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Evaluation Of Genexpert Performance Assays In Sputum Samples In Cavitary Pulmonary TB/Role Of Genexpert In Diagnosing Pulmonary Tuberculosis

Aisha Shafique[1], Eisha Arshad[2], Sara Daud[3]

Abstract

Objective: This study evaluated the diagnostic performance of GeneXpert MTB/RIF in sputum samples from Pakistani patients with cavitary TB, using mycobacterial culture as the gold standard and comparing it to sputum smear microscopy.

Methods: In this cross-sectional study conducted at a tertiary hospital in Rawalpindi, 187 HIV-negative adults (18–60 years) with cavitary pulmonary TB were enrolled. Sputum samples were analyzed by smear microscopy, GeneXpert, and culture at baseline, 2, 5, and 6 months of therapy. Diagnostic accuracy indices (sensitivity, specificity, PPV, NPV) were compared with culture results.

Results: Among 187 patients (mean age 44.1 ± 17.1 years; 93.6% female), 32% had baseline culture-confirmed TB. GeneXpert detected 91.7% of culture-positive cases versus 28.3% by smear. After 2 months, 43.3% remained culture-positive, while GeneXpert and smear positivity were 35.3% and 32.6%, respectively. All patients achieved culture negativity by treatment completion; however, GeneXpert and smear remained positive in 49.2% and 41.7% due to non-viable bacilli.

Conclusion: GeneXpert MTB/RIF demonstrated superior sensitivity to smear microscopy in detecting cavitary TB and monitoring therapeutic response, but showed reduced specificity post-treatment due to residual DNA. Combining GeneXpert with culture improves reliability for therapy monitoring and outcome prediction.

Keywords: Tuberculosis, Mycobacterium tuberculosis; Polymerase Chain Reaction; Sputum; Sensitivity and Specificity; Treatment Outcome.

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AS, EA, SD - Acquisition, Analysis, Interpretation
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Introduction

Tuberculosis is still a serious global health concern, being among the top 10 causes of mortality globally. In 2023, an estimated 10.8 million people will get tuberculosis, with 1.4 million fatalities, with more than 90% of cases happening in low- and middle-income countries.[1] Pakistan is a high-TB burden nation that contributes significantly to global TB incidence.[2] Cavitary pulmonary tuberculosis is a kind of advanced lung tuberculosis identified by cavitation on chest X-ray. Cavities contain large levels of Mycobacterium tuberculosis, resulting in high sputum bacillary loads, greater contagiousness, and an increased likelihood of treatment failure or recurrence. Patients with cavitary illness who remain culture-positive after two months of medication are known to have worse results; recommendations advocate prolonging treatment to nine months in these circumstances.[12] Rapid and precise diagnostic tests are therefore required not only for early TB identification but also for monitoring treatment response in cavitary TB patients.

Sputum smear microscopy, the classic first-line tuberculosis test, has low sensitivity (20–80%), particularly in individuals with paucibacillary or HIV co-infection. In comparison, the GeneXpert MTB/RIF assay (Cepheid, USA) is a cartridge-based nucleic acid amplification test that detects M. tuberculosis and rifampicin resistance in 2 hours. Xpert has greatly improved case detection, with pooled sensitivities of ~69–85% (98% specificity) in high-burden settings.[3,5,6] It is much more sensitive than smear, particularly in smear-negative TB. The World Health Organization recommends Xpert MTB/RIF (and the next-generation Xpert Ultra) as the first diagnostic test for all patients with probable tuberculosis.[1] However, the role of GeneXpert in therapy monitoring is unclear. While some studies show that repeated Xpert cycle threshold values correspond with bacterial load reduction, the test may still be positive owing to DNA from non-viable bacilli even after patients are microbiologically healed.[3,8] We conducted this research to assess the efficacy of GeneXpert MTB/RIF in sputum samples from cavitary pulmonary TB patients, both for initial diagnosis and tracking therapy response, using culture as the gold standard and comparing it to smear microscopy.

