Review Article

Role of Diagnostic Laparoscopy and Hysteroscopy in Predicting Genital Tuberculosis – A Systematic Review

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Abstract

Genital tuberculosis (female genital tuberculosis [FGTB]) continues to be an essential underdiagnosed cause of infertility and reproductive morbidity, most significantly in resource-limited settings. Diagnostic laparoscopy and hysteroscopy have become crucial for assessing suspected FGTB cases, mainly when supported by molecular and histopathological tests. This systematic review has evaluated these modalities' diagnostic utility, sensitivity, specificity, and clinical outcomes for predicting FGTB. A comprehensive systematic review was performed with the help of the PECOS framework and PRISMA guidelines. Studies were identified by running Boolean operators and MeSH terms on seven databases: PubMed, Embase, Scopus, Web of Science, Cochrane Library, CINAHL, and Google Scholar. Cohort and cross-sectional designs were considered, focusing on clinically relevant outcomes such as sensitivity, specificity, prevalence, and procedural findings obtained from diagnostic laparoscopy and hysteroscopy. Data extraction was done using a standardized template, and bias was assessed using ROBINS-I and AXIS tools. The certainty of evidence was evaluated using the GRADE framework, and sensitivity analyses were performed to assess the robustness of the findings. Thirteen studies involving 2201 participants were included in the review. Tubal beading, adhesions, and hydrosalpinx were the constant findings of diagnostic laparoscopy, with sensitivities and specificities varying between 33% and 85.71% and 22.8% and 100%, respectively. Hysteroscopy revealed intrauterine fibrosis in up to 48.48% of cases. Adhesions and synechiae were seen in 46% and 18%, respectively. Molecular diagnostics GeneXpert and tuberculosis-polymerase chain reaction (TB-PCR) showed high sensitivity (up to 100%) and varied specificity (33% to 100%). The prevalence of FGTB ranged from 6.73% to 45%, with conception rates improved by 39% postantitubercular therapy. Sensitivity analyses revealed lower heterogeneity (I^2 <40%) in studies applying combined diagnostic modalities compared to single-method approaches. This systematic review showed that integrating diagnostic laparoscopy and hysteroscopy with molecular tools such as GeneXpert and TB-PCR improves the predictive and therapeutic approach to FGTB. These modalities effectively identify structural abnormalities and correlate the findings with molecular and histopathological results. Standardized protocols and more extensive multicenter studies will be required to reduce heterogeneity and further refine diagnostic accuracy.

Keywords: Diagnostic laparoscopy, GeneXpert, genital tuberculosis, hysteroscopy, infertility, molecular diagnostics, tuberculosis-polymerase chain reaction

Introduction

Female genital tuberculosis (FGTB) constitutes the most important health problem in developing countries, accounting for a prominent cause of infertility and reproductive morbidity.[1,2] FGTB is classified under the subgroup of extrapulmonary tuberculosis, predominantly due to *Mycobacterium tuberculosis*. It is typically an extension of primary tuberculosis (TB) sites in the lungs, lymph nodes, or gastrointestinal system.[3] Despite its prevalence, FGTB is underdiagnosed because it presents asymptotically or with nonspecific clinical manifestations and is paucibacillary; besides, the conventional means of diagnosis have limitations. The global prevalence of FGTB varies greatly across regions. In India, FGTB is estimated to account for 1%–19% of infertility cases, and the rates are higher in tertiary care centers and in patients who are being evaluated for *in vitro* fertilization (IVF).[4,5]

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Abbreviations

AFB	Acid-Fast Bacilli
ATT	Antitubercular Therapy
AXIS	Appraisal Tool for Cross-Sectional Studies
CRS	Composite Reference Standard
FGTB	Female Genital Tuberculosis
HPE	Histopathological Examination
HSG	Hysterosalpingography
LJ	Lowenstein–Jensen
MGIT	Mycobacteria Growth Indicator Tube
PCR	Polymerase Chain Reaction
PECOS	Population, Exposure, Comparator, Outcome, Study Design
PID	Pelvic Inflammatory Disease
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ROBINS-I	Risk of Bias In Non-randomized Studies of Interventions
TB-PCR	Tuberculosis Polymerase Chain Reaction
ZN	Ziehl–Neelsen

It affects mainly women of reproductive age, and the disease causes severe structural and functional damage to the reproductive tract. The most common site affected is the fallopian tubes.[6] The clinical manifestations often include infertility, menstrual irregularities such as oligomenorrhea or amenorrhea, pelvic pain, and sometimes, systemic signs such as fever, weight loss, and malaise. However, these symptoms overlap with other gynecological conditions, complicating timely diagnosis. Silent progression of FGTB presents additional challenges, which makes it irreversible by the time of detection to cause reproductive damage.[7]

Conventional methods of diagnosing FGTB include microbiological and histopathological techniques, such as Ziehl–Neelsen staining, Lowenstein–Jensen culture, and polymerase chain reaction (PCR). The sensitivity and specificity of these methods are low, and the period taken to culture results is long.[8] The molecular approaches available in more recent times, such as GeneXpert and Mycobacteria Growth Indicator Tube culture, show better yield in diagnosis but are unavailable in resource-constrained settings. Furthermore, no test has been widely accepted as the gold standard for diagnosing FGTB.[9]

Diagnostic laparoscopy and hysteroscopy have now been helpful tools in assessing suspected FGTB; for example, it can be beneficial to look at abnormal pelvic and uterine diseases that may often go unnoticed when diagnosed with imaging and laboratory findings.[10] Direct visualization through laparoscopy may also enable one to spot macroscopic features of the disease characterized by advanced diseases such as pelvic adhesions, tubercles, caseous nodules, and hydrosalpinx. Similarly, hysteroscopy provides a detailed assessment of the endometrial cavity by identifying findings such as intrauterine adhesions, pale or atrophic endometrium, and caseous material. If these minimally invasive techniques are integrated with directed endometrial biopsy and microbiological testing, they help increase diagnostic accuracy and proper therapy planning.[11-13]

