Evaluation of health-related quality of life and adherence among pre-extensively drug-resistant tuberculosis patients receiving either Bedaquiline or Delamanid regimen at a teaching hospital in Eastern India

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ABSTRACT

Background: The foremost concern and challenge in managing drug-resistant tuberculosis is ensuring a high health-related quality of life (HRQoL). The effectiveness of pre-extensively drug-resistant (Pre-XDR) tuberculosis management hinges on patients adhering to therapy, a crucial factor in averting the development of drug-resistant strains, ultimately enhancing HRQoL. **Methodology:** This analytical longitudinal study spanned two years at a teaching hospital and involved collaboration between the Departments of Pharmacology and Pulmonary Medicine. A case record form was utilized to gather baseline data, encompassing patient demographics, medication details, WHO BREF HRQoL scores, and treatment adherence. Patients were classified as either adherent or nonadherent using three distinct criteria: the guidelines of the Revised National Tuberculosis Programme (RNTCP), the Morisky-Green-Levine Scale (MGLS), and the Batalla test. The sample size was determined based on 30% nonadherence rates from preliminary analysis of prior data, resulting in 86 patients included in the study. The association between the improvement of HRQoL score from the baseline with the predictor variables was assessed with a linear regression model. Comparison of nonadherence with the different predictors of the study population was assessed with binary logistic regression model. **Results:** Analysis of demographic data revealed no notable differences in age and BMI between the Bedaquiline and Delamanid groups. However, there was a gender-related difference in treatment distribution, with more men in the Bedaquiline group. Other factors, such as marital status, socioeconomic status, employment status, stigma/discrimination, comorbidity, and addiction, showed no significant differences between the groups. Comparing HRQoL scores at baseline and after six months showed substantial improvements in all domains, indicating a positive impact of the treatment. Linear regression analysis revealed a strong association between QoL improvement and adherence. Adherence patterns did not significantly differ between the two treatment groups, as assessed by various criteria. The patients with high stigma, newly diagnosed Pre-XDR cases, and the presence of adverse events had higher odds of nonadherence. **Conclusion:** This study highlights the substantial impact of Bedaquiline and Delamanid treatment on the HRQoL of Pre-XDR TB patients in Eastern India. Adherence to treatment plays a crucial role in improving QoL, and factors like stigma, newly diagnosed Pre-XDR patients, and adverse drug reactions influence adherence adversely. The findings emphasize the importance of patient support and education to enhance treatment outcomes.

Keywords: Bedaquiline, Delamanid, Eastern India, health-related quality of life, Pre-XDR TB, treatment adherence

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Introduction

Tuberculosis (TB) is a highly contagious disease caused by *Mycobacterium tuberculosis*.[1] In the context of drug-resistant TB, there are two significant classifications: pre-extensively drug-resistant TB (Pre-XDR TB), indicating multidrug-resistant tuberculosis (MDR-TB) with resistance to either a fluoroquinolone (Fq) or a second-line injectable (SLI) agent, but not both; and extensively drug-resistant (XDR) TB, involving resistance to at least isoniazid and rifampicin, along with any of the Fqs and any of the three SLIs, namely amikacin, capreomycin, and kanamycin. Together, these categories make up approximately 9.5% of MDR-TB.[1] In India, the incidence rates for XDR TB and Pre-XDR TB are 1.9% and 7.9%, respectively.

Health-related quality of life (HRQoL) refers to an individual's self-evaluation that encompasses their physical, mental, emotional, and social well-being, along with their perceptions of their roles in life. HRQoL is significant because patients value their ability to function well, their overall sense of well-being, and their holistic experience of illness, not merely the elimination of the disease. Additionally, doctors may sometimes not fully realize the extent to which the disease and treatment impact a patient's HRQoL.[2]

Failure to adhere to prescribed TB treatment raises significant concerns, contributing to the development of drug-resistant TB and requiring extended treatment.[3,4] Successfully managing tuberculosis heavily relies on patients adhering to medication guidelines, preventing the development of drug-resistant strains. In India, as many as 50% of TB patients deviate from their treatment plans.[5,6] Various factors contribute to this, including the lengthy treatment duration, drug side effects, forgetfulness, travel, missed appointments, lack of support, poor communication with healthcare providers, and insufficient medication.[7] Ineffectual use of TB drugs prolongs suffering, heightens mortality risk, facilitates disease transmission, and escalates the likelihood of treatment resistance.

