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Original Research Article

ROLE OF GENE-XPERT IN PEDIATRIC TUBERCULOSIS DIAGNOSIS: A STUDY FROM NAVI MUMBAI, INDIA

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ABSTRACT

Background: Tuberculosis (TB) remains a significant global health challenge, particularly in children, due to its paucibacillary nature, nonspecific clinical symptoms, and challenges in sample collection. Conventional diagnostic methods, such as smear microscopy and culture, have limitations in pediatric populations. Gene-Xpert MTB/RIF, a rapid molecular diagnostic tool, has emerged as a promising method for detecting Mycobacterium tuberculosis and rifampicin resistance. This study evaluates the utility of Gene-Xpert in diagnosing presumptive TB in children and its correlation with other diagnostic modalities.

Material and Methods: This prospective observational study included 44 children with symptoms suggestive of TB, conducted at Dr. D.Y. Patil Medical College, Hospital, and Research Centre, Navi Mumbai, over 18 months. Detailed clinical evaluations, radiological assessments (chest X-ray and CT), Mantoux tuberculin skin test (TST), and microbiological testing (Gene-Xpert MTB/RIF and MGIT culture) were performed. The final diagnosis was categorized into pulmonary and extra-pulmonary TB with and without microbiological confirmation. Statistical analysis included sensitivity, specificity, and p-values for diagnostic correlations.

Results: The majority of the study population (63.6%) were aged 6–12 years, with fever (81.8%) and cough (65.9%) as the most common symptoms. Radiological findings showed that 22.7% of chest X-rays and 69.2% of CT scans were suggestive of TB. Gene-Xpert identified TB in 20.5% of cases, with 88.9% drug-sensitive and 11.1% rifampicin-resistant cases. Extra-pulmonary TB without microbiological confirmation was the most common diagnosis (50%). Gene-Xpert demonstrated a higher correlation with CT findings ($p = 0.102$) compared to chest X-rays ($p = 0.56$).

Conclusion: Gene-Xpert is a valuable diagnostic tool for pediatric TB, particularly for identifying rifampicin resistance. However, its limitations as a rule-out test emphasize the need for a multimodal diagnostic approach that includes clinical evaluation, imaging, and histopathological analysis. Addressing implementation challenges in resource-limited settings is crucial to improve access to this rapid diagnostic method.

Keywords: Pediatric tuberculosis, Gene-Xpert MTB/RIF, diagnostic methods, extra-pulmonary tuberculosis, Mantoux test, CT chest, microbiological confirmation.

INTRODUCTION

Tuberculosis (TB) remains a critical public health concern worldwide, disproportionately affecting vulnerable populations such as children. According to the World Health Organization (WHO), approximately.[1] 1 million children developed TB in 2020, resulting in an estimated 226,000 deaths, highlighting the severe burden of the disease.[1] Pediatric TB presents unique challenges due to its paucibacillary nature, nonspecific clinical symptoms, and difficulties in obtaining adequate sputum samples, all of which contribute to diagnostic delays.[2]

Traditional diagnostic methods for TB, such as smear microscopy and culture, have well-documented limitations, particularly in pediatric populations. Smear microscopy, a commonly employed method, has poor sensitivity in children, often yielding negative results even in cases of active disease.[3] Culture, regarded as the gold standard for TB diagnosis, provides higher sensitivity but is time-intensive, with results taking several weeks to obtain, thereby delaying the initiation of treatment.[4]

The development of molecular diagnostic techniques, particularly the Xpert MTB/RIF assay (commonly referred to as Gene-Xpert), has transformed TB diagnostics by enabling rapid and accurate detection of Mycobacterium tuberculosis complex and rifampicin resistance within a two-hour timeframe.[5] The WHO has recommended Gene-Xpert for the diagnosis of pulmonary TB in both adults and children due to its superior sensitivity compared to smear microscopy and its ability to detect drug resistance.[6] However, its diagnostic performance in pediatric TB, which is often paucibacillary, has shown variability depending on factors such as sample type, HIV co-infection, and the prevalence of TB in the population.[7]

Studies have reported that Gene-Xpert significantly improves diagnostic yield in smear-negative pediatric TB cases, particularly in high-burden settings.[8] Despite these advantages, the implementation of Gene-Xpert in resource-limited settings—where the burden of childhood TB is highest—poses logistical challenges. These include the need for stable electricity, temperature-controlled environments, and trained personnel, alongside concerns about its cost-effectiveness.[9,10] Addressing these barriers is critical to realizing the full potential of Gene-Xpert in improving TB diagnosis among children.

