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Correlation of Hrct, Mmp-9, Molecular Rapid Test, Hba1c and Quality of Life In Patients With and Without Tb-Dm Sequel

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ABSTRACT

Tuberculosis (TB) is a chronic infectious disease that can cause permanent lung damage (sequelae). Diabetes Mellitus (DM) is a comorbidity that can worsen TB healing. Evaluation of sequelae through various examination approaches such as: