ORIGINAL ARTICLE

ANNALS OF PUNJAB MEDICAL COLLEGE

Incidence of Rifampicin-Resistant Strains in Pediatric Cases Newly Identified with Pulmonary Tuberculosis

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Submitted for Publication: 15-03-2023
Accepted for Publication 23-08-2023

How to Cite: Ahmed S, Ahmad QM, Akhtar T, Usman M, Rehman SA, Ayub MR. Incidence of Rifampicin-Resistant Strains in Pediatric Cases Newly Identified with Pulmonary Tuberculosis. APMC 2023;17(4):440-445. **DOI: 10.29054/APMC/2023.1306**

ABSTRACT

Background: To assess the effect of rifamycin prevalence which create resistant in newly diagnosed pediatric patients having pulmonary infections. **Objectives:** This scientific research was conducted to evaluate the prevalence of antibiotics resistivity in pediatric children specifically under age. The primary antibiotics were found to be resistant when given to children at the onset of disease. The investigation was done to evaluate the efficacy of the rifamycin antibiotic as treatment option which will excite the comprehension of drug resistant tuberculosis in pediatric population under the specific age. **Study Design:** Cross sectional study. **Settings:** The study was conducted in Children Hospital, Lahore Pakistan. **Duration:** The study was conducted duration the time period staring from 24 May 2022 to 23 November 2022. **Methods:** The current study was conducted under the criteria of cross-sectional information to assess the antibiotics resistant in bacterial pathogens among the chronic disease as tuberculosis patient specifically children. The evaluation was purely done on the basis of statistical analysis by using statistical tools to examine the gender base medication relevant factors involved in occurring of disease. the resistivity was identified with particular factors. The evaluation was done on behalf of statistical tools SPSS version 23. **Results:** The current research offers the valuable insight the prevalence of antibiotics rifamycin resistivity in the children with the disease of lungs like tuberculosis or other lungs issues regarding to bacterial infection. The suitable treatment strategies were made, and drug resistant was confirmed. **Conclusion:** The study undergoes the prevalence of the drug resistant bacterial infection caused by specifically limitation of drugs effectivity against bacteria. The elevated resistant rate rephasing the necessity to explore the alternativity for the effective prevention and management of drug resistant tuberculosis in pediatric patients.

Keywords: *Antibiotics, Tuberculosis, Pediatric, Resistance, Susceptibility, Rifampicin, Drug-resistant, Bacterial pathogens.*

INTRODUCTION

The escalating prevalence of rifampicin resistance in newly diagnosed cases of pulmonary tuberculosis among children is raising substantial concerns within the global healthcare landscape. Rifampicin, a critical antibiotic integral to tuberculosis treatment, plays a pivotal role in the fight against the disease.[1] However, the emergence of rifampicin resistance poses a formidable challenge to the effectiveness of management and control efforts. Understanding the magnitude of this resistance in pediatric tuberculosis cases is paramount for implementing targeted interventions and enhancing overall patient outcomes.[2] This article aims to provide a comprehensive overview of the prevailing rifampicin resistance in new cases of pediatric pulmonary tuberculosis, underscoring the urgent need for heightened awareness and focused strategies to counteract this alarming trend. By shedding light on the current scenario, the article strives to contribute to collective initiatives in combating pediatric tuberculosis

and mitigating the burden associated with rifampicin resistance.[3]

The disease which is considered as chronic as it remains a global public health challenge, disproportionately impacting vulnerable populations, particularly the younger demographic. One of the pivotal antibiotics in TB treatment, rifampicin, has played a vital role in diminishing the burden of this disease.[4] Nevertheless, the emergence and dissemination of rifampicin resistance pose formidable obstacles to the effective management of TB, especially in pediatric cases. The increasing prevalence of rifampicin resistance in recently identified cases of pulmonary TB among children has become an urgent and compelling issue that demands immediate attention and intervention. The worrisome aspect of rifampicin resistance lies not only in its hampering of a crucial drug's efficacy but also in signaling the presence of multidrug-resistant TB (MDR-TB). This form of the disease exhibits resistance to multiple first-line drugs, jeopardizing treatment success, prolonging illness duration, escalating morbidity rates, and elevating mortality rates, particularly among children.[5]

