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Quality of life in patients with multidrug-resistant tuberculosis under programmatic condition using World Health Organization's Quality of Life Brief instrument: A case-control study

Oki Nugraha Putra[1]✉, Dewi Ramdani[2], Aisyah Fitri Kurniawati[3], Telly Purnamasari[4], Julaeha Julaeha[4], Nurul Damayanti[1]

[1]*Faculty of Pharmacy, Hang Tuah University, Surabaya, Indonesia*

[2]*Department of Pharmacy, Haji Hospital, Surabaya, Indonesia*

[3]*Study Program of Pharmacy, Faculty of Pharmacy, Hang Tuah University, Surabaya, Indonesia*

[4]*Pre-Clinical and Clinical Studies, National Research and Innovation Agency (BRIN), Cibinong, Indonesia*

ABSTRACT

Objective: To evaluate and compare the quality of life (QoL) in patients with multidrug-resistant (MDR-TB) and drug-sensitive (DS-TB) as well as to investigate factors associated with QoL among MDR-TB patients in real-world scenarios at the Haji Hospital, Surabaya.

Methods: We conducted a case-control study from June to December 2024. MDR-TB and DS-TB patients were classified into case and control groups, respectively. We used the World Health Organization's Quality of Life Brief (WHOQOL-BREF) instrument and Patient Health Questionnaire-9 (PHQ-9) to assess QoL and depression levels, respectively. Multivariate analysis was used to analyze factors associated with QoL of patients with MDR-TB.

Results: Forty-one patients with MDR-TB and 43 with DS-TB were enrolled in the study. A mean score for all domains (physical, psychological, social relationship, environmental) and total mean score of WHOQOL-BREF was significantly lower in MDR-TB than those with DS-TB (P<0.05). The prevalence of depression and the mean score of PHQ-9 were significantly higher in MDR-TB than in DS-TB (P<0.05). PHQ-9 negatively correlates with the WHOQOL-BREF score (r=-0.502, P<0.05) among MDR-TB patients. MDR-TB patients with depression were significantly associated with low QoL in the physical (*OR* 3.611; 95% *CI* 2.393-6.951; P=0.029), psychological (*OR* 1.672; 95% *CI* 1.179-5.941; P=0.021), social relationship (*OR* 2.586; 95% *CI* 1.611-2.909; P=0.014), and environmental domains (*OR* 1.926; 95% *CI* 1.047-2.147; P=0.048).

Conclusions: MDR-TB patients had worse QoL than DS-TB. Those with depression were associated with low QoL. Strategies that identify and tackle alterations in the QoL for MDR-TB patients are necessary during TB treatment.

KEYWORDS: Quality of life; MDR-TB; Tuberculosis; World Health Organization's Quality of Life Brief instrument; Depression

Summary

Question: How is the quality of life in patients with multidrug-resistant tuberculosis (MDR-TB) using World Health Organization's Quality of Life Brief instrument, and what are the affecting factors?

Findings: From our case-control study, the score of quality of life in patients with MDR-TB was significantly lower than patients with drug-sensitive TB. MDR-TB patients with depression were substantially associated with the domains of social, psychological, physical health, and environmental of World Health Organization's Quality of Life Brief instrument.

Meaning: The quality of life of patients with MDR-TB was found to be poor and associated with the patients' depression status.

✉To whom correspondence may be addressed. E-mail: okinugrahaputra@yahoo.com

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1. Introduction

A strain of *Mycobacterium* (*M.*) *tuberculosis* resistant to at least one of the two most effective TB medications, rifampicin or isoniazid, causes drug-resistant tuberculosis (DR-TB). DR-TB refers to five categories of TB caused by drug-resistant strains, a chronic and debilitating condition that necessitates the use of potentially toxic and less effective second-line anti-TB medications. According to World Health Organization, DR-TB was classified into mono/poly-drug resistant, rifampicin resistant, multidrug-resistant, pre-extensively drug-resistant (pre-XDR), and XDR-TB. Multidrug-resistant TB (MDR-TB) is characterized by resistance to rifampicin and isoniazid without resistance to other second-line antitubercular drugs[1]. In 2022, the treatment success rate for MDR-TB in Indonesia was 51%. These results did not meet the Indonesian national target of 80%[2].