This study aims to evaluate the utility of Gene-Xpert in diagnosing presumptive tuberculosis in children, focusing on its diagnostic accuracy compared to conventional methods, its impact on clinical decision-making, and its role in guiding treatment strategies. By shedding light on these aspects, the findings will contribute to the growing body of evidence on Gene-Xpert and inform guidelines for pediatric TB diagnosis in resource-constrained settings.

MATERIALS AND METHODS

This study was conducted as a prospective observational study to evaluate the utility of Gene-Xpert in diagnosing presumptive tuberculosis (TB) in children. The research was carried out at the Department of Pediatrics, Dr. D. Y. Patil Medical College, Hospital, and Research Centre, Nerul, Navi Mumbai, over a duration of 18 months, from October 2022 to April 2024. Ethical approval was obtained from the Institutional Review Board prior to commencement, and the study adhered strictly to Good Clinical Practice guidelines throughout its duration. Written informed consent was obtained from the parents or legal guardians of all participants before enrollment.

The study population included children presenting with symptoms suggestive of TB, as defined by the World Health Organization (WHO) criteria. Inclusion criteria comprised all children with symptoms such as prolonged cough, fever, weight loss, and a history of contact with TB patients. Children with BCG adenitis, congenital TB, or whose parents declined to participate were excluded from the study. A total of 44 children meeting these criteria were enrolled.

Upon enrollment, each participant underwent a detailed clinical evaluation. This included obtaining a comprehensive medical history, with a focus on TB-related symptoms, duration of illness, and exposure history. A thorough physical examination was performed, and findings were documented in a standardized proforma. Radiological evaluations were conducted for all participants, with chest X-rays (CXR) interpreted by a radiologist blinded to the clinical and microbiological data. Additionally, for 13 participants, chest computed tomography (CT) was performed to evaluate detailed pulmonary involvement.

All children were administered the Mantoux tuberculin skin test (TST), and results were interpreted after 48–72 hours. Microbiological assessments involved the collection of appropriate samples such as sputum, gastric aspirates, or other bodily fluids, as clinically indicated. Each sample was subjected to Gene-Xpert MTB/RIF testing, which detects the presence of Mycobacterium tuberculosis complex and rifampicin resistance within two hours. These samples were also cultured using the Mycobacteria Growth Indicator Tube (MGIT) system, considered the gold standard for TB diagnosis. Positive MGIT cultures were further confirmed as Mycobacterium tuberculosis complex using standard identification methods.

The collected data were classified into two main categories: presumptive tuberculosis (cases with clinical and radiological features suggestive of TB

without microbiological confirmation) and microbiologically confirmed tuberculosis (cases with positive results on Gene-Xpert or MGIT culture). Performance characteristics of Gene-Xpert, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were calculated using MGIT culture as the gold standard. The diagnostic performance was analyzed across different subgroups, such as sample types and patient characteristics.

To ensure quality and reliability, all laboratory procedures were conducted in accordance with standardized operating protocols, and Gene-Xpert and MGIT systems were regularly calibrated. A subset of samples was sent to a reference laboratory for external quality assurance. Data analysis was performed using SPSS software (version 22), and statistical significance was assessed using appropriate tests such as chi-square and Fisher's exact test, with a p-value <0.05 considered statistically significant.

This detailed methodology ensured a robust assessment of Gene-Xpert's role in pediatric TB diagnosis, contributing valuable insights into its utility in clinical and resource-limited settings.

RESULTS

The study analyzed data from 44 children with presumptive tuberculosis (TB) using SPSS version 22. The majority of the study population, 63.6%, belonged to the 6–12 years age group, followed by 25% in the 1–5 years group, and 11.4% were under 1 year of age. Among the participants, 54.5% were female, and 45.5% were male. The most common presenting symptom was fever, reported in 81.8% of cases, followed by cough in 65.9% and weight loss in 31.8%. History of contact with TB cases was noted in 22.7% of children. Signs of undernutrition were observed in 68.2% of the study population, while pallor was present in 50%, and lymphadenitis was seen in 20.5%. Notably, all 44 children had a visible BCG scar.