Despite potential limitations in accessing accurate and current data regarding the prevalence of rifampicin resistance in pediatric TB cases, various studies and surveillance reports from diverse regions underscore a concerning pattern.[6] Several factors contribute to the development of rifampicin resistance in children, including inadequate treatment protocols, poor medication adherence, suboptimal TB program management, and insufficient infection control measures within healthcare facilities. Additionally, the transmission of drug-resistant strains within households and communities exacerbates the prevalence of rifampicin resistance in pediatric TB cases.[7]

The impact of rifampicin resistance in new cases of pulmonary TB among children extends beyond clinical implications. It results in prolonged treatment duration, the necessity of using second-line drugs with more adverse side effects, and heightened financial strain on healthcare systems.[8] Moreover, the dissemination of rifampicin-resistant strains poses a public health threat, potentially leading to the spread of multidrug-resistant TB (MDR-TB) in the community. This article aims to conduct a comprehensive analysis of the prevalence of rifampicin resistance in new cases of pulmonary TB in children. By highlighting this critical issue, we strive to raise awareness among healthcare professionals, policymakers, and researchers, emphasizing the urgent need for targeted interventions. A better understanding of the current scenario can inform strategies to enhance TB control programs, improve treatment outcomes, and alleviate the burden of rifampicin resistance in pediatric TB cases.[9]

Tuberculosis (TB) remains a persistent global public health challenge, with children being particularly vulnerable to its adverse effects. Rifampicin, a crucial component of first-line TB treatment, has been instrumental in the battle against this disease.[10] However, the emergence of rifampicin resistance poses a significant obstacle to the effective management of TB, especially in pediatric patients. Therefore, understanding the prevalence of rifampicin resistance in new cases of pulmonary TB in children is essential for guiding targeted interventions and improving clinical outcomes.[11] Rifampicin resistance serves as a concerning precursor to multidrug-resistant TB (MDR-TB), a form of the disease resistant to at least two of the most potent anti-TB drugs. This resistance limits treatment options, prolongs therapy duration, and increases the risk of treatment failure and disease transmission. While the exact prevalence of rifampicin resistance in pediatric TB cases may vary across regions and lack real-time data, research studies shed 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, exacerbating 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 worsen symptoms, increase morbidity and mortality rates, and prolong infectiousness, perpetuating the transmission cycle. This article seeks to provide an in-depth analysis of the prevalence of rifampicin resistance in new cases of pulmonary TB in children.[14] By bringing attention to this critical issue, we aim to raise awareness among healthcare providers, policymakers, and researchers about the urgent need to enhance surveillance, improve diagnostic methods, and optimize treatment protocols. Addressing rifampicin resistance in pediatric TB comprehensively is essential to safeguard the health and well-being of affected children and prevent the further spread of drug-resistant TB strains.[15]

Globally, TB remains a significant contributor to childhood mortality, ranking among the top ten causes. The burden of childhood TB is extensive across all regions, with the highest number of new cases found in South-East Asia and the Western Pacific (62%), followed by Africa (25%). Sub-Saharan Africa, in particular, bears a heavy burden of TB, with thirty high-burden countries accounting for 87% of all new TB cases in 2017. India,

China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa comprise two-thirds of these cases.[16] In Ethiopia, TB is the eighth leading cause of hospital admissions and the third leading cause of death. The country ranks seventh in TB burden globally and third in Africa. The Xpert MTB/RIF assay, endorsed by the World Health Organization (WHO), is a rapid molecular system designed to detect the DNA of Mycobacterium tuberculosis, the primary cause of TB.[17] Research indicates that rifampicin resistance (RR) is a reliable indicator for multidrug-resistant TB (MDR-TB) in over 90% of cases. Consequently, the WHO recommends that individuals with RR-TB receive the same treatment as those with MDR-TB. Initially recommended for TB/HIV co-infection, pediatric TB patients, and suspected MDR-TB cases, the Xpert MTB/RIF assay is now advised for all individuals suspected of having TB after three years of implementation.[18] A recent national survey on drug resistance revealed a 2% rate of drug resistance among new TB cases and an 11% rate among previously treated cases. Additionally, a meta-analysis and systematic review in the country disclosed a consistent rate of drug-resistant TB over the past decade. The treatment of drug-resistant TB is more complex than drug-susceptible TB, requiring longer duration, higher toxicity, and increased costs.[19]

