

DIAGNOSTIC ROLE OF GENE XPERT IN SUSPECTED CHILDHOOD PULMONARY TUBERCULOSIS

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Abstract

Background: Childhood pulmonary tuberculosis (TB) poses diagnostic challenges due to its atypical presentation and paucibacillary nature. This prospective study investigates the Diagnostic Role of Gene Xpert in Suspected Childhood Pulmonary Tuberculosis. **Material & Methods:** We enrolled 150 pediatric cases (6 months to 12 years) based on clinical, radiological, and Mantoux test criteria. Specimens included gastric aspirate, sputum, and pleural fluid, analyzed by Gene Xpert and Acid-Fast Bacilli (AFB) staining. **Results:** In 150 pediatric cases, Gene Xpert demonstrated an 8.0% positivity rate, outperforming Acid-Fast Bacilli (AFB) staining. Sensitivity was 25%, specificity reached 100%, with a positive predictive value of 100% and a negative predictive value of 93.88%. Comparison with Mantoux test and AFB results highlighted Gene Xpert's superiority, emphasizing its role in enhancing diagnostic precision for childhood pulmonary tuberculosis. Ongoing research is crucial for addressing challenges and optimizing sensitivity. **Conclusion:** Gene Xpert enhances diagnostic precision in childhood pulmonary TB, providing reliable results with high specificity. Challenges persist in achieving optimal sensitivity, emphasizing the need for ongoing research.

INTRODUCTION

In the dynamic landscape of pediatric health, where the intricacies of childhood diseases demand constant scrutiny, childhood pulmonary tuberculosis (TB) stands out as a formidable global health challenge.^[1] Caused by *Mycobacterium tuberculosis*, the impact of TB on children, often underestimated, beckons for meticulous investigation. It is within this context that our present study undertakes a profound exploration into the Diagnostic Role of Gene Xpert, a cutting-edge nucleic acid amplification test, in suspected cases of childhood pulmonary tuberculosis.^[2]

Childhood TB presents a unique set of challenges, primarily attributed to its atypical clinical presentation, paucibacillary nature, and the inherent difficulties associated with obtaining appropriate samples for accurate diagnosis.^[3] Traditional diagnostic methods, such as sputum smear microscopy and culture, which find widespread application in adult cases, exhibit limitations when extrapolated to the pediatric population.^[4] The inadequacies of these conventional approaches in capturing the elusive nature of childhood TB underscore a pressing need for more sensitive and

efficient diagnostic tools tailored to the specific nuances of pediatric cases.^[4]

The advent of molecular diagnostic techniques has ushered in a new era in the realm of tuberculosis diagnosis, offering a ray of hope in overcoming the challenges posed by childhood TB. Gene Xpert, a nucleic acid amplification test, stands out as a beacon of promise, holding the potential to unravel the diagnostic intricacies inherent in childhood pulmonary TB.^[5] This automated, cartridge-based system facilitates the rapid and simultaneous detection of *Mycobacterium tuberculosis* and rifampicin resistance, ushering in a paradigm shift in the diagnostic approach to childhood TB.^[6]

The crux of our study lies in the meticulous evaluation of the Diagnostic Role of Gene Xpert in suspected cases of childhood pulmonary tuberculosis. By delving into the sensitivity, specificity, and overall diagnostic accuracy of Gene Xpert in a pediatric cohort, our aim is to make a substantive contribution to the ongoing discourse surrounding childhood TB diagnosis. The significance of our research extends beyond the academic realm; it holds the potential to enhance diagnostic precision and, consequently, impact clinical decision-making significantly. This becomes particularly crucial in resource-limited settings

where prompt and accurate diagnosis becomes a lifeline for effective disease management.^[7]

The exploration of the Diagnostic Role of Gene Xpert in Suspected Childhood Pulmonary Tuberculosis is not merely an academic endeavor; it represents a critical intersection of technology and pediatric healthcare. Our pursuit extends beyond the realm of theoretical knowledge, aiming to generate tangible insights that can directly inform and transform clinical practice. The ultimate goal is to catalyze improved outcomes for the youngest victims of this age-old malady, aligning technological advancements with compassionate healthcare practices. As we unravel the potential of this molecular diagnostic tool, our commitment remains steadfast, driven by the conviction that our findings can pave the way for a brighter, healthier future for children grappling with the challenges of childhood pulmonary tuberculosis.

MATERIALS AND METHODS

Study Setting: This prospective analytical study was conducted at the Institute of Pediatrics, Government Rajaji Hospital, Madurai, in collaboration with the Department of Thoracic Medicine and Institute of Microbiology at Madurai Medical College. The study aimed to investigate the Diagnostic Role of Gene Xpert in childhood pulmonary tuberculosis.

Study Period: The study was conducted over a period of one year to ensure systematic data collection and analysis. The study period spanned from August 2017 to July 2018.

Study Participants

The participants included both in-patients and out-patients aged between 6 months to 12 years who exhibited suspected pulmonary tuberculosis based on the national childhood TB diagnostic algorithm.

