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The GeneXpert Test for The Diagnosis of Childhood Pulmonary Tuberculosis in Suspected Cases: Study in a Tertiary Care Hospital in Bangladesh

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Abstract: ***Background:*** Pulmonary tuberculosis (PTB) remains a significant health issue in children. Early and accurate diagnosis is critical but challenging, The GeneXpert test, a rapid and accurate molecular diagnostic tool, has improved TB detection by identifying Mycobacterium tuberculosis and resistance to rifampicin within hours. ***Aim of the study****:* This study aimed to assess the role of the GeneXpert test in diagnosing pulmonary tuberculosis in clinically suspected pediatric cases. ***Methods:*** This cross-sectional observational study was conducted in the department of pediatrics, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from March 2021 to August 2022. In this study, 280 pediatric cases, all under 12 years old and clinically suspected, were enrolled using purposive sampling. Diagnostic tests, including chest X-ray, Mantoux test, microscopy of sputum or gastric aspirate, and GeneXpert, were conducted to validate the clinical diagnoses. Data analysis was carried out using the SPSS version 23.0 program. ***Results:*** In our study, the GeneXpert test demonstrated high sensitivity (96.79%), effectively identifying true positives, but had moderate specificity (51.61%), resulting in more false positives. The positive predictive value was 71.56%, and the negative predictive value was 92.75%, indicating higher accuracy in correctly identifying true negatives. Overall, the test achieved an accuracy of 76.79%, showing it reliably determined the disease status in most cases. ***Conclusion:*** GeneXpert test is an effective diagnostic procedure for detecting pulmonary tuberculosis in clinically suspected pediatric patients. It shows high sensitivity and moderate specificity in diagnosing pulmonary tuberculosis in clinically suspected or presumptive pediatric cases.

Keywords: Clinically suspected, Diagnosis, GeneXpert test, Pediatric, Pulmonary tuberculosis.

Research Paper

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INTRODUCTION

Tuberculosis (TB) remains a prominent health issue, particularly in children who often face diagnostic challenges due to non-specific symptoms and difficulty in obtaining high-quality sputum samples [1]. Diagnosing childhood pulmonary tuberculosis (PTB) is challenging due to several factors, including the low bacterial load associated with the disease, difficulties in collecting adequate sputum samples, limitations of current diagnostic tests, and the similarity in respiratory symptoms with those seen in Human Immune Deficiency Virus (HIV) infections [2]. The World Health Organization (WHO) supports using the Xpert MTB/RIF test as a primary diagnostic tool for TB in children [3]. The GeneXpert MTB/RIF test, a molecular diagnostic tool, has become an essential tool for detecting Mycobacterium tuberculosis in pediatric cases. Unlike traditional diagnostic methods like sputum microscopy, which is less sensitive in children, the GeneXpert test

provides an efficient, rapid alternative that detects TB DNA using real-time PCR within approximately two hours [4]. The GeneXpert test has transformed pediatric TB diagnostics by offering high sensitivity, even in samples with low bacterial counts, which is common in children's respiratory samples [5]. This attribute is particularly beneficial, as pediatric TB cases often present with extrapulmonary or paucibacillary disease, making traditional methods less effective. In addition to detecting TB, the GeneXpert test identifies rifampicin resistance, a marker for multidrug-resistant TB (MDR-TB), which is critical for timely intervention in affected children [6]. In high-burden settings, the use of the GeneXpert test is precious, as it requires minimal processing and can be deployed in decentralized clinics, improving accessibility to accurate diagnostics [7]. For instance, studies have shown that the test's integration into routine diagnostics significantly increases TB detection rates in children compared to conventional microscopy [8]. The test has been endorsed by the World Health Organization (WHO) as a primary diagnostic tool for pediatric TB due to its high diagnostic accuracy, which surpasses that of traditional methods [9]. However, the GeneXpert test is not without limitations. Its higher cost and need for specialized equipment have posed challenges for widespread implementation, particularly in resource-constrained regions [10]. Additionally, while the test is highly accurate for pulmonary TB, its sensitivity may decrease in very young children or cases of extrapulmonary TB, necessitating the use of additional diagnostic tools [11]. This study aimed to assess the role of the gene GeneXpert test in diagnosing pulmonary tuberculosis in clinically suspected pediatric cases.

