Section: Microbiology

Original Research Article

IMPACT OF PRIOR ANTIBIOTIC EXPOSURE ON THE DEVELOPMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS: A RETROSPECTIVE COHORT STUDY

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Abstract

Background: The emergence of multi-drug-resistant tuberculosis (MDR-TB) poses a significant global health challenge, and prior antibiotic exposure has been identified as a potential risk factor. This study investigates the impact of previous antibiotic use on the development and treatment outcomes of MDR-TB in a cohort of tuberculosis (TB) patients. **Materials and Methods:** A retrospective cohort analysis was conducted on 100 TB patients, primarily aged 25-40 years (60%), with a male predominance (55%) and a notable prevalence of comorbidities such as diabetes and HIV (40%). Prior antibiotic exposure, particularly to fluoroquinolones (45%) and macrolides (23%), was recorded in 68% of patients. Statistical analysis, including odds ratio and confidence intervals, assessed the association between antibiotic exposure and MDR-TB development. **Result:** Among patients with prior antibiotic exposure, 52.9% developed MDR-TB compared to only 17.2% in non-exposed individuals (OR: 4.9; 95% CI: 2.1–11.4; $p < 0.001$). Treatment outcomes were significantly poorer in MDR-TB patients, with a success rate of 45% compared to 78% in non-MDR-TB patients. Furthermore, relapse rates were higher in MDR-TB patients (30%) than in non-MDR-TB patients (12%), with antibiotic-exposed individuals within the MDR-TB cohort showing an even higher relapse rate (30%) compared to 20% in non-exposed individuals. **Conclusion:** Prior antibiotic exposure is strongly associated with the development of MDR-TB and poorer treatment outcomes. These findings underscore the need for cautious antibiotic stewardship to mitigate MDR-TB risks.

INTRODUCTION

Tuberculosis (TB) remains one of the leading causes of infectious disease-related mortality worldwide, with approximately 10 million new cases annually.[1] The rise of multi-drug-resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampicin, presents a critical challenge to global TB control. MDR-TB not only complicates treatment but also contributes to higher morbidity, mortality, and healthcare costs.[2] The increasing prevalence of MDR-TB has been linked to multiple factors, including prior exposure to antibiotics, which can drive resistance through selection pressure on Mycobacterium tuberculosis.[3,4]

The overuse or inappropriate use of antibiotics—especially fluoroquinolones and macrolides—has been highlighted as a significant contributor to the development of antibiotic resistance across various bacterial infections.[5,6] Although these antibiotics are not primarily used in TB treatment, their widespread use in other infections may inadvertently impact TB resistance patterns.[7] Patients with a history of antibiotic exposure may, therefore, have a heightened risk of developing MDR-TB due to the selection of resistant TB strains.

This retrospective cohort study seeks to explore the association between prior antibiotic exposure and the development of MDR-TB. By examining a sample of TB patients, this study evaluates key demographic and clinical factors, rates of MDR-TB development, and differences in treatment outcomes between those with and without prior antibiotic exposure. The findings aim to contribute to the growing body of evidence on antibiotic stewardship's role in TB control and highlight the need for targeted interventions to reduce MDR-TB prevalence.

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MATERIALS AND METHODS

Study Design and Setting

This retrospective cohort study was conducted at the Maharajah's Institute of Medical Sciences in Vizianagaram. The study spanned from March 2023 to February 2024 and included patients diagnosed with tuberculosis (TB) who received treatment or follow-up care at the institution. The study was designed to assess the impact of prior antibiotic exposure on the development of multi-drug-resistant tuberculosis (MDR-TB) and examine treatment outcomes among MDR-TB and non-MDR-TB patients.

Study Population

The study included a total of 100 patients diagnosed with TB during the study period. Eligibility criteria required patients to have a confirmed TB diagnosis and documented information on prior antibiotic use. Patients with incomplete medical records or those with drug-resistant TB at initial diagnosis were excluded to ensure the study's focus on the development of MDR-TB.