Inclusion Criteria

All suspected cases of pulmonary TB aged between 6 months to 12 years were considered eligible based on the following criteria

Clinical Criteria

- Fever and/or cough persisting for more than 2 weeks
- Unexplained loss of weight or failure to gain weight; loss defined as more than 5% of the recorded weight in the past three months
- History of contact with a suspected or diagnosed TB case within the last 2 years
- Children with persistent pneumonia

Radiological Features

- Primary complex
- Hilar, paratracheal, subcarinal lymphadenopathy
- Consolidation
- Pleural effusion
- Collapse
- Calcification
- Bronchiectasis
- Miliary spread

Tuberculin Skin Test: 5 TU purified protein derivative (PPD) used. Mantoux's test or PPD skin test considered positive if the induration is 10 mm or more.

Exclusion Criteria

Individuals known to be on TB treatment were excluded from the study. Participants were selected through a systematic approach following the national childhood TB diagnostic algorithm.

Study Methodology: The diagnostic evaluation involved obtaining specimens through two methods:

1. Early Morning Gastric Aspirate: The child fasted for approximately 6 hours, and an appropriately sized intra-gastric tube was used for sample collection. The aspirate was drawn from the stomach, followed by washing with 15-30 ml saline.
2. Sputum: Two consecutive days of early morning sputum samples were collected and subjected to smear microscopy and nucleic acid amplification test (Gene Xpert test).

Statistical Analysis

The data analysis was carried out using IBM SPSS version 25. We employed the chi-square test for cross-tabulations and kappa statistics to predict the k value. This statistical approach aimed to assess the diagnostic accuracy of Gene Xpert in childhood pulmonary TB cases.

Ethical Issues

The study strictly adhered to ethical considerations. Informed consent was obtained from parents or guardians, and suspected participants were included in the study only after ethical approval. The research followed ethical guidelines, ensuring the rights and well-being of the pediatric participants were protected throughout the study.

RESULTS

In this prospective analytical study, the study cohort's age distribution showcased a mean age of 6 years, ranging from a minimum of 4/12 years to a maximum of 12 years, illustrating the diversity in age within the participants (Standard Deviation = 3.74). Among the 150 participants, the gender distribution was nearly balanced, with 74 males (49.3%) and 76 females (50.7%). The study primarily focused on children aged 6 months to 12 years presenting with suspected pulmonary tuberculosis, identified through the national childhood TB diagnostic algorithm.

Further exploration of demographic characteristics unveiled that 17.3% of participants had a history of contact with tuberculosis patients, while 82.7% did not report such contact. Additionally, 71.3% of participants exhibited a visible BCG scar. The Mantoux test, a vital diagnostic criterion, yielded a positive result in 24.0% of cases. Radiological findings before treatment included heterogeneous opacity (n=91), pleural effusion (n=18), hilar adenopathy (n=2), and a normal X-ray in 39 cases.

Specimen analysis revealed that the majority (n=133) were gastric aspirates, followed by sputum (n=17) and pleural fluid (n=17). Acid-Fast Bacilli (AFB) staining results indicated a low positive rate (2.0%), with 147 participants (98.0%) testing negative. Notably, GeneXpert results demonstrated an 8.0% positivity rate, underscoring its potential to enhance diagnostic accuracy. The comparison between GeneXpert and AFB results revealed a kappa value of 0.4, signifying good agreement. Regarding treatment initiation, 22.0% of participants (n=33) commenced Anti-Tuberculosis Treatment (ATT), while 78.0% (n=117) did not. Among those on treatment, AFB staining was positive in 3 cases, while GeneXpert identified 12 positive cases, indicating a higher yield for GeneXpert. Additionally, 20 patients positive for the Mantoux

test were initiated on ATT; however, the comparison with GeneXpert results revealed disparities, with only 9 cases showing agreement. [Tables 1-3] offer a detailed comparison between GeneXpert and AFB staining results, providing valuable insights into their respective diagnostic performances for various specimen types. The results underscore the potential of GeneXpert as a more sensitive tool in the diagnosis of childhood pulmonary tuberculosis. Gene Xpert exhibited 8.0% positivity, outperforming AFB staining. Sensitivity was 25%, specificity 100%, positive predictive value 100%, and negative predictive value 93.88%. Comparison with Mantoux test and AFB results demonstrated Gene Xpert's superiority in diagnosing pediatric TB.

Table 1: Comparison between results from GeneXpert and AFB results for all samples

AFB result	GeneXpert		Total	k- value
	Positive	Negative	N (%)	
Positive	3 (100.0)	0 (0.0)	3 (100.0)	0.4
Negative	9 (6.1)	138 (93.9)	147 (100.0)	

Table 2: Comparison between results from GeneXpert and AFB results for gastric aspirate

AFB result	GeneXpert		Total	k- value
	Positive	Negative	N (%)	
Positive	3 (100.0)	0 (0.0)	3 (100.0)	0.2
Negative	9 (6.1)	138 (93.9)	147 (100.0)	

Table 3: Comparison between results from GeneXpert and AFB results for sputum

AFB result	GeneXpert		Total	k- value
	Positive	Negative	N (%)	
Positive	2 (100.0)	0 (0.0)	2 (100.0)	1
Negative	0 (0.0)	14 (100.0)	14 (100.0)	

DISCUSSION

Pediatric tuberculosis (TB) presents a formidable challenge in diagnosis due to the absence of distinctive clinical features and limitations associated with traditional diagnostic methods.^[8] In our prospective analytical study, we aimed to assess the efficacy of the Xpert TB assay in children suspected of pulmonary TB, employing respiratory specimens, gastric aspirates, and pleural fluid for analysis among 150 high-risk patients.