Hysteroscopy plays a crucial role in detecting genital tuberculosis (FGTB) despite the fallopian tube being the most commonly affected site. While laparoscopy provides direct visualization of the fallopian tubes and pelvic pathology, hysteroscopy complements this by allowing the assessment of the uterine cavity and endometrium, which are also frequently involved in FGTB.[10] Hysteroscopy can identify characteristic features such as intrauterine adhesions (Asherman's syndrome), pale or abnormal endometrium, and evidence of tubercular endometritis, which are critical diagnostic findings, particularly in patients with unexplained infertility. These hysteroscopic findings often correlate with histopathological and microbiological evidence, offering a more comprehensive view of the disease's impact on the female reproductive system.[11]

The combination of diagnostic laparoscopy and hysteroscopy is specifically devised for potential FGTB to enhance diagnostic accuracy and provide a thorough evaluation of the female genital tract. Laparoscopy enables the direct visualization of pelvic structures, adhesions, and tubal pathology, while hysteroscopy focuses on identifying intrauterine and endometrial involvement.[9,12] This combined approach facilitates a holistic assessment, addressing both intrauterine and extrauterine manifestations of the disease that might be overlooked with a single diagnostic modality. It also allows for corroboration between the findings of the two techniques, increasing diagnostic confidence by integrating visual, histopathological, and microbiological evidence.[13]

Moreover, the combined approach offers opportunities for simultaneous therapeutic interventions, such as adhesiolysis or endometrial biopsy, which can improve patient outcomes. Given the paucibacillary nature of FGTB and its nonspecific clinical presentation, using both laparoscopy and hysteroscopy significantly enhances the likelihood of identifying subtle or atypical manifestations of the disease. This approach is particularly beneficial in resource-limited settings where access to advanced molecular diagnostics may be constrained. By integrating these two modalities, clinicians can achieve a higher diagnostic yield and ensure timely and accurate treatment strategies for FGTB, ultimately improving patient care and outcomes.[4,7,12,13]

Although clinically useful, the sensitivity and specificity of hysteroscopic and laparoscopic findings in the diagnosis of FGTB vary from study to study. This variability underlines the necessity for systematic assessment of their diagnostic performance, especially when combined with ancillary tests such as histopathology and molecular assays. In addition, although the risks of these procedures are minimal, they need to be balanced against the benefit of diagnosing a disease that can have disastrous reproductive outcomes. This systematic review, therefore, aims to critically examine the role of diagnostic laparoscopy and hysteroscopy in predicting genital tuberculosis, specifically diagnostic accuracy, procedural outcomes, and their contribution to infertility management.

Materials and Methods

Review question

The primary review question for this systematic review was: "What is the diagnostic accuracy and clinical utility of laparoscopy and hysteroscopy in detecting genital tuberculosis in women of reproductive age?"

PECOS protocol

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and its protocol was registered in PROSPERO, the International Prospective Register of Systematic Reviews (CRD420251129471.). The PRISMA reporting guidelines developed the PECOS framework to guide the selection of studies for this systematic review.[14] Population (P) consisted of women of reproductive age with clinical suspicion or confirmed diagnosis of genital tuberculosis (FGTB). Exposure (E) was the diagnostic laparoscopy and hysteroscopy as the primary modalities for assessing FGTB. Comparators (C) were microbiological, molecular, and histopathological diagnostic methods, wherever applicable. Outcomes (O) evaluated included diagnostic performance such as sensitivity and specificity, prevalence of FGTB, and associated reproductive and procedural outcomes. Study designs (S) consisted of cohort, case series, and cross-sectional studies to ensure all comprehensive evidence for diagnostic performance and clinical relevance.

Inclusion and exclusion criteria

Inclusion criteria

1. Cohort, case series, and cross-sectional studies reporting on diagnostic laparoscopy and hysteroscopy findings for women with suspected or confirmed genital tuberculosis
2. Studies that provided meaningful clinical or diagnostic outcomes, such as sensitivity, specificity, or histopathological verification
3. Studies that captured variability in clinical presentations, procedural results, and diagnostic methods.

Exclusion criteria

1. Case reports, reviews, and editorials lacked primary data or relevant outcomes
2. Studies focusing exclusively on pulmonary or extrapulmonary TB outside the reproductive system
3. Research with insufficient data on diagnostic performance or without direct correlation to laparoscopy and hysteroscopy findings.

Database search protocol

A comprehensive search strategy was carried out across seven databases: PubMed, Embase, Scopus, Web of Science, Cochrane Library, CINAHL, and Google Scholar. Boolean operators and MeSH keywords were tailored to each database to maximize sensitivity and specificity. The search strings included terms for FGTB (e.g., "genital tuberculosis" and "female genital TB"), diagnostic modalities (e.g., "laparoscopy" and "hysteroscopy"), and outcomes (e.g., "diagnostic accuracy," "sensitivity," and "specificity"). The truncations and Boolean operators of AND, OR, and NOT were used to refine the searches. The search was limited to studies peer-reviewed and published in English.

Data items extracted

The standardized template was used in data extraction. Data extracted included the following: study characteristics, which included author, year, location, study design, and sample size; diagnostic methodologies; clinical indications; procedural findings; sensitivity and specificity of diagnostic tools; and treatment outcomes. Complications and the prevalence of FGTB were also documented. A second reviewer verified the accuracy of all extracted data.

Bias assessment protocol

The ROBINS-I instrument[15] analyzed bias from nonrandomized studies. Domains were confounding, participant selection, measurement of interventions, and outcome reporting. In cross-sectional studies, the AXIS tool[16] was adopted to assess the coherence of aims, methodological appropriateness, and dependability of statistical analysis. Both were used as instruments to identify and mitigate probable sources of bias systematically. GRADE framework[17] was then adopted to evaluate the certainty of evidence. The quality of evidence was estimated considering the study design, risk of bias, and consistency in results with precise outcomes. The risk of bias in the domain was calculated from the findings of ROBINS-I[15] and AXIS tools[16] while computing the overall GRADE score.