METHODOLOGY

This was a cross-sectional observational study that was conducted in the Department of Pediatrics (OPD), Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh from March 2021 to August 2022. A total of 280 pediatric cases, all clinically suspected and under 12 years of age, were enrolled as study subjects. Sample selection was conducted using convenient purposive sampling.

Inclusion criteria:

- Age within 12 years.
- Fever and cough for more than two weeks.
- Contact with TB patients within one year.

Exclusion criteria:

- Age over 12 years.
- Children already undergoing treatment for tuberculosis.
- Children who did not complete the required investigations.

The entire intervention adhered to the principles of human research outlined in the Helsinki Declaration [12] and complied with current regulations and the General Data Protection Regulation (GDPR) [13]. Written informed consent was obtained for all study participants before data collection. Diagnostic procedures including chest X-ray, Mantoux test, microscopy of sputum or gastric aspirate, and GeneXpert were performed to confirm clinical diagnoses. Data analysis was conducted using the SPSS version 23.0 program.

RESULT

In this study, the largest group of cases (44.3%) was in the 5-10 years age range, followed by 30.7% in the more than 10 years age group, and 25% in the less than 5 years group. Most participants were female (54.6%), with males comprising 45.4%. Additionally, 47.9% of cases were from middle-class families, and 37.9% were from lower-class families. The clinical status of our participants showed that everyone in the study experienced fever and cough. Weight loss was observed in roughly 85% of cases, while poor appetite was found in about 38.2%% of the cases. In this study, out of 211 cases, 151 were true positives for both GeneXpert and clinical diagnostic findings, while 60 were false positives, clinically negative yet GeneXpert positive. Among 69 clinically negative cases, 59 were true negatives with corroborating GeneXpert results, but 10 were false negatives, being GeneXpert negative despite clinical positivity. These figures can be employed to calculate important performance metrics such as sensitivity, specificity, and predictive values for the GeneXpert test. The GeneXpert tests demonstrated a high sensitivity of 96.79% and a moderate specificity of 51.61%. The positive predictive value was 71.56%, and the negative predictive value was 92.75%. The overall accuracy of the GeneXpert test was 76.79%.

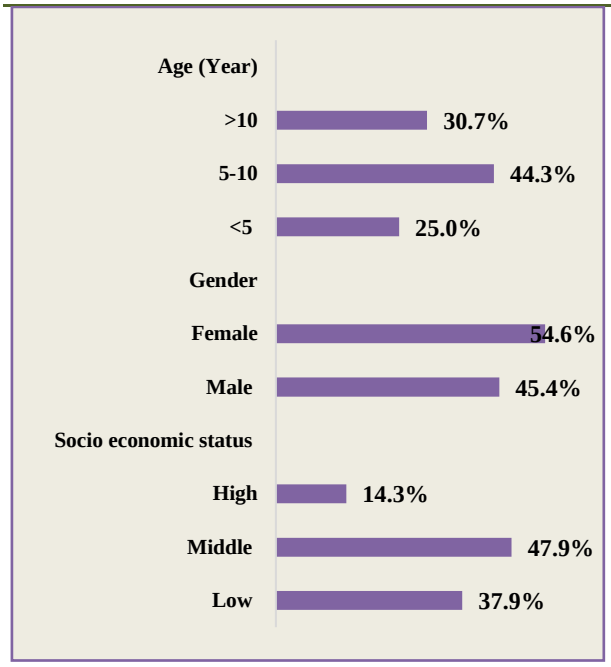

Figure 1: Socio-demographic data

Table 1: Clinical characteristics

Findings	n	%
Fever	280	100%
Cough	280	100%
Poor appetite	107	38.2%
Weight loss	239	85.4%
History of contact	77	27.5%
Hemoptysis	56	20.0%

Table 2: GeneXpert and other clinical diagnostic findings

Methods		GeneXpert		Total
		+ve	-ve	
Clinical	+ve	151	60	211
	-ve	10	59	69
Total		**161**	**119**	**280**