Radiological findings revealed that 22.7% of children had chest X-rays suggestive of TB, while 77.3% had normal X-rays. CT chest scans were performed on 13 children, with findings suggestive of TB in 69.2%, highlighting its higher sensitivity compared to chest X-rays. The Mantoux tuberculin skin test (TST) was conducted on all participants, with 22.7% showing positive results, while 77.3% tested negative. Gene-Xpert MTB/RIF testing identified Mycobacterium tuberculosis complex in 20.5% of cases, with 88.9% of these being drug-sensitive and 11.1% rifampicin-resistant. Results from Line Probe Assay (LPA) aligned with the Gene-Xpert findings, showing similar proportions of drug-sensitive (88.9%) and drug-resistant cases (11.1%). [Table 1]

Histopathological analysis further confirmed TB in 100% of lymph node biopsy samples, while 58.3% of body fluid analyses indicated TB. Among the study participants, pulmonary TB with microbiological confirmation was diagnosed in 11.4% of cases, while 29.5% were diagnosed with pulmonary TB without microbiological confirmation. Extra-pulmonary TB without microbiological confirmation was the most common diagnosis, comprising 50% of cases, followed by extra-pulmonary TB with microbiological confirmation in 9.1% of cases. [Table 2]

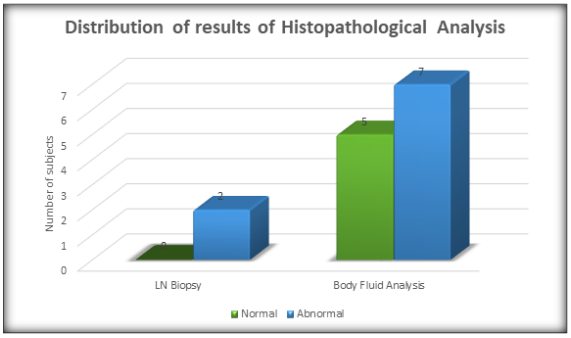

Figure 1: Distribution of results of Histopathological Analysis

Statistical comparisons revealed a higher correlation between Gene-Xpert results and CT chest findings (p = 0.102) compared to chest X-rays (p = 0.56). Among children with a positive TST, 40% also had chest X-rays suggestive of TB (p = 0.13). Gene-Xpert positivity was observed in 30% of children with a positive TST, compared to 17.6% of those with a negative TST (p = 0.39). [Table 4]

These results emphasize the utility of Gene-Xpert as a rapid diagnostic tool, particularly when combined with radiological imaging and clinical assessments, to improve TB diagnosis in children. The predominance of extra-pulmonary TB cases without microbiological confirmation underscores the challenges in diagnosing pediatric TB. [Table 5]

Table 1: Demographic Characteristics, Clinical Symptoms, Physical Signs, and BCG Scar Status of Children with Presumptive Tuberculosis

		Frequency	Percentage
Age(in years)	<1	5	11.4%
	1-5	11	25%
	6-12	28	63.6%
	Total	44	100%
Gender	Female	24	54.5%
	Male	20	45.5%
	Total	44	100%
Symptoms	Fever	36	81.8%

	Cough	29	65.9%
	Weight loss	14	31.8%
	H/O contact	10	22.7%
	Lymphadenitis	7	15.9%
	Convulsions (chronic meningitis)	2	4.5%
	Gibbus	1	2.3%
Signs	Undernutrition	30	68.2%
	Pallor	22	50%
	Lymphadenitis	9	20.5%
	Edema	1	2.3%
	Gibbus	1	2.3%
BCG Scar	Present	44	100%
	Absent	0	0
	Total	44	100%

Table 2: Radiological, Microbiological, and Drug Sensitivity Findings in Children with Presumptive Tuberculosis

			No. of Study population
Chest CT	Normal	4	30.8%
	Suggestive of Tuberculosis	9	69.2%
Chest X-Ray	Normal	34	77.3%
	Suggestive of Tuberculosis	10	22.7%
TST	Positive	10	22.7%
	Negative	34	77.3%
Gene-Xpert	Positive	9	20.5%
	Negative	35	79.5%
Drug Sensitivity (Gene-Xpert)	Drug-Sensitive	8	20.5%
	Drug-Resistant	1	11.1%
Drug Sensitivity (LPA)	Drug-Sensitive	8	20.5%
	Drug-Resistant	1	11.1%

Table 3: Final Diagnosis Distribution of Pulmonary and Extra-pulmonary Tuberculosis in Children

Final Diagnosis	Frequency	Percentage
Pulmonary Tuberculosis with Microbiological confirmation	5	11.4%
Pulmonary Tuberculosis without Microbiological confirmation	13	29.5%
Extra pulmonary Tuberculosis with Microbiological confirmation	4	9.1%
Extra pulmonary Tuberculosis without Microbiological confirmation	22	50%
Total	44	100%

Table 4: Correlation of Gene-Xpert Results with Imaging Modalities and Tuberculosis Types