Delamanid (Dlm) and Bedaquiline (Bdq) represent two novel anti-TB drugs introduced through the Controlled Access Program. They are incorporated into the treatment regimen for MDR/Pre-XDR tuberculosis. Bedaquiline, classified as a diarylquinoline [Bdq], specifically targets the mycobacterial ATP synthase enzyme,[8] a pivotal component in the energy production of Mycobacterium TB. On the other hand, Delamanid [Dlm], a pro-drug, belonging to the nitro-dihydro-imidazo-oxazole family, stands as the pioneering treatment for MDR tuberculosis. It functions by inhibiting the synthesis of crucial constituents of the mycobacterial cell wall, specifically methoxy mycolic acid and ketomycolic acid.

To the best of our knowledge, there is a notable scarcity of published research addressing the evaluation of HRQoL and adherence to Pre-XDR treatment regimens within the Eastern Indian population. This study endeavors to comprehensively investigate the impact of bedaquiline and delamanid therapies on both the HRQoL and adherence to treatment among patients grappling with Pre-XDR TB while receiving care at a teaching hospital in eastern India.

The primary objective of this study entails evaluating the enhancement in HRQoL, as measured by the WHO BREF questionnaire, among the participating individuals at the outset and after a duration of 6 months. The secondary objectives encompass: 1) comparing therapy nonadherence among study participants at the subsequent visit, 2) scrutinizing the correlation between QoL and adherence, 3) identifying factors influencing HRQoL, and 4) identifying factors contributing to nonadherence.

Material and Methods

This is a longitudinal analytical study conducted over a period of 2 years in collaboration between the Department of Pharmacology and the Department of Pulmonary Medicine, situated within the hospital premises. A comprehensive case record form was devised to capture baseline data encompassing patient demographics [along with a modified Kuppuswamy scale (five classes upper class, upper middle, lower middle, upper lower, lower based on education, occupation, and per capita income), addiction status (as yes/no where subsets are smoking status, alcohol intake, and tobacco intake where if anyone is present is considered as yes), stigma/discrimination scale was measured using four questions adapted from internalized AIDS-related stigma scale], prescribed medication details, WHO BREF Quality of Life (QoL) scores, and adherence to the prescribed treatment regimen. Data acquisition occurred through interactions with patients within the in-patient department (IPD) and/or via telephonic consultations at different time frames as explained below.

Inclusion criteria encompassed patients of both genders aged 6-18 years for the Delamanid (Dlm) group, and above 18 years for both Bedaquiline (Bdq) and Delamanid (Dlm) groups. Consideration was given to patients with comorbid conditions such as Type II diabetes mellitus or hypertension, coinfection with HIV, and a diagnosis of chronic obstructive pulmonary disease (COPD). Additionally, patients with stable, controlled arrhythmia following cardiac consultations were included. Conversely, the study excluded vulnerable populations such as pregnant and lactating women, patients with a history of torsades de pointes or ventricular arrhythmias, and those displaying hypersensitivity to the active substance or any excipients.