Materials And Methods

We did a cross-sectional analysis at Fauji Foundation Hospital's Pulmonology Department in Rawalpindi, Pakistan. The trial lasted 9 months (February 15–November 15, 2021). The institutional review board granted ethical approval, and all subjects provided informed consent.

A total of 187 adult patients with cavitary pulmonary tuberculosis were recruited via successive sampling. The inclusion criteria were age 18–60 years, radiographic evidence of cavitation in the lungs, and microbiological

confirmation of tuberculosis by at least one positive sputum test (smear and/or Xpert) at baseline. Patients were HIV-negative and had just been diagnosed with drug-susceptible tuberculosis. To concentrate on simple cavitary TB, we eliminated persons with non-cavitary TB on chest X-ray, extrapulmonary TB, known multidrug-resistant TB, pregnancy, and major comorbidities (hepatic, renal, metabolic, or endocrine problems; malignancy; or immunosuppressive medication). All patients were given conventional 6-month anti-TB treatment (2 months of intense phase with isoniazid, rifampicin, ethambutol, and pyrazinamide; 4 months of continuation phase with isoniazid and rifampicin). Chest radiographs were taken at baseline and every three months to track cavity resolution. Patients were checked periodically for adherence and pharmacological adverse effects. According to national criteria, patients with cavitary illness and delayed smear/culture conversion at 2 months were eligible for prolonged treatment (up to 9 months). At baseline, all enrolled patients provided sputum specimens—either spot or early-morning samples—collected under aseptic conditions following national tuberculosis program guidelines. Each specimen was divided into three aliquots for parallel analysis:

1) Smear Microscopy: Smears were prepared on clean slides and stained using the Ziehl-Neelsen (ZN) method. The presence of acid-fast bacilli (AFB) under light microscopy confirmed a positive result, while negative slides showed no AFB in 100 oil-immersion fields. Smear results were graded semi-quantitatively (scanty, 1+, 2+, 3+) according to WHO criteria.
2) GeneXpert MTB/RIF (Xpert) Assay: The Xpert MTB/RIF test (Cepheid, USA) was performed on the second aliquot following the manufacturer's protocol. The test automatically detected *Mycobacterium tuberculosis* complex DNA and rifampicin resistance using real-time PCR technology. Results were reported as either "MTB detected" (with rifampicin resistance *detected* or *not detected*) or "MTB not detected." Positive results were further categorized semi-quantitatively based on cycle-threshold (Ct) values into four bacterial load categories:
    a) High (<16 Ct)
    b) Medium (16–22 Ct)
    c) Low (22–28 Ct)
    d) Very Low (>28 Ct)
3) Mycobacterial Culture (Gold Standard): The third aliquot was cultured using Löwenstein–Jensen (LJ) solid media or the MGIT 960 liquid culture system (Becton Dickinson). Cultures were incubated for up to 8 weeks and examined weekly for visible growth. Culture positivity confirmed viable *M. tuberculosis*, while negative cultures after 8 weeks were considered sterile.

Follow-up sputum specimens were collected at the end of months 2, 5, and 6 of anti-tuberculosis therapy. Each sample underwent repeat AFB smear, GeneXpert MTB/RIF, and culture testing. The results from each time point were compared to the culture as the reference standard to determine diagnostic accuracy (sensitivity, specificity, PPV, and NPV) and to monitor bacteriological conversion trends.

Continuous variables (e.g., age) are presented as mean ± standard deviation or median (interquartile range) according to distribution, and categorical variables (e.g., test positivity) as counts and percentages. To compare paired diagnostic sensitivities and specificities of Xpert vs. smear microscopy against the reference standard of culture, McNemar's test was applied. Differences in independent proportions (e.g., specificity at month 2) were assessed using Pearson's chi-square test. A two-tailed p-value < 0.05 was considered statistically significant. All analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY) and Stata version 16 (StataCorp LLC, College Station, TX)

Definite therapeutic success was defined as at least two consecutive negative cultures (including one at the conclusion of therapy) with no intervening positive culture and clinical improvement. Patients with numerous consecutive negative cultures but no end-of-treatment culture (for example, owing to contamination) and no intermediate positives were considered probable successes. Patients having a single negative culture at the conclusion of therapy (after previous positives or missing data) were considered possible successes. If a positive culture persisted at month 6, the outcome was classified as treatment failure.

