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Original Article

Internal Medicine Section

# Correlation of Cartridge Based Nucleic Acid Amplification Test Grading Based on Cycle Threshold Value with Clinicoradiological Profile and Time to Culture Positivity in Pulmonary Tuberculosis Patients: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Tuberculosis (TB) remains a global health challenge, with India bearing the highest burden, including Multidrug-Resistant (MDR) TB. Early diagnosis is critical in controlling transmission, often achieved using GeneXpert *Mycobacterium tuberculosis*/Rifampicin (MTB/RIF), which detects TB bacilli, RIF resistance and provides Cycle Threshold (CT) values reflecting bacillary load. Correlating CT values with clinical, radiological and microbiological parameters can enhance the evaluation of disease severity and guide management.

**Aim:** To evaluate the correlation of Cartridge Based Nucleic Acid Amplification Test (CBNAAT) CT values with clinical, radiological and microbiological parameters to assess bacillary load and disease severity in pulmonary TB.

**Materials and Methods:** This cross-sectional study was conducted at Institute of Respiratory Diseases, Sawai Man Singh Medical College, Jaipur, Rajasthan, India from April 2023 to April 2024. Patients diagnosed with pulmonary TB based on CBNAAT were enrolled. The study period spanned 12 months. The study included 110 participants (calculated for 95% confidence, 80% power and 7.5% error, based on 62% smear-positive prevalence and 90.5% GeneXpert sensitivity). Eligible participants were adults (≥18 years) providing consent, including all sputum smear-positive cases and smear-negative suspects. Patients with extrapulmonary TB, undetectable sputum CBNAAT-MTB, and pregnant women were excluded. Data collected included name age, sex, symptoms and signs (cough, expectoration, fever, breathlessness, weight loss, chest pain, haemoptysis, clubbing, icterus, pallor, cyanosis, lymph node, oedema, chest examination), vitals (blood pressure, oxygen saturation, heart rate, temperature, respiratory rate, Body Mass Index (BMI), mid upper arm circumference) Bandim scores, co-morbidities and demography, Chest X-ray (CXR) grading, sputum fluorescent microscopy grading and time to positivity in liquid culture. Correlation analyses were performed using Spearman's rho and Pearson's tests. IBM Statistical Package for the Social Sciences (SPSS) version 29.0 was used for statistical analysis, and a p-value <0.05 was considered significant.

**Results:** The study included 110 patients, with the largest group (41) aged 21-40 years, followed by 30 patients in the 41-60 years age range. The mean age of the participants was 44.93±18.07 years. It demonstrated significant correlations between CBNAAT CT values and various diagnostic parameters. CBNAAT CT values were inversely correlated with Bandim scores (Spearman's rho=-0.82, p-value <0.001), chest X-ray grading (Pearson's r-value=-0.429, p-value=<0.001), and sputum fluorescent microscopy grading (Spearman's rho=-0.63, p-value=<0.005), indicating lower CT values were associated with higher bacillary loads. Conversely, a positive correlation was observed between CBNAAT CT values and liquid culture time to positivity. Bivariate analysis showed that high bacillary loads were significantly associated with higher Bandim scores, advanced chest X-ray grading and elevated sputum microscopy grading (p-value <0.05). Conversely, low bacillary loads were characterised by higher CBNAAT CT values, milder radiological findings and reduced sputum microscopy grading. These findings underscore the utility of these variables in distinguishing between low and high bacillary load cases.

**Conclusion:** CBNAAT CT values are strongly correlated with clinical, radiological and microbiological parameters in pulmonary TB. Lower CT values are indicative of higher bacillary loads, while higher CT values suggest lower bacillary loads. These findings highlight the potential of CBNAAT CT values as a surrogate marker for bacillary burden in pulmonary TB.