The study adhered to ethical standards outlined in the Helsinki Declaration, securing necessary approvals from the Institutional Ethics Committee, and obtaining written informed consent from participating patients before commencement. Following a clear explanation of the study's purpose and the provision of written informed consent, we administered the questionnaire. Patients were assured of the anonymity and confidentiality of their data. To identify cases of Pre-XDR TB, a battery of

microbiological tests, including drug susceptibility testing (DST), cartridge-based nucleic acid amplification test (CBNAAT), line probe assay (LPA), and bacterial cultures, was employed. After diagnosis, all patients underwent a comprehensive series of clinical, serological, and laboratory assessments to establish baseline data. A patient was categorized as having Pre-XDR TB if they exhibited multidrug-resistant TB (MDR TB) with resistance to fluoroquinolones (Fq-r) or second-line injectable (SLI-r) agents.[1,8]

Patients received prescribed medications during the initial visit, and adherence was assessed in subsequent visits. The study comprised 85 patients, with 65 receiving Bdq and 20 receiving Dlm as part of an optimized background regimen. Trained investigators conducted HRQoL measurement using the WHO QoL-BREF questionnaire, which was already available in the vernacular language (Odia) on the WHO website.[8] We conducted face-to-face interviews with all patients to fill out the questionnaires twice: once before initiating treatment, along with collecting baseline data, and again at the end of the 6-month treatment completion. The instrument consists of 26 items, with 24 items dedicated to assessing HRQoL across various domains: physical (7 items), psychological (6 items), social relationships (3 items), and environmental factors (8 items). Additionally, two items evaluate general HRQoL and overall health. Multiple facets represent each domain, and questions are structured using a Likert response scale. The scale gauges intensity (ranging from "nothing" to "extremely"), capacity (from "nothing" to "completely"), frequency (from "never" to "always"), and assessment (from "very dissatisfied" to "very satisfied" or "very bad" to "very good"), with all scales featuring five levels (one to five). In this study, all domains are exclusively captured, comprising a total of 24 items.

Patients were systematically classified into adherent or nonadherent groups, employing three distinct criteria: the guidelines of the Revised National Tuberculosis Programme (RNTCP), deemed the most crucial criterion; the Morisky-Green-Levine Scale (MGLS), reflecting patients' attitudes; and the Batalla test, assessing patients' knowledge levels. According to the RNTCP guidelines, individuals were labeled as nonadherent if they failed to take the prescribed doses for over one month during the course of treatment.[9] The MGLS is a four-item assessment tool that evaluates a patient's attitudes toward their treatment regimen. This tool has been previously employed to identify nonadherent patients with diabetes and hypertension.[10] The MGLS questionnaire encompassed four key aspects of nonadherence, including forgetfulness, carelessness, discontinuing medication when feeling better, and initiating treatment when feeling worse. Patients were deemed adherent to their medication if they responded negatively to all four questions. The developers proposed categorizing medication adherence into three levels using this score: high, medium, and low adherence with 0, 1–2, and 3–4 points, respectively.[10] The Batalla test was created to evaluate the study population's awareness of fundamental aspects of the disease, serving as an indicator of their tuberculosis

knowledge. If a patient was aware of all three parameters, he or she was supposed to have adequate knowledge of TB. Participants who correctly answered "Yes" to all the items on this test were considered to possess sufficient knowledge about TB. All questions in these assessments had binary responses of either "Yes" or "No".

The sample size was determined using the formula $n = (z^2_{(1-\alpha/2)} P(1-P) / d^2)$. A preliminary analysis of prior data revealed a nonadherence rate of approximately 30% and an adherence rate of about 70%. Taking into account a confidence level of 95% ($\alpha = 0.05$), an expected population proportion (P) of 70%, and a margin of error (d) of 10%, the calculated minimum sample size was 80. Taking into account an attrition rate of 10%, the ultimate sample size was determined to be 88. However, two participants from the Bdq group and one from the Dlm group did not respond to the questionnaire and were consequently excluded from the study. Consequently, the final sample size was adjusted to 85.

We collected essential data from 85 consecutive cases meeting inclusion and exclusion criteria admitted to the in-patient Department of Pulmonary Medicine (sourcing information from hospital and laboratory records, and cross-referenced it with records from nursing faculties and discharge certificates to ensure treatment accuracy). Demographic, baseline, clinical, medication, HRQoL, and adherence details were systematically recorded in an Excel sheet using a specially designed proforma.

