



# Effect of Body Mass Index, Sputum Conversion Status, and Adverse Drug Events Severity On Health-Related Quality of Life of Drug-Resistant Tuberculosis Patients

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## Abstract

**Background:** Adherence to treatment guidelines and bacteriological conversion are the main indicators of successful treatment of drug-resistant tuberculosis patients. Evaluation of health-related quality of life (HRQoL) and the effect of treatment on HRQoL are often ignored. HRQoL assessment is an interesting outcome to evaluate and improve. Drug-resistant tuberculosis patients suffer not only from the disease but also from the effects of the treatment.

**Method:** This study used a cross-sectional design to determine the correlation of body mass index (BMI), sputum conversion status, and adverse drug events severity with the HRQoL of drug-resistant tuberculosis patients. Quality of life assessment using the WHOQoL-BREF questionnaire. The study was conducted in October 2022 at dr. Moewardi Hospital, Surakarta and Dr. Ario Wirawan, Salatiga. Determination of the sample by total sampling method.

**Results:** HRQoL in 33 study subjects ie, 15 subjects had good HRQoL and 18 subjects had poor HRQoL. The media for each quality of life domain are the physical domain 43.00±6.20, psychological domain 33.21±8.83, social domain 28.21±11.01, and environmental domain 33.45±6.38. Statistical analysis with rank Spearman showed that there were a relationship between BMI (P=0.018), sputum conversion status (P=0.002), and adverse drug events severity (P=0.0001) with HRQoL of drug-resistant tuberculosis patients.

**Conclusion:** BMI, sputum conversion status, and drug adverse events severity affect HRQoL of drug-resistant tuberculosis patients.

**Keywords:** drug-resistant tuberculosis, HRQoL

## INTRODUCTION

The tuberculosis (TB) control program is aimed at optimizing microbiological cures and using microbiological parameters as indicators of

treatment success. Although this is highly important from a public health perspective, such an approach does not adequately address the physical, mental, and social suffering of patients caused by TB. Patients

suffer not only from the symptoms of the disease but also from a general decline in their quality of life. Patients' perceptions of their illness and health remain largely unexplored.<sup>1,2</sup>

Quality of life is a broad and complex multidimensional concept that encompasses physical, social, psychological, economic, and spiritual domains. It is difficult to define and measure but can be broadly described as an individual's perception of their position in life within the context of the culture and value systems in which they live and concerning their goals, expectations, standards, and concerns. Quality of life is more an expression of the preferences and values of patients rather than a judgment made by physicians.<sup>3,4</sup>

Studies on health-related quality of life (HRQoL) of drug-resistant tuberculosis (DR-TB) patients undergoing treatment with anti-TB drugs are still limited. Research on the factors influencing the quality of life of drug-resistant TB patients will provide new insights into the management of these patients. The author aims to investigate the HRQoL of DR-TB patients receiving treatment, as well as the correlation between body mass index (BMI), sputum conversion status, and the severity of adverse drug events with the quality of life of these patients.

## METHOD

This study employed a cross-sectional design and was conducted in October 2022 at the MDR-TB clinics of dr.

Moewardi Hospital, Surakarta and dr. Ario Wirawan Hospital, Salatiga. The target population consisted of DR-TB patients undergoing treatment at these facilities during the study period. The accessible population included all DR-TB patients registered at the PMDT clinics of the aforementioned hospitals in October 2022.

The research sample was selected using consecutive sampling, whereby all eligible subjects meeting predefined criteria were included. Inclusion criteria comprised DR-TB patients aged 18 years or older who were within the first to sixth months of treatment and provided written informed consent to participate in the study. Exclusion criteria included incomplete medical record data relevant to the study and DR-TB patients with pre-existing conditions before treatment initiation, such as anemia, gout arthritis, cardiac arrhythmias, hearing impairment, mental disorders, hepatitis, or chronic kidney failure.

HRQoL was assessed using the WHOQoL-BREF questionnaire. A total score of <60 was classified as a "poor" quality of life, while a score of  $\geq 60$  was classified as "good." The WHOQoL-BREF instrument also evaluates four distinct domains of quality of life: physical, psychological, social, and environmental.

This study received ethical approval from the Ethical Review Committee of Dr. Moewardi Hospital on October 7, 2022 (approval number: 1.028/X/HREC/2022). All procedures adhered to ethical standards for research involving human subjects.