Data Collection

Data were retrospectively collected from patient medical records, including demographic information (age, gender), clinical data (presence of comorbidities like diabetes and HIV), and antibiotic history. Prior antibiotic exposure was recorded, with particular attention to the use of fluoroquinolones and macrolides, which are commonly prescribed for various infections but are associated with an increased risk of resistance in TB.

Outcome Measures

The primary outcome of interest was the development of MDR-TB, defined as resistance to both isoniazid and rifampicin, which was confirmed through laboratory testing. Secondary outcomes included treatment success rates and relapse rates among MDR-TB and non-MDR-TB patients. Treatment success was defined as the absence of TB symptoms and a negative laboratory result at the end of the treatment period. Relapse was noted if symptoms reappeared or TB was confirmed again after completing treatment.

Statistical Analysis

Data were analyzed to determine the association between prior antibiotic exposure and MDR-TB development. Descriptive statistics were used to summarize demographic and clinical characteristics. Chi-square tests were employed to compare MDR-TB rates between antibiotic-exposed and non-exposed groups. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the likelihood of MDR-TB development among patients with prior antibiotic exposure. P-values < 0.05 were considered statistically significant. Treatment outcomes and relapse rates were compared between MDR-TB and non-MDR-TB groups using appropriate statistical tests.

RESULTS

This retrospective cohort study assessed the impact of prior antibiotic exposure on the development of multi-drug-resistant tuberculosis (MDR-TB) in a sample of 100 patients. Key characteristics of the sample are presented in [Table 1]. The majority of participants were between 25–40 years of age (60%), with a male predominance (55%). Comorbidities were present in 40% of patients, including diabetes and HIV, which are known to influence immune response and tuberculosis treatment outcomes.