We assessed the normality of the distribution for continuous/discrete variables using the QQ plot. If the points on the QQ plot closely follow a straight line, it suggests that the data is approximately normally distributed. Continuous variables were summarized as mean with standard deviation (SD) or median with interquartile range (IQR), while categorical variables were presented as frequency (percentage). For groups with normally distributed data, we employed the independent *t*-test; for skewed datasets, we utilized the Mann-Whitney U test to analyze continuous/discrete variables. Nominal variables among groups were evaluated using either Pearson's Chi-square test or Fisher's exact test. We compared HRQoL scores across domains using the independent *t*-test. The linear regression model assessed the association between differences in HRQoL scores across domains at baseline and after 6 months with predictor variables. Binary logistic regression was employed to assess nonadherence compared to different predictors within the study population. *P* < 0.05 was considered significant for all tests.

Result

In the study involving 85 enrolled patients, we performed a thorough analysis of demographic data to compare two distinct groups: the Bedaquiline group and the Delamanid group. The associated *P* values are presented in Table 1. Initially, no statistically significant differences were observed in "Age" and

Table 1: Comparisons of the Demographic Parameters of the Study Population among both groups

Variable	Frequency/mean±SD [median (IQR)]		*P*
	Bedaquiline	**Delamanid**	
Age	36.22±14.28 [32 (25−45)]	31±12.1 [28 (21.25−41.5)	0.227*
BMI	16.92±3.08 [16.65 (14.78−18.52)	17.5±3.84 [18.12 (14.03−20.90)	0.483**
Gender			
Male	55	12	0.018
Female	10	08	
Martial status			
Married	39	09	0.237
Unmarried	26	11	
Socioeconomic status			
LIG or below	43	12	0.615
MIG or above	22	08	
Currently employed			
Yes	13	03	0.578
No	50	17	
HIV Coinfection			
Present	0	02	0.053
Absent	65	18	
Previously treated for Tb			
Yes	06	02	1.000
No	59	18	
Stigma/discrimination status as per scale			
Low	46	15	0.713
High	19	05	
Comorbidity status			
Yes	14	06	0.435
No	51	14	
Addiction status			
Yes	35	10	0.763
No	30	10	

*Mann-Whitney *U* test, **independent *t*-test, and remaining are Pearson's Chi-square test

"BMI" between the two groups. This suggests that the choice of treatment did not have a significant impact on the age and body mass index of the patients. On the other hand, the "Gender" distribution showed a substantial disparity, with a significantly higher number of males in the Bedaquiline group, denoting a gender-related difference in treatment distribution ($P = 0.018$). Meanwhile, "Martial Status," "Socioeconomic Status," "Currently Employed," "Stigma/Discrimination Status," "Comorbidity Status," and "Addiction Status" did not exhibit noticeable differences between the two groups. Notably, the presence of HIV coinfection suggested a potential difference though it was not statistically significant ($P = 0.053$), while "Previously Treated for TB" demonstrated no significant variation ($P = 1.000$).

The comparison of various domains of the WHO BREF HRQoL score at two points in time: baseline and after 6 months is illustrated in Table 2. It indicates significant enhancements across various aspects of well-being, such as physical, physiological, social, and environmental health, over the 6-month period. This implies that the intervention has notably improved the overall quality of life for the individuals participating in the study. Nevertheless, the enhancement in the social domain of health does not align with the improvements observed in the other three

Table 2: Comparisons of different domains WHO BREF QoL score at baseline and at the end of 6 months

Domains of WHO BREF Scale	At the baseline (Mean±SD)	At the end of 6 months (Mean±SD)	*P*
Physical state	10.479±1.871	26.920±7.321	0.000
Psychological state	10.041±2.156	23.329±6.011	0.000
Social state	6.466±1.581	11.452±2.141	0.000
Environmental state	14.384±2.497	31.726±8.516	0.000
Total BREF score	41.370±4.689	93.420±23.159	0.000

*Independent *t*-test

domains. This indicates that social life remains significantly and persistently affected even after the completion of treatment.