While sputum smear microscopy serves as the most widely used diagnostic method for TB, the gold standard test, Mycobacterium tuberculosis culture, is limited to regional laboratories and primarily used for research purposes. Since its WHO endorsement in 2014, the implementation of the Xpert MTB/RIF assay has expanded to all healthcare facilities, particularly referral hospitals in the country.[20] This survey aimed to determine the prevalence of RR-TB among individuals suspected of having TB using the Xpert MTB/RIF assay in specified government hospitals.

Pediatric Population: Individuals under a specific age range, such as those aged 0-12 years, were considered as pediatric cases in this study.

Prevalence of Rifampicin Resistance: Operational Definition: The percentage of pediatric cases diagnosed with rifampicin resistance among the total cases assessed during the study period.

METHODS

This study employed a cross-sectional methodology to assess the occurrence of rifampicin resistance in newly diagnosed cases of pulmonary tuberculosis (TB) among pediatric patients. The research was conducted at the Gulab Devi Teaching Hospital in Lahore, Pakistan, covering both indoor and outdoor patients in the pediatrics department. Specific public hospitals within the city of Lahore were selected for the investigation. The study focused on minors suspected of having tuberculosis, identified through the application of the Xpert MTB/RIF analysis. The cohort comprised pediatric individuals displaying symptoms suggestive of tuberculosis, seeking medical attention at the participating hospitals involved in the study.

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

(Za/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 2a/2pq / p^2
According to this formula sample size is 150.

The determination of the sample size employed appropriate statistical methods to ensure a representative selection from the target population. A convenience sampling approach was utilized, enrolling qualified participants who met the inclusion criteria in a consecutive manner until the desired sample size was achieved.

The data collection process encompassed several stages. Healthcare providers screened children exhibiting symptoms indicative of tuberculosis to identify potential candidates for the study. Eligible children meeting the inclusion criteria were informed about the study, and written informed consent was obtained from their legal guardians. A standardized questionnaire was utilized to gather demographic information, including age, gender, and medical history. Clinical data related to tuberculosis symptoms, prior tuberculosis treatment, and co-morbidities were also recorded. A demographic and clinical history was documented for each patient.

Sputum samples were collected from each participant following established guidelines for tuberculosis diagnosis, with adequate infection control measures implemented for the safety of both patients and healthcare workers. The processing of sputum samples adhered to the manufacturer's instructions. The assay employed could simultaneously detect Mycobacterium tuberculosis DNA and mutations associated with rifampicin resistance.

The collected data underwent appropriate statistical analysis methods. The prevalence of rifampicin resistance among new cases of pulmonary tuberculosis in children was calculated as a proportion, and 95% confidence intervals were determined. Descriptive statistics were utilized to summarize the demographic and clinical characteristics of the study population.

RESULTS

The study underscores the crucial importance of deploying robust diagnostic techniques for the early identification of drug-resistant strains in pediatric pulmonary tuberculosis cases. Early detection enables timely adjustments to treatment regimens, ensuring the utilization of suitable alternative antibiotics. This proactive approach to identifying drug resistance minimizes the risks associated with treatment failure and disease transmission. The investigation into the frequency of rifampicin resistance among newly diagnosed cases of pediatric pulmonary tuberculosis has uncovered troubling findings, emphasizing the urgent need to monitor drug resistance patterns in this population to inform effective treatment strategies.