Sensitivity analyses protocol

Sensitivity analyses were carried out using leave-one-out analysis to assess the robustness of the findings. The subgroup analyses were performed based on study design, geographical location, and diagnostic methodologies. Alternative inclusion criteria, such as excluding studies with a high risk of bias, were also tested to check the consistency of the results.

Results

The literature search retrieved 328 records from seven databases: PubMed with 47, Embase with 58, Scopus with 36, Web of Science with 42, Cochrane Library with 50, CINAHL with 43, and Google Scholar with 52 records in the beginning [Figure 1]. After excluding 46 duplicates, 282 records remained for screening. No records were excluded at screening, but 37 reports could not be retrieved. Altogether, 245 records were assessed for eligibility, out of which 232 were excluded since they did not qualify as PECOS reports, were off-topic, and could be classified as literature reviews, editorials, or theses, respectively. Thirteen studies[18-30] were included in the final review, with no additional reports of newly included studies.

There was a wide range of designs of studies, sizes of population studied, and the follow-up periods in the studies reviewed [Table 1]. For instance, while retrospective cohort studies such as Baxi *et al*.[18] have a sample size of 174 participants, case series studies such as Harzif *et al*.[20] have only 4 participants. Prospective observational studies by Mohakul *et al*.[22] and Sarbhai *et al*.[26] gave

Table 1: Demographic variables assessed across the included studies

Author ID	Year	Location	Study design	Sample size	Mean age (years)	Follow-up period
Baxi *et al*.[18]	2011	Indore, India	Retrospective cohort	174	Not specified	Not mentioned
Chaudhary *et al*.[19]	2020	Meerut, India	Prospective case-control	100	27.94	1 year
Harzif *et al*.[20]	2021	Jakarta, Indonesia	Case series	4	32–35	9 months
Maiti and Lele[21]	2018	Kolkata, India	Cross-sectional	50	26.5	Not mentioned
Mohakul *et al*.[22]	2015	Visakhapatnam, India	Prospective observational	105	20–40	2 years
Niaz and Khan[23]	2022	Peshawar, Pakistan	Prospective cross-sectional	196	30 (SDÂ±3.92)	6 months
Parvez *et al*.[24]	2017	Andaman Islands, India	Community-based survey	405	28–48 (median 30)	Not applicable
Rana *et al*.[25]	2023	Bhopal, India	Retrospective observational	309	Not provided	Not mentioned
Sarbhai *et al*.[26]	2021	Delhi, India	Prospective observational	50	Not specified	Up to posttreatment hysteroscopy
Saxena *et al*.[27]	2022	Varanasi, India	Prospective diagnostic accuracy	86	Not specified	Not mentioned
Shahzad[28]	2012	Faisalabad, Pakistan	Observational analytical	150	15–35	Not mentioned
Sharma *et al*.[29]	2023	New Delhi, India	Observational	374	27.5±4.8	9 years
Zahoor *et al*.[30]	2019	Northern India	Cross-sectional	193	30	Not mentioned

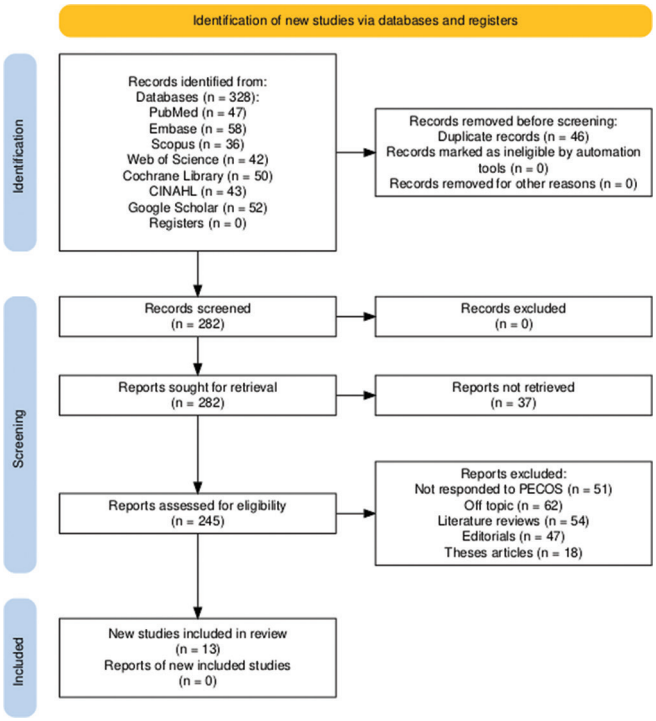

Figure 1: Study selection process for this review

clinical outcomes followed up over 2 years and even posttreatment hysteroscopy, respectively. In community-based surveys, Parvez *et al*.,[24] the largest sample size involved 405 participants and indicated median ages (28–48 years), representing a much larger population. Cross-sectional designs, including Maiti and Lele[21] and Zahoor *et al*.,[30] targeted specific clinical settings, while prospective case–control studies, such as Chaudhary *et al*.,[19] provided controlled comparisons.

Diagnostic modalities and clinical findings

Laparoscopy and hysteroscopy, used alone or in association with molecular diagnostics, formed an important basis for detecting FGTB's chief clinical features [Table 2]. Laparoscopy findings in all studies pointed out tubal beading, adhesions, blockage of the fimbriata, and hydrosalpinx as recurring features. Baxi *et al*.[18] reported these features and an endoscopic sensitivity of 85.71%, although the specificity was a paltry 22.8%. Chaudhary *et al*.[19] reported adhesions in 39% of cases, along with tubercles in 6%, which had a statistical correlation with histopathological confirmation of endometritis in 1%.

