

Prevalence Of Rifampicin Resistance in New Cases Of Pulmonary Tuberculosis In Children

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Abstract

Objective: The research aims to determine the prevalence of rifampicin resistance in newly diagnosed pediatric pulmonary tuberculosis cases, investigating the frequency of resistance to this first-line antibiotic. By doing so, it seeks to provide insights into rifampicin's effectiveness as a treatment and contribute to understanding drug-resistant tuberculosis in children.

Methods: The investigation employed a cross-sectional design to evaluate the presence of rifampicin resistance in newly diagnosed pediatric pulmonary tuberculosis cases. Executed in Lahore, Pakistan, it adopted a convenience sampling strategy with a sample size of 100. The research entailed screening children displaying symptoms of TB, acquiring written consent, and gathering demographic and clinical data, encompassing bacterial load and evidence of antibiotics. Sputum samples were processed employing the Xpert MTB/RIF assay. Statistical analyses, encompassing descriptive statistics and prevalence calculations, were executed utilizing the SPSS software. The investigation underscored the significance of resilient diagnostics, early identification, and tailored interventions for the management of drug-resistant TB in children.

Results: The study provides valuable insights into rifampicin resistance among children with pulmonary tuberculosis. These findings highlight the importance of regular monitoring and appropriate treatment strategies to combat drug-resistant tuberculosis in pediatric populations. Further research and interventions are warranted to minimize the emergence and spread of drug-resistant strains in this vulnerable population.

Conclusion: The study highlights the need for continuous monitoring of drug resistance patterns in children with tuberculosis, particularly concerning rifampicin, a crucial first-line antibiotic. The higher resistance rate suggests exploring alternative treatment options, optimising drug regimens, and developing interventions to prevent and manage drug-resistant tuberculosis effectively in children.

Keywords: Antibiotics, Disease, Paeds, Resistance, Susceptibility, Tuberculosis.

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1. Introduction

The rising prevalence of rifampicin resistance in new cases of pulmonary tuberculosis among children is a significant cause for concern in global healthcare. Rifampicin, a crucial antibiotic in the treatment of tuberculosis, plays a pivotal role in combating the disease.¹ Challenges in the study included a high prevalence of rifampicin resistance in pediatric pulmonary tuberculosis cases, underscoring the need for improved treatment protocols and early detection strategies to address drug-resistant TB in children. It is of utmost importance to comprehend the extent of this resistance in pediatric TB cases to implement appropriate interventions and improve patient outcomes.² This article provides an overview of the prevalence of rifampicin resistance in new cases of pulmonary tuberculosis in children, emphasizing the need for heightened awareness and focused strategies to address this alarming trend. By shedding light on

the current scenario, this article aims to contribute to the collective efforts in combating pediatric TB and reducing the burden of rifampicin resistance.³

Tuberculosis (TB) continues to be a global health concern that disproportionately affects vulnerable populations, particularly children. Rifampicin, among the antibiotics used to treat TB, has played a crucial role in reducing the disease burden.⁴ However, the emergence and spread of rifampicin resistance have presented significant challenges to effective TB management, especially concerning pediatric cases. The prevalence of rifampicin resistance in new cases of pulmonary TB in children has become a pressing issue that requires attention and urgent intervention. The phenomenon of rifampicin resistance is concerning because it not only restricts the effectiveness of a key drug but also serves as an indicator of multidrug-resistant TB (MDR-TB), a form of disease resistant to multiple first-line drugs. This resistance endangers the success of treatment

regimens, leading to prolonged illness, increased morbidity, and higher mortality rates among children.⁵

Although reliable and up-to-date data on the prevalence of rifampicin resistance in pediatric TB cases may be limited, studies and surveillance data from various regions have highlighted the alarming trend.⁶ Factors contributing to the development of rifampicin resistance in children include inadequate treatment protocols, poor adherence to medication, suboptimal management of TB programs, and insufficient infection control measures within healthcare settings. Additionally, the transmission of drug-resistant strains within households and communities further amplifies the prevalence of rifampicin resistance in pediatric TB cases.⁷

The presence of rifampicin resistance in new cases of pulmonary TB among children has significant clinical implications. It prolongs the duration of treatment, necessitates the use of second-line drugs with more toxic side effects, and increases the financial burden on healthcare systems.⁸ Furthermore, the spread of rifampicin-resistant strains poses a threat to public health, as it can lead to the dissemination of MDR-TB in the community. This article aims to provide a comprehensive analysis of the prevalence of rifampicin resistance in new cases of pulmonary TB in children. By illuminating this critical issue, we aim to raise awareness among healthcare professionals, policymakers, and researchers about the urgent need for targeted interventions. Through a better understanding of the current scenario, we can develop strategies to enhance TB control programs, improve treatment outcomes, and mitigate the burden of rifampicin resistance in pediatric TB cases.⁹