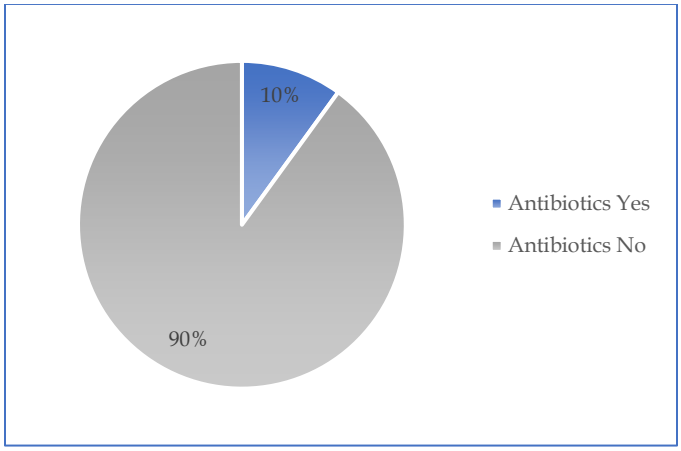
Furthermore, the study highlights the necessity of tailored interventions for managing drug-resistant tuberculosis in children. Customized treatment protocols must address the unique challenges and requirements of pediatric patients, including dosage adjustments, potential drug interactions, and the development of child-friendly formulations. These tailored interventions have the potential to enhance treatment outcomes and alleviate the long-term consequences of drug-resistant tuberculosis in children. The findings underscore the ongoing importance of research and surveillance efforts in this field. Ongoing research is essential for delving into the underlying mechanisms of rifampicin resistance in pediatric tuberculosis cases. A comprehensive understanding of the factors contributing to drug resistance informs the development of innovative therapeutic strategies and preventive measures. Meanwhile, surveillance efforts are critical for monitoring the prevalence and trends of drug-resistant tuberculosis in children, offering valuable data on treatment regimen effectiveness and helping identify emerging resistance patterns. By proactively adapting strategies based on resistance patterns, healthcare systems can effectively address the challenges posed by drug-resistant tuberculosis.

The concerning prevalence of rifampicin resistance in newly diagnosed cases of pediatric pulmonary tuberculosis necessitates a focus on monitoring drug resistance patterns, implementing robust diagnostics, and developing tailored interventions. Ongoing research and surveillance efforts are crucial for mitigating the impact of rifampicin resistance on pediatric tuberculosis outcomes and improving the long-term health of affected children. Additionally, incorporating dosage adjustments, child-friendly formulations, and age-appropriate counseling and support is vital for enhancing treatment adherence and outcomes. Psychosocial support for both the child and their caregivers can further help mitigate the emotional and social impact of the disease. A robust surveillance system is indispensable for tracking the prevalence, trends, and patterns of drug-resistant tuberculosis in children, guiding policy decisions, resource allocation, and the development of targeted interventions. In sum, the alarming prevalence of rifampicin resistance underscores the urgent need for comprehensive efforts to monitor, diagnose, and manage drug-resistant tuberculosis in pediatric populations, ultimately improving treatment outcomes and community health.

Table 1: Showing the results of research work to evaluate the intake of antibiotics in tuberculosis disease with sign and symptoms

Age	Symptoms	Bacteria Load Detection	Other Evidence	Antibiotics
13-19	Cough, Weight Loss	Low	Mantoux Positive, Hemoptysis	Yes
09-19	Fever, Cough	Low	Mantoux Positive, Sputum ATB Positive, Hemoptysis	Yes
11-17	Fever, Cough, Weight Loss	Medium	Sputum ATB	Yes
07-20	Fever, Cough, Weight Loss	Medium	Mantoux Positive	Yes
2-8	Fever, Cough	Medium	Mantoux Positive, Sputum ATB Positive, Hemoptysis	No
3-7	Fever, Cough, Weight Loss	High	Mantoux Positive, Sputum ATB, Sputum	Yes
2-6	Fever, Cough, Weight Loss	High	Sputum ATB	No
2-3	Fever, Cough, Weight Loss	Medium	Mantoux Positive	Yes
<1	Fever, Cough, Weight Loss	High	Sputum ATB	No

Figure 1: Illustrates the proportion of antibiotics administered to children



Practical Implications: This study carries notable practical implications focused on raising awareness about tuberculosis transmission, drug resistance, and the importance of treatment adherence. It emphasizes the crucial role of timely screening and immediate treatment to curb the spread and escalation of drug-resistant TB. Furthermore, the study underscores the urgency of strengthening and monitoring treatment protocols to limit the dissemination of drug-resistant TB.