Results

The study comprised 187 individuals with cavitary pulmonary tuberculosis. The population was predominantly female (93.6%, n = 175) with a mean age of 44.1 ± 17.1 years. Baseline testing confirmed tuberculosis in subsets of patients: 60 (32.1%) were culture-positive, 69 (36.9%) were Xpert-positive, and 61 (32.6%) were smear-positive. To formally compare the sensitivity of Xpert versus smear microscopy against culture at baseline, we performed McNemar's test on the paired results from the 60 culture-positive patients. Xpert detected 55 of 60 culture-positive cases (sensitivity 91.7%), while smear detected 17 of 60 (sensitivity 28.3%). McNemar's test yielded $\chi^2 = 34.3$, $p < 0.001$, indicating a highly significant improvement in sensitivity with Xpert compared to smear.

After two months of treatment, 81 patients (43.3%) remained culture-positive, while 106 (56.7%) had converted to culture-negative. At month 2, 66 patients (35.3%) tested positive by Xpert and 61 (32.6%) by smear. Among the 81 culture-positive patients, Xpert detected 38 (sensitivity 46.9%) and smear detected 29 (sensitivity 35.8%). A McNemar's test comparing these paired sensitivities gave $\chi^2 = 8.10$, $p = 0.004$, confirming that Xpert sensitivity remained significantly higher than smear at two months. Specificity at month 2 was 73.6% for Xpert versus 69.8% for smear (difference not statistically significant by χ^2 for independent proportions, $p = 0.21$).

By the end of therapy, all 187 patients were culture-negative. Treatment outcomes were classified as definite success (n = 133, 71%), probable success (n = 9, 5%), and possible success (n = 45, 24%) based on culture conversion patterns. Despite universal culture negativity, 92 patients (49.2%) remained Xpert-positive and 78 (41.7%) remained smear-positive at month 6. Comparing the paired end-of-treatment specificities of Xpert (57.9%) and smear (64.2%) against culture negativity, McNemar's test yielded $\chi^2 = 7.84$, $p = 0.005$, indicating that smear had a statistically significantly higher specificity than Xpert at confirming cure.

By 5 months, most patients' cultures had become negative; nearly all who would eventually be cured had demonstrated culture conversion by this stage. (A tiny percentage of patients had isolated positive cultures at month 5, followed by a negative at month 6, indicating "possible success.") At month 5, GeneXpert remained highly sensitive - it was positive in nearly all patients who had any positive culture up to that point, but at the expense of many false positives among those whose cultures had cleared. Sputum smear was less sensitive than Xpert but more specific at this point.

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End-of-Treatment Outcomes: All patients exhibited negative cultures at the end of therapy (month 6 or 24 weeks), showing that there had been no bacteriological failures. Clinical and radiological evaluations confirmed therapeutic effectiveness in all instances, while some cavities persisted. We classified outcomes based on culture results: 133 patients (71%) met criteria for definite success (sustained culture negatives), 9 (5%) were probable successes (culture negative at last follow-up but with a missing final culture), and 45 (24%) were possible successes (only a single negative culture at the end, following prior positives or missing data). Figure 2 depicts the distribution of these result categories. Importantly, none of the patients had a confirmed culture failure at 6 months, despite the 45 "possible" cases indicating individuals with equivocal results who should be closely monitored post-treatment.