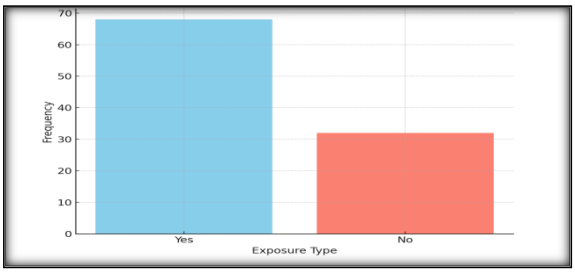

Figure 1: Prior Antibiotic Exposure Among Patients

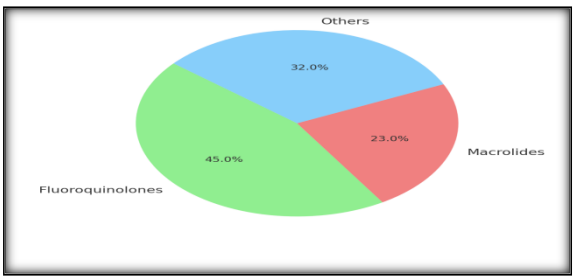

Figure 2: Types of Antibiotics Used Among Exposed Patients

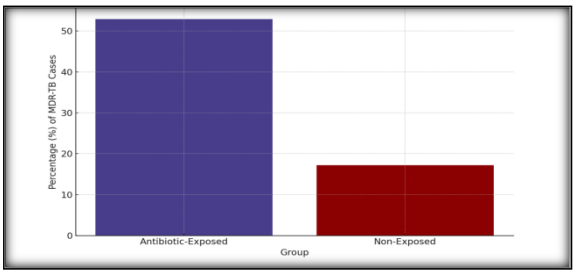

Figure 3: Development of MDR-TB by Antibiotic Exposure

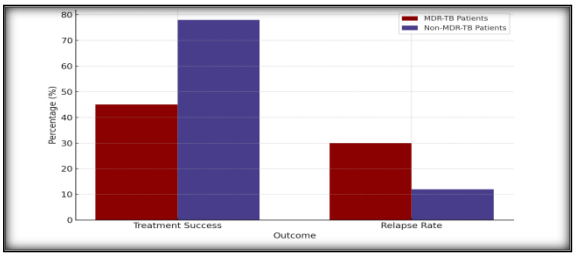

Figure 4: Treatment Outcomes for MDR-TB and Non -MDR-TB Patients

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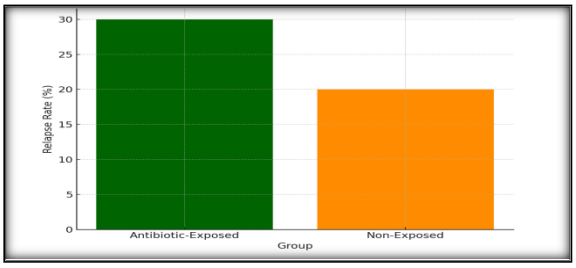

Figure 5: Relapse Rates in MDR-TB Patients Based on Prior Antibiotic Exposure

Prior Antibiotic Exposure: Prior antibiotic exposure was observed in 68% of patients [Table 2]. Among these, the most frequently used antibiotics were fluoroquinolones (45%) and macrolides (23%).
Development of MDR-TB: A significant proportion of the cohort, 41%, developed MDR-TB. Patients with a history of antibiotic exposure demonstrated a markedly higher rate of MDR-TB at 52.9%, compared to only 17.2% in the non-exposed group [Table 3]. The statistical analysis indicated that prior antibiotic exposure was associated with a significantly elevated likelihood of MDR-TB development, with an odds ratio of 4.9 (95% CI: 2.1–11.4) and a p-value < 0.001, highlighting a strong association between prior antibiotic use and MDR-TB [Table 4].
Treatment Outcomes: Treatment success rates varied considerably between MDR-TB and non-MDR-TB patients. Among MDR-TB patients, the treatment success rate was only 45%, while non-MDR-TB patients achieved a significantly higher success rate of 78% [Table 5]. Relapse rates were also notably different, with 30% of MDR-TB patients experiencing relapse compared to 12% of non-MDR-TB patients.
Relapse Rates in MDR-TB Patients by Antibiotic Exposure: Within the MDR-TB cohort, relapse rates were examined in relation to prior antibiotic exposure. Patients with prior antibiotic exposure showed a higher relapse rate of 30%, compared to 20% in those without prior exposure [Table 6].

Table 1: Sample Characteristics.

Characteristic	Frequency	Percentage (%)
Age		
18–24	20	20%
25–40	60	60%
41–60	15	15%
61+	5	5%
Gender		
Male	55	55%
Female	45	45%
Comorbidities		
Diabetes	20	20%
HIV	10	10%
Other	10	10%
None	60	60%

Table 2: Prior Antibiotic Exposure Among Patients

Exposure Type	Frequency	Percentage (%)
Prior Antibiotic Use		
Yes	68	68%
No	32	32%
Types of Antibiotics Used		
Fluoroquinolones	31	45% of exposed
Macrolides	16	23% of exposed
Others	21	32% of exposed

Table 3: Development of MDR-TB by Antibiotic Exposure

Group	Total Patients	MDR-TB Cases	Percentage (%)
Antibiotic-Exposed	68	36	52.9%
Non-Exposed	32	5	17.2%
Total	100	41	41%

Table 4: Statistical Significance of MDR-TB Development Based on Prior Antibiotic Exposure

Statistic	Value
Odds Ratio	4.9
95% Confidence Interval	2.1 – 11.4
P-Value	<0.001

Table 5: Treatment Outcomes for MDR-TB and Non-MDR-TB Patients

Outcome	MDR-TB Patients (N=41)	Non-MDR-TB Patients (N=59)
Treatment Success	45%	78%
Relapse Rate	30%	12%

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Table 6: Relapse Rates in MDR-TB Patients Based on Prior Antibiotic Exposure

