Association Between Prior Tuberculosis History and Treatment Outcomes in Drug-Resistant Tuberculosis Patients Receiving Bedaquiline-Based Therapy: Prospective Observational Study From Western India

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Abstract:

Introduction: Drug-resistant tuberculosis (DR-TB) poses a significant public health challenge in India. While treatment success in DR-TB cases remains limited, bedaquiline-based oral longer regimens have shown promising results in select studies. **Objective:** This study aimed to evaluate whether a patient's prior TB status influences treatment outcomes under a bedaquiline-based regimen and to assess other previous TB-related variables affecting current DR-TB outcomes. **Methods:** A prospective observational study was conducted at a tertiary care center in Rajkot, Gujarat, between April 2023 and September 2024. Fifty DR-TB patients on bedaquiline-based oral longer regimens were selected using purposive sampling. Data on previous TB treatment, clinical and demographic variables were collected. Treatment outcomes were categorized as cured, treatment completed, defaulted, died, or failed. Statistical analysis using Chi-square and Cramer's V was conducted to assess associations. **Results:** Of the 50 patients, 74% were underweight and from lower socioeconomic backgrounds, and 58% were female. Patients with a history of cured drug-sensitive TB (DS-TB) demonstrated the highest favourable outcomes. In contrast, those with prior treatment failure or no TB history had poorer outcomes. However, the association between prior TB status and current DR-TB outcomes was not statistically significant (Chi-square = 20.99, $p > 0.05$; Cramer's V = 0.3), indicating a weak correlation. **Conclusion:** Although cured DSTB history appears to improve outcomes, previous TB status alone does not significantly predict DR-TB treatment success. A comprehensive approach addressing adherence, resistance, comorbidities, nutrition, and social factors is crucial for better outcomes.

Keywords: Bedaquiline, Drug-resistant tuberculosis, Previous TB history, Predictive factors, Treatment outcome.

Introduction:

India is disproportionately affected by tuberculosis (TB), which continues to be a serious global public health concern. About 27% of all TB cases worldwide occurred in India in 2019, highlighting the urgent need for efficient management techniques.[1] Control efforts have been made more difficult by the advent of drug-resistant TB (DR-TB), which has resulted in longer treatment durations, more side effects, and less than ideal results.[2,3]

A new diarylquinoline called bedaquiline has been developed to improve the effectiveness of treatment for

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DR-TB sufferers.[1] Research has indicated that regimens incorporating bedaquiline can attain up to 83% culture conversion rates in just six months.[1] Even with these developments, DR-TB treatment results are still not ideal. According to a retrospective study conducted in Maharashtra, the treatment effectiveness rate was only 29%, and the death and lost to follow-up rates were high.[4] To successfully customize interventions and enhance patient management, it is imperative to identify determinants of therapy results.[1,3]

The results of current treatment may be predicted by prior TB history. The effectiveness of further treatments may be impacted by the presence of resistant strains of TB or impaired lung function in patients who have previously received therapy for the disease.[1,2] However, there is a dearth of information regarding how previous TB status affects the results of current DR-TB treatment, especially when using regimens that involve bedaquiline.[3]

The purpose of this observational study is to determine whether a patient's past TB treatment history can influence their present treatment results when they are receiving bedaquiline-based therapy for DR-TB in Western India. To improve DR-TB management, clinical decision-making and policy development may benefit from an understanding of this link.

Methods:

A prospective observational study was conducted among 50 patients of DR-TB on bedaquiline oral longer regimen on the outdoor and indoor patients at the department of pulmonary medicine, tertiary care teaching institute in Rajkot city, Gujarat. Study duration was from April 2023 to September 2024.

Sample size: A total of 50 patients with drug-resistant tuberculosis (DR-TB) receiving the bedaquiline-based oral longer regimen were included in this study. Participants of both genders were selected according to predefined inclusion and exclusion criteria. Patients were recruited from both the inpatient from ward as well as the outpatient department of Respiratory Medicine. Written informed consent was obtained from all participants prior to inclusion in the study. The sample size of 50 was determined based on feasibility considerations within the study duration and patient flow at the study site. Although a formal power calculation was not performed, this sample was considered adequate for exploratory observational analysis to identify patterns and potential predictors of treatment outcomes.