**Keywords:** Bacillary load, Bandim score, Chest X-ray grading, Sputum fluorescent microscopy grading

## INTRODUCTION

The TB constitutes a significant challenge to public health, with a global incidence of 10.6 million cases, out of which 3.0 million are reported in India, making it the country with the highest TB burden in the world. The incidence of laboratory-confirmed MDR TB globally stands at 167,000 cases, with India contributing one-third of this burden, amounting to 57,000 cases [1]. It's crucial to emphasise the control of TB transmission as a primary measure in reducing the burden, as transmission often occurs before the patient receives diagnosis and treatment, affecting numerous susceptible contacts. The World Health Organisation (WHO) recommends GeneXpert (Xpert) as a first-line diagnostic test for TB, serving as an alternative to smear microscopy. Xpert provides CT values, which may offer insights into the concentration of TB bacilli [2]. CT value is defined

as the number of amplification cycles required to reach a fixed background level of fluorescence, indicating the transition from a negative to a positive diagnostic result in real-time PCR [3].

Quantifying the mycobacterium load holds significance in determining disease severity, evaluating transmission risk and predicting treatment failure and relapse among pulmonary TB patients. The assessment of bacillary burden encompasses various methods such as grades of smear positivity, culture methods (TTCP), Bandim TB score and evaluating the severity of lesions observed on CXR [4-6].

The Bandim TB score involves a systematic assessment of five self-reported symptoms (cough, chest pain, dyspnoea, haemoptysis and night sweats) and six signs identified during examination (temperature >37°C, anaemia, pulse >90 beats/min, positive findings at lung auscultation, BMI <18.0 kg/$m_2$/<16.0 kg/$m_2$, and Mid-Upper Arm Circumference (MUAC) <220 mm/<200 mm). Based on this score, three Severity Classes (SCs) are determined: SC I (score 0–5), SC II (score 6-7), and SC III (score 8–13 points) [6].

Active Pulmonary TB typically manifests on CXR as focal or diffuse pulmonary infiltrates, consolidation, cavitation and nodular opacities [7]. The severity of the lesions is categorised into four groups: No lesion, minimal lesion, moderately advanced and far advanced, using the classification of the National Tuberculosis and Respiratory Disease Association of the USA [8].

Previous studies explored GeneXpert CT values for predicting smear status and mycobacterial load, CXR findings in paediatric TB and correlations between CT values and clinical scores like Bandim TB and Karnofsky Performance Score [9-11]. Additionally, CT value correlations with smear, culture time-to-positivity and clinical factors have also been examined [12].

This study, conducted in Jaipur, aims to expand upon this research by establishing correlations between CBNAAT CT value, clinical (Bandim score) and radiological presentations, sputum fluroscent microscopy grading and liquid culture time to positivity, providing a more comprehensive understanding of TB bacilli burden and validating CT values as reliable indicators of disease severity.

## MATERIALS AND METHODS

This hospital-based cross-sectional observational study was conducted over one year (from 12/04/2023 to 11/04/2024) at the Institute of Respiratory Diseases, Sawai Man Singh Medical College, Jaipur, Rajasthan, India. Necessary permission was taken from Ethical Committee and Research Review Board of Sawai Man Singh Medical College, Jaipur (316/MC/EC/2023). The study investigated the relationship between CBNAAT grading, based on CT values and clinical presentations, radiological findings, sputum fluoroscent microscopy and time to culture positivity in pulmonary tuberculosis patients.

**Inclusion criteria:** Individuals aged 18 years and above who provided written informed consent. All diagnosed cases with sputum smear-positive results and all individuals suspected of having TB with sputum smear-negative results were included in the study.

**Exclusion criteria:** Individuals with extrapulmonary TB, if the sputum CBNAAT-MTB test did not detect the presence of MTB, or if they were pregnant women were excluded from the study.

**Sample size:** The sample size was calculated to be 110 cases, with a confidence interval of 95% and study power of 80%, considering an allowable error of 7.5%. This calculation is based on the prevalence of smear-positive patients at 62% and the assumed sensitivity of the GeneXpert CT test at 90.5% [9].

**Outcome variables:**

- Clinicoradiological profile: Presenting symptoms, physical examination findings (Bandim Score) and radiological assessments.
- Sputum AFB microscopy grading : Evaluated using auramine thiazine red staining.
- CT value of CBNAAT: Recorded for each sample.
- Time to culture positivity: Measured in days from sample collection to positive culture growth.

**Clinical evaluation:** Patients underwent clinical evaluation for TB, encompassing symptom assessment (cough, fever, dyspnoea, haemoptysis, night sweats), detailed medical history (smoking, alcohol, diabetes) and comprehensive physical examination (pallor, lung sounds, MUAC, BMI, vitals). These findings were used to determine the Bandim TB score, a tool classifying TB severity into three classes (SC I, II, III) based on five self-reported symptoms and six examination signs (temperature, anaemia, pulse, auscultation, BMI, MUAC) [6].