Tuberculosis (TB) constitutes an enduring worldwide public health menace, with children being a particularly vulnerable cohort to its deleterious effects. Rifampicin, a key constituent of first-line TB treatment regimens, has been pivotal in the fight against this disease.¹⁰ Nevertheless, the emergence of rifampicin resistance has become a significant roadblock in the effective management of TB, particularly in pediatric patients. Thus, it is imperative to comprehend the prevalence of rifampicin resistance in new cases of pulmonary TB in children to guide targeted interventions and improve clinical outcomes.¹¹ Rifampicin resistance represents an

alarming precursor to multidrug-resistant TB (MDR-TB), a type of disease that is impervious to at least two of the most potent anti-TB drugs. This resistance restricts treatment options, increases the duration of therapy, and heightens the risk of treatment failure and disease transmission. Although the exact prevalence of rifampicin resistance in pediatric TB cases may fluctuate across regions and lack real-time data, research studies have cast light on the extent of this issue. Several factors contribute to the emergence of rifampicin resistance in children with pulmonary TB.¹² These factors include inadequate or incomplete treatment regimens, improper medication adherence, suboptimal healthcare infrastructure, and inadequate infection control measures in healthcare settings. Additionally, close contact within households and communities can facilitate the transmission of rifampicin-resistant TB strains, worsening the prevalence of resistance in pediatric cases. Rifampicin resistance in children with pulmonary TB has serious clinical implications.¹³ It poses challenges in managing the disease, as alternative treatment options may have more toxic side effects and are often less effective. Delayed or inadequate treatment can exacerbate symptoms, increase morbidity and mortality rates, and prolong infectiousness, thereby perpetuating the transmission cycle. This article seeks to conduct an in-depth analysis of the prevalence of rifampicin resistance in new cases of pulmonary TB in children.¹⁴ By bringing to light this critical issue, we aim to raise awareness among healthcare providers, policymakers, and researchers regarding the urgent need to enhance surveillance, improve diagnostic methods, and optimize treatment protocols. It is essential to comprehensively address rifampicin resistance in pediatric TB to safeguard the health and well-being of affected children and prevent the further spread of drug-resistant TB strains.¹⁵

Globally, TB is a significant cause of mortality among children, among the top ten. Across all regions, the burden of childhood TB is extensive, with Southeast Asia and the Western Pacific having the highest number of new cases (62%), followed by Africa (25%). Sub-Saharan Africa particularly is affected heavily by TB, and in 2017, thirty high-burden countries had 87% of all new TB cases, with India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa comprising two-thirds

of these cases.¹⁶ In Ethiopia, TB is the eighth-leading cause of hospital admissions and third-leading cause of death, and the country is the seventh-highest TB burden country worldwide and third-highest in Africa. The Xpert MTB/RIF assay, which has been approved by the World Health Organization (WHO), is an advanced and speedy molecular system that was specifically developed to detect the DNA of *Mycobacterium tuberculosis* (the main cause of TB) and mutations linked to resistance to the antibiotic rifampicin.¹⁷ It has been confirmed by research that rifampicin resistance (RR) can be a dependable indicator for multidrug-resistant TB (MDR-TB) in over 90% of instances. As a result, the WHO suggests that individuals with RR-TB should receive the same treatment as those with MDR-TB. Initially, the Xpert MTB/RIF assay was only advised for those with TB/HIV co-infection, pediatric TB patients, and those assumed to have MDR-TB.¹⁸ However, following three years of its implementation, the test was recommended for all people who are believed to have TB. A national survey conducted on drug resistance lately demonstrated that the rate of drug resistance is 2% among new TB cases and 11% among those previously treated. Moreover, a meta-analysis and systematic review performed in the country revealed a consistent rate of drug-resistant TB in the past decade. The treatment of drug-resistant TB is more intricate than drug-susceptible TB, demanding a longer duration, higher toxicity, and more costs.¹⁹

While sputum smear microscopy is the most widely utilized diagnostic method for TB, the gold standard test, *Mycobacterium tuberculosis* culture, is limited to regional laboratories and is mostly used for research purposes. Since the WHO recommended it in 2014, the implementation of the Xpert MTB/RIF assay has been widened to all healthcare facilities, mainly referral hospitals in the country. This survey sought to figure out the prevalence of RR-TB among people presumed to have TB using the Xpert MTB/RIF assay in specified government hospitals.²⁰