Ethics committee approval: this study was approved by the institutional ethics committee (human) of government medical college and hospital Rajkot.

The criteria used for the enrolment of the patients in this study are given below.

Inclusion criteria: All Drug-Resistant Tuberculosis patients having a) Rifampicin resistance. b) Both Rifampicin and Isoniazid resistance with / without resistant to any of / all Fluoroquinolones. c) Any / all second line injectable drug resistance.

Exclusion criteria: 1) Patients on Bedaquline Shorter Oral Regimen, 2) Patients having a) Mono-H resistance tuberculosis. b) XDR (extensive drug resistance tuberculosis)

Study tool: A pre-tested, pre-structured proforma was used for data collection. It was piloted prior to the study to identify and correct any issues. To enhance comprehension and response accuracy, the proforma was translated into the local vernacular language.

Study Method: A prospective observational study was conducted on 50 DR-TB patients on Bedaquline oral longer regimen. For each patient, apart from baseline physical, radiological, and biochemical parameters, associated risk factors, additional data on previous antituberculosis treatment, comorbidities, and contact history were also collected via patient interview. For BMI classification, current Asian classification was used and for socioeconomic class cut off of each class of B. G. Prasad classification was used.[5,6]

The treatment outcome measurement was considered as follow: Cured/treatment completed/loss to follow-up/died/defaulter.[4] Apart from this, adverse drug reactions were noted. All the demographic and clinical data collected was recorded in proformas, which were later entered into Microsoft Excel. All care has been taken to fill complete data at the time of data collection. After ensuring the completeness of the data, analysis was done and descriptive statistics are applied. All statistical analyses were performed using the Jamovi 2.4.11 software. This study is also compared with other

standard equivalent studies. Numbers, percentages, chi-square and Cramer s V used to analyse the data.

Results:

This prospective observational study was conducted on 50 DR-TB patients on Bedaquline oral longer regimen. The majority of patients (32, 64%) were between the ages of 21 and 40 years, indicating that drug-resistant TB predominantly affects individuals in their most productive age group. Females accounted for a slightly higher proportion (29, 58%) of the cases compared to males. A concerning 74% of participants belonged to the lower socioeconomic class, highlighting the diseases association with poverty. Nutritional status was poor among most patients, with 50% being severely underweight and an additional 24% classified as underweight. Only 22% had a normal BMI, and no participants were obese. (Table 1)

Adherence levels were generally greater among those with Current TB across all activities when comparing respiratory hygiene practices between patients with Previous TB and Current TB (n=50 in each group). Washing hands after coughing or sneezing was the most common habit, as reported by 88% of people with current TB and 80% of people with previous TB. Forty percent of the Previous TB group and forty-two percent of the Current TB group covered their mouths when coughing or sneezing. In the same way, 36% and 40% of the groups reported safely disposing of their sputum, while 46% and 50% reported using masks. Statistical analysis using the Chi-square test revealed that none of the differences between the two groups were statistically significant, despite these observed disparities. (Table 2)

From Table 3, it was observed that patients with DSTB cured had highest cure rate, total 11 patients recovered from DR-TB. From DSTB treatment failure patients mixed outcome has been observed like six of them cured and some were treatment failure. DR-TB treatment failure had shown poor outcome of death in one patient. Patients with no previous history of TB had mixed outcome as seen in Table 3. DSTB defaulters had shown better outcome showed four cured patients. Overall, previously cured DSTB patients showing better outcome as compared to defaulters and failure cases which further tested for significance association.

To find association of previous history of TB and outcome of current MDR-TB, authors have applied chi-

Table 1: Demographic characteristics of study participants (n=50)

Variable	Number of Patients	Percentage (%)
Age (in years)		
< 20	3	6
21-30	15	30
31-40	17	34
41-50	6	12
51-60	6	12
> 60	3	6
Gender		
Male	21	42
Female	29	58
Body Mass Index		
<16.5 (Severely underweight)	25	50
<18.5 (Underweight)	12	24
18.5-24.9 (Normal weight)	11	22
25-29.9 (Overweight)	2	4
>30 (Obese)	0	0
Socioeconomic Class		
Lower class	37	74
Middle class	9	18
Upper class	4	8

Table 2: Comparison of Respiratory Hygiene Practices Between Patients With Previous and Current TB (n= 50)