**Radiological evaluation:** Chest radiographs were obtained for all patients to assess pulmonary involvement in TB. Radiographic findings, typically manifesting as focal or diffuse infiltrates, consolidation, cavitation and nodular opacities, were classified according to lesion severity [7]. Categories included mild disease (no and minimal lesion) and severe disease (moderate, and far advanced lesion) using the classification system of the National Tuberculosis and Respiratory Disease Association of the USA [8]. This classification aids in evaluating the extent of pulmonary involvement and helps establish correlations with clinical and microbiological findings.

**Microbiological evaluation:** Sputum samples were collected in sterile containers. Two aliquots are prepared from each sample.

**CBNAAT processing:** One sample underwent CBNAAT testing (GeneXpert), which allows for the detection of *Mycobacterium tuberculosis*, determination of RIF resistance status and provides CT values indicating the bacterial load. The results are categorised as very low (28<CT≤38), low (22<CT≤28), medium (16<CT≤22), and high (CT ≤16) based on the CT value for MTB detection [13].

**Fluorescent microscopy and culture:** Sputum samples were stained with auramine-thiazine red for AFB detection and graded as follows:

Fluorescent Microscopy Grading (Union/WHO Scale, 400X magnification, 1 length of 2 cm=40 fields) [14]:

- Negative: Zero AFB/1 length (40 fields)
- Scanty: 1-19 AFB/1 length (40 fields) (Confirmation required if <3 AFB/1 length)
- 1+: 20-199 AFB/1 length (40 fields)
- 2+: 5-50 AFB/1 field
- 3+: >50 AFB/1 field

This grading system quantifies bacterial load, aiding in assessing disease severity, treatment response and potential drug resistance. Samples were also cultured on Middlebrook 7H9 medium (NALC-NaOH method) at 37°C for up to six weeks, with growth identified by serpentine cording and confirmed by MPT64 antigen detection [15].

**Data management:** Data from clinical evaluations, radiological assessments and microbiological results were entered into a secure database. Unique identifiers ensure patient confidentiality.

## STATISTICAL ANALYSIS

Statistical tests, including the Chi-square test for categorical data and Pearson or Spearman correlations were used to analyse the relationships between variables IBM SPSS version 29.0 was used for statistical analysis. The main emphasis was on examining the correlation between CBNAAT CT values, sputum fluorescent microscopy grades and liquid culture time to positivity. Statistical significance was considered for p-values <0.05.

## RESULTS

The 110 participants were distributed across the following age groups: 0-20 years (9.09%, n=10), 21-40 years (37.27%, n=41), 41-60 years (27.27%, n=30), 61-80 years (23.63%, n=26), and 81-100 years (2.72%, n=3), with the majority (41) falling into the 21-40 years of age range, followed by 30 in the 41-60 years age range. The mean age of the patients was 44.93±18.07 years. Detailed demographic information is available in [Table/Fig-1].

The presenting complaints of the participants, broken down by gender, were as follows: cough {76 males (100%), 31 females (91.18%); total 107 (97.27%)}, dyspnoea {41 males (53.95%), 19 females (55.88%); total 60 (54.55%)}, night sweats/fever {47 males (61.84%), 18 females (52.94%); total 65 (59.09%)}, haemoptysis {21 males (27.63%), 11 females (32.35%); total 32 (29.09%)}, and chest pain {20 males (26.32%), 8 females (23.53%); total 28 (25.45%)}.

The most common symptom reported was cough, followed by fever in males and dyspnoea in females [Table/Fig-2].

Patients without fever had higher GeneXpert CT values, longer culture times, and slightly lower smear positivity compared to patients with fever. Additionally, patients without dyspnoea had higher GeneXpert CT values, similar culture times, and slightly lower smear positivity compared to patients with dyspnoea as shown in [Table/Fig-3].