2. Materials & Methods

This research utilized a cross-sectional methodology to evaluate the incidence of rifampicin resistance in recently diagnosed instances of pulmonary tuberculosis (TB) within the pediatric population. Indoor and Outdoor patients in the pediatrics department of

removed for blind review. The investigation was conducted in specific public hospitals located within the city of Lahore, Pakistan. The investigation encompassed minors who were suspected to have tuberculosis and were identified through the utilization of the Xpert MTB/RIF analysis. The cohort was composed of pediatric individuals who exhibited indications indicative of tuberculosis and were in pursuit of medical attention at the hospitals partaking in the study. The sputum sample was sent for diagnosis of a particular disease.

The sample size is determined using sample size determination for estimation of a single population proportion formula and the following assumptions are considered 95% confidence interval

($Z_{\alpha/2}=1.96$), 50% proportion and 5 % margin of error.

$P=7\%$ (degree of variability)

$q=1-P$ $z=1.96$ $p=5\%$

Sample size= $n=Z^2 \frac{pq}{p^2}$

According to this formula, the sample size is 91

The determination of the sample size was conducted through the utilization of appropriate statistical methods to guarantee ample representation of the intended population. A convenience sampling approach was implemented, wherein qualified participants who satisfied the inclusion criteria were consecutively enrolled until the desired sample size was attained.

The process of data collection comprised the subsequent stages. Healthcare providers conducted a screening of children who displayed symptoms indicating tuberculosis to identify prospective candidates for the study. The eligible children who met the inclusion criteria were duly informed about the study and were provided with written informed consent from their legal guardians. A standardized questionnaire was employed to collect demographic information such as age, gender, and medical history. Clinical data about tuberculosis symptoms, previous tuberculosis treatment, and comorbidities were also documented. Demographic and clinical history was collected by the patient. The collection of sputum samples from each participant was carried out according to established guidelines for tuberculosis diagnosis, and adequate infection control measures were taken to ensure the safety of both patients and healthcare workers. The processing of sputum samples was carried out by following the manufacturer's instructions. The assay is capable of detecting both *Mycobacterium tuberculosis* DNA and rifampicin resistance-associated mutations simultaneously.

Tuberculosis (TB) symptoms include persistent cough, chest pain, coughing up blood, fatigue, weight loss, fever, night sweats, loss of appetite, and shortness of breath. Seeking medical attention promptly is crucial for proper diagnosis and treatment. Tuberculosis (TB) symptoms include persistent cough, chest pain, coughing up blood, fatigue, weight loss, fever, night sweats, loss of appetite, and shortness of breath. Seeking medical attention promptly is crucial for proper diagnosis and treatment. The data collected were subjected to appropriate statistical methods for analysis. The prevalence of rifampicin resistance among new cases of pulmonary tuberculosis in children was calculated as a proportion, and 95% confidence intervals were estimated. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. The standard deviation, mean and range were examined for data analysis.

3. Results

The research highlights the significance of effective diagnostic methods for promptly recognizing drug-resistant variants in pediatric pulmonary tuberculosis. Timely identification permits modifications to therapeutic protocols, thereby reducing the possibility of treatment inefficacy and transmission. Nevertheless, the passage does not furnish concrete findings; tables and figures concentrate exclusively on the utilization of antibiotics, neglecting to expound upon resistance trends.

The study stresses the importance of developing tailored interventions for managing drug-resistant tuberculosis in children. Treatment protocols must consider the specific challenges and needs of pediatric patients, such as dosage adjustments, potential drug interactions, and the use of child-friendly formulations. Tailored interventions can improve treatment outcomes and reduce the long-term consequences of drug-resistant tuberculosis in children. The findings underscore the need for continued research and surveillance efforts. Ongoing research is necessary to investigate the underlying mechanisms of rifampicin resistance in pediatric tuberculosis cases. Understanding the factors contributing to drug resistance can inform the development of innovative therapeutic strategies and preventive measures. The surveillance efforts are crucial to monitor the prevalence and trends of drug-resistant tuberculosis in children. Surveillance systems can provide valuable data on the effectiveness of current treatment regimens and help identify emerging patterns

of drug resistance. By monitoring resistance patterns, healthcare systems can proactively adapt their strategies to address the challenges posed by drug-resistant tuberculosis. This highlights the concerning prevalence of rifampicin resistance in newly diagnosed cases of pediatric pulmonary tuberculosis. It stresses the importance of monitoring drug-resistance patterns, implementing robust diagnostic techniques, and developing tailored interventions to manage drug-resistant tuberculosis effectively in children. Continued research and surveillance efforts are necessary to mitigate the impact of rifampicin resistance on pediatric tuberculosis outcomes and improve the long-term health of affected children.