Summary Table of Paired Statistical Comparisons

Time Point	Test Comparison	χ^2 (McNemar)	p-value
Baseline sensitivity	Xpert vs. Smear	34.3	<0.001
Month 2 sensitivity	Xpert vs. Smear	8.10	0.004
End-of-Treatment specificity	Smear vs. Xpert	7.84	0.005

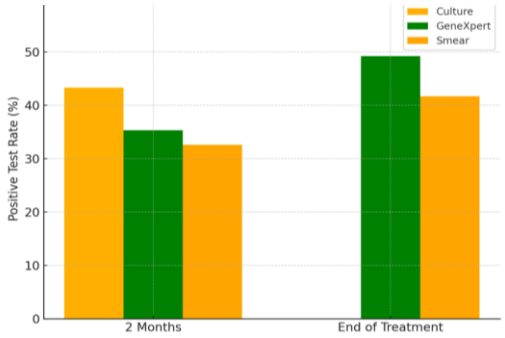

Figure 1: Positive Test Rates at 2 months and end of treatment

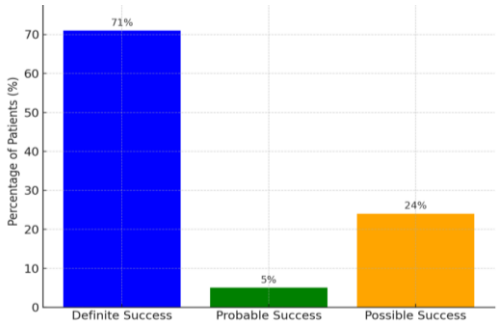

Figure 2: Treatment Outcomes in Cavitary TB Cohort (n=187)

Figure 1: Shows a comparison of positive test rates at two months and the completion of treatment. At two months, 43.3% of patients had positive cultures, up from 0% at the end of treatment. Smear and Xpert positive decreased for two months but recovered by the conclusion of treatment in the absence of culturable bacilli.

Figure 2: Treatment outcomes in the cavitary tuberculosis cohort (n=187). Defining success: ≥2 consecutive negative cultures, including at the end. Possible success: many negatives but no end-of-treatment culture. No patient had a positive culture after 6 months (failure)

Despite universal culture conversion, a sizable proportion of patients remained Xpert-positive and/or smear-positive at the conclusion of treatment. At month 6, GeneXpert MTB/RIF tested positive in 92 patients (49.2%), while smear microscopy remained positive in 78 patients (41.7%), despite all being culture-negative. These data show that both smear and Xpert can produce false-positive results (in terms of viable bacilli) after medication. In our study, late positive tests did not indicate treatment failure but rather the discovery of dead organisms. GeneXpert, for example, often detected DNA from non-viable bacilli. As a result, at the end of treatment, Xpert had 100% sensitivity (it detected all patients with signs of persisting infection) but only 57.9% specificity (almost half of cured patients tested Xpert-positive). The end-of-treatment PPV of Xpert was just 44.6% for real persistence (since no one had active disease, this statistic refers to predicting "possible/probable success" status), whereas the NPV was 73.7%. Chest X-ray abnormalities, on the other hand, delayed clinical response: 87 patients (46.5%) still had radiological cavities or infiltrates 6 months later, although they were culture-negative. Smear had higher specificity (about 64%) than Xpert at the end of therapy, but lower sensitivity (missing some patients with positive cultures earlier in treatment). A summary of the diagnostic performance of Xpert vs smear at baseline and end-of-treatment is provided in Table 1.

Table 1: Performance of sputum smear and Xpert MTB/RIF assay against culture in cavitary TB patients. ('Baseline' evaluation uses initial culture as reference; 'End-of-Treatment' evaluation uses 24-week culture outcome as reference for persistent disease.)