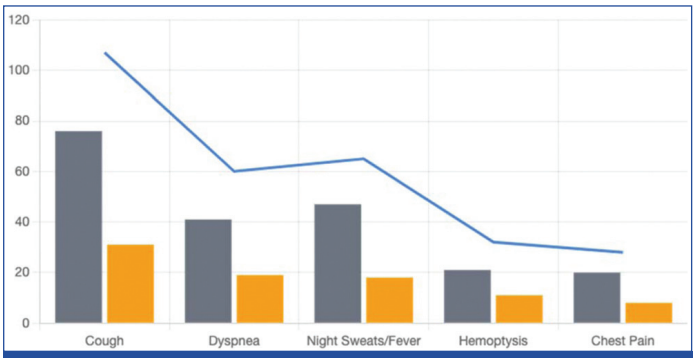
Furthermore, patients with Bandim TB scores ranging from 0 to 5 had an average GeneXpert CT value of approximately 24.12. In the 6 to 7 score range, the GeneXpert CT value decreased significantly to about 16.02. For the highest Bandim TB score of 8 to 13, the GeneXpert CT value further decreased slightly to 15.60. These findings indicate a negative correlation between the Bandim TB Score and the GeneXpert CT Value with rho -0.82 and p-value <0.001, as detailed in [Table/Fig-4,5].

Among the total cases, 52.7% (58 cases) were categorised as severe TB based on chest X-ray findings, comprising 'Moderately Advanced' and 'Far Advanced' gradings. Additionally, 47.3% (52 cases) were classified as Mild TB, including 'Minimum' and 'No lesion' gradings. It is noteworthy that a higher number of mild cases are associated with medium and low GeneXpert CT categories, while severe TB cases are more prevalent in the high and medium GeneXpert categories indicating a negative correlation between GeneXpert CT value and disease severity based on CXR, with r value -0.429 and a significant p-value of <0.001, as indicated in [Table/Fig-6,7].

Out of 110 patients, 88 tested positive for sputum fluorescent microscopy, while 22 tested negative, as illustrated in [Table/Fig-8,9]. There was a negative correlation between GeneXpert CT value and sputum fluroscent microscopy grading, as the GeneXpert CT value decreases, the sputum fluroscent microscopy grading increases from negative to positive, indicating a negative correlation between the two with r value of -0.63 and p-value <0.05.

| Category | Subcategory | n (%) |
|---|---|---|
| Age statistics (years) | Mean±SD | 44.93±18.07 |
| | Median | 46 |
| | Range | 18-89 |
| Gender distribution | Males | 76 (69.1) |
| | Females | 34 (30.9) |
| Residence | Urban | 53 (48.18) |
| | Rural | 57 (51.82) |
| Health status | New cases | 66 (60) |
| | Recurrent | 44 (40) |
| | H/O smoking (Yes) | 54 (49.09) |
| | H/O Alcohol Intake (Yes) | 31 (28.18) |
| | HIV positive | 3 (2.7) |
| | Diabetic | 12 (10.9) |

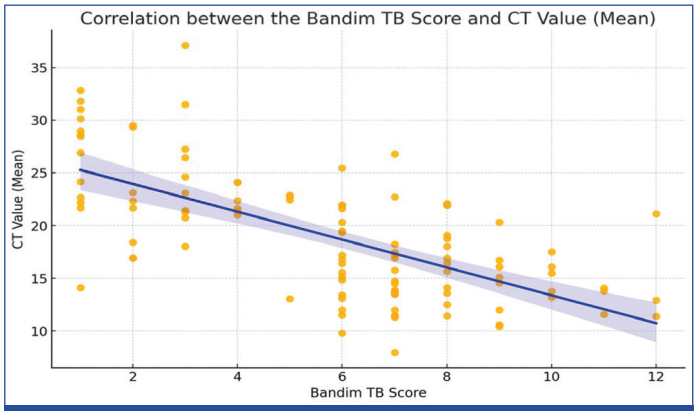
**[Table/Fig-1]:** Demographics of patients who participated in the study.