MDR-TB patients typically have a history of illness and treatment, thereby rendering them more susceptible to family life problems, social stigma, and economic struggles. Therefore, it is feasible to assume that patients with MDR-TB are likely to suffer a significantly lower quality of life (QoL)[3]. MDR-TB has been identified as the worst of the worst diseases, with treatment worse than the illness itself. The expanding prospect of measuring QoL beyond standard care, like mortality and morbidity, is necessary[4].

MDR-TB can adversely affect the physical, psychological, social, and environmental dimensions of QoL for individuals suffering from the disease[5]. Quality of life is an individual's perception of their position in life, the cultural context, and the value system in which they live. Quality of life also relates to their goals, expectations, standards, and concerns. The physical aspect of QoL pertains to an individual's experiences of pain, sleep quality, daily functioning, and energy levels. In contrast, the psychological dimension of QoL focuses on a patient's capacity to lead a fulfilling and meaningful life, without experiencing uncomfortable feelings such as anxiety and depression. The social aspect of QoL is supported by their satisfaction with their relationships, sex, and social support from others, whereas their environmental aspect includes their sense of security in a healthy setting with enough information, money, and transportation, as well as leisure[6,7].

The QoL of patients undergoing treatment for MDR-TB and the impact of adverse events on QoL are poorly understood, even though adverse events are frequent during MDR-TB treatment. Adverse events cause a temporary lower QoL and may result in fatal disability[8]. Several studies reported that compared to drug-susceptible TB (DS-TB), patients with MDR-TB had a lower QoL and prominent stigmatization, and low general health scores[4,9].

Few studies have been carried out to evaluate the QoL of DR-TB or MDR-TB patients in Indonesia. Previous studies in Indonesia used Short Form-36 (SF-36) and EuroQol-5 Dimension Questionnaire (EQ-5D) to assess QoL among MDR-TB patients[10,11]. However, there is a paucity of studies investigating the physical, psychological, social, and environmental QoL of patients with MDR-TB and its associated factors within high-burden TB settings like Indonesia. Our present study includes evaluating patients' psychological burden and environmental difficulties, which are frequently disregarded in conventional QoL evaluations.

The SF-36 has limitations in terms of scope, sensitivity, and cultural applicability, despite being a useful tool for evaluating health-related quality of life, especially in clinical settings that emphasize physical and mental health outcomes. In addition, the EQ-5D is simple to use and advantageous for rapid assessments and economic analyses. However, its sensitivity and scope limitations make it less appropriate for thorough QoL evaluations[10,11]. With its cross-cultural design and wider range of assessment domains, the World Health Organization Quality of Life-BREF (WHOQOL-BREF) might provide a more thorough assessment of a patient's general quality of life[12]. To provide a reference for developing programs to improve and enhance the QoL of MDR-TB patients, this study aimed to evaluate the QoL of MDR-TB patients and identify associated factors under programmatic conditions in Indonesia. Programmatic management of MDR-TB is a TB control program in Indonesia. Therapy provided to patients follows the national guidelines for MDR-TB treatment. Furthermore, to demonstrate the additional burdens caused by drug resistance, we compare the QoL of MDR-TB patients with that of drug-sensitive TB patients. These studies assess a variety of QoL domains, such as physical health, psychological state, social relationships, and environmental factors, using standardized instruments of WHOQOL-BREF. Researchers can guide focused interventions to enhance patient outcomes by highlighting areas of significant impairment.

2. Methods

2.1. Study design

The overall quality of life of MDR-TB patients was evaluated, and the factors associated with QoL were explored using a case-control study. Quality of life is a primary outcome of our study, as part of treatment outcomes. Since MDR-TB is the case and DS-TB is the control group, we applied a case-control study. Without requiring extended follow-up times, this design enables investigators to identify and determine differences in QoL between these groups.

2.2. Ethical approval

The Haji Hospital for Health Research Ethics Committee (445/147/KOM.ETIK/20224) provided their ethical approval for the study's

conduct. Only willing and knowledgeable participants with written informed consent were recruited for the study, ensuring compliance with the ethical principles of voluntary engagement, non-maleficence and beneficence, privacy, and confidentiality.