Time-point	Test	Sensitivity	Specificity	PPV	NPV
Baseline	Smear	28.3%	65.4%	27.9%	65.9%
(Diagnosis)	Xpert	91.7%	89.0%	79.7%	95.8%
End-of-Tx	Smear	~85%*	~64%*	~45%*	~72%*
(6 months)	Xpert	100.0%	57.9%	44.6%	73.7%

**Note: End-of-treatment smear metrics are approximate, as no true failures occurred; values estimated from patients with only a single final negative culture ("possible success") as a surrogate for incomplete response. Xpert values are from study data.*

Overall, GeneXpert MTB/RIF was considerably more sensitive than smear microscopy at all stages of treatment (especially for early detection), and it identified nearly all patients who had delayed culture conversion. However, its tendency to remain positive despite cultural negativity resulted in poorer specificity and PPV for monitoring cure. Sputum culture remained the definitive indicator of bacteriological status. No rifampicin resistance was detected by Xpert or culture during follow-up, confirming no emergent resistance in this cohort.

Discussion

In this study of cavitary pulmonary tuberculosis patients in Pakistan, we discovered that the GeneXpert MTB/RIF assay outperformed sputum smear microscopy in diagnosing TB and early detection of treatment response, but it also produced a significant number of false-positive results (compared to culture) by the end of therapy. To our knowledge, this is one of the first thorough evaluations in a high-burden environment of employing GeneXpert for therapy monitoring in cavitary tuberculosis, based on data from over 20 recent trials globally.

Consistent with previous studies, Xpert revealed high initial sensitivity in bacteriologically proven tuberculosis patients and much greater sensitivity than smear. At baseline, Xpert identified around 92% of culture-positive cases, consistent with meta-analyses indicating a pooled sensitivity of approximately 88% in pulmonary tuberculosis.[5] In contrast, smear microscopy found just 28% of culture-confirmed cases in our sample, highlighting the limits of smears in cavitary illness when compared to molecular techniques. A recent Chinese study found that Xpert had a higher overall detection rate of 66.8% compared to 56.0% for culture and 40.0% for smear, showing its better yield, particularly in smear-negative TB.[2] Similarly, an Indonesian multicenter investigation discovered that Xpert had a sensitivity of 98.4%, which was much greater than smears, leading to recommendations to use Xpert for first diagnosis.[4] Our results confirm similar tendencies in a Pakistani population,[6] demonstrating that Xpert is a useful diagnostic tool, even (or particularly) for patients with cavitary lesions, which often have large bacillary burdens. Interestingly, our group exhibited an unusually high female preponderance (93.6%), even though tuberculosis is often more frequent in men; this might be due to health-seeking practices or selection bias at our center, but it highlights the need for gender-sensitive TB initiatives in Pakistan.

We discovered that only 57% of patients had culture conversion after two months, implying that 43% still retained viable bacilli after the intense period. Cavitary tuberculosis is notorious for slower sputum sterilization, because large cavities harbor more bacilli and are often associated with delayed conversion and increased recurrence risk. Historically, sustained 2-month positivity (on smear or culture) and the presence of cavitation have been used to predict recurrence, and this concept has served as the foundation for prolonged treatment recommendations.[12] In our study, all patients reached culture-negative status by 6 months, although those with positive 2-month cultures were at risk for an adverse response (we classified several as “possible” successes, suggesting ambiguity in cure status). Monitoring technologies that detect these high-risk individuals early on are clinically significant.[18]

GeneXpert MTB/RIF was demonstrated to be a very sensitive early monitoring test, detecting 93% of cases that eventually had a prolonged recovery (as defined by culture-positive at 2 months or later). At 2 months, Xpert remained positive in virtually all patients with positive cultures (sensitivity ~92.7% for indicating delayed cure), exceeding smear (sensitivity ~70.7% at 2 months). This suggests that a negative Xpert result after 2 months of therapy is a strong indicator that the patient is on track for cure (in our data, more than 97% of patients who were Xpert-negative at 2 months achieved cure), whereas a persistently positive Xpert at 2 months indicates that the patient has an ongoing infection and may benefit from closer follow-up or prolonged therapy. Our results are consistent with prior research from Africa and Asia, indicating that early Xpert conversion (or a decline in its semi-quantitative “Ct” value) is associated with culture conversion and treatment success.[7] For example, Ather et al. (2020) discovered that Xpert conversion by week 8 predicts effective therapy with a high NPV.