**[Table/Fig-2]:** Symptom distribution by gender.

| | Bandim score severity | | | Kruskal-Wallis test | | |
|---|---|---|---|---|---|---|
| | 0 to 5 | 6 to 7 | 8 to 13 | $\chi^2$ | p-value | Spearmans (ρ) |
| CT value Mean±SD | 24.12± 5.15 | 16.02± 4.33 | 15.60± 3.44 | 49.696 | <0.001 | -0.82 (p-value <0.001) |

**[Table/Fig-4]:** Comparison and correlation of the 3 Subgroups of Bandim TB Score-category with GeneXpert CT value.




**[Table/Fig-5]:** Scatter plot between Bandim Score and GeneXpert CT Value (n=110), (Spearmans rho=-0.82) and (p-value=<0.001).

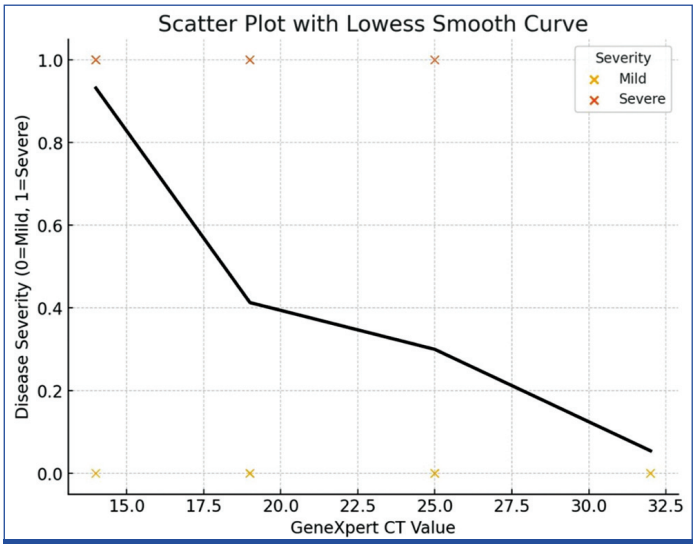
| Variable | Category | GeneXpert CT value median | | Liquid culture time to positivity median | | Sputum fluroscent microscopy grading | |
|---|---|---|---|---|---|---|---|
| | | (IQR) | p-value | (IQR) | p-value | N (%) | p-value |
| Fever | No | 21.6 (16.7-24.2) | <0.001 | 20.0 (14.0-24.0) | 0.002 | 65 (59.1) | 0.06 |
| | Yes | 15.1 (13.1-18.2) | | 15.0 (13.0-18.0) | | 45 (40.9) | 0.06 |
| Dyspnoea | No | 20.3 (16.2-22.6) | 0.03 | 18.0 (14.25-23.0) | 0.15 | 50 (45.5) | 0.42 |
| | Yes | 16.4 (13.6-22.0) | | 15.5 (13.0-21.0) | | 60 (54.5) | 0.42 |
| Cough | Yes | 18.040 (13.9-22.3) | 0.77 | 17.0 (14.0-22.0) | 0.80 | 107 (97.3) | 0.97 |
| | No | 14.1 (13.6-21.5) | | 14.0 (12.5-22.0) | | 3 (2.7) | 0.97 |
| Treatment status | New | 17.2 (14.6-21.9) | 0.95 | 16.5 (14.0-21.75) | 0.90 | 66 (60.0) | 0.35 |
| | Re-current | 19.9 (13.7-22.8) | | 18.0 (14.0-22.0) | | 44 (40.0) | 0.35 |

**[Table/Fig-3]:** The univariate analysis of clinical variables associated with "GeneXpert CT value", "Liquid culture time to positivity (days)", and "Sputum Fluroscent Microscopy Grading".

Present study found that out of 110 cases, the highest percentage of culture positivity (48.18%) was observed in the 14-21 days group.

| GeneXpert CT value | Mild TB | Severe TB | Chi-sq and p-value | r-value |
|---|---|---|---|---|
| Very low (28<CT≤38) | 10 | 0 | 35.44 (p-value <0.001) | -0.429 (p-value=<0.001) |
| Low (22<CT≤28) | 14 | 10 | | |
| Medium (16<CT≤22) | 23 | 18 | | |
| High CT ≤16 | 5 | 38 | | |
| Total | 52 | 58 | | |

**[Table/Fig-6]:** The analysis of the GeneXpert CT value and disease severity on CXR Grading, with r value -0.429 and a significant p-value of <0.001.