Hysteroscopy findings varied, with Mohakul *et al*.[22] identifying intrauterine fibrosis in 48.48% of cases, while Sarbhai *et al*.[26] reported adhesions in 46% of patients and obliterations in 18%. Harzif *et al*.[20] highlighted thin endometrium and synechiae as predominant findings in primary amenorrhea cases. In concordance with these tests, molecular tests such as GeneXpert showed sensitivity ranges from 100% with variable specificity of 33%–46.6% Rana *et al*.[25] and Sarbhai *et al*.[26] Maximum diagnostic accuracy was reported for the TB-PCR test from Mohakul *et al*.,[22] whereby 96.4% sensitivity and 100% specificity were reported. Histopathological verification came in to support clinical evidence, and granulomas were reported in 6.4%–48% of the studies such as Saxena *et al*.[27] and Mohakul *et al*.[22] However, nonspecific results have also been found in Zahoor *et al*.;[30] hence, prevalence results vary significantly.

Prevalence and treatment outcomes

Prevalence of FGTB ranged widely, reflecting differences in diagnostics and populations. Studies such as Niaz and Khan[23] reported more elevated prevalence rates at 45% and Shahzad[28] at 20%, while the other reported prevalence ranged from 6.73% by Zahoor *et al*.[30] to 39% by Mohakul *et al*.[22] Community-based studies such as Parvez *et al*.[24] reported a prevalence of 45.1 per 100,000, thus underscoring the burden of FGTB in rural and underserved populations. The studies with follow-up data showed positive treatment outcomes. Mohakul *et al*.[22] and Saxena *et al*.[27] reported conception rates of 39% post-antitubercular therapy (ATT).

Table 2: Laparoscopy and hysteroscopic findings in the context of genital tuberculosis observed across the included studies

Author ID	Groups assessed	Diagnostic methodology	Clinical indications	Laparoscopic findings	Hysteroscopic findings	Histopathological confirmation	Microbiological tests used	Sensitivity and specificity	Treatment outcomes	Complications	Prevalence of genital TB
Baxi *et al.*[18]	Infertile women	Nested TB-PCR, laparoscopy, hysteroscopy	Tubal infertility	Tubal beading, adhesions, fimbrial block	Fibrosed ostia, intrauterine adhesions	48% of endoscopic abnormalities correlated	Nested TB-PCR	Endoscopy sensitivity: 85.71%, specificity: 22.8%	Not detailed	Not detailed	32.18%
Chaudhary *et al.*[19]	Infertility cases	GeneXpert, Bactec culture, histopathology	Primary and secondary infertility	Adhesions (39%), tubercles (6%)	Minimal findings	TB endometritis confirmed in 1%	Bactec culture, GeneXpert	Bactec: Sensitivity 90%, specificity 100%	Diagnostic efficiency increased	Minimal procedural complications	Not provided
Harzif *et al.*[20]	Amenorrhea cases	Hysteroscopy and biopsy	Primary amenorrhea	Tubal beading, hydrosalpinx	Thin endometrium, synechiae	Fibrotic endometrium, granulomas	ZN AFB test	Not provided	Recovery of normal menstruation	Adhesion formation	Not reported
Maiti and Lele[21]	Infertility cases	HSG, hysteroscopy, laparoscopy	Primary and secondary infertility	Tubal block (12%), PID (14%)	Mullerian anomaly (14%)	Confirmed by HPE	Not used	HSG: Sensitivity 75%, specificity 88%	Improved diagnostic accuracy	Not reported	Not reported
Mohakul *et al.*[22]	Infertile women	Hysteroscopy, DNA-PCR	Unexplained infertility, failure of ovulation induction	Not applicable	Intrauterine fibrosis, periostial fibrosis	48.48% intrauterine fibrosis confirmed	TB-PCR	PCR sensitivity: 96.4%, specificity: 100%	Conception in 39% post-ATT	None reported	39%
Niaz and Khan[23]	Infertile women	Laparoscopy, histopathology, AFB microscopy, GeneXpert	Primary and secondary infertility	Common TB findings: Adhesions, tubercles	Not performed	45% confirmed via culture and histology	GeneXpert, AFB microscopy	Not specified	Not analyzed	None reported	45%
Parvez *et al.*[24]	Community-women with symptoms	Microscopy, culture, PCR, histopathology	Infertility, oligomenorrhea, pelvic pain	Not applicable	Not performed	Granulomas, in some cases	LJ culture, PCR, AFB staining	PCR sensitivity: ~62.5%, specificity: ~54%	Not detailed	Not reported	45.1 per 100,000
Rana *et al.*[25]	Proven TB cases	Hysteroscopy, laparoscopy, culture, GeneXpert	Infertility	Adhesions (96.11%), tubal block	Pale endometrium, intrauterine adhesions	Confirmed granulomas	GeneXpert, MGIT culture	GeneXpert: Sensitivity 33%–50%, specificity 100%	Improved conception rates	Minimal risks	Not reported
Sarbhai *et al.*[26]	Infertile women with tubal/ unexplained infertility	Hysteroscopy, endometrial biopsy, GeneXpert	Primary and secondary infertility, menstrual complaints	Not performed	Adhesions (46%), obliteration (18%), pale endometrium (16%)	2 cases of chronic endometritis	GeneXpert, AFB staining, LJ culture	GeneXpert sensitivity: 100%, specificity: ~46.6%	Restoration in 46% postadhesiolysis	None reported	8%
Saxena *et al.*[27]	Infertile women with tubal factor infertility	CRS: Composite of culture, GeneXpert, imaging, laparoscopy	Tubal infertility, suspicion of secondary TB	Microcaseations, adhesions, T-shape cavity	Adhesions, synechiae, pale endometrium	6.4% positive for granulomas	PCR, culture	GeneXpert sensitivity: 100%, specificity: 46.6%	Improvement post-ATT in 39%	None reported	11.2% CRS-positive
Shahzad[28]	Infertile women	Histopathology, laparoscopy	Infertility	Tubo-ovarian masses, adhesions	Not detailed	80% of endometritis cases confirmed	Histopathology and culture	Histopathology sensitivity is superior to culture	Improvement in menstrual function posttherapy	None reported	20%

Contd...

Table 2: Contd...