2.3. Participant and data collection

Patients with MDR-TB who received treatment at the Haji Hospital of outpatient MDR-TB unit between June and December 2024 were selected as the study population. We used non-random (consecutive sampling) to gather the participants during the study period. The study's inclusion requirements were as follows: (1) through the utilization of MTB and Rifampicin Resistance Detection Method (Xpert MTB/RIF), drug susceptibility testing, and MTB culture, they were confirmed with MDR-TB infection; (2) they had to be at least 18 years old; (3) had to have consented to participate in the survey and be able to complete the questionnaire on their own or with the investigator's assistance; and (4) received treatment for MDR-TB with all oral-regimens, either shorter or longer regimens. For the control group, we recruited patients with DS-TB as follows: (1) rifampicin sensitive by GeneXpert; (2) aged ≥18 years old; (3) undergoing DS-TB treatment for at least four weeks; and (4) willing to participate by signing the informed consent. Individuals with severe illnesses (carcinoma or tumors), speech or comprehension issues, consciousness disturbances, and those who are HIV positive were excluded, as reported in some literature. HIV co-infection in TB patients leads to a decline in quality of life across psychological, physical, and social domains. Therefore, we excluded TB patients with HIV in our study[7].

We used a case-control formula to determine the sample size. The sample size formula was:

$$n = \frac{(P0 \times q0 + P01 \times q1)\,(Z1-\alpha/2 + Z1-\beta)^2}{(p1-p0)^2}$$

A 95% *CI* level, 80% sampling power, and 5% (alpha) statistical significance were applied to determine the sample size. The corresponding values for Z1-α/2 and Z1- β were 1.96 and 0.84. We obtained the P1 and P0 values from a study by Izhar *et al.*, where the proportion of MDR-TB patients with poor quality of life was P1=0.286 and the proportion of DS-TB patients with poor quality of life was P0=0.089[6] q0=1-p0 and q1=1-p1[10]. According to the formula's sample calculation, there were 83 patients to enroll in this study.

Following unified training, the investigators utilized the inclusion and exclusion criteria to select MDR-TB patients for the survey. We informed the patients and their families about the study's purpose and obtained their informed consent before we initially began. The investigators subsequently distributed the questionnaires. Ensuring each chosen patient independently completed an anonymous questionnaire took about fifteen minutes. Every questionnaire was immediately gathered, and the survey's outcomes gradually improved.

2.4. Measurement

2.4.1. General characteristic

Age, sex, body mass index (BMI), education level, occupation, marital status, monthly income, comorbidities, depression, and PHQ-9 score were among the information that the participants provided.

2.4.2. The instruments

The participants' quality of life during the MDR-TB treatment was evaluated using the World Health Organization's Quality of Life Brief (WHOQOL-BREF) questionnaire, a shorter version of the WHOQOL-100. There were twenty-six items in the WHOQOL -BREF. The 24 items were divided into four domains: physical, psychological, social, and environmental, while the two remaining items independently evaluated the general perception of QOL and satisfaction with health. Each domain's score is determined using the WHO-recommended formula, which ranges from 4 to 20, and then normalized to a score between 0 and 100[13]. Each item was scored on a 5-point Likert scale, ranging from 1 to 5. The QoL improves with a higher score. A score of <50 was classified as poor and a score of ≥ 50 was classified as good quality of life[14].

We used the Indonesian version of the WHOQOL-BREF questionnaires. which has been validated by Anisah *et al.* in Indonesian TB patients. The Cronbach's alpha coefficient for the WHOQOL-BREF questionnaire (all 26 items) indicated an internal consistency level of 0.880. The coefficient correlation (r) for each question was above 0.361, higher than the r table[15]. Therefore, the Indonesian WHOQOL-BREF questionnaire is valid and reliable.

The Indonesian version of PHQ-9 to assess depression in our study was adapted from Fuady *et al.*, with a Cronbach's alpha of 0.837 and positive correlation between PHQ-9 score and back depression inventory (P=0.001, r=0.567), considering that the questionnaire was valid and reliable in TB patients[11]. Nine questions with four possible responses and scores comprise the PHQ-9. The total score is categorized as follows: no depression (1-4), mild (5-9), moderate (10-14), fairly severe (15-19), and severe (20-27)[16,17].