Data were analyzed using SPSS 21 for Windows. The primary objective of this study was to examine the relationship between HRQoL and factors such as body mass index (BMI), sputum conversion status, and the severity of adverse drug events. The Spearman's rank correlation test was used to assess the association between independent and dependent variables. A value of  $P < 0.05$  was considered statistically significant, and the strength of the correlation was determined by the r-value.

## RESULT

The subjects of this study were 33 DR-TB patients undergoing treatment and fulfilling the inclusion and exclusion criteria at dr. Moewardi Hospital and dr. Ario Wirawan Hospital. The characteristics of the research subjects are presented in Table 1.

Table 1. Subject characteristic

Characteristic	n	%
Sex		
Male	25	75.8%
Female	8	24.2%
Age		
18 - 39	10	30.3%
40 - 60	17	51.5%
>60	6	18.2%
Education		
Bachelor	1	3.3%
Senior high school	12	36.1%
Junior high school	15	45.5%
Elementary school	3	9.1%
No education	2	6.1%
Employment status		
Employed	12	36.4%
Unemployed	21	63.6%
BMI (Mean±SD; Min-max)	20.00±2.81	13.82-25.81

Most subjects were men (75.8%) in their productive age. Most of the education levels are junior and high school, which shows that education plays a role in understanding TB disease and its treatment.

Table 2. HRQoL of DR-TB patients

HRQoL	n (%)
Good (score $\geq 60$ )	15 (45.45%)
Poor (score $< 60$ )	18 (54.55%)

The quality of life assessment indicates that 54.55% of patients experience a diminished quality of life. The physical, psychological, social, and environmental categories exhibited low ratings, signifying that patients encountered a substantial effect of the disease and therapy on their quality of life. Meanwhile, Table 3 displays the score for the assessment of HRQoL.

Table 3. HRQoL of DR-TB patients

HRQoL Domain	Score
Physique	43.00±6.20
Psychological	33.21±8.83
Social	28.21±11.01
Environment	33.45±6.38

The study found that there was a moderate relationship between BMI and HRQoL, with the value of  $P = 0.018$ . This shows that patients with a better BMI tend to have a better quality of life. The statistical test for the relationship between BMI and HRQoL of DR-TB patients is shown in Table 4.

Table 4. Relationship between BMI and HRQoL in DR-TB patients

Variable	HRQoL	
	R	P
BMI	0.409	0.018*

Note: Spearman rank test; \*) Significant at  $\alpha = 5\%$

Table 5. Relationship between sputum conversion status and adverse events (Aes) severity with HRQoL in DR TB patients

Variable	HRQoL		P	r
	Poor	Good		
Sputum Conversion Status				
Not yet converted	15 (45.45%)	5 (15.15%)	0.002*	0.510
Converted	3 (9.09%)	10 (30.30%)		
AEs severity				
No AEs	3 (9.09%)	9 (27.27%)	0.0005*	-0.594
Mild	5 (15.15%)	6 (18.18%)		
Moderate	6 (18.18%)	0 (0.00%)		
Severe	4 (12.12%)	0 (0.00%)		
Life-threatening	0 (0.00%)	0 (0.00%)		

Note: Spearman rank test. \*) Significant at  $\alpha=5\%$

A weak correlation exists between sputum conversion status and HRQoL ( $P=0.002$ ), indicating that patients who have undergone sputum conversion exhibit superior quality of life compared to those who have not. Adverse drug effects were observed in 21 patients (63.64%). The findings indicate a moderate and substantial correlation between the intensity of pharmacological side effects and HRQoL ( $P=0.0005$ ), with individuals experiencing milder side effects reporting a superior quality of life. Table 5 presents the statistical analysis of the correlation between sputum conversion status and the severity of adverse drug events with HRQoL in DR-TB patients.