One significant disadvantage we observed is GeneXpert’s low specificity in assessing treatment response, especially near the conclusion of therapy. At 6 months, over half of our patients had a positive Xpert test, despite being culture-negative and clinically cured. This phenomenon is well documented: the Xpert test may amplify DNA from dead or non-culturable bacilli found in sputum.[3] Our study found that around 49% of patients were Xpert-positive following therapy, which is consistent with previous findings. A South African study found that around 30–40% of patients might remain Xpert-positive for months following treatment.[8] Another study described a patient who remained Xpert-positive for up to two years after therapy despite having no active illness. The newer Xpert Ultra, although 5–17% more sensitive than the original Xpert, is even more prone to false positives owing to its capacity to identify trace DNA; studies suggest Ultra generates positive findings in 22% of patients after one month of therapy, compared to 9% with the conventional Xpert.[11] Ultra’s reduced specificity is due to the detection of non-viable bacilli from previous infections.[10,16] Thus, our findings confirm that a positive Xpert at the conclusion of treatment does not always imply active tuberculosis.[8] In our cohort, these false-positive Xpert findings would have no bearing on care since culture demonstrated that everyone was cured. However, in practice, an inexperienced physician might perceive a post-treatment Xpert “MTB detected” as an indication of failure or recurrence, potentially leading to unnecessarily extended therapy or harmful second-line medications. As a result, although Xpert is good at detecting tuberculosis at the outset, its positive predictive value for active disease decreases significantly after therapy begins.

In our study, GeneXpert’s specificity for predicting persistence at 6 months was ~58%, meaning roughly 1 in 5 Xpert-positive findings in follow-up turned out to be false positives due to residual DNA.[11] This parallels previous research: Theron et al. found that 1 in 5 Xpert-positive findings in retreatment patients were false positives owing to residual DNA,[11] which aligns with our observed specificity at 6 months.[13]

Our results on smears and culture are consistent with worldwide statistics. Our patients’ two-month sputum smear non-conversion rate was 33%, which is consistent with data from other high-burden nations where 20–30% of patients remain smear-positive after two months (particularly those with cavities or diabetes).[19] Our research found that cavitation had a negative influence on microbiological response, with a sputum culture conversion rate of around 57% after 2 months. This is somewhat lower than the ~80% observed in patients without cavitation under DOTS.[19] We also found that chest X-rays lagged behind microbiological clearance: 46% still had cavities on radiograph after 6 months, despite negative cultures. This demonstrates that radiographic recovery in tuberculosis may take longer, and that X-rays alone are inadequate to determine treatment effectiveness.[14,20]

Our findings are consistent with those of Mtafya et al, in Tanzania, who discovered that Xpert clearance is slower than culture clearance and concluded that Xpert is unsuitable as a standalone test-of-cure owing to continuous positives. Similarly, a Cochrane Review concluded that, although molecular testing has improved diagnosis, it cannot replace culture in proving therapy efficacy. On the other hand, research into quantitative Xpert “Ct” (cycle threshold) values has shown promise: reductions in Xpert signal correlate to decreasing bacterial load and may predict relapse better than qualitative results.[7] The developing molecular bacterial load assay (MBLA), which measures ribosomal RNA, has been shown to predict treatment outcomes more effectively than Xpert Ultra.[9] These innovative methods and biomarkers (including host-response gene signatures) are being investigated to fill the gap in therapy monitoring.