The diagnostic landscape for pediatric TB is marked by atypical clinical presentations and challenges in obtaining accurate samples, which hinders the effectiveness of conventional diagnostic methods like sputum smear microscopy.^[9] In our study, the Xpert TB assay emerged as a promising tool, providing a rapid and automated platform for detecting TB and rifampicin resistance simultaneously.^[10] The endorsement by the World Health Organization (WHO) underscores its potential as a replacement for sputum smear microscopy, especially in cases of suspected extra-pulmonary TB.^[10]

Our study results demonstrated the superiority of the Xpert TB assay over smear microscopy, particularly in gastric aspirate specimens where 10 cases tested positive out of 133, highlighting the assay's ability to address the paucibacillary nature of pediatric TB.^[11] Furthermore, out of 17 sputum specimens, 2 cases were positive for both smear and Xpert, reinforcing the diagnostic accuracy of the gene Xpert test.^[11] The discordance observed between Xpert and smear results, with only 3 out of 12 positive Xpert cases aligning with smear examination, emphasizes the higher yield of Xpert, especially in the context of the limited sensitivity of smear microscopy.^[12]

The sensitivity of the Gene Xpert assay, defined as the probability of the test correctly identifying positive cases when the disease is present, was found to be 25%. This sensitivity aligns with findings from other studies and highlights the persistent challenge in achieving high sensitivity, particularly in the context of pediatric TB where clinical presentations are often atypical and the disease exhibits a paucibacillary nature.^[13]

On the other hand, the specificity of the Gene Xpert assay, representing the probability of correctly identifying negative cases when the disease is absent, was determined to be 100%. This high specificity underscores the reliability of the Gene Xpert assay in ruling out TB in cases where the disease is not present, providing confidence in the accuracy of negative results.^[14]

The positive predictive value (PPV) of the Gene Xpert assay, indicating the likelihood that a positive test result truly corresponds to the presence of the disease, was determined to be 100%. This high PPV is crucial in clinical decision-making, affirming that a positive Gene Xpert result is a reliable indicator of pediatric TB.^[15]

The negative predictive value (NPV), which signifies the probability that a negative test result correctly reflects the absence of the disease, was calculated to be 93.88%. This NPV is essential in reassuring clinicians that a negative Gene Xpert result is a strong indicator of the absence of TB, contributing to effective patient management and resource allocation.^[16]

It's important to note that while the specificity and PPV of the Gene Xpert assay in our study are high, the sensitivity falls within the range observed in other studies. This emphasizes the ongoing need for research to optimize sensitivity, particularly in the challenging landscape of pediatric TB diagnosis. The limitations associated with the paucibacillary nature of the disease, small sample sizes, and infrequent sampling may contribute to the observed sensitivity, and addressing these factors in future studies could enhance the diagnostic performance of the Gene Xpert assay in pediatric TB.

Comparison with other studies revealed a range of sensitivities for the Xpert TB assay, emphasizing the need for comprehensive research to optimize sensitivity, especially in the context of pediatric TB diagnosis.^[9-12] The advantages of the Xpert assay, including its speed, simultaneous detection of TB and rifampicin resistance, and applicability in challenging scenarios like smear-negative and HIV-associated TB, underscore its potential to revolutionize pediatric TB diagnostics.^[14]

Our study contributes valuable insights into the diagnostic role of the Xpert TB assay in childhood pulmonary TB. The assay's superiority over smear microscopy, particularly in gastric aspirate specimens, highlights its potential to enhance diagnostic precision in pediatric populations. Despite the limitations, such as the need for electricity and cartridge shelf life, the Xpert TB assay holds promise as an essential tool for early diagnosis and initiation of treatment, particularly in resource-limited settings. Further research endeavors with expanded sample sizes and refined sampling strategies are warranted to unlock the full potential of this molecular diagnostic tool in the context of pediatric TB.

CONCLUSION

The present study on the Diagnostic Role of Gene Xpert in Suspected Childhood Pulmonary Tuberculosis highlights the significance of this molecular diagnostic tool in pediatric TB diagnosis. The assay demonstrated a sensitivity of 25% and specificity of 100%, highlighting its reliability in confirming positive cases. The high positive predictive value of 100% affirms the accuracy of positive results, supporting clinicians in decision-making. The assay's negative predictive value of 93.88% assures its effectiveness in ruling out TB when the disease is absent. While challenges persist in achieving optimal sensitivity, the study emphasizes Gene Xpert's valuable role in enhancing diagnostic precision, particularly in resource-limited settings where prompt and accurate diagnosis is crucial for improved outcomes in pediatric TB cases.

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