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Original Research Article

Rifampicin resistance in pulmonary and extra pulmonary tuberculosis cases in of children

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ABSTRACT

Background: The prevalence of Rifampicin-resistant MTB/EPTB in children in India is a growing concern. Globally a large proportion of childhood tuberculosis (TB) cases are diagnosed based only on clinical findings. This study was undertaken to measure MTB positivity and their rifampicin resistance rates in different clinical samples from children.

Materials and Methods: Different samples of clinically suspected tuberculosis in children were included. All the samples were tested for Tuberculosis positivity and Rifampicin (Rif) resistance by GeneXpert assay.

Results: A total of 1420 samples were received from presumptive TB patients of all age group from February 2023 to January 2024. Total 1420 samples were analyzed for this study, of which 30% were male and 70% were females. Respiratory samples and extra-pulmonary samples were 1261 (88.8%) and 159 (11.2%) respectively. Among 1420, 211(14.86%) samples were from children and among these 75 (35.55%) were found MTB positive and 7 (9.33%) were Rif resistant MTB. Of 75 MTB detected patients, 77.8% and 22.2% MTB detected in female and male children respectively.

Conclusion: There are higher prevalence of Rif resistant MTB in children so it is important for healthcare providers in India to be vigilant in timely diagnosis, individualized treatment and enhance surveillance. It is essential to combat this growing threat and protect the health of children.

1. Introduction

Rifampicin (RIF) resistance poses a significant challenge in the management of children with Mycobacterium tuberculosis (MTB) infections, particularly in cases of extrapulmonary tuberculosis (EPTB). EPTB, characterized by TB infection outside the lungs, often presents unique diagnostic and therapeutic dilemmas owing to its diverse clinical manifestations and limited availability of specimens for microbiological confirmation. In children here the disease may exhibit atypical symptoms, and the immune response differs from adults, timely and accurate diagnosis coupled with effective treatment is crucial to prevent morbidity, mortality, and transmission within communities.[1]

Several studies have reported an increasing trend in the prevalence of Rifampicin-resistant MTB/EPTB among children in India.[2,3] The emergence of rifampicin resistance complicates this scenario, as rifampicin is a cornerstone drug in the treatment of both pulmonary and extrapulmonary TB due to its potent bactericidal activity and role in shortening the treatment duration. Resistance to rifampicin often signifies multidrug-resistant TB (MDR-TB), which further limits treatment options, increases the treatment duration, and increases the risk of adverse outcomes. In children, the management of rifampicin-resistant MTB/EPTB requires a delicate balance between

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achieving therapeutic efficacy, minimizing drug toxicity, and ensuring treatment adherence.[4]

With the advent of GeneXpert MTB/RIF, more TB cases in children are being reported. Xpert MTB/RIF, a highly sensitive and specific rapid tool, offers a promising solution in addressing these challenges. This study was undertaken to evaluate the Pulmonary and extrapulmonary Tuberculosis with susceptibility of Rifampicin in children.

2. Materials and Methods

The total of 1420 samples were collected having 211 samples from pediatric population under RNTCP during the duration of February 2023 to January 2024. All specimen pulmonary and non-pulmonary were collected from suspected tuberculosis individuals as per the guideline of Revised National Tuberculosis Control Program (RNTCP), India. The samples were collected for diagnosis of TB in Department of Microbiology at RNTCP facility, Mycobacteriology laboratory, Government Institute of Medical Sciences, Greater Noida. The data was examined retrospectively and patient details such as age, gender, nature of specimen, prior medical background, were collected from the RNTCP requisition form. These specimens were initially subjected to GeneXpert MTB/RIF test.

The GeneXpert MTB/RIF assay, frontline test for diagnosis of TB was performed on all sample as per the manufacturer potocol.[5] The samples were mixed and vortexed with the reagent and followed by the incubation period of 15 minutes. The 2ml of the mix were transfer to GeneXpert machine cartridge and loaded onto the machine (Cepheid, Dx System Version 4.0c). The result were recorded as detected, not detected or invalid/error for MTB. Rifampicin resistance results were also reported as susceptible, resistant, or indeterminate.

3. Result

The study analyzed 1420 presumptive TB patient (30% male and 70% females) from February 2023 to January 2024. The age of the patients ranged from 1 month to 18 years with median age of 15 years. The 88.8% (1261 Sample) of the samples included in the study were respiratory samples collected from sputum 72.5% (1029 Samples), gastric aspirate 10.5% (18 Samples), bronchoalveolar lavage 3.5% (50 Samples) and pleural fluid 2.4% (34 Samples). The extra-pulmonary samples were 11.2% (159 Samples) including cerebrospinal fluid (CSF) and pus 6.5% (92 Samples) and 4.7% (67 Samples) respectively. Out of 1420, 46.34% (658) were found positive with 5.32% (35) Rif resistant. Among 1420, 211(14.86%) samples were from children and among these 75 (35.55%) were found MTB positive and 7 (9.33%) were Rif resistant MTB. Of 75 MTB detected patients, 77.8% and 22.2% MTB detected in female and male children respectively.