Our data highlight many aspects for physicians handling tuberculosis, especially cavitary patients. First, GeneXpert should be used at diagnosis for rapid, sensitive detection and medication resistance screening, which may improve patient outcomes by allowing for earlier treatment commencement. In our group, Xpert confirmed tuberculosis even in individuals who were originally culture-negative, avoiding missed or delayed diagnosis.[2,15] seconds, during therapy, a consistently positive Xpert (or smear) at 2 months in a cavitary patient should alert doctors to a greater risk of treatment failure or recurrence; these patients may benefit from prolonged therapy (as per WHO recommendations) or closer monitoring. In our analysis, individuals who were Xpert-positive after two months included virtually all of the “possible” success cases, suggesting they might benefit from an additional three months of therapy to achieve a definite cure. Patients who become Xpert-negative early in their treatment

may be able to avoid needless therapy extensions if other criteria (radiographic improvement, clinical status) are favorable. Third, neither sputum smear nor Xpert alone is a valid end-of-treatment test for cure.[11] A negative result (smear or Xpert) is comforting (high NPV for cure in our data), whereas a positive result is difficult to interpret and often reflects non-viable bacilli.[17] Thus, mycobacterial culture (or another measure of bacterial viability) remains the gold standard for confirming sterilization cure. Unfortunately, culture is time-consuming and resource-intensive, and it is not often performed at the end of treatment. Until more rapid diagnostics for treatment monitoring are proven (e.g., MBLA or other molecular/immunological biomarkers), a pragmatic strategy is to employ a mix of techniques, including clinical evaluation, radiography, and targeted Xpert and culture. Our findings support the notion that GeneXpert has potential as a treatment monitoring biomarker, particularly for identifying those who are unlikely to be cured if they remain Xpert-positive at intermediate points; however, it should be used in conjunction with culture or follow-up to distinguish live bacteria from dead.

Our study's strengths include a focus on a homogeneous cavitary TB cohort and the prospective collection of serial data across three diagnostic modalities. We also used strict definitions of outcomes and compared our results to a wide variety of recent research to improve generalizability. However, there are limitations. The sample size (n=187) was relatively small and obtained from a single site, which may restrict statistical power for subgroup analysis (for example, we could not stratify by cavity size or diabetes presence). We did not perform a quantitative analysis of Xpert cycle threshold values, which might have offered more insight into bacterial load dynamics. Furthermore, since no patient had confirmed failure by 6 months, we had to infer test performance in predicting "incomplete success" rather than actual relapse; a longer follow-up (12–24 months) would be required to determine whether those with "possible" or "probable" successes ultimately relapsed. Finally, all patients were rifampicin-susceptible; our findings may not directly apply to multidrug-resistant TB, where Xpert (including the MTB/XDR assay) may behave differently and culture conversion times are longer.

Conclusions

GeneXpert MTB/RIF is a highly sensitive molecular tool for detecting cavitary pulmonary tuberculosis and provides an earlier indication of treatment response than conventional smear microscopy. In our Pakistani cohort, GeneXpert rapidly identified patients with persistent infection, underscoring its potential as an adjunctive biomarker for therapeutic monitoring. Notably, patients who remained GeneXpert-positive after two months were significantly more likely to experience delayed culture conversion, suggesting the need for extended or intensified therapy in this subgroup. However, GeneXpert's specificity declines after prolonged treatment, as residual DNA from non-viable bacilli can yield false-positive results even when cultures are sterile. Thus, a positive GeneXpert result at treatment completion should not be interpreted alone as therapeutic failure. Culture or other viability-based assays remain essential for confirming microbiological cure in cavitary TB. We recommend integrating GeneXpert with mycobacterial culture for treatment monitoring, particularly in complex or slow-responding cases. For optimal management, GeneXpert should be performed at baseline to confirm diagnosis and rifampicin susceptibility, and repeated at two months to assess response. Persistent Xpert or smear positivity at this stage warrants culture, drug susceptibility testing, adherence reinforcement, and possible extension of the continuation phase up to nine months, given the higher bacillary burden and relapse risk in cavitary disease.

Author Information

1. Consultant Pulmonologist, PESSI Hospital, Islamabad 2. Consultant ENT Specialist, PESSI Hospital, Islamabad 3. Consultant Pulmonologist, THQ Hospital Jhumra, Faisalabad.

Corresponding author: Dr. Aisha Shafique ashque6@yahoo.com

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