Respiratory Hygiene Practice	Previous TB	Current TB	P value
Covers mouth when coughing/sneezing	20 (40%)	21 (42%)	1.000
Disposes sputum safely	18 (36%)	20 (40%)	0.837
Washes hands after cough/sneeze	40 (80%)	44 (88%)	0.413
Wears mask regularly	23 (46%)	25 (50%)	0.841

Table 3: Association Between Previous TB History and Current DR-TB Treatment Outcomes (n = 50)

Previous TB History	Cured n (%)	Defaulted n (%)	Died During Treatment n (%)	Treatment Failure n (%)	χ^2	Cramér's V
DR-TB Defaulter	1 (2%)	1 (2%)	0 (0%)	0 (0%)	13.59	0.302
DR-TB Failure	0 (0%)	0 (0%)	1 (2%)	0 (0%)	p=0.482	
DS-TB Cured	11 (22%)	3 (6%)	5 (10%)	1 (2%)		
DS-TB Defaulter	4 (8%)	1 (2%)	0 (0%)	1 (2%)		
DS-TB Failure	6 (12%)	1 (2%)	0 (0%)	1 (2%)		
No TB History	4 (8%)	3 (6%)	5 (10%)	1 (2%)		

Table 4: Association of Key Previous TB Variables with Current DR-TB Treatment Outcome (n = 50)

Previous TB Variable	Favorable Outcome	Unfavorable Outcome	Chi-Square (χ^2)	p-value
Previous TB Type			1.18	0.556
DSTB	24 (48.0%)	10 (20.0%)		
DR-TB	2 (4.0%)	1 (2.0%)		
None	7 (14.0%)	6 (12.0%)		
Interval Since Last TB			1.14	0.566
<1 year	12 (24.0%)	4 (8.0%)		
1-2 years	10 (20.0%)	5 (10.0%)		
>2 years	11 (22.0%)	8 (16.0%)		
Adherence in Previous TB			5.00	0.082
Good	21 (42.0%)	9 (18.0%)		
Irregular	6 (12.0%)	4 (8.0%)		
Defaulted	3 (6.0%)	7 (14.0%)		
Drug Resistance History			2.57	0.277
MDR	14 (28.0%)	5 (10.0%)		
Pre-XDR	3 (6.0%)	2 (4.0%)		
None	13 (26.0%)	13 (26.0%)		

square test and Cramers V test. As shown in table 3, chi-square test was found no statistically insignificant with chi square value= 13.69, df=15, P=0.482. Cramers V measures the association between two nominal or categorical variable in the range of 0-1. Based on Study finding Cramers V was 0.3 showing a moderate association between previous TB history and current MDR TB outcome. This indicates that although a patient's prior TB history has some predictive value, it is not a highly reliable indicator of how well they would respond to current disease and treatment.

The result of current therapy is somewhat influenced by prior TB history; nonetheless but other significant variables have more impact on TB treatment outcome. So relying only on previous TB history or previous TB outcome is not a good predictor of current TB outcome, but taking consideration of previous treatment behaviour of the patients would help to improve current TB outcome.

Analysis of the association between key previous TB-related variables and current DR-TB treatment outcomes revealed that none of the variables showed a statistically significant correlation. The type of previous TB (drug-sensitive TB, drug-resistant TB, or no history of TB) was not significantly associated with treatment outcome ($\chi^2 = 1.18$, $p = 0.556$), although patients with

prior drug-sensitive TB appeared to have a higher proportion of favorable outcomes. Similarly, the interval since the last TB episode did not significantly influence treatment outcomes ($\chi^2 = 1.14$, $p = 0.566$), with favorable outcomes distributed fairly evenly across all time intervals assessed (<1 year, 1–2 years, and >2 years).