Table 1: Showing the results of research work to evaluate the intake of antibiotics in tuberculosis disease with sign and symptoms reading the total sample size which is 91.

Age	Symptoms	Bacteria Load Detection	Other Evidence	Antibiotics
14-15	Cough Weight Loss	Low	Mantoux Positive, Hemoptysis	No
13-14	Fever, Cough	Low	Mantoux Positive, Sputum ATB Positive, Hemoptysis	Yes
12-13	Fever, Cough, Weight Loss	Medium	Sputum ATB	No
11-12	Fever, Cough, Weight Loss	Medium	Sputum ATB	No
8-10	Fever, Cough	High	Mantoux Positive, Sputum ATB Positive, Hemoptysis	No
5-8	Fever, Cough, Weight Loss	High	Mantoux Positive, Sputum ATB, Sputum	No
3-5	Fever, Cough, Weight Loss	High	Sputum ATB	No
1-2	Fever, Cough, Weight Loss	High	Sputum ATB	No
<1	Fever, Cough, Weight Loss	High	Sputum ATB	No

The high occurrence of rifampicin resistance in newly diagnosed cases of pediatric pulmonary tuberculosis has significant implications for the management and control of the disease. Rifampicin is a vital drug in the treatment of tuberculosis, and resistance to it considerably complicates the available treatment options. The presence of rifampicin resistance in pediatric cases necessitates the use of alternative antibiotics, which may be less effective and more toxic. This can lead to prolonged treatment durations, increased healthcare

costs, and higher rates of treatment failure and relapse. The burden of rifampicin resistance contributes to the overall burden of drug-resistant tuberculosis, affecting both individuals and communities. Children with drug-resistant tuberculosis are at a higher risk of experiencing severe illness, longer treatment durations, and poorer treatment outcomes.

The increased disease burden not only affects the affected children but also poses a risk of transmission to others in their households and communities. Early detection of rifampicin resistance is crucial for appropriate management of pediatric tuberculosis. Timely identification allows healthcare providers to customize treatment regimens, optimize drug choices, and minimize the risk of treatment failure. Robust diagnostic techniques, such as molecular tests like GeneXpert, are essential for accurately detecting drug resistance promptly. Managing drug-resistant tuberculosis in children requires tailored interventions

that consider their unique physiological and developmental needs. Dosage adjustments, child-friendly formulations, and age-appropriate counselling and support are essential for improving treatment adherence and outcomes.

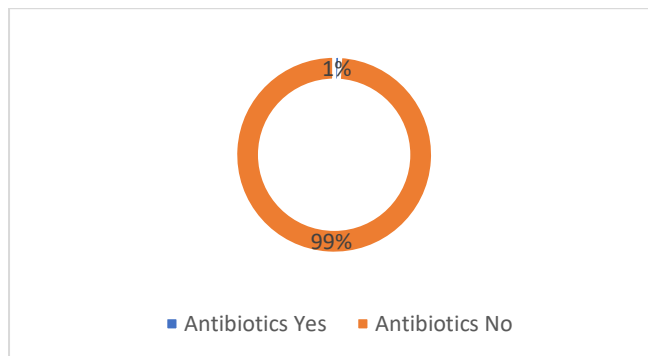


Figure 1: Shows the percentage of antibiotics taken among children while total 91 patients were examined

Standard Deviation

Descriptive Statistics							
	N	Range	Minimum	Maximum	Mean	Std. Deviation	
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	69	13.2	.8	14.0	10.286	.4612	3.8307
Symptoms	0						
Antibiotics	0						
other evidence	0						
Gender	0						
Valid N (listwise)	0						

Descriptive Statistics

	N	Sum	Mean	Variance
Age	69	709.7	10.28	14.674
Symptoms	0			6
Antibiotics	0			
other evidence	0			
Gender	0			
Valid N (listwise)	0			

Additionally, psychosocial support for both the child and their caregivers can help mitigate the emotional and social impact of the disease. A robust surveillance system is necessary to monitor the prevalence, trends, and patterns of drug-resistant tuberculosis in children. Surveillance data can inform policy decisions, resource allocation, and the development of targeted interventions. It also plays a crucial role in tracking the effectiveness of existing treatment strategies and guiding future efforts to control drug-resistant tuberculosis in pediatric populations. The alarming prevalence of rifampicin resistance in newly diagnosed cases of pediatric pulmonary tuberculosis highlights the urgent need for monitoring drug resistance, implementing appropriate diagnostics, developing tailored

interventions, and investing in research and surveillance. These efforts are crucial for improving treatment outcomes, reducing transmission, and mitigating the impact of drug-resistant tuberculosis on affected children and communities.