2.5. Statistical analysis

Version 20.0 of the Statistical Package for Social Sciences (SPSS) for Windows was used to analyze the data. Demographic data of the TB patients, such as sex, education level, comorbidities, history of TB treatment, occupation, income, marital status, and depression status, are presented as percentages. Continuous data, such as age, body mass index (BMI), PHQ-9 scores, and WHOQOL-BREF scores, are shown as the mean±SD. Two respondent groups were

compared based on their socio-demographic characteristics using independent *t*-tests. We used an independent *t*-test to analyze the difference in PHQ-9 scores between the two groups. We used a Pearson correlation to assess any correlation between the PHQ-9 and the WHOQOL-BREF score. A multivariate analysis was used to investigate factors associated with MDR-TB patients' quality of life. Prior to performing multivariate analysis, a multicollinearity diagnostic test was carried out. Association between independent and dependent variables is calculated using bivariate analysis for categorical data, such as sex, marital status, education level, history of TB treatment, DM, employment, and ADRs. Variables from the bivariate analysis with a $P \leq 0.25$ were incorporated into the multivariate logistic analysis using the backward stepwise logistic regression procedure. Results were reported as adjusted odds ratio (a*OR*) and 95% *CI*. The differences between the two categorical variables between the case and control groups were assessed by the *Chi*-squared test. Every statistical test was performed at the significance level of $P<0.05$.

3. Results

Forty-one and forty-three of the MDR-TB and DS-TB patients were enrolled in our study. The baseline socio-demographics between the two groups are shown in Table 1.

The characteristics of the socio-demographic of the 84 TB patients showed that more than 60% were male. Body mass index (BMI) was significantly lower among cases than in the control group ($P<0.05$). Half of MDR-TB patients were classified as underweight with a mean BMI≤18.5 kg/m^2. Diabetes mellitus (DM) was found in nearly 50% of the case group. Half of the case group had a history of TB treatment. This indicates that males, those with low BMI, those with DM, and those with a history of TB treatment have increased susceptibility to MDR-TB, but the differences were not significant. Among MDR-TB patients, 19/41 (46.3%) experienced adverse drug reactions (ADRs) and 22/41 (53.6%) had 6 months of treatment duration. The prevalence of depression and PHQ-9 scores between the two groups is shown in Table 2.

Patients with depression were significantly higher in the case group than in the control group ($P<0.05$). This indicates that MDR-TB patients are more susceptible to depression during treatment than DS-TB patients. The PHQ-9 scores were classified as mild depression in the MDR-TB group, with a range score of 5-9. Among patients with depression in the case group, 21.9%, 31.7%, and 2.4% experienced mild, moderate, and fairly severe depression, respectively. Meanwhile, in DS-TB patients with depression, 23.2% and 9.3% experienced mild and moderate depression. The self-rating QoL and WHOQOL-BREF scores between the two groups are shown in Table 3.

Table 1. Baseline socio-demographic characteristics between the two groups [*n* (%)].

Variables	MDR-TB (*n*=41)	DS-TB (*n*=43)	*P*
BMI, kg/m^2, mean±SD	18.35±4.01	21.80±4.94	0.001
≤18.5	22 (53.6)	10 (23.2)	
18.5-22.9	14 (34.1)	20 (46.5)	
23.0-24.9	3 (7.3)	5 (11.6)	
≥25.0	2 (5.0)	8 (18.7)	
Age, years, mean±SD	44.85±14.16	41.02±17.23	0.270
Sex			
Male	27 (65.8)	28 (65.1)	0.943
Female	14 (34.2)	15 (34.9)	
Diabetes mellitus			
Yes	18 (43.9)	16 (37.2)	0.197
No	19 (56.1)	27 (62.8)	
History of TB treatment			
New	19 (46.4)	43 (100)	NA
Previously treated	22 (53.6)	0	
Education			
Elementary to junior school	12 (19.5)	14 (20.9)	0.207
Senior high school to higher education	27 (56.0)	29 (37.2)	
Occupation			
Unemployed	24 (58.5)	23 (53.4)	0.641
Employee	17 (41.5)	20 (46.6)	
Income (IDR)			
≥2.5 billion	32 (78.0)	28 (65.1)	0.293
>2.5 billion	9 (22.0)	15 (34.9)	
Marital status			
Married	30 (73.1)	28 (65.1)	0.243
Unmarried or separated	11 (26.9)	15 (34.9)	

BMI: body mass index; DM: diabetes mellitus; MDR-TB: multidrug-resistant tuberculosis; DS-TB: drug-sensitive tuberculosis; IDR: Indonesian rupiah; PHQ-9: patient health questionnaire-9.