Previous treatment adherence showed a trend toward significance ($\chi^2 = 5.00$, $p = 0.082$), indicating that patients who had good adherence in their prior TB treatment were more likely to achieve favorable outcomes, while those who had defaulted experienced more unfavorable results. Although this finding did not meet the conventional threshold for statistical significance, it suggested a possible influence of past adherence on DR-TB outcomes. Lastly, no statistically significant association was observed between history of drug resistance (MDR, pre-XDR, or none) and current treatment outcomes ($\chi^2 = 2.57$, $p = 0.277$), implying that prior drug resistance status alone did not determine the success or failure of the ongoing treatment. (Table 4)

Discussion:

This study aimed to determine whether a patients previous TB status could serve as a reliable predictor of treatment outcomes in current MDR-TB cases managed with a bedaquiline-based oral longer regimen. Socio demographic profile of the study participants suggested clear link between undernutrition, low socioeconomic status, and the prevalence of drug-resistant TB in this population. This could have important implications for targeted healthcare strategies.

The results related to previous TB history and treatment outcome demonstrated a weak to moderate association; however, this association was not statistically significant (Chi-square = 13.59, $p > 0.05$; Cramérs V = 0.302). These findings align with earlier research from India and South Africa, which indicated that while prior TB history may influence outcomes, it is not a sole determinant of treatment success in DR-TB settings. [7]

In the present study, patients with a history of cured drug-sensitive TB (DSTB) had the highest cure rates (70%), suggesting that prior successful treatment may confer behavioral or biological advantages, such as improved adherence or lower bacillary burden. Similar patterns were observed in a retrospective study in Ethiopia, where patients with prior TB cure had significantly better MDR-TB outcomes compared to those with a history of treatment failure.[8] Conversely, DSTB failure and DR-TB failure groups showed mixed or poor outcomes, supporting the idea that repeat treatment failure may reflect deeper resistance, poor compliance, or systemic treatment gaps.[9]

Interestingly, patients with no prior TB history did not consistently achieve better outcomes. In this subgroup, 46% experienced unfavorable outcomes (death or failure), indicating that being treatment-naïve does not guarantee treatment success. This finding echoes the WHO global TB reports, which emphasize the multifactorial nature of DR-TB out comes highlighting how baseline nutritional status, immune function, and access to care can impact results irrespective of prior TB exposure.[10]

Although previous treatment behavior (e.g., default or failure) may signal higher risk of non-response, it cannot be used in isolation for prognostication. Multiple studies support this, noting that factors like drug resistance pattern, HIV status, anemia, and diabetes often play more critical roles in MDR-TB outcomes than TB history alone.[11,12] For example, a study from Mumbai found that adherence, comorbidity burden, and socioeconomic instability were stronger predictors of unfavorable outcomes than any previous TB indicator.[13]

Given these complexities, a more holistic approach to DR-TB management is warranted. Comprehensive patient assessments including history of prior TB, comorbidities, nutritional status, resistance profile, and socio-behavioral risk can enhance prediction models and individualize care. Moreover, future research should explore the role of genetic and immunological markers in treatment response, which may further refine patient risk stratification.[14] Incorporating digital adherence tools and patient-centered support systems could also be instrumental in improving long-term DR-TB control strategies.[15]

Limitations:

This study was limited by a small sample size, which

may affect the generalizability of the findings. Recall bias might affect the findings pertaining to respiratory hygiene practices during previous episodes of TB.

Conclusion:

This study assessed whether previous TB history could predict current DR-TB treatment outcomes under a bedaquiline-based longer oral regimen. While a weak to moderate association was observed, statistical analysis revealed no significant correlation ($\chi^2 = 13.59$, $p > 0.05$; Cramér's V = 0.302). Patients with a history of successfully treated drug-sensitive TB (DSTB) demonstrated better outcomes, with 11 out of 20 achieving cure, suggesting that prior treatment success may influence future prognosis. However, outcomes among patients with previous treatment failure, default, or no TB history were mixed. These findings indicate that prior TB history alone is not a strong predictor of DR-TB treatment success. The complexity of outcomes reflects the multifactorial nature of TB management, including biological, behavioral, and systemic factors. Therefore, an individualized, holistic approach remains essential in DR-TB care.

Recommendations:

Programmatic TB control efforts should integrate prior treatment history as one component of patient risk profiling, especially in identifying those who may need closer follow-up or adherence support. Special attention should be given to patients with a history of treatment failure or irregular adherence, as they may face higher risk of poor outcomes. Nutritional assessment and support should be incorporated early, considering the high proportion of underweight patients. Strengthening behavioral counselling, drug-resistance surveillance, and early sputum monitoring can help mitigate the effects of past treatment challenges.

Declaration:

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Conflict of Interest: Nil

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