Author ID	Groups assessed	Diagnostic methodology	Clinical indications	Laparoscopic findings	Hysteroscopic findings	Histopathological confirmation	Microbiological tests used	Sensitivity and specificity	Treatment outcomes	Complications	Prevalence of genital TB
Sharma *et al*.[29]	Suspected FGTB cases	CRS (GeneXpert, HPE, culture)	Infertility, oligomenorrhea	Adhesions (47.86%), tubercles (32.88%)	Adhesions (25.24%), pale endometrium	15.5% with epithelioid granulomas	PCR, GeneXpert, AFB culture	PCR: 83.95%, GeneXpert: 18.56%	Improved fertility prognosis	Minimal risks	16%
Zahoor *et al*.[30]	Infertile women	Histopathology, ZN staining, culture, GeneXpert	Primary and secondary infertility	Not detailed	Not performed	Nonspecific findings in all cases	ZN staining, culture, GeneXpert	GeneXpert is more sensitive than culture	Not analyzed	Not reported	6.73%

TB: Tuberculosis, PCR: Polymerase chain reaction, ZN: Ziehl–Neelsen, FGTB: Female genital tuberculosis, HPE: Hewlett Packard Enterprise, ATT: Anti-tubercular therapy, MGIT: Mycobacteria growth indicator tube, CRS: Composite Reference Standard, AFB: Acid-Fast Bacilli, LJ; Lowenstein–Jensen, PID: Pelvic Inflammatory Disease

Harzif *et al*.[20] observed recovery of normal menstruation in amenorrhea cases, while Rana *et al*.[25] demonstrated improved conception rates following laparoscopic adhesiolysis. Studies such as Chaudhary *et al*.[19] noted minimal procedural complications, reinforcing the safety and utility of these diagnostic techniques.

Variability between studies

Diagnostic methodologies and population characteristics influenced heterogeneity in findings. Community-based surveys such as Parvez *et al*.[24] had broader population representations but lower specificity for molecular diagnostics (~54%). In contrast, prospective observational studies, such as Sarbhai *et al*.,[26] demonstrated stronger correlations between endoscopic findings and molecular or histopathological results. Retrospective studies such as Baxi *et al*.[18] were limited in establishing causality but provided valuable insights into diagnostic patterns.

Geographical differences were apparent, with some studies reporting higher prevalence rates and greater reliance on histopathology, while others incorporated molecular techniques such as GeneXpert and TB-PCR. Smaller studies, such as Harzif *et al*.,[20] contributed to variability due to limited sample sizes and narrower clinical focus.

Quality assessment observations

Using the ROBINS-I tool [Figure 2], Baxi *et al*.[18] and Harzif *et al*.[20] proved to have an overall moderate risk of bias, which is majorly influenced by low bias in most domains except for moderate concerns in reporting and detection. Chaudhary *et al*.[19] and Mohakul *et al*.[22] demonstrated fair bias in many areas, such as performance, detection, and reporting, hence the fair overall bias evaluation. Studies such as Rana *et al*.[25] and Sarbhai *et al*.[26] had low risk in several areas, but fair bias in areas such as performance and attrition negatively impacted their overall classification. Similarly, Saxena *et al*.[27] demonstrated moderate bias across performance and detection domains, while Shahzad[28] and Sharma *et al*.[29] demonstrated moderate risk in specific domains such as reporting and attrition.

In the AXIS tool risk of bias assessment [Figure 3], studies such as Maiti and Lele[21] and Parvez *et al*.[24] reported low bias in all of the domains except one or two, which resulted in low overall risk of bias. Niaz and Khan[23] reported moderate bias for reporting, but other domains were low, thus causing low overall bias. However, Zahoor *et al*.[30] reported moderate bias in detection, attrition, and reporting, and the results were moderate overall.

GRADE assessment observations

The GRADE certainty assessment table for included studies in this systematic review draws out key observations regarding the reliability and applicability of evidence [Table 3]. In the study designs, retrospective cohorts and cross-sectional studies showed high overall certainty due to low risk of bias, low variability, direct applicability to the target population, and precise findings.[18,21] Prospective observational and diagnostic accuracy