Group	Total MDR-TB Patients	Relapse Cases	Percentage (%)
Antibiotic-Exposed	36	11	30%
Non-Exposed	5	1	20%

DISCUSSION

The findings of this study underscore a strong association between prior antibiotic exposure and the development of multi-drug-resistant tuberculosis (MDR-TB) in patients treated at the Maharajah's Institute of Medical Sciences in Vizianagaram. This association aligns with evidence from other studies, suggesting that prior antibiotic exposure, particularly to fluoroquinolones and macrolides, increases the risk of resistance in Mycobacterium tuberculosis (Migliara et al,[8] 2021; Murray et al,[9] 2019). The results indicate that a history of antibiotic exposure significantly elevates the risk of developing MDR-TB, with an observed odds ratio of 4.9, meaning that patients with prior antibiotic use are nearly five times more likely to develop MDR-TB compared to non-exposed patients. Similar findings in the literature link the extensive or inappropriate use of antibiotics to increased resistance in TB, complicating its treatment and control (Dookie et al,[10] 2018; Xi et al,[12] 2022).

Fluoroquinolones, widely used for respiratory and other bacterial infections, may inadvertently select for resistant strains of M. tuberculosis, further complicating TB control efforts (Murray et al,[9] 2019). This unintended selection pressure mirrors the increased risks seen with Klebsiella pneumoniae and other multidrug-resistant organisms in intensive care settings, reinforcing the importance of antibiotic stewardship to limit resistance development (Migliara et al,[8] 2021). Our study showed that treatment success rates for MDR-TB patients (45%) were significantly lower than those for non-MDR-TB patients (78%), highlighting the treatment challenges posed by drug-resistant TB (Jang & Chung,[11] 2020). Moreover, the study revealed a higher relapse rate among MDR-TB patients (30%) compared to non-MDR-TB patients (12%), with even greater relapse in antibiotic-exposed MDR-TB patients (30%) compared to non-exposed MDR-TB patients (20%). This aligns with findings by Mikiashvili et al,[13] (2024) that underscore the lasting impact of prior antibiotic use on TB treatment outcomes, emphasizing the need for more effective management strategies for MDR-TB. The increasing incidence of MDR-TB and extensively drug-resistant TB further stresses the need for innovative antimicrobial approaches (Haydel,[14] 2010) and personalized treatment strategies to optimize outcomes in high-risk populations (Dookie et al,[10] 2018).

Implications for Practice and Policy

These findings highlight the importance of cautious and judicious use of antibiotics, especially in high-TB-burden areas. Antibiotic stewardship programs targeting the appropriate use of fluoroquinolones and macrolides in non-TB infections could help reduce the risk of MDR-TB development. This study also underscores the need for improved diagnostic practices to ensure that antibiotics are prescribed only when absolutely necessary, thereby limiting the selection pressure that promotes resistance.

Limitations

This study has certain limitations. As a retrospective cohort study, it relies on the accuracy and completeness of medical records, which may introduce biases. Additionally, other factors not accounted for in this study, such as patient adherence to treatment and environmental exposure to TB, may have influenced MDR-TB development. Further studies with a prospective design and a larger sample size could provide more robust evidence on the causal relationship between antibiotic exposure and MDR-TB development.

CONCLUSION

This study demonstrates a significant association between prior antibiotic exposure and the development of multi-drug-resistant tuberculosis (MDR-TB) among TB patients, with an odds ratio of 4.9, indicating a nearly fivefold increased risk. Patients exposed to antibiotics, especially fluoroquinolones and macrolides, showed higher MDR-TB rates (52.9%) and poorer treatment outcomes, with a success rate of 45% compared to 78% in non-MDR-TB patients. Relapse rates were also higher in antibiotic-exposed MDR-TB patients. These findings underscore the need for stringent antibiotic stewardship and targeted interventions to mitigate the impact of antibiotic misuse on TB resistance and treatment outcomes.

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