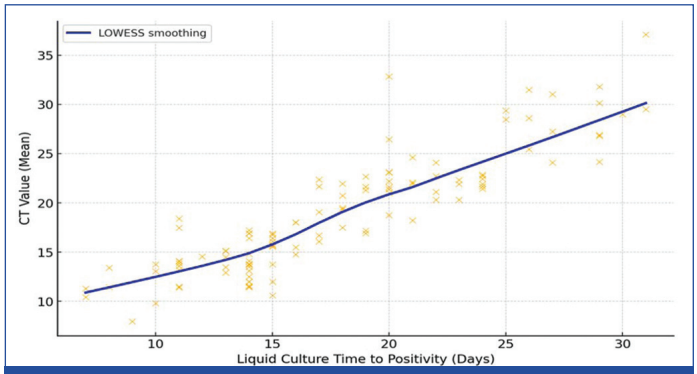

**[Table/Fig-7]:** Scatter plot between GeneXpert CT value and disease severity on CXR basis (r value -0.429) and (p-value <0.001).

positivity times and higher MTB detection levels, while longer times correlate with lower detection levels as illustrated in [Table/Fig-10].

| Liquid culture time to positivity category (days) | Very low (28<CT≤38) | Low (22<CT≤28) | Medium (16<CT≤22) | High CT ≤16 | r-value |
|---|---|---|---|---|---|
| <14 | 0 | 0 | 3 | 20 | 0.67 (p-value <0.001**) |
| 14-21 | 1 | 7 | 24 | 21 | |
| 21-28 | 4 | 10 | 11 | 0 | |
| >28 | 6 | 3 | 0 | 0 | |

**[Table/Fig-10]:** Distribution and correlation of liquid culture time to positivity and GeneXpert CT value.

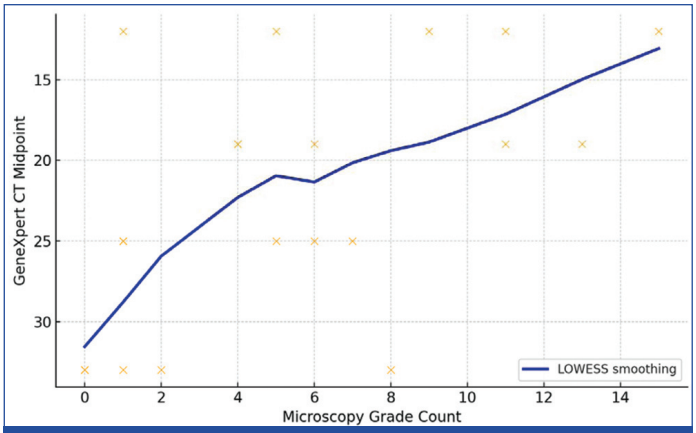
The scatter plot in [Table/Fig-11] depicts a positive correlation between the GeneXpert CT value and the liquid culture time to positivity. As the days increase, the GeneXpert CT value also tends to increase.




**[Table/Fig-11]:** Scatter Plot of GeneXpert CT value vs liquid culture time to positivity (days) r-value 0.67.

| GeneXpert CT value | Sputum fluorescent microscopy grading | | | | | | p-value (Chi-square test) | Pearson correlation coefficient (r value) |
|---|---|---|---|---|---|---|---|---|
| CT value category | Negative | Scanty | 1+ | 2+ | 3+ | Total | 0.00059* | -0.63 (p-value <0.001**) |
| Very Low (28<CT≤38) | 8 (7.3%) | 2 (1.8%) | 1 (0.9%) | 0 | 0 | 11 (10.0%) | | |
| Low (22<CT≤28) | 5 (4.5%) | 7 (6.4%) | 6 (5.5%) | 1 (0.9%) | 1 (0.9%) | 20 (18.2%) | | |
| Medium (16<CT≤22) | 4 (3.6%) | 6 (5.5%) | 13 (11.8%) | 11 (10.0%) | 4 (3.6%) | 38 (34.5%) | | |
| High (CT ≤16) | 5 (4.5%) | 1 (0.9%) | 9 (8.2%) | 11 (10.0%) | 15 (13.6%) | 41 (37.3%) | | |
| Total | 22 (20.0%) | 16 (14.5%) | 29 (26.4%) | 23 (20.9%) | 20 (18.2%) | 110 (100.0%) | | |

**[Table/Fig-8]:** Comparison between semiquantitative mycobacterial load defined by GeneXpert CT value: Very low (28<CT≤38), Low (22<CT≤28), Medium (16<CT≤22) and High (CT ≤16) and Sputum Fluorescent Microscopy Grading.