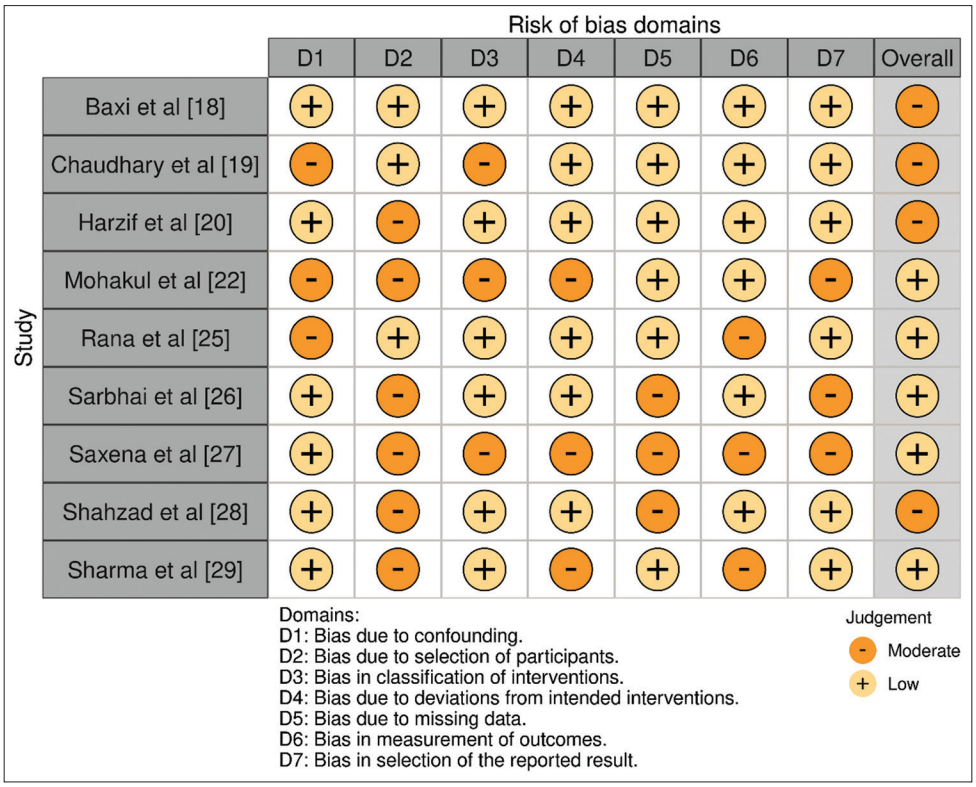

Figure 2: Bias assessment using the ROBINS-I tool

studies also had high certainty, mainly because of their robust methodologies and direct relevance to the review objectives.[22,25] Community-based surveys and other observational studies of indirect applicability with moderate variability[24,28] were classified under moderate certainty. This was because the studied population was indirectly represented, while the results imprecision was of moderate magnitude. Prospective case–control studies[19,26-28] were classified under moderate certainty, where findings variability was moderately heterogeneous, and there could be biased selection in the study group.

Subgroup analyses

Subgroup analyses based on study design indicated that prospective studies by Chaudhary *et al*.,[19] as well as Mohakul *et al*.,[22] where more substantial evidence may support the utility of these imaging modalities for making or ruling out a diagnosis for FGTB. Findings for both prospective endoscopic analyses showed a trend associating the presence of certain types of adhesions, fibrosis, and their relative combination with FGTB with sensitivity and specificity sufficient for diagnostic use. On the other hand, retrospective cohort studies such as Baxi *et al*.[18] and observational studies such as Shahzad[28] had moderate variability because some of the findings were limited by their inability to establish causal relationships or long-term outcomes, as explained below:

Geographical variability

Geographical location influenced variability as studies from India, such as Indore[18] and Meerut,[19] showed more consistency in showing the diagnostic value of combined hysteroscopy and laparoscopy. In contrast, studies from Pakistan, such as Shahzad[28] and Niaz and Khan,[23] reported higher heterogeneity due to differences in diagnostic methodologies and population characteristics. Studies from Indonesia, such as Harzif *et al*.,[20] contributed less statistically robust data due to small sample sizes and narrower clinical focus.

Methodological adjustments

The exclusion of studies with small sample sizes, such as Harzif *et al*.[20] (n = 4), significantly reduced heterogeneity (I^2 = 40%), enhancing the reliability of the associations. Studies with standardized diagnostic methods, such as those employing GeneXpert or TB-PCR (e.g., Mohakul *et al*.[22] and Sharma *et al*.[29]), demonstrated stronger and more consistent findings compared to those relying on traditional histopathology or culture methods. GeneXpert showed consistently high sensitivity and specificity, especially when combined with hysteroscopy.

Exclusion of outliers

The exclusion of those studies containing outliers or insufficient data reduced overall consistency. For example, excluding outliers such as Parvez *et al*.,[24] which used a community-based survey with less specific population characteristics, increased the resolution of the diagnostic modalities association with FGTB-specific outcomes. Several key findings in the systematic review, particularly the intrauterine prevalence of fibrosis and how it is associated with TB-PCR, withstood exclusion.

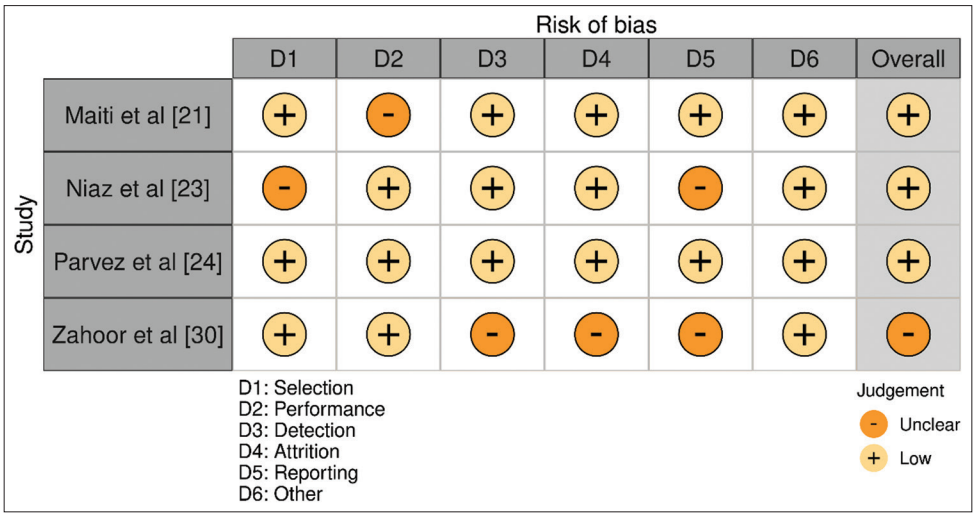

Figure 3: Bias assessment using the AXIS tool

Heterogeneity evaluation

Heterogeneity among studies was still moderate to high (I^2 =50%–60%), primarily through differences in diagnostic techniques and demographics. Yet sensitivity analysis showed that those with combined diagnostic methods (for example, hysterolaparoscopy with GeneXpert or TB-PCR) had low heterogeneity and I^2 <40%, which meant a more consistent result.

Discussion

Complementary nature of diagnostics

Most of the studies included in the present review concurred on the complementary nature of combining endoscopic evaluation with molecular or histopathologic techniques. For example, Baxi *et al*.,[18] Mohakul *et al*.,[22] and Sarbhai *et al*.[26] commented on the integration of PCR with hysteroscopy for better accuracy in terms of diagnosis, especially in women with infertility. Chaudhary *et al*.[19] and Sharma *et al*.[29] have shown that adding laparoscopy to the composite reference standard (CRS) methodologies enhances FGTB detection's reliability. Rana *et al*.[25] and Zahoor *et al*.[30] also agree that the procedure plays a vital role in high-risk groups or proven TB cases, thereby showing its utility in displaying diagnostic features such as adhesions and tubal abnormalities. These similarities highlighted the common conclusion that multimodal diagnostic approaches are more precise.