Association between the predicted variables and improvement in HRQoL score was depicted in Table 3. In this linear regression model, Nagelkerke adjusted R^2 value was 0.939, which means 93.9% variability was explained by the variables included in the model. The statistical exploration revealed a statistically significant association ($P < 0.001$) between the improvement in HRQoL score and the variable of adherence (categorized as 'Yes'), while maintaining nonadherence (categorized as adherence 'No') as the reference category indicating a strong positive association between

these two parameters. This analysis helps in identifying key factors affecting the enhancement of quality of life in the study population.

Figure 1 illustrates the adherence patterns within two study groups, Bedaquiline and Delamanid, across different categories. It assesses adherence according to the RNTCP, MGLS, and Batalla test, providing the frequency of individuals falling into

Table 3: Linear Regression Analysis of HRQoL Score Improvement in Relation to Predictor Variables				
Predictor variables	Estimate	SE	*t*	*P*
Age	0.0974	0.0833	1.1692	0.246
BMI	−0.1021	0.2239	−0.4559	0.65
Sex				
Male/female	1.6168	1.8845	0.8579	0.394
Marital status				
Single/married	4.2275	2.2416	1.8859	0.064
Currently working				
Yes/no	−0.9665	1.9671	−0.4914	0.625
Socioeconomic status				
LIG or below/MIG or above	1.4727	1.6215	0.9083	0.367
Stigma-scale				
High/low	−0.3857	2.0805	−0.1854	0.853
Presence of comorbidity				
Yes/No	0.9582	1.6811	0.57	0.571
Addiction status				
Yes/no	2.8395	1.433	1.9815	0.052
Previously treated				
Yes/no	0.1511	2.4984	0.0605	0.952
Regimen				
Bedaquiline/Delamanid	0.7327	1.6861	0.4346	0.665
Adherence (RNTCP)				
No/yes	−52.5162	2.1219	−24.7497	<.001
Adverse events noticed/reported				
Yes/no	1.3826	1.5405	0.8975	0.373

Reference level and model coefficients−QOL difference

different adherence levels. Remarkably, there are no substantial differences in adherence between the two groups for any of the criteria, as evidenced by the relatively high *P* values. This suggests that the choice between Bedaquiline and Delamanid treatment options does not significantly impact adherence according to these particular measures.

Over a 6-month period, there was a remarkable enhancement in the HRQoL across all parameters for patients who adhered to therapy, as illustrated in Figure 2. In the adherent group, the distribution of changes in HRQoL parameters, as depicted in the violin plot, exhibited greater vertical symmetry compared to the nonadherent group.