## DISCUSSION

Assessing the quality of life in patients with chronic illnesses, such as tuberculosis, is a critical responsibility for healthcare personnel. The extended duration of treatment and the necessity for compliance substantially impact mental and social well-being. Numerous research indicates that assessing patients' quality of

life functions as a criterion for the quality of healthcare services. Assessing a patient's quality of life helps provide a standard for enhancing therapy and health services.<sup>4,5</sup>

Quality of life is defined as an individual's evaluation of physical and mental well-being and its impact on physical, psychological, economic, spiritual, and social-relational functions. The assessment of quality of life elucidates the patient's condition in relation to their illness and its impact on personal functioning and everyday activities.<sup>4,5</sup>

The male proportion is 75.8%, surpassing the female proportion of 24.2% in this study. The findings of this study align with those of Widyasrini et al, which indicated that the proportion of male DR-TB patients was 57.7%, and Kurniawan et al, which reported a proportion of 63.4% of male DR-TB patients. Gender influences mycobacterial exposure through variations in social roles, risk behaviors, and activities. Men may engage in more frequent travel, maintain a greater number of social connections, and participate in occupations linked to an elevated risk of tuberculosis. Moreover, there is evidence of physiologic

disparities between genders that may influence susceptibility to mycobacterial infection.<sup>6-9</sup>

Animal studies have shown that male C57BL/6 mice have a lower ability to control *Mycobacterium tuberculosis* (*M. tuberculosis*) infection than female mice. This is due to less effective innate and adaptive immune responses, characterized by higher bacterial loads in the lungs and faster mortality. Differences in the early stages of the innate immune response also influence the level of bacterial load and the subsequent development of the adaptive immune response.<sup>6-9</sup>

Pathogen recognition and inflammatory and antimicrobial responses also differ between male and female mice, with genetic and hormonal factors playing important roles. Estrogen is known to enhance the ability of macrophages to kill bacteria such as *Streptococcus pneumoniae*, while peritoneal macrophages from female mice show stronger antimicrobial activity against *Mycobacterium intracellulare* than male mice.<sup>6-9</sup>

IFN $\gamma$  is an important cytokine produced by CD4+ and CD8+ T cells that plays a role in enhancing the antibacterial function of macrophages. Invariant Natural Killer T (iNKT) cells, which act as a link between innate and adaptive immunity, can recognize *M. tuberculosis*-infected macrophages, produce IFN $\gamma$ , and kill intracellular bacteria. Estradiol has also been shown to increase IFN $\gamma$  production by iNKT cells in female mice.<sup>6-9</sup>

Castration or removal of the estradiol receptor reduces IFN $\gamma$  production, which can be restored by estradiol injection. Testosterone has anti-inflammatory effects by inhibiting pro-inflammatory factors such as TNF- $\alpha$  and increasing IL-10 production. Castration of male mice increases TNF- $\alpha$  secretion, and TB susceptibility can be reduced by castration, suggesting that testosterone may be a factor that increases TB susceptibility. Female mice exhibit higher T cell activity, including the production of Th1-type cytokines such as IFN $\gamma$ , as well as stronger antibody responses than male mice.<sup>6-9</sup>

These differences in adaptive immunity may contribute to the inability of male mice to control *M. tuberculosis* infection over the long term. In addition to hormonal factors, sex differences in TB are also influenced by genetic factors, such as the expression of immunity-related genes on the X chromosome and the advantage of genetic diversity in female mice due to cellular mosaicism and genes that escape X chromosome inactivation. Thus, the difference in susceptibility to TB between male and female mice is the result of a complex interaction between hormonal and genetic factors.<sup>6-9</sup>

The majority of patients in this study were of productive age. A study by Abrori et al reported that DR-TB patients in Banyumas, Indonesia mostly occurred in adolescents and adults. A study by Dela et al reported that DR-TB in India was found in the majority at the age of 21-60 years. High mobility and higher social interaction

are the causes of the high incidence of DR-TB cases in this age range.<sup>10,11</sup>

The educational level of the patients in this study mostly had lower secondary education. This research is in line with the research of Abrori et al and Bawoente et al. Level of education is a risk factor for tuberculosis transmission. Education level is related to knowledge and understanding of tuberculosis prevention. The level of education is also related to knowledge about homes and environments that meet health requirements. Someone with a good level of knowledge tends to develop a clean and healthy lifestyle.<sup>11,12</sup>