Table 3: Sensitivity, specificity, and accuracy of GeneXpert tests

Statistic	Value	95% CI
Sensitivity	96.79%	92.68-98.95%
Specificity	51.61%	42.47-60.68%
Positive LR	2.00	1.66-2.40
Negative LR	0.06	0.03-0.15
Disease prevalence	55.71%	49.68-61.62%
Positive PV	71.56%	67.68-75.16%
Negative PV	92.75%	84.16-96.86%
Accuracy	76.79%	71.39-81.60%

LR: Likelihood Ratio, **PV:** Predictive Value

DISCUSSION

In this study, the largest group of cases fell within the 5-10 years age range, followed by nearly one-third in the more than 10 years age group and one-fourth in the less than 5 years group. A similar age distribution was noted in another study [14]. Most participants in this study were female, whereas another study [15] reported a male predominance. Additionally, 47.9% of the cases were from middle-class families, while 37.9% were from lower-class families. The clinical status of the participants in this study revealed that all experienced fever and cough. Weight loss was observed in approximately 85% of the cases, and poor appetite was noted in about 56%. Das *et al.,* [14] reported a similar trend, with weight loss in 84.5% of their participants. In contrast, a study by Roma *et al.,* [16] showed poor appetite in 91% of participants. Out of our 211 cases, 151 were confirmed as true positives by both GeneXpert and clinical findings, whereas 60 were false positives, showing positive GeneXpert results but negative clinical findings. Among the 69 clinically negative cases, 59 were confirmed as true negatives with matching GeneXpert results, and 10 were false negatives, with negative GeneXpert results despite being clinically positive. These numbers can be used to calculate key performance metrics, including sensitivity, specificity, and predictive values for the GeneXpert test. According to an updated Cochrane systematic review, when GeneXpert is initially used to replace smear microscopy in diagnosing PTB, the GeneXpert MTB/RIF test has an overall sensitivity of 88% and a pooled specificity of 98%, compared to culture [17]. In our study, the GeneXpert test exhibited high sensitivity, effectively identifying individuals with the disease, although its moderate specificity indicated it was less effective at ruling out those without the disease. The positive predictive value was 71.56%, meaning a positive test result had a 71.56% probability of being accurate. The negative predictive value was 92.75%, indicating that a negative result had a 92.75% likelihood of being correct. The overall accuracy suggested the test was generally reliable for the population studied. Detjen *et al.,* [18] noted significant variations in GeneXpert's sensitivity across different studies and specimen types, with specificity ranges between 93-100%. In contrast, Venkatesh KS *et al.,* [19] reported a sensitivity of 73.3% i.e. lower than our study, and a higher specificity of 93.6%.

CONCLUSION & RECOMMENDATION

The GeneXpert test is a highly effective tool for diagnosing pulmonary tuberculosis in children. Its high sensitivity accurately identifies most true positive cases, minimizing missed diagnoses. However, due to its moderate specificity, there's a risk of false positives, requiring further clinical evaluation. Despite this, its benefit in initial screening makes it valuable for pediatric

TB diagnosis, providing rapid results while supporting thorough clinical decision-making.