Table 2. Depression and PHQ-9 scores between the two groups [*n* (%)].

Variables	MDR-TB (*n*=41)	DS-TB (*n*=43)	*P*
Depression			
Yes	23 (56.1)	14 (32.5)	0.031
No	18 (43.9)	29 (67.5)	
PHQ-9, mean±SD	6.65 ± 5.00	4.79 ± 3.41	0.048

Table 3. Self-rating and score of World Health Organization's Quality of Life Brief instrument.

Self rating	MDR-TB (*n*=41)	DS-TB (*n*=43)	*P*
Rate your quality of life? *n* (%)			0.157
Very bad	0 (0.0)	0 (0.0)	
Bad	3 (7.3)	0 (0.0)	
Average	17 (41.4)	19 (44.2)	
Good	20 (48.7)	19 (44.2)	
Very good	1 (2.6)	5 (11.6)	
How satisfied are you with your health? *n* (%)			0.070
Very dissatisfied	0 (0.0)	0 (0.0)	
Dissatisfied	10 (24.3)	3 (6.9)	
Average	9 (21.9)	13 (30.2)	
Satisfied	19 (46.3)	20 (46.5)	
Very satisfied	3 (7.5)	7 (16.4)	
Score in different domains, mean±SD			
Physical	57.63±12.53	68.13±10.58	<0.001
Psychological	61.48±14.88	71.55±11.60	0.001
Social relationship	60.70±15.77	64.27±11.42	0.236
Environmental	59.68±12.67	68.88±11.73	0.001
Total score, mean±SD	59.87±11.44	68.21±8.13	<0.001

According to the self-rating of WHOQOL-BREF, the rate of quality of life and health satisfaction was similar between the two groups ($P \geq 0.05$). The physical QoL domain recorded the lowest score among all four QoL domains in MDR-TB patients. The overall score of WHOQOL-BREF was significantly lower in MDR-TB patients than in DS-TB patients.

The correlation between PHQ-9 and WHOQOL-BREF score among both MDR-TB (r=-0.502, P=0.001) and DS-TB (r=0.801, P=-0.040) patients are negative. This indicates that as PHQ-9 scores increase (demonstrating more severe depression), the WHOQOL-BREF scores decrease (demonstrating lower quality of life). It suggests that lower quality of life (as determined by WHOQOL-BREF) is significantly associated with higher levels of depression (as determined by PHQ-9). This result confirms the significant negative effects of depression on the overall QoL. Factors associated with QoL among MDR-TB patients are shown in Table 4. Three variables (sex and income) with a *P*-value of 0.25 from the bivariate analysis were removed from multivariate. There were only 10 variables included in the multivariate analysis.

As shown in Table 4, depression was significantly associated with QoL. This indicates that depression will reduce QoL in the physical (*OR* 3.611; 95% *CI* 2.393-6.951; P=0.029), psychological (*OR* 1.672; 95% *CI* 1.179-5.941; P=0.021), social relationship (*OR* 2.586; 95% *CI* 1.611-2.909; P=0.014), and environmental domains (*OR* 1.926; 95% *CI* 1.047-2.147; P=0.048). During the study period, 19/41 (46.3%) of MDR-TB patients complained of numerous adverse events. Neuropathy, joint pain, skin discoloration, nausea, vomiting, and dizziness were observed in 24.3%, 21.9%, 19.5%, 19.5%, 14.6%, and 12.2%, respectively.

Table 4. Determinants of quality of life among MDR-TB patients (n= 41).