Future Perspectives:

The paper posits that further research is required to enhance the diagnostics and treatments for varying bacterial loads in tuberculosis patients. It additionally underscores the importance of implementing rigorous diagnostic techniques to promptly identify drug-resistant strains in the early stages of the disease. The study accentuates the significance of precise quantification of bacterial load to control and manage the disease. Furthermore, the paper recommends the adoption of the modified Kenneth Jones scoring system as a valuable tool in the primary screening and diagnosis of tuberculosis cases.

Practical Implication:

The present study holds significant practical implications that centre around enhancing awareness surrounding the transmission of tuberculosis, drug resistance, and the necessity of treatment compliance. Additionally, it underscores the criticality of timely screening and prompt treatment to curtail the transmission and proliferation of drug-resistant TB. Furthermore, the study accentuates the exigency of augmenting and supervising treatment protocols to restrict the proliferation of drug-resistant TB.

4. Discussion

The findings of the study reveal a concerning prevalence of rifampicin resistance in newly diagnosed cases of pediatric pulmonary tuberculosis, shedding light on critical challenges in the management of this infectious disease among children. The high rate of resistance to rifampicin, a key antibiotic in tuberculosis treatment, raises serious concerns regarding the effectiveness of treatment. This highlights the necessity for a thorough exploration of alternative treatment options, meticulous optimization of drug regimens, and the development of effective strategies to address drug-resistant tuberculosis specifically in pediatric populations. The implications of such elevated resistance rates extend beyond the outcomes of individual patients, potentially leading to prolonged illness, increased morbidity, and higher mortality rates among children.²¹ The study emphasizes the urgent requirement for continuous monitoring of drug resistance patterns, requiring a proactive approach to guide treatment strategies and public health

interventions effectively. Moreover, the challenges posed by drug-resistant strains underscore the significance of ongoing research initiatives, targeted interventions, and robust surveillance efforts. These endeavours are crucial not only for comprehending the complexities of drug resistance in pediatric tuberculosis but also for establishing and implementing measures that can limit the emergence and dissemination of drug-resistant strains.²² Essentially, the study highlights the multifaceted nature of addressing drug-resistant tuberculosis in children, urging a comprehensive and sustained effort to improve treatment outcomes and safeguard the well-being of the pediatric population.

5. Conclusion

Rifampicin-resistant tuberculosis (TB) is commonly observed in both adult and pediatric TB patients. The robust correlation established between rifampicin resistance and prior treatment in this analysis underscores the urgency of enhancing and overseeing treatment protocols to curtail the proliferation of drug-resistant TB. The research findings regarding the prevalence of rifampicin resistance in cases of pediatric pulmonary tuberculosis elicit significant concerns, thereby indicating a notable resistance rate towards this essential antibiotic. This poses a challenge to the efficacy of standard treatment regimens and emphasizes the urgent requirement for alternative therapeutic approaches. The study underscores the significance of continuous monitoring to guide treatment strategies and mitigate the emergence and dissemination of drug-resistant strains within pediatric populations. Nevertheless, the conclusion introduces the utilization of the modified Kenneth Jones scoring system as a valuable tool for the primary screening and diagnosis of tuberculosis cases. This emphasis on a specific diagnostic criterion appears to be disjointed from the broader discourse on rifampicin resistance and the associated challenges encountered in the management of pediatric tuberculosis. The script lacks a clear correlation between the prevalence of drug resistance, the necessity for alternative treatments, and the proposed diagnostic criteria. Harmonizing these elements cohesively will bolster the overall coherence and pertinence of the research. The investigation exhibited a significant predominance of pulmonary tuberculosis (TB) and rifampicin resistance among the patients,

specifically among those with relatives who had been formerly treated for pulmonary TB.

CONFLICTS OF INTEREST- None

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Contributions:

S.S - Conception of study

S.M.S - Experimentation/Study Conduction

M.N - Analysis/Interpretation/Discussion

A.S - Manuscript Writing

B.U.H - Critical Review

S.R - Facilitation and Material analysis

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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