REFERENCES

1. Ogunbayo, A. E. (2018). Comparison of methods and samples used in the diagnosis of childhood PTB and characterization of mycobacterium tuberculosis isolates.
2. Sekadde, M. P., Wobudeya, E., Joloba, M. L., Ssengooba, W., Kisembo, H., Bakeera-Kitaka, S., & Musoke, P. (2013). Evaluation of the Xpert MTB/RIF test for the diagnosis of childhood pulmonary tuberculosis in Uganda: a cross-sectional diagnostic study. *BMC infectious diseases*, *13*, 1-8.
3. Chipinduro, M., Mateveke, K., Makamure, B., Ferrand, R. A., & Gomo, E. (2017). Stool Xpert® MTB/RIF test for the diagnosis of childhood pulmonary tuberculosis at primary clinics in Zimbabwe. *The International Journal of Tuberculosis and Lung Disease*, *21*(2), 161-166. doi:10.5588/ijtld.16.0357.
4. Atherton, R. R., Cresswell, F. V., Ellis, J., Kitaka, S. B., & Boulware, D. R. (2019). Xpert MTB/RIF ultra for tuberculosis testing in children: a mini-review and commentary. *Frontiers in pediatrics*, *7*, 34.
5. Habib, Z. G., Dayyab, F. M., Sanda, A., Tambuwal, S. H., Dalhat, M. M., Muhammad, H., ... & Habib, A. G. (2015). Role of GeneXpert MTB/Rif assay in diagnosing tuberculosis in pregnancy and puerperium. *Case Reports in Infectious Diseases*, *2015*(1), 794109. doi:10.1155/2015/794109.
6. Naz, Farah, (2021). "High rate of successful treatment outcomes among childhood rifampicin/multidrug-resistant tuberculosis in Pakistan: a multicenter retrospective observational analysis." BMC Infectious Diseases 21: 1-11.
7. Rachow, A., Clowes, P., Saathoff, E., Mtafya, B., Michael, E., Ntinginya, E. N., ... & Hoelscher, M. (2012). Increased and expedited case detection by Xpert MTB/RIF assay in childhood tuberculosis: a prospective cohort study. *Clinical infectious diseases*, *54*(10), 1388-1396.
8. Kiruthiga, S. (2019). *Role of Cartridge Based Nucleic Acid Amplification Test (CBNAAT-Genexpert) in the Diagnosis of Pediatric Pulmonary Tuberculosis* (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
9. World Health Organization. (2024). *WHO consolidated guidelines on tuberculosis. Module 3: diagnosis–rapid diagnostics for tuberculosis detection*. World Health Organization.
10. Denkinger, C. M., Kik, S. V., Cirillo, D. M., Casenghi, M., Shinnick, T., Weyer, K., ... & Pai, M. (2015). Defining the needs for next generation assays for tuberculosis. *The Journal of infectious diseases*, *211*(suppl_2), S29-S38.
11. Velen, K., Podewils, L. J., Shah, N. S., Lewis, J. J., Dinake, T., Churchyard, G. J., ... & Charalambous, S. (2021, April). Performance of GeneXpert MTB/RIF for diagnosing tuberculosis among symptomatic household contacts of index patients in South Africa. In *Open Forum Infectious Diseases* (Vol. 8, No. 4, p. ofab025). US: Oxford University Press.
12. World Medical Association. (2001). World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bulletin of the World Health Organization, 79 (4), 373 - 374. World Health Organization. https://apps.who.int/iris/handle/10665/268312.
13. Voigt, P., & Von dem Bussche, A. (2017). Enforcement and fines under the GDPR. The EU General Data Protection Regulation (GDPR).
14. Das, A., Anupurba, S., Mishra, O. P., Banerjee, T., & Tripathi, R. (2019). Evaluation of Xpert MTB/RIF assay for diagnosis of tuberculosis in children. *Journal of tropical pediatrics*, *65*(1), 14-20.
15. Zhang, H., Li, H., Tan, M., Liu, Z., Gu, J., Zhang, Y., & Sheng, H. (2022). GeneXpert MTB/RIF combined with conventional methods for tuberculosis in Shanghai Regional Medical Center: a retrospective diagnostic study. *Annals of Translational Medicine*, *10*(10).
16. Roma, K., Shrestha, S. K., Bhandari, N., Shah, G. J., & Khetan, S. (2023). Assessment of geneXpert test for diagnosis of pediatric pulmonary tuberculosis. *Birat Journal of Health Sciences*, *8*(2), 2024-2028.
17. Steingart, K. R., Sohn, H., Schiller, I., Kloda, L. A., Boehme, C. C., Pai, M., & Dendukuri, N. (2013). Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane database of systematic reviews*, (1).
18. Detjen, A. K., DiNardo, A. R., Leyden, J., Steingart, K. R., Menzies, D., Schiller, I., ... & Mandalakas, A. M. (2015). Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in children: a systematic review and meta-analysis. *The lancet respiratory medicine*, *3*(6), 451-461.
19. Roma, K., Shrestha, S. K., Bhandari, N., Shah, G. J., & Khetan, S. (2023). Assessment of geneXpert test for diagnosis of pediatric pulmonary tuberculosis. *Birat Journal of Health Sciences*, *8*(2), 2024-2028.