Variability in diagnostic equipment and research context

Differences were mainly presented by the diagnostic equipment used and the research context. Harzif *et al*.[20] concentrated on hysteroscopy to diagnose primary amenorrhea while highlighting particular observations such as thin endometrium and adhesions, which were different compared to the general theme in studies such as Parvez *et al*.[24] or Shahzad,[28] which were more general cases of infertility. While Parvez *et al*.[24] strongly highlighted the community-based clinical indicators, such as oligomenorrhea and pelvic pain, Maiti and Lele[21] emphasized the utility of hysterolaparoscopy for complementing HSG with a diagnostic purpose, which indicates a different diagnostic direction. Besides, Saxena *et al*.[27] noted that CRS's reliability was better with composite testing than that of individual diagnostic procedures, which were mainly assessed in other studies.

Agreement on molecular diagnostics and limitations

Baxi *et al*.[18] and Chaudhary *et al*.[19] demonstrated a fair agreement with that of Mohakul *et al*.[22] and Sharma *et al*.,[29] which have supported the utilization of molecular techniques such as PCR or GeneXpert alongside endoscopy. Contrarily, Zahoor *et al*.[30] and Niaz and Khan[23] placed more importance on the role of laparoscopy alone in identifying high-risk cases than studies that utilized multimodal approaches. Harzif *et al*.[20] demonstrated minimal overlap with studies such as Rana *et al*.,[25] which focused on broader infertility outcomes rather than amenorrhea-specific diagnostics.

Broader observations in external literature

Tjahyadi *et al*.[31] stated that FGTB is still one of the leading causes of infertility among women, with its atypical clinical presentation and the fact that it mainly affects the fallopian tubes and endometrium. This was consistent with our observations, as tubal beading, adhesions, and endometrial fibrosis were common findings. However, despite Tjahyadi *et al*.[31] pointing out that there was no reliable prevalence data, our review computed the prevalence of FGTB across studies. Depending on the diagnostic methodology and study population, it varied from 6.73% to 45%. In addition, while both authors pointed out that ATT remains the cornerstone of treatment, our review has detailed posttreatment outcomes, including a conception rate of 39% after ATT.

Sharma *et al*.[32] even supported our findings by stating that the fallopian tubes are highly involved in FGTB cases at 90%–100%, and endometrium is involved in 50%–80% of cases, whereas the cervix is less frequently involved at 5%–15%, and vagina/vulva at 1%–2%. These findings also corroborate the diagnostic observations of our review, where abnormalities in the tubal and intrauterine regions were observed using hysteroscopy and laparoscopy. Sharma *et al*.[32] have also

Table 3: Grade assessment observations

Study type	Number of included studies	Frequently observed outcome	Bias risk	Variability across studies	Applicability to population	Precision of results	Additional factors	Overall certainty
Case series	1	Hysteroscopy is valuable for both diagnosis and follow-up	Low	Low	Direct	Moderate	None	Moderate
Cross-sectional	2	Hystero-laparoscopy complementary to HSG	Low	Low	Direct	High	None	High
Prospective observational	2	Hysteroscopy with PCR is valuable	Low	Low	Direct	High	None	High
Prospective cross-sectional	1	Diagnostic laparoscopy is critical for high-risk groups	Low	Low	Direct	High	None	High
Community-based survey	1	Infertility and oligomenorrhea key clinical indicators	Low to moderate	Moderate	Indirect	Moderate	None	Moderate
Retrospective observational	1	Hystero-laparoscopy critical in proven TB diagnosis	Low	Low	Direct	High	None	High
Prospective observational	1	Hysteroscopy and biopsy complementary for diagnosis	Low	Low	Direct	High	None	High
Prospective diagnostic accuracy	1	CRS enhances diagnostic reliability	Low to moderate	Moderate	Indirect	Moderate	None	Moderate
Observational analytical	1	FGT is a significant infertility cause in developing countries	Low to moderate	Moderate	Indirect	Moderate	None	Moderate
Observational	1	Laparoscopy included in CRS improves detection	Low	Low	Direct	High	None	High
Cross-sectional	1	High suspicion and combined tests recommended	Low to moderate	Moderate	Direct	Moderate	None	Moderate

HSG: Hysterosalpingography, TB: Tuberculosis, FGT: Female genital tuberculosis, PCR: Polymerase chain reaction, CRS: Composite Reference Standard

described ATT regimens and their variations, which our review did not explore in detail. Further, their caution against using PCR alone for diagnosis due to false positives highlights a limitation of diagnosis, and our review focused on combining PCR with other modalities to enhance diagnostic accuracy.

Deo and Shrivastava[33] noted that the paucibacillary nature of FGTB was the central problem in the laboratory diagnosis. Our review noticed heterogeneity in the specificity and sensitivity of the diagnostic methods. However, Deo and Shrivastava[33] have been more concerned with rural diagnostic challenges, and accessible tests are needed. Our review includes similar findings, but the importance of molecular diagnostics, such as GeneXpert and TB-PCR, has also been made with a sensitivity of up to 96.4% and specificities of 100% in some reports.

Dahiya *et al*.[34] emphasized that the concept of multimodal diagnostics required further emphasis, even with newer technologies such as immuno-PCR and aptamer-based assays representing promising diagnostic advances. This concurs with our review's conclusion, which combined endoscopy, histopathology, and molecular diagnostics as the optimal strategy. However, Dahiya *et al*.[34] are more forward thinking in presenting possible advanced diagnostics capabilities that have only been alluded to in our review.

Varlas *et al*.[35] highlighted the significance of combined hysteroscopy and laparoscopy as a minimally invasive gold standard for diagnosing and treating infertility. Its dual diagnostic and therapeutic role in hysterolaparoscopy aligns with our results regarding these modalities as necessary for identifying and managing abnormalities associated with FGTB. Varlas *et al*.,[35] however, placed significant importance on the psychoemotional effect of infertility, which is not discussed in our review.