DR-TB patients in this study mostly had poor quality of life. The HRQoL of DR-TB patients in this study consisted of 15 patients (45.54%) with good quality of life and 18 patients (54.55%) with poor quality of life. The HRQoL of patients in this study is in line with the studies of Dhelaimi et al and Jaber et al. HRQoL is defined as the extent to which a patient's subjective perception of physical, mental and social well-being is affected by the disease and its treatment every day. The need to assess quality of life becomes important because of the broader concept of measuring health status beyond conventional indicators such as mortality and morbidity. HRQoL is an indicator of the effects of disease and morbidity on daily activities and functions.<sup>13,14</sup>

Malnutrition and TB are major problems in almost all developing countries in the world. Both tend to interact with each other. Poor nutritional status will affect the body's defense system which

causes an individual to be more susceptible to infection with a disease. Tuberculosis also causes metabolic changes in the body where there is an increase in metabolism as a response to the body's infection so that there is a decrease in appetite, malabsorption of macro and micro-nutrients, a decrease in fat-free mass, and fat mass which ultimately increases morbidity and mortality rates.<sup>15-17</sup>

In conditions of infection, there is an increase in metabolism which uses the protein as an energy source to fight pathogenic germs, causing degradation of muscle protein and a decrease in protein in the blood circulation. Selection of protein types that contain complete amino acids also called high-quality protein and are easily digested by the body are the main choices in determining the type of protein to be consumed because it affects its ability to be used immediately by the body and is beneficial for preventing a decrease in fat-free mass in the body which ultimately improves the quality of life of TB patients.<sup>15,16</sup>

Sputum conversion plays an important role in determining DR-TB treatment and indicators of treatment effectiveness. Sputum that does not convert or is late in converting until the end of 4 months of intensive phase treatment often indicates unfavorable outcomes such as treatment failure and death. Late sputum conversion has negative impacts such as prolonging the therapy period and less than optimal treatment compliance with the consequences of treatment failure. Sputum conversion in DR-TB patients in

79.5% of patients occurred in the first two months of treatment. Sputum conversion indicates treatment effectiveness, reduced risk of TB transmission to others, improvement in clinical symptoms, and improved quality of life of patients.<sup>18,19</sup>

This study identified the impact of sputum conversion status on HRQoL in DR-TB patients. These findings align with the research conducted by Dar et al. The research conducted by Dar et al analyzed the HRQoL of tuberculosis patients at the onset of treatment and following the completion of the intense phase. The research indicated enhancements in HRQoL during the intensive phase of tuberculosis medication. The dimensions of quality of life that underwent the most significant enhancement were the physical and psychological domains.<sup>20,21</sup>

Enhancements in the physical aspect of quality of life were associated with the amelioration of tuberculosis symptoms following the completion of the intense treatment period. A subsequent investigation by Dujaili et al yielded analogous findings. The research conducted by Dujaili et al indicated that enhancements in physical well-being, functional well-being, and overall quality of life ratings were observed following the completion of the intense phase of anti-tuberculosis therapy.<sup>20,21</sup>

The treatment for DR-TB requires a greater number of drug combinations compared to drug-sensitive tuberculosis, hence elevating the probability and intensity of AEs. The evaluation of adverse events is essential for decreasing morbidity

and mortality associated with DR-TB. The majority of adverse events are minimal and can be managed without altering or discontinuing the prescription regimen. Severe pharmacological side effects can significantly jeopardize health, need hospitalization, or perhaps threaten life.<sup>5,22</sup>

The frequency of drug AEs in this study was 63.64%. The frequency of drugs AEs in this study is in line with a study by Ahmad et al in Pakistan at 72%, Nilamsari et al at 70% in Indonesia and Dela et al in India at 57.6%. Variations in the reported frequency of AEs may be due to differences in attitudes towards therapy such as lack of medication adherence, default rates, differences in opinion of patients and doctors regarding reporting of drugs AEs, differences in support programs, initial assessment, and management of drugs AEs.<sup>11,23–25</sup>

Tuberculosis significantly seriously affects patients' quality of life. The occurrence and severity of drug adverse events associated with DR-TB treatment are well-documented; nevertheless, the impact of these medication adverse events on patients' quality of life remains largely unexplored. The research by Dela et al indicated that the occurrence of drug adverse events diminished the HRQoL of DR-TB patients, and a correlation existed between HRQoL and adherence to treatment guidelines.<sup>11,23</sup>