Table 4 displays the outcomes of a binomial regression model designed to examine the correlation between nonadherence and various predictors within the study population. In this particular binomial regression model, the Nagelkerke adjusted pseudo R2 value was 0.681, indicating that 68.1% of the variability was accounted for by the variables incorporated into the model. The variables like age, BMI, gender and treatment regimen (Delamanid vs Bedaquiline) showed no significant impact on nonadherence. Whether patients were single or married did not affect nonadherence significantly. Addiction and comorbidity status did not show significant associations with nonadherence. Stigma-scale exhibited a substantial impact, with individuals reporting high stigma having 20.27 times higher odds of nonadherence. Noteworthy, patients with a history of adverse events had a striking 23.46 times higher odds of nonadherence. Individuals without a history of prior treatment have 16.53490 times higher odds of not adhering to the RNTCP protocol compared to those with a history of previous treatment. These findings underscore the multifaceted nature of adherence, emphasizing the importance of psychosocial factors and adverse events in shaping patient behavior within tuberculosis treatment programs. Table 5 presents data on relationship between
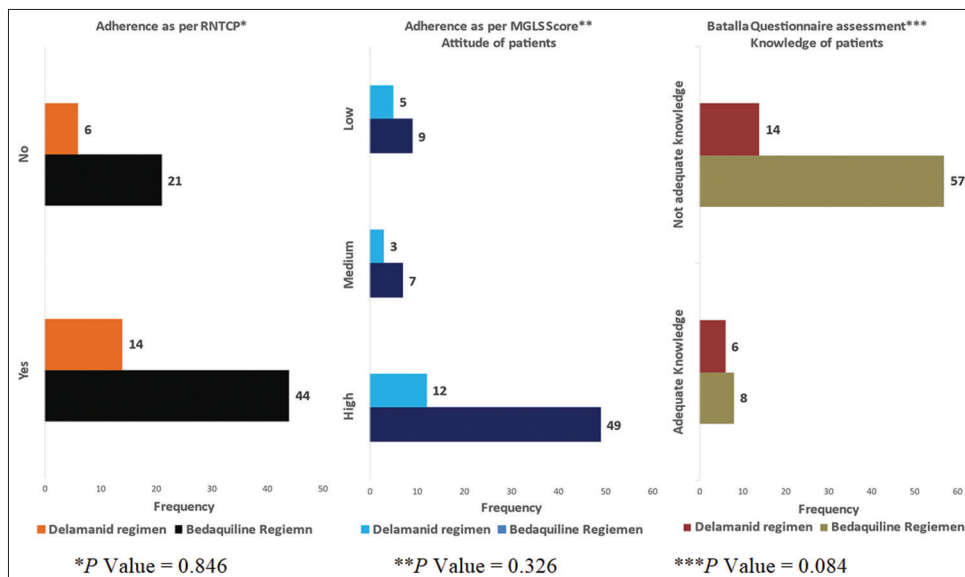

Figure 1: Adherence of the study population according to the RNTCP criteria, MGLS, and Batella test
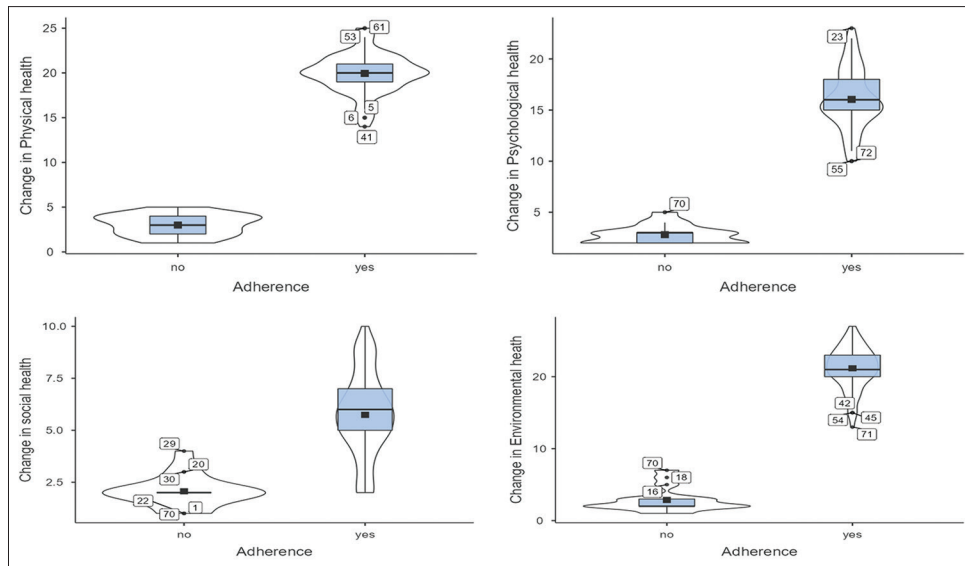
Figure 2: Relationship of adherence with HRQoL as per WHO BREF score

Table 4: Binomial regression model showing comparison of nonadherence with the different predictors of the study population