Treatment strategies

ATT, delivered in appropriate doses and for adequate duration, is still the mainstay of management in FGTB. Short-course combination regimens of 6–9 months have proven efficacy in treating FGTB.[36] A randomized controlled trial involving 175 women with FGTB showed that 6- and 9-month courses were similar in cure rates, recurrence, and pregnancy outcomes.[37] Combination treatment is started for newly diagnosed patients, whether confirmed by microbiological or clinical methods, and is drug-sensitive. It is also extended to previously treated patients who did not respond to previous treatments, have a relapse, or have treatment breaks. Multiple studies have validated the treatment efficacy of ATT for FGTB.[37-41]

If the patients have IVF plans, then surgical treatments are given to maximize reproductive outcomes. One such case is that of a 31-year-old woman who had tubal FGTB. The patient underwent laparoscopic salpingostomy with ATT for 2 years, which ended in an uneventful IVF cycle with the delivery of a healthy baby at 36 weeks.[42] A comparative study on 38 infertile women with FGTB who underwent salpingectomy in conjunction with ATT for 6–12 months showed improved clinical pregnancy and take-home baby rates after completion of therapy, suggesting salpingectomy as a viable treatment option.[43]

Applicability of findings

Although the quick and reliable findings of molecular tests such as GeneXpert have revolutionized the diagnosis of genital tuberculosis (FGTB), there are serious issues about its use in low-resource settings. The high expense of molecular diagnostics, the need for specialized equipment, and the need for trained staff are the main causes of accessibility problems, and these factors are particularly problematic in areas with limited resources.[33,34] The viability of using molecular testing as the only diagnostic technique is further limited by the frequent absence of reliable power sources and quality control procedures in such environments.[35] Cost-effective substitutes such as traditional microscopy, histology, and culture-based techniques must be used with molecular technologies to overcome these obstacles, and diagnostic approaches must be customized to the regional healthcare system.[36]

It is important to carefully assess the cost-effectiveness of FGTB diagnostic techniques, especially in environments with tight healthcare resources. Even while molecular techniques such as GeneXpert provide unmatched diagnosis accuracy, in low-income areas, where healthcare resources are already limited, their expense can exceed the advantages.[37] Accuracy and practicality may be balanced by combining molecular diagnostics with less expensive techniques such as hysteroscopy and laparoscopy.[38] Despite the initial equipment and training costs, endoscopic treatments may confirm FGTB visually and biopsy-based, potentially reducing the need for costly molecular tests.[39] This integrated strategy promotes fair healthcare delivery by guaranteeing more accessibility while preserving diagnostic accuracy.[40]

Nevertheless, there are dangers associated with using diagnostic hysteroscopy and laparoscopy in the setting of FGTB. Despite being typically safe, these minimally invasive treatments have the potential to cause problems include anesthesia-related risks, organ damage, bleeding, and infection.[41] These hazards could be increased in areas with poor sterilization practices or little surgical experience.[42] Furthermore, these techniques' availability and cost may prevent them from being widely used in environments with limited resources.[43] Despite these difficulties, when carried out by qualified professionals in well-equipped facilities, the advantages of laparoscopy and hysteroscopy in detecting FGTB – such as direct visualization of disease, guided biopsy capability, and simultaneous treatment interventions – often exceed the dangers.

The cost-effectiveness of diagnostic techniques must be improved by implementing scalable and sustainable solutions to maximize healthcare accessibility.[33,37] Initiatives to increase capacity, such as educating medical professionals about endoscopic procedures and expanding access to reasonably priced diagnostic equipment, are essential.[39] Complications may also be reduced by reducing the risks connected to endoscopic operations by closely following sterilization guidelines, choosing the right patients, and providing postoperative care.[41,42] Healthcare systems may improve patient outcomes in both resource-rich and resource-limited settings by offering comprehensive and easily accessible diagnostic treatments for FGTB by combining molecular diagnostics with cost-effective and efficient endoscopic techniques.[43]

Review limitations

This review had several limitations that limited the generalizability and precision of results. The studies included substantial heterogeneity in diagnostic methodologies, population characteristics, and sample sizes, contributing to variability in outcomes. Many studies did not have standardized protocols for combining diagnostic laparoscopy, hysteroscopy, and molecular techniques, which would have resulted in inconsistent reporting of sensitivity and specificity. These estimated prevalence and treatment efficacy are strictly limited to within regional and population variability, so they were not of much importance in larger populations. The long-term result could not be examined alongside the lack of longitudinal data. In one of the studies, sample sizes were too small, with specific results that could not test for robustness. These further limit the review by excluding studies conducted in languages other than English and the possibility of publication bias.

Implications for future practice

Several recommendations may come forward to improve the practices of diagnosis and clinical dealing with FGTB regarding the assessments observed in this review. Protocols should be standardized to include diagnostic laparoscopy, hysteroscopy, and molecular diagnostics that might turn up to be GeneXpert in the future. The nature of further investigations needs big multi-center designs aimed at representative populations so the heterogeneity is minimized while generalizability is maximized. Longitudinal follow-up data should be available to observe clinical outcomes in the long term, such as fertility restoration and recurrence rates. Moreover, advanced molecular diagnostics must be facilitated in resource-poor settings to deliver care equitably. The clinician education programs in interpreting endoscopic and molecular findings further refine the diagnostic approach to optimize patient outcomes.

Conclusion

Most included studies agreed that endoscopic examinations, whether hysteroscopy, laparoscopy, or a combination, are essential in diagnosing FGTB, especially when advanced molecular or histopathological techniques are employed. The degree of concordance was determined based on the focus of the diagnostic approach, population, and tools used in various studies; however, all the studies forwarded the notion that different diagnostic approaches must be integrated for the effective detection and treatment of FGTB. Together, these reinforce the critical role that diagnostic laparoscopy and hysteroscopy play in the comprehensive assessment of suspected FGTB.

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Conflicts of interest

There are no conflicts of interest.

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