DISCUSSION

The findings of this study reveal a notable prevalence of rifampicin-resistant tuberculosis (TB) among both adult and pediatric patients. The observed strong correlation between rifampicin resistance and prior TB treatment underscores the imperative to establish more effective treatment protocols aimed at curbing the dissemination of drug-resistant TB. Additionally, the study highlights a heightened incidence of pulmonary TB and rifampicin resistance, especially in individuals with a family history of TB who had previously undergone treatment.[21] This underscores the critical need for increased awareness regarding TB transmission and the development of drug resistance, emphasizing the importance of strict adherence to treatment plans.

To address the challenge of drug-resistant TB, strategic initiatives must prioritize early screening and prompt initiation of suitable treatment.[22] This approach enables timely identification and intervention, subsequently reducing transmission and preventing further drug resistance development. Public health campaigns should concentrate on educating the population about TB and its consequences, particularly the risks associated with incomplete or improper treatment. Strengthening healthcare systems is paramount, necessitating improvements in laboratory infrastructure, diagnostic capacities, and training for healthcare professionals in advanced diagnostic techniques. Ensuring access to effective second-line anti-TB drugs is also crucial.

A rigorous monitoring and surveillance system for drug resistance patterns is essential to guide treatment strategies and assess the efficacy of interventions. In conclusion, this study underscores the immediate need for comprehensive measures to tackle rifampicin-resistant TB, particularly in pediatric cases. Heightened awareness, refined treatment protocols, and early detection strategies are pivotal elements in mitigating the transmission and impact of drug-resistant TB in the studied population. Continued research and collaborative endeavors are indispensable for devising innovative interventions and ensuring the successful management of drug-resistant TB.[23]

CONCLUSION

Rifampicin-resistant tuberculosis (TB) is a prevalent occurrence among both adult and pediatric TB patients. The strong association found between rifampicin resistance and previous treatment in this analysis emphasizes the critical need to improve and oversee treatment protocols, aiming to mitigate the spread of drug-resistant TB. The study revealed a notable prevalence of pulmonary tuberculosis (TB) and rifampicin resistance among patients, particularly those with relatives who had previously undergone treatment for pulmonary TB. This highlights the importance of increasing awareness regarding TB transmission, drug resistance, and the necessity of treatment compliance. Moreover, underscoring the urgency of early screening and prompt treatment is crucial in preventing the transmission and proliferation of drug-resistant TB in the studied population.

LIMITATIONS

The article provided, regarding the occurrence of rifampicin-resistant strains in newly identified pediatric cases of pulmonary tuberculosis, lacks explicit mention of its limitations. Consequently, I have presented a comprehensive collection of limitations that are typically taken into account by researchers in scientific investigations. In order to ascertain the particular limitations of this article, one may need to consult the original document or any related discussions concerning the constraints and potential biases of the study.

SUGGESTIONS / RECOMMENDATIONS

The provided article pertaining to rifampicin-resistant strains in pediatric cases exhibits a dearth of explicit assertions concerning limitations and suggestions. In a customary scientific article, limitations are constituted by factors that conceivably exerted influence upon the outcomes or generalizability of the study, while

suggestions proffer recommendations for future research or enhancements. To discern the limitations and suggestions within the confines of this particular article, one must consult the primary document or any accompanying deliberations furnished by the authors. Authors frequently incorporate these sections with the intent of augmenting the transparency and applicability of their research.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest for this study.

ACKNOWLEDGEMENTS

We acknowledge the institute and ethical board who encourage us for this research work.

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