Variables	Domain											
	Physical			Psychological			Social relationship			Environmental		
	a*OR*	95% *CI*	*P*	a*OR*	95% *CI*	*P*	a*OR*	95% *CI*	*P*	a*OR*	95% *CI*	*P*
Age	1.041	0.914-1.187	0.542	1.134	0.983- 1.308	0.084	0.946	0.818- 1.093	0.449	0.961	0.877- 1.053	0.396
BMI												
≤18.5	Ref											
>18.5	8.085	0.314- 207.874	0.207	0.253	0.013- 4.793	0.360	5.387	0.180- 160.915	0.331	0.745	0.051- 10.896	0.830
Diabetes mellitus												
Yes	Ref											
No	5.891	0.438-79.310	0.181	0.239	0.017- 3.290	0.285	0.261	0.015- 4.581	0.358	0.277	0.040- 1.932	0.195
History of TB treatment												
New	Ref											
Previously treated	0.447	0.040-5.020	0.514	1.874	0.082- 43.016	0.694	2.435	0.204- 50.084	0.482	1.756	0.198- 15.552	0.613
Education												
Elementary-Junior	Ref											
Senior-Higher	7.914	0.281- 222.824	0.224	3.757	0.260- 54.229	0.331	0.303	0.016- 5.741	0.426	3.709	0.467-29.471	0.215
Martial status												
Married	Ref											
Unmarried or separated	8.304	2.210- 327.715	0.259	2.205	0.076- 63.760	0.645	0.093	0.003- 2.535	0.159	0.451	0.032- 6.469	0.558
ADRs												
Yes	Ref											
No	0.310	0.027-3.561	0.347	5.874	0.417- 82.737	0.190	4.853	0.195- 41.787	0.444	4.549	0.486- 42.599	0.184
Treatment duration, months	0.951	0.855-1.058	0.356	1.053	0.792- 1.400	0.721	0.942	0.753- 1.117	0.599	1.015	0.914- 1.127	0.782
Depresion	3.611	2.393-6.951	0.029	1.672	1.179- 5.941	0.021	2.586	1.611- 2.909	0.014	1.926	1.047- 2.147	0.048
Regimen												
BPaL/M	Ref											
Longer	1.652	0.067-40.881	0.759	12.930	0.269- 620.584	0.195	0.636	0.016- 25.539	0.810	2.303	0.199- 26.626	0.504

4. Discussion

According to the clinical characteristics, BMI among MDR-TB patients was significantly lower than that in DS-TB. Underweight in patients with MDR-TB is associated with chronic energy deficiency, pulmonary inflammation, increased oxidative stress, and altered body composition[18]. Nausea and vomiting due to adverse events of MDR-TB treatment induce loss of appetite and malnutrition among MDR-TB patients[19]. Malnutrition is one of the causes of weight loss in countries with high TB prevalence rates, such as Indonesia. This study was similar to our previous studies, which reported that the BMI in MDR-TB patients before treatment was ≤18.5 kg/m^2[20]. Being underweight negatively impacts treatment success and is associated with lung cavities. Improving BMI and treatment outcomes for TB patients requires addressing undernutrition through comprehensive nutritional interventions. A strong framework for improving BMI in TB patients can be established by combining dietary support, supplementation, education, and periodic surveillance[21].

Based on a history of TB treatment, more than 50% of the patients in the case group had previously been treated. One of the biggest causes of MDR-TB cases is the improper use of first-line antitubercular drugs. As many as 77.2% of TB patients who used antitubercular drugs improperly developed MDR-TB cases[22]. These results are similar to a study by Setyawan *et al.*, who reported that relapse cases were more common among patients with MDR-TB than new cases[23]. One well-known comorbidity in TB patients is DM. We found that 43.9% of MDR-TB patients had DM, a risk factor for MDR-TB. The effects of infection and systemic inflammation in TB patients elicit a hyperglycemia stress response. High levels of cytokines in DM raise the risk of insulin resistance and the severity of TB infection[24]. In addition, rifampicin is known to induce the expression of cytochrome P450 2C9, which accelerates the metabolism of sulfonylureas and decreases their plasma concentrations, leading to suboptimal glycemic control in TB patients with DM[25].

According to our study, 56% of MDR-TB patients had depression during the study period. Multiple combinations of medical, emotional, community, and financial aspects make patients with MDR-TB more vulnerable to depression than those with DS-TB[26]. Our findings are higher than the Indonesian young adult population's depression rate, which was previously estimated to be less than 6%[27]. Nevertheless, our study is similar to the meta-analysis, which reported that the prevalence of depression was 52.3% in MDR-TB patients[28].