Predictor Variables	Estimate	SE	Z	P	Odds ratio	Confidence interval	
						Lower	Upper
Age	0.056	0.045	1.2442	0.213	1.0576	0.96829	1.155
BMI	−0.0257	0.147	−0.1747	0.861	0.9747	0.73069	1.3
Gender							
Male/female	0.2017	1.1089	0.1819	0.856	1.2234	0.13922	10.751
Marital status							
Single/married	−0.7098	1.3331	−0.5324	0.594	0.4918	0.03606	6.706
Currently working							
Yes/no	−2.5181	1.7081	−1.4742	0.14	0.0806	0.00283	2.292
Socioeconomic status							
LIG or below/MIG or above	0.216	0.9609	0.2248	0.822	1.2411	0.18875	8.161
Addiction status							
Yes/no	0.7495	0.8698	0.8618	0.389	2.116	0.38475	11.637
Presence of comorbidity							
Yes/no	−0.0777	0.9039	−0.0859	0.932	0.9253	0.15736	5.44
Stigma-scale							
High/low	3.0092	0.9737	3.0904	0.002	20.271	3.00629	136.684
Previously treated							
No/yes	2.8055	1.3935	2.0132	0.044	16.53490	1.07701	253.85
Regimen							
Delamanid/Bedaquiline	−0.0862	1.0538	−0.0818	0.935	0.9174	0.1163	7.237
Adverse events noticed/reported							
Yes/no	3.1553	1.1001	2.8682	0.004	23.4594	2.71603	202.627

Model Coefficients – Adherence (RNTCP), Note. Estimates represent the log odds of "Adherence (RNTCP) = No is the comparator " vs. "Adherence (RNTCP) = Yes is the reference"

tuberculosis medication adherence as per RNTCP criteria as compared to attitude based Morisky Green Levine scale and knowledge based on Batalla Scale questionnaires. Morisky Green Levine results indicate significantly lower adherence in those who forget (most common), are careless, or stop medication when feeling better (second most common) or worse ($P < 0.001$). In the Batalla Scale, while knowledge on tuberculosis varies, overall adherence is not strongly associated with perceptions of TB being a lifelong disease or medication control. This underscores the importance of addressing specific behavioural factors affecting adherence for effective tuberculosis management in healthcare interventions and patient education programs.

Discussion

In this longitudinal study, the incorporation of Bedaquiline or Delamanid in Pre-XDR TB patients exhibited a promising trend toward enhancing HRQoL. Our discoveries suggest enhancements

Table 5: Association of Medication Adherence with Morisky Green Levine and Batalla Scale Assessments					
Question	**As per RNTCP criteria (*n*=85)**		**Total**	**χ^2**	**P**
	Adherence	**Nonadherence (*n*=27)**			
Adherence according to Morisky Green Levine Scale Questionnaire					
Do you forget to take your medicine?					
No	58	07	65	56.2	<0.001
Yes	0	20	20		
Are you careless at times about taking your medications?					
No	58	12	70	39.1	<0.001
Yes	0	15	15		
Do you stop taking your medicine when you start feeling better?					
No	58	09	67	49.1	<0.001
Yes	0	18	18		
If sometimes you feel worse when you take the medicine, do you stop taking it?					
No	58	21	79	13.9	<0.001
Yes	0	06	06		
Adherence according to Batalla Scale Questionnaire					
Is tuberculosis a lifelong disease?					
No	14	05	19		0.78
Yes	44	22	66		
Can tuberculosis be controlled through medication?					
No	44	20	64		1.000
Yes	14	07	21		
Could you name one or more organs that may be damaged by tuberculosis?					
No	44	18	62		0.435
Yes	14	09	23		
Good knowledge of TB as per Batalla test					
No	44	27	71		0.004
Yes	14	0	14		

in all HRQoL domains among Pre-XDR patients, as assessed by the WHO BREF scale. In contrast, research conducted by Chang B *et al.* and Hansel NN *et al.* posits that within TB patients, psychosocial burdens may exert a more pronounced impact than clinical symptoms.[11,12] A cross-sectional investigation led by Laxmeshwar C *et al.* among patients with MDR-TB at two tuberculosis clinics in Mumbai disclosed that the psychological domain experienced the most significant impact, closely trailed by the physical domain.[2]