The adverse effects of anti-tuberculosis medications, particularly second-line agents for drug-resistant tuberculosis, can profoundly affect a patient's quality of life through multiple

routes. Physically, adverse effects including anorexia, nausea, vomiting, visual disturbances, alterations in urine color, pruritus, erythema, and auditory impairment can diminish the patient's overall physical health, thereby restricting the capacity to engage in daily activities, reducing mobility, and inducing persistent discomfort.<sup>24,26,27</sup>

Moreover, these medications may adversely impact the patient's psychological condition, exacerbating mental health issues such as depression and, in extreme instances, potentially inducing hallucinations and a sense of hopelessness. The psychological and physical effects may diminish a patient's motivation to persist with therapy, resulting in non-compliance, which can subsequently impede recovery, elevate the risk of drug resistance, and exacerbate the overall state of tuberculosis. The absence of social support can exacerbate the deterioration of the quality of life for these individuals.<sup>24,26,27</sup>

## CONCLUSION

The majority of DR-TB patients receiving anti-tuberculosis therapy exhibit diminished HRQoL. The body mass index, sputum conversion status, and severity of drug adverse events are correlated with the HRQoL of DR-TB patients. Substandard quality of life can influence treatment adherence in DR-TB patients. The treatment of DR-TB should prioritize not only patient healing but also the enhancement of patient quality of life.

## REFERENCES

1. Brown J, Capocci S, Smith C, Morris S, Abubakar I, Lipman M. Health status and quality of life in tuberculosis. *International Journal of Infectious Diseases*. 2015;32:68–75.
2. Khan S, Tangiisuran B, Imtiaz A, Zainal H. Health Status and Quality of Life in Tuberculosis: Systematic Review of Study Design, Instruments, Measuring Properties and Outcomes. *Health Science Journal*. 2017;11(1):484.
3. Febi AR, Manu MK, Mohapatra AK, Praharaj SK, Guddattu V. Psychological stress and health-related quality of life among tuberculosis patients: a prospective cohort study. *ERJ Open Res*. 2021;7(3):00251–2021.
4. Rachmawati DS, Nursalam N, Hargono R, Otok BW. Quality of Life and Subjective Well-Being Modeling of Pulmonary Tuberculosis Patients. *J Public Health Res*. 2021;10(2):2180.
5. Salehitali S, Noorian K, Hafizi M, Dehkordi AH. Quality of life and its effective factors in tuberculosis patients receiving directly observed treatment short-course (DOTS). *J Clin Tuberc Other Mycobact Dis*. 2019;15:100093.
6. Widiasrini ER, Probandari AN, Reviono R. Factors Affecting the Success of Multi Drug Resistance (MDR-TB) Tuberculosis Treatment in Residential Surakarta. *Journal of*