Table 1: Status of MTB

S. No.	Description	Total
1.	Total tests performed using CBNAAT	1420
2.	Total cases of MTB detected (MTB+)	658 (46.34%)
3.	Total Pediatric sample tested	211 (14.86%)
4.	MTB detected in Children	75 (35.55%)

Table 2: Status of Rif susceptibility

S.No.	Description	Total
1.	Total cases of MTB detected and RIF sensitive	623 (94.68%)
2.	Total cases of MTB detected and RIF resistant	35 (5.32%)
3.	MTB detected in children and RIF sensitive	68 (90.67%)
4.	MTB detected in children and RIF resistant	7 (9.33%)

Table 3: Demographic details of MTB positive children

	Total MTB detected n(%)	MTB detected /Rif R
Age		
<5	3 (4)	0
5-10	6 (8)	0
11-15	30 (40)	3 (33.3)
16-18	36 (48)	6 (66.7)
Gender		
Male	24 (32)	2 (22.2)
Female	51 (68)	7 (77.8)
Sample		
Gastric Aspirate	8 (10.7)	0
CSF	4 (5.3)	0
Pleural Fluid	1 (1.3)	0
BAL	2 (2.7)	0
PUS	3 (4)	2 (22.2)
Sputum	57 (76)	7 (77.8)

4. Discussion

The present analysis has provided an estimate of 35.55% of samples were MTB positive for population aged > 18 years. Utilizing the GeneXpert assay, the study analyzed 1,420 clinical samples from February 2023 to January 2024, with a focus on 211 pediatric samples. The findings revealed that 35.55% of the pediatric samples were MTB positive, with 9.33% of these cases showing Rifampicin resistance. A notable gender disparity was observed, with female children having a higher detection rate of MTB and Rifampicin resistance than males.

Rifampicin-resistant tuberculosis poses a significant threat to children worldwide, presenting unique challenges in diagnosis and management. WHO has recommended GeneXpert MTB/RIF assay for the initial diagnostic test in all children suspected of having TB. The ambitious goal of Government of India to eliminate the TB till 2025. To meet this goal of National Strategic Plan, various initiatives including notification of new cases to the government by private health providers, active case discovery, medication resistance surveys, and nutritional support for TB patients have been launched. The countrywide TB prevalence survey has been launched by the Ministry of Health, Government of India to determine the prevalence of disease at the national and subnational levels.[6]

The study highlights the growing concern of Rifampicin-resistant MTB/EPTB in children, which is often diagnosed based on clinical findings rather than laboratory confirmation. This poses significant challenges due to the diverse clinical manifestations of EPTB and the limited availability of specimens for microbiological confirmation. The GeneXpert MTB/RIF assay has become a crucial tool in addressing these challenges, offering rapid and accurate diagnosis, which is particularly important in pediatric populations where the disease may present atypically.

In the current study, the overall MTB in children was found to be 35.55%. In contrast, the prevalence of TB in our finding was higher as compared to studies done in the other part of India.[7] We found 9.3% MTB were Rifampicin resistant. The rates of drug resistance was higher among children TB cases observed in the present study are higher than reported earlier in India.[8]

The main factors like age and sex were considered to study the distribution TB cases. Many similar studies on gender basis among different populations suggested that the males were highest predisposed to the disease as compared to females which was also in line with other studies done in different ethical populations of the world like China, Cambodia, Ethiopia, Bangladesh, Pakistan etc.[9–12] In present study among 75 positive MTB cases, 51 females and 24 males pediatric cases were enrolled for the study, the number of females cases were higher for the detection of Rifampicin resistance as compared to the males. However, some studies reported the same results.[8] A study by Mushtaq MU et al., has shown the prevalence of TB increases with age which was in agreement with another study in TB surveillance statistics of Pakistan study. [23] In our study also patient with age 15 to 18 got more infection than patients less than 15-year age.[13–15]

The variation in magnitude could potentially stem from differences in the study population, geographic diversity, study environment, and tuberculosis (TB) control measures, such as the practices under the Directly Observed Treatment, Short Course program. Furthermore, sample heterogeneity may also influence the outcomes of the GeneXpert MTB/RIF assay sensitivity.

The study highlights the growing concern of Rifampicin-resistant MTB/EPTB in children, which is often diagnosed based on clinical findings rather than laboratory confirmation. This poses significant challenges due to the diverse clinical manifestations of EPTB and the limited availability of good quality specimens for microbiological confirmation. The GeneXpert MTB/RIF assay has become a crucial tool in addressing these challenges, offering rapid and accurate diagnosis, which is particularly important in pediatric populations where the disease may present atypically.

Although empirical treatment regimens for TB usually involve combination therapy based on local epidemiology, the presence of rifampicin resistance complicates treatment decisions. To address the issue of rifampicin-resistant MTB/EPTB in children, a comprehensive approach is required.[16] When faced with rifampicin-resistant MTB/EPTB in children, it is essential to consider the challenges in diagnosis and treatment due to resistance.

Studies have shown that the rates of Rifampicin-resistant MTB/EPTB in children are increasing, further complicating treatment outcomes. Furthermore, the emergence of rifampicin resistance adds complexity to the treatment regimen and increases the risk of treatment failure and disease progression.

5. Conclusion

Rifampicin-resistant tuberculosis in children presents a complex clinical, therapeutic, and public health challenge. By understanding the clinical presentation, treatment approaches, and public health implications of this condition, healthcare providers, policymakers, and communities can work together to improve outcomes for children affected by rifampicin-resistant tuberculosis. The prevalence of TB and rifampicin resistance TB in children was higher in our finding. Enhanced surveillance, timely diagnosis, individualized treatment, and community-based interventions are key components of a comprehensive strategy to combat this growing threat and safeguard the health of children worldwide.

6. Sources of Funding

None.

7. Conflict of Interest

None.

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