The peak enhancement in HRQoL occurred within the initial 2–3 months, aligning with findings from studies by Chang B *et al.* and Othman Q *et al.*[11,14] Our study also reflected this trend, with significant improvement observed at the 6-month mark.[13,14] Nonetheless, a systematic review spearheaded by T. Kastien-Hilka revealed consistent HRQoL outcomes in diverse studies on tuberculosis (TB). The findings suggested that physical health domains experienced more significant adverse effects compared to mental health domains. Although all health domains exhibited improvement during TB treatment, lingering physical impairments persisted after treatment completion. This indicates that current measurement methods may not entirely encompass the comprehensive impact of TB on HRQoL.[15]

In studies conducted by Kruijshaar ME *et al.*[16] and Lutge *et al.*,[17] factors indicative of lower HRQoL before the initiation of treatment, such as depression and low socioeconomic status,

were identified. However, our study uniquely revealed that the sole factor leading to minimal HRQoL improvement from baseline was nonadherence to therapy (*P* < 0.001). Investigating the association between HRQOL and adherence specific to TB in future research can enhance treatment programs, identify limitations in TB control, and inform targeted interventions to improve the health status of high-burden TB populations.[15] A comprehensive analysis of qualitative studies underscored the intricate relationship between HRQoL and adherence to tuberculosis (TB) treatment. Common factors influencing both include aspects like TB therapy, health status, socioeconomic and demographic factors, and the quality of healthcare services. Investigating this correlation throughout the course of TB treatment provides valuable insights, contributing to the improvement of treatment effectiveness and the optimization of care for individuals undergoing TB therapy.[18]

Results from a study conducted at a tertiary health institution in Southeast Nigeria and South Ethiopia revealed nonadherence rates for anti-TB drugs at 24.5% and 24.2%, respectively, while our study reported a higher adherence rate of 31.76% to the Pre-XDR regimen.[6,19] According to our findings, the most common subjective causes of nonadherence were feeling worse during therapy (59.25%) and feeling better due to symptom improvement (18.51%). This contrasts with studies by Munro *et al.*[18] and a World Health Organization review, where patients

often stopped treatment prematurely either due to perceived well being improvement or no improvement in health status.[20] Factors significantly associated with nonadherence in our Pre-XDR TB patient study include high stigma, newly diagnosed cases, and reported adverse events, highlighting the complex influences on adherence beyond individual health beliefs.[15]

There is a pressing need for patient-friendly DR-TB treatment regimens, free from injectables, featuring shorter durations, and exhibiting reduced short as well as long-term toxicity to reduce the number of pills required.[12] Notably, our study refutes pill burden as a factor for nonadherence. We assert the robustness of our study, meeting all criteria for an ideal QoL study on TB outlined by Brown J *et al.*[21] Employing the WHO BREF QoL tool in the vernacular language of the study population ensures representativeness, and our longitudinal approach assesses QoL improvements at the study's conclusion, accounting for comorbidities and socioeconomic status.

Limitations of this study probably include potential subject bias arising from the use of questionnaires and the risk of recall bias. Another limitation is the use of a research design characterized by a relatively small sample size and a brief duration. Moreover, it is essential to acknowledge that quality of life is influenced by factors beyond mere adherence and health improvement. One perspective asserts that the economic burden associated with suffering from tuberculosis, including associated direct, indirect, and intangible costs, has not been fully considered in this study.

Conclusion

Significant improvement in overall quality of life emerged at the study's conclusion, particularly among individuals adherent to their treatment regimens. The choice between Bedaquiline and Delamanid did not significantly affect adherence. Adherence complexities include individuals with high stigma levels, those without prior tuberculosis treatment (new Pre-XDR patients), and those experiencing more adverse events exhibiting higher nonadherence. The key to successful implementation of antitubercular treatment lies in providing comprehensive disease knowledge and effectively addressing specific nonadherence factors.

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Conflicts of interest

There are no conflicts of interest.

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