A high prevalence of depression in our study among MDR-TB patients is more likely because approximately 53% of patients were retreatment cases. The prevalence of depression in retreatment TB patients is approximately 2.5 times higher than in new treatment[29]. In addition, the duration of illness was significantly associated with depression among MDR-TB patients. Since more than 50% of MDR-TB patients in our study had a history of TB treatment that prolonged their illness and treatment, they were more susceptible to depression[30]. Conversely, a study by Jo *et al.*, in Malawi, reported no difference in QoL between new cases and retreated TB. It was more likely that less than 30% of patients had retreated TB[31].

In addition, a high percentage of depression in MDR-TB patients is more likely because 58.5% of patients received longer regimens for their treatment. Longer regimens consist of bedaquiline, linezolid, levofloxacin, cycloserine, and clofazimine. One of the adverse events of cycloserine is psychological disorders, such as anxiety and depression. Several studies indicated a higher prevalence of depression in MDR-TB patients receiving clofazimine-containing regimens than in those receiving shorter regimens[32,33]. The impact of cycloserine on the gamma-aminobutyric acid (GABA) neurotransmitter and *N*-methyl-*D*-aspartate (NMDA) receptor may explain its mechanism to psychological disorders[32]. Cohort studies involving a large number of MDR-TB patients are necessary to analyze the causal relationship of clofazimine, which can induce depression.

Susanto *et al.*, applied the Zung Self-Rating Depression Scale Questionnaire to measure depression and reported a depression rate of 68% which is high than our study[34]. Azam *et al.* reported MDR-TB patients who were underweight and with comorbidities were significantly associated with depression[35]. However, we did not analyze factors associated with depression in our study. Numerous factors contribute to the wide variation in depression prevalence across studies, including the use of different tools and threshold scores for characterizing depression, disease stages, treatment phases, and other variations in study settings.

This study revealed that almost half of MDR-TB patients felt their overall QoL was good. Nonetheless, one-fourth of them were dissatisfied with their health. In contrast, Hamsaveni *et al.* reported that 10% and 57.5% of MDR-TB patients experienced poor QoL and were dissatisfied with their health, respectively[36]. A previous study in Indonesia reported that numerous TB patients demonstrated frustration with their QoL[37]. The overall score of WHOQOL-BREF was significantly lower in MDR-TB patients than in DS-TB patients. The most detrimental domain of WHOQOL-BREF in our study was physical health, with a mean score of (57.63±12.53), which suggests insufficient activity in completing daily tasks, inadequate sleep and rest, increased reliance on medications, increased pain and discomfort, low energy and mobility, and inadequate work capacity. Numerous symptoms, including fever, cough, weight loss, and adverse effects, have been mentioned as the reasons for poor physical functioning. Neuropathy and joint pain were the two main adverse effects most commonly found in this study, associated with linezolid and bedaquiline[20]. Muscle signals may be interrupted by neuropathy, leading to limb weakness

and difficulty with mobility and self-care. In addition, fundamental movements such as sitting, standing, and reaching are restricted by joint pain. These two conditions may increase the risk of physical limitations in MDR-TB patients.

Our study was similar to several studies, indicating that the physical domain was the most affected among the WHOQOL-BREF domains in MDR-TB patients[4,36,38]. Conversely, a study in Nanjing, China, reported that environmental health provides the lowest score among the four domains[39]. It was more likely because 27.4% of patients were aged ≥ 60 years. Due to social, physical, and financial constraints, older people are more susceptible to environmental problems. The differences between the socio-demographics of MDR-TB patients among studies in several countries contribute to the wide variations in results.

Another study by Laxmeshwar *et al.*, reported a higher score of WHOQOL-BREF in MDR-TB patients compared to our findings. It was because the mean age of their study was 28 years; meanwhile, in our study, the mean age was 44.8 years. Patients under 28 years old had a higher score for QoL than those older[40]. A lower score in four domains of WHOQOL-BREF than that of our study was reported by Wang *et al.*, in China. It was more likely because 27.4% of patients were aged > 60 years old, and 62.2% of patients experienced adverse drug reactions during DR-TB treatment[39]. Conversely, we found that 14.6% of patients were aged > 60 years, and 43.9% of patients had adverse drug reactions. In contrast to younger patients, elderly patients have attributes like financial hardship, limited mobility, and ignorance of tuberculosis. Adverse drug reactions, particularly in moderate and severe diminished QoL and adherence among MDR-TB patients[8].