**[Table/Fig-9]:** Scatter plot of GeneXpert CT value vs sputum fluroscent microscopy grading r value of -0.63 and p-value <0.001.

In this group, the GeneXpert CT grading was medium in 26 cases and high in 23 cases. For cases with culture positivity in less than 14 days, 20.9% showed high GeneXpert CT grading. In contrast, for cases with culture positivity in more than 28 days, only 8.18% showed very low GeneXpert CT grading. These findings suggest a correlation (r-value=0.67, p<0.001) between quicker culture

In the bivariate regression analysis, significant associations were found between several parameters and bacillary load in TB patients. A shorter liquid culture time to positivity (low vs. high) was significantly associated with a higher bacillary load (B=9.46, 95% CI: 8.09-10.84, p-value <0.001). Higher sputum fluroscent microscopy grades (1+, 2+, 3+, Scanty vs. negative) were significantly associated with increased bacillary load (B=2.3, 95% CI: 1.8-2.8, p-value=0.02). Higher Bandim scores (reflecting increased clinical severity) were significantly associated with elevated bacillary load (B=1.5, 95% CI: 1.2-1.8, p-value=0.03). Severe TB (moderate to far advanced lesions) on chest X-ray was significantly associated with higher bacillary load compared to mild TB (minimal or no lesions) (B=3.7, 95% CI: 3.2-4.2, p-value=0.04) as shown in [Table/Fig-12].

## DISCUSSION

The relationship between Bandim TB scores and GeneXpert CT values indicates a strong connection between TB severity and bacterial load. Cases with Bandim scores ranging from 0 to 5, representing milder symptoms, had an average CT value of 24.12±5.15. In contrast, those with scores of 6 to 7, indicating moderate severity, showed an average CT value of 16.02±4.33, while the most severe cases (scores of 8 to 13) demonstrated an

| Variable | Category | Beta coefficient (B) | 95% CI | p-value |
|---|---|---|---|---|
| Liquid cultures time to positivity (days) | Low (ref: High) | 9.461785 | (8.089-10.835) | <0.001** |
| Sputum fluroscent microscopy grading | 1+, 2+, 3+, Neg, Scanty | 2.3 | (1.8-2.8) | 0.02* |
| Bandim score | 0 to 5, 6 to 7, 8 to 13 | 1.5 | (1.2-1.8) | 0.03* |
| CXR Grading | Mild TB (minmum, no lesion), Severe TB (moderate, far advance) | 3.7 | (3.2-4.2) | 0.04* |

**[Table/Fig-12]:** Bivariate regression of GeneXpert CT value with liquid culture time to positivity, sputum fluorescent microscopy grading, bandim score and CXR grading.

average CT value of 15.60±3.44. This pattern suggests that as TB symptoms worsen, the bacterial load increases, as evidenced by the decreasing CT values. The variability in the interquartile range for each score category emphasises the range of results, and the Kruskal-Wallis test ($\chi^2$=49.696, rho -0.82, p-value <0.001) confirms a statistically significant difference in CT values across the Bandim TB score categories, indicating a strong inverse relationship between CT values and backerial load.

The study conducted by Sarkar K et al., demonstrated a strong inverse correlation between Bandim TB scores and mean CT values, with statistical significance (rho=-0.82, p-value <0.001). The decrease in median CT values across severity subgroups underscores the effectiveness of Bandim scores in accurately reflecting disease progression [11].

Additionally, patients with severe TB (moderately advanced lesion and far advanced lesion) typically present with lower CT values, indicating higher bacterial loads, while those with mild disease (no lesion and minimal lesion) display a wider range of CT values, including more instances of higher values. This significant difference underscores the potential of GeneXpert CT values in assessing TB severity. Advanced TB patients generally exhibit lower CT values, pointing to a higher bacterial load, whereas those with milder forms show a wider range of CT values, including more instances in the lower ranges. This notable distinction highlights the utility of GeneXpert CT values as a crucial diagnostic tool for distinguishing between mild and severe TB cases.

