screening test. However, given its inability to confirm active genital disease, IGRA results must be interpreted alongside anatomical and microbiological evidence.
- GeneXpert MTB/RIF, while highly specific, showed modest sensitivity. This finding is consistent with previous studies and reflects uneven mycobacterial distribution within endometrial tissue. PCR and histopathology showed intermediate diagnostic performance, emphasizing their complementary role rather than standalone use.
  Laparoscopy proved particularly valuable, not only for diagnosis but also for assessing disease extent and pelvic damage. Typical findings such as adhesions, tubercles, hydrosalpinx, and tubo-ovarian masses were frequently observed.
  The use of a CRS allowed better case detection by compensating for the shortcomings of individual tests. This approach aligns with emerging recommendations for diagnosing extrapulmonary tuberculosis in low-bacillary-load settings.

Limitations

The study is limited by its small sample size, retrospective design, and absence of long-term fertility outcome assessment following treatment. Additionally, potential confounders, such as prior pelvic infections and socioeconomic factors, were not considered, and reliance on histopathology may introduce sampling bias.

Future Scope

Prospective multicentre studies with larger populations and evaluation of post-treatment reproductive outcomes, including assisted reproductive techniques, are warranted.

Conclusion

Female genital tuberculosis remains a hidden yet significant contributor to infertility in endemic regions. Accurate diagnosis cannot be achieved through a single investigation. A composite, multimodal diagnostic approach incorporating immunological tests, molecular assays, histopathology, and laparoscopy substantially improves detection and facilitates timely management, potentially preserving fertility

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