- Epidemiology and Public Health. 2017;02(01):45–57.
7. Kurniawan S, Reviono R, Sutanto YS. Pengaruh faktor usia, berat badan, dosis dan rejimen terhadap waktu timbulnya efek samping gastrointestinal, hepatotoksik, dan kesembuhan pada tuberkulosis resisten obat. Universitas Sebelas Maret. Surakarta: Universitas Sebelas Maret; 2020. p. 41–60.
  8. Humayun M, Chirenda J, Ye W, Mukeredzi I, Mujuru HA, Yang Z. Effect of Gender on Clinical Presentation of Tuberculosis (TB) and Age-Specific Risk of TB, and TB-Human Immunodeficiency Virus Coinfection. *Open Forum Infect Dis*. 2022;9(10):ofac512.
  9. Dutta NK, Schneider BE. Are There Sex-Specific Differences in Response to Adjunctive Host-Directed Therapies for Tuberculosis? *Front Immunol*. 2020;11:1465.
  10. Abrori I, Ahmad RA. Gambaran Kualitas Hidup Penderita Tuberkulosis Resistan Obat dan Karakteristiknya di Kabupaten Banyumas, Provinsi Jawa Tengah, Periode Tahun. *Berita Kedokteran Masyarakat*. 2018;34(2):55–61.
  11. Dela AI, Tank NKD, Singh AP, Piparva KG. Adverse drug reactions and treatment outcome analysis of DOTS-plus therapy of MDR-TB patients at district tuberculosis centre: A four year retrospective study. *Lung India*. 2017;34(6):522–6.
  12. Bawonte TG, Mambo CD, Masengi ASR. Faktor-Faktor Yang Mempengaruhi Tuberculosis Multidrug Resistance (TB MDR). *eBiomedik*. 2021;9(1):117–25.
  13. Omar Dhelaimi G, Alsaedi TS, Alharbi MO, Alkaraiem F, Altarjami AS, Alkaraiem AA, et al. Multidimensional Health-Related Quality-of-Life Among Patients with Pulmonary Tuberculosis in Saudi Arabia. *World Journal of Public Health*. 2018;3(2):48–56.
  14. Jaber AAS, Ibrahim B. Health-related quality of life of patients with multidrug-resistant tuberculosis in Yemen: prospective study. *Health Qual Life Outcomes*. 2019;17(1):142.
  15. Koethe JR, von Reyn CF. Protein-calorie malnutrition, macronutrient supplements, and tuberculosis. *The International Journal of Tuberculosis and Lung Disease*. 2016;20(7):857–63.
  16. Chandrasekaran P, Saravanan N, Bethunaickan R, Tripathy S. Malnutrition: Modulator of Immune Responses in Tuberculosis. *Front Immunol*. 2017;8:1316.
  17. Mahapatra A, Thiruvengadam K, Nair D, Padmapriyadarsini C, Thomas B, Pati S, et al. Effectiveness of food supplement on treatment outcomes and quality of life in pulmonary tuberculosis: Phased implementation approach. *PLoS One*. 2024;19(7):e0305855.
  18. Ismail N, Ismail F, Omar S V., Blows L, Gardee Y, Koornhof H, et al. Drug-resistant tuberculosis in Africa:

- Current status, gaps and opportunities. *Afr J Lab Med.* 2018;7(2):781.
19. Bade AB, Mega TA, Negera GZ. Malnutrition is Associated with Delayed Sputum Culture Conversion Among Patients Treated for MDR-TB. *Infect Drug Resist.* 2021;14:1659–67.
  20. Dar SA, Shah NN, Wani ZA, Nazir D. A prospective study on quality of life in patients with pulmonary tuberculosis at a tertiary care hospital in Kashmir, Northern India. *Indian Journal of Tuberculosis.* 2019;66(1):118–22.
  21. Dujaili JA, Sulaiman SAS, Hassali MA, Awaisu A, Blebil AQ, Bredle JM. Health-related quality of life as a predictor of tuberculosis treatment outcomes in Iraq. *International Journal of Infectious Diseases.* 2015;31:4–8.
  22. Sineke T, Evans D, Schnippel K, van Aswegen H, Berhanu R, Musakwa N, et al. The impact of adverse events on health-related quality of life among patients receiving treatment for drug-resistant tuberculosis in Johannesburg, South Africa. *Health Qual Life Outcomes.* 2019;17(1):94.
  23. Atif M, Ahmed W, Iqbal MN, Ahmad N, Ahmad W, Malik I, et al. Frequency and Factors Associated With Adverse Events Among Multi-Drug Resistant Tuberculosis Patients in Pakistan: A Retrospective Study. *Front Med (Lausanne).* 2022;8:790718.
  24. Ahmad N, Javaid A, Sulaiman SAS, Afridi AK, Zainab, Khan AH. Occurrence, Management, and Risk Factors for Adverse Drug Reactions in Multidrug Resistant Tuberculosis Patients. *Am J Ther.* 2018;25(5):e533–40.
  25. Nilamsari WP, Rizqi MF, Regina NO, Wulaningrum PA, Fatmawati U. Adverse drug reaction and its management in tuberculosis patients with multidrug resistance: a retrospective study. *J Basic Clin Physiol Pharmacol.* 2021;32(4):783–7.
  26. Zhang Y, Wu S, Xia Y, Wang N, Zhou L, Wang J, et al. Adverse Events Associated with Treatment of Multidrug-Resistant Tuberculosis in China: An Ambispective Cohort Study. *Medical Science Monitor.* 2017;23:2348–56.
  27. Massud A, Syed Sulaiman SA, Ahmad N, Shafqat M, Chiau Ming L, Khan AH. Frequency and Management of Adverse Drug Reactions Among Drug-Resistant Tuberculosis Patients: Analysis From a Prospective Study. *Front Pharmacol.* 2022;13:883483.