In a study conducted by Behzadmehr R and Nejadkehkha E revealed a significant increase in the frequency of cavitation presentation with higher grading of smears (1+, 2+, and 3+), while the frequency of reticulonodular presentations decreased significantly [16]. Additionally, Awang H et al., identified a strong association between positive pretreatment AFB sputum smear results and severe pulmonary TB, particularly in children and adolescents [10]. Similarly, Martin-Higuera et al., found that cavitation was linked to a higher bacillary burden, indicating more severe disease. The severity of pulmonary TB is closely tied to the extent of lung lesions or the presence of cavitation, with larger cavities correlating with a higher bacilli count and increased risk of transmission. GeneXpert CT values not only reflect the size of lesions or cavities but also serve as a direct measure of a patient's infectiousness and disease severity [12].

A negative correlation was identified between the mean GeneXpert Ct values and sputum fluroscent microscopy grading, indicating that as the GeneXpert Ct values decreses, the sputum fluroscent microscopy grading transitions from negative to positive. This suggests that higher levels of *Mycobacterium tuberculosis* detection correspond with an increased probability of a positive sputum grading result. Such a correlation highlights the importance of GeneXpert Ct values in predicting sputum grading, which is crucial for evaluating bacterial load and is significant for the diagnosis and management of TB.

The study by Fradejas I et al., highlighted that samples from smear-negative patients had a higher mean CT value compared to those from smear-positive patients, indicating a lower bacterial load in smear-negative cases [9]. Similarly, Kashyap B et al., reported a strong correlation between CT values and smear grades, demonstrating that higher smear grades were associated with lower GeneXpert CT values [17].

Furthermore, high bacterial loads, indicated by low CT values, were found to be associated with shorter liquid culture time to positivity (TTCP) of 0-14 and 14-21 days, while lower bacterial loads, reflected by high CT values, corresponded to longer TTCP of 21-28 days and beyond. This suggests that GeneXpert CT values can be an effective measure of bacterial load in TB patients, allowing clinicians to evaluate disease severity more efficiently and make timely treatment decisions.

In a related study, Khalil MM et al., found a significant relationship between CBNAAT grading and positive culture results, with median CT values decreasing as microscopy grades improved. Additionally, a significant inverse relationship was noted between Time to Culture Positivity and CBNAAT grading [18]. Beynon F et al., also supported the idea that Xpert MTB/RIF CT values serve as a reliable indicator of bacillary burden, correlating well with smear grades and moderately with Time to Positivity in liquid cultures [19].

The scatter plot from the current study illustrates a clear positive correlation between mean GeneXpert CT values and Liquid Culture Time to Positivity in days, emphasising the potential of GeneXpert CT values as a predictive tool for bacterial load and TTCP. This finding is crucial for assessing TB severity and guiding timely treatment interventions.

### Limitation(s)

This study has several limitations. First, it was a single-centre study conducted at a tertiary care hospital, which may limit the generalisability of the findings to other settings. Second, the observational design of the study limits the ability to draw causal inferences. Third, the sample size was relatively small, which may have reduced the statistical power of the study. Future research should address these limitations by conducting multi-center studies with larger sample sizes and using experimental designs to establish causal relationships.

## CONCLUSION(S)

This cross-sectional study provides robust evidence that the CBNAAT (GeneXpert) CT value is a meaningful surrogate marker for bacillary load and disease severity in pulmonary TB. A strong inverse correlation was observed between CBNAAT CT values and Bandim TB scores, chest X-ray severity grading and sputum fluorescent microscopy grading, indicating that lower CT values correspond to higher bacillary burden and greater clinical and radiological disease severity. Similarly, lower CT values were significantly associated with shorter time to culture positivity, further reinforcing their role as indicators of higher bacterial load. Present study findings highlight that CT values can reliably differentiate between low and high bacillary load cases, offering a rapid, objective and quantifiable method to assess TB severity. This can aid clinicians not only in diagnosing TB but also in stratifying patients according to disease severity, monitoring progression and prioritising those who may benefit from more intensive management or closer follow-up. Moreover, incorporating CT values into routine reporting could enhance the precision of TB care, especially in high-burden settings where timely treatment initiation is critical to curbing transmission and improving outcomes.

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