	Imaging	Gene-Xpert		p-value
		Positive	Negative	
Imaging	**X-ray Chest**			0.56
	Normal	7 (77.8%)	30 (85.7%)	
	Suggestive of Tuberculosis	2 (22.2%)	5 (14.3%)	
	CT Chest			
	Normal	7 (77.8%)	26 (74.3%)	0.102
	Suggestive of Tuberculosis	1 (11.1%)	9 (25.7%)	
Type	Pulmonary	5 (27.8%)	13 (72.2%)	0.31
	Extra pulmonary	4 (15.4%)	22 (84.6%)	

Table 5: Association of TST Results with Imaging Findings and Gene-Xpert Results

		TST		p-value
		Positive	Negative	
ChestX-ray	Suggestive of Tb	4 (40%)	6 (17.6%)	0.13
	Normal	6 (60%)	28 (82.4%)	
CT Chest	Suggestive of Tb	3 (23.1%)	6 (46.2%)	0.18
	Normal	0	4 (30.7%)	
GeneXpert	Positive	3 (30%)	6 (17.6%)	0.39

DISCUSSION

The diagnosis of tuberculosis (TB) in children remains a formidable challenge due to the paucibacillary nature of the disease, difficulty in obtaining quality samples, and nonspecific clinical presentations. This study evaluated the utility of Gene-Xpert MTB/RIF in diagnosing presumptive TB in children, comparing its diagnostic performance with conventional methods and exploring its implications for clinical decision-making and treatment strategies.

Gene-Xpert MTB/RIF, a rapid molecular diagnostic tool, demonstrated significant advantages in identifying Mycobacterium tuberculosis complex and rifampicin resistance. In this study, Gene-Xpert identified TB in 20.5% of cases, with 88.9% being drug-sensitive and 11.1% rifampicin-resistant. This

aligns with previous studies showing that Gene-Xpert has superior sensitivity compared to smear microscopy, particularly in pediatric populations where smear sensitivity is often limited due to paucibacillary disease.[1-3] Despite its higher sensitivity, the present study corroborates findings that Gene-Xpert alone cannot rule out TB, emphasizing the need for complementary diagnostic methods.[4]

Radiological findings played a critical role in TB diagnosis, with chest CT scans showing a higher diagnostic yield (69.2%) compared to chest X-rays (22.7%). This reinforces evidence that CT imaging can detect subtle abnormalities not visible on X-rays, making it a valuable tool for TB diagnosis in children.[5-6] However, access to CT imaging may be limited in resource-constrained settings, underscoring the need for affordable and effective diagnostic algorithms that incorporate widely available tools like chest X-rays and clinical assessments.[7]

The Mantoux tuberculin skin test (TST), although positive in only 22.7% of cases, provided supportive evidence when combined with clinical and imaging findings. TST remains useful in high-burden settings but is limited by cross-reactivity with Bacille Calmette-Guérin (BCG) vaccination and environmental mycobacteria, as documented in previous research.[8]

The predominance of extra-pulmonary TB (59.1%) in this study highlights the diagnostic challenges associated with non-pulmonary forms of the disease, where microbiological confirmation is often difficult. Studies have emphasized the importance of integrating clinical, radiological, and microbiological evidence to improve diagnostic accuracy for extra-pulmonary TB.[9-10] The WHO-recommended strategy of upfront Gene-Xpert testing for all presumptive TB cases aligns with this integrated approach, enhancing the early detection and management of pediatric TB.[11]

Despite its advantages, the implementation of Gene-Xpert in resource-limited settings remains challenging. The cost of cartridges, requirements for stable electricity, and trained personnel are significant barriers, particularly in high-burden regions.[12] Recent studies have called for the optimization of Gene-Xpert use, including targeted testing for high-risk groups and combining it with affordable diagnostic methods.[13]

CONCLUSION

This study highlights the utility of Gene-Xpert MTB/RIF as a rapid and effective diagnostic tool for pediatric tuberculosis (TB), particularly in resource-limited settings. Gene-Xpert demonstrated higher sensitivity compared to conventional methods, especially in detecting paucibacillary TB cases, and provided crucial information on rifampicin resistance. However, its limitations as a rule-out test underscore the importance of integrating Gene-Xpert with other diagnostic modalities, such as clinical evaluation, imaging (especially CT chest), and supportive tests like the tuberculin skin test (TST).

The predominance of extra-pulmonary TB without microbiological confirmation in this study reflects the diagnostic challenges associated with this form of the disease, emphasizing the need for a comprehensive, multimodal diagnostic approach. Additionally, the logistical and cost-related barriers to implementing Gene-Xpert in resource-constrained settings warrant attention to ensure equitable access to this valuable diagnostic tool.

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