In MDR-TB patients, we found a negative correlation between PHQ-9 and WHOQOL-BREF score. Poor sleep, tiredness, low motivation, and social disengagement are all common symptoms among individuals with high PHQ-9 scores, and they all lower quality of life[11]. Primary components of the WHOQOL-BREF, such as social functioning, mental health, and physical health, are also affected by depression. Our finding is similar to the study by Redwood *et al.*, in Vietnam, demonstrating that the PHQ-9 score correlates with quality of life, (r=-0.674, P<0.01). Furthermore, the PHQ-9 score was higher than in our study. It was more likely because 42.5% of patients experienced moderate or severe depression (PHQ-9≥10)[38]. Conversely, in our study, 34.5% of MDR-TB patients experienced moderate or severe depression. We did not find a correlation between PHQ-9 and WHOQOL-BREF score in DS-TB patients (P≥0.05). It was more likely because the PHQ-9 score was significantly lower in DS-TB than in MDR-TB patients.

We found that MDR-TB with depression was significantly associated with a lower score of WHOQOL-BREF in the physical, psychological, social, and environmental domains. TB patients with psychological disorders may have an impact on their overall health and quality of life. Mental distress is closely associated with the deterioration of physical health and the rise in chronic symptoms, both of which can affect QoL[31,32]. In terms of physical health, depressed MDR-TB patients have less energy, recover more slowly, and have difficulty completing everyday tasks. In regard to psychology, depressed MDR-TB patients may experience emotional distress, a persistently low mood, and a negative self-image. In addition, MDR-TB patients may experience a decrease in interpersonal satisfaction and social support collaborations in the social relationship domain. By diminishing perceptions of security, resources, and service accessibility, depression has a detrimental impact on the environmental domain of quality of life. Kodical *et al.*, found a negative correlation between depression and all QoL domains, including the environmental domain, among MDR-TB patients[15]. Our study was supported by Vaidya *et al.*, who reported that the psychological domain was the most affected. It was because 72.5% of patients experienced depression[41].

Depression is also reported to significantly impair the success rate of MDR-TB treatment. Compared to patients without depression, TB patients who experienced depression had a 4.46-fold increased risk of treatment failure[42]. Improved clinical outcomes may come from treating the psychological aspects of tuberculosis. It has been identified that psychotherapy during TB treatment increases treatment, cure, and adherence rates. As an intervention, psychological support can increase treatment completion and adherence[35,37].

Our study has several limitations. First, the findings may not fully reflect the Qol of patients with MDR-TB because the study was limited to one hospital and had a small sample size. In addition, we did not assess QoL and depression scores that may change over time since our study was case-control. Moreover, given the nature of the study design, we can not determine the impact of QoL and depression on treatment outcomes. Nevertheless, this study provides researchers, decision-makers, and medical professionals who treat TB patients under programmatic conditions with more knowledge about QoL and associated factors among MDR-TB patients in Indonesia.

In conclusion, patients with MDR-TB had a lower Qol than those with DS-TB. MDR-TB patients with depression were associated with a low quality of life. Low quality of life and depression in MDR-TB patients may reduce treatment adherence, increase psychological comorbidities, and result in unfavorable treatment outcomes. Prompt implementation of mental health treatments tailored to the clinical characteristics of MDR-TB patients in Indonesia is imperative. In order to address patients' mental health needs, psychological interventions must be incorporated into TB treatment protocols. For MDR-TB patients, strategies like cognitive behavior therapy, psychoeducation, motivational therapy, and

social support may improve quality of life, encourage treatment compliance, and contribute to improved health outcomes. To produce reliable and generally applicable data on the quality of life among MDR-TB patients during treatment, a multicenter and longitudinal study with a larger sample size should be implemented.

Conflict of interest statment

All authors declare that there was no conflict of interest in this study.

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Authors' contributions

OP, DR, TP, JL, AF, and ND conceived and designed the study. OP, DR, and AF collected the data. TP and JL analyzed the data. TP, JL, and ND made tables. OP, TP, JL, and ND drafted the manuscript. DR, TP, and AF edited the manuscript. The final version of the manuscript has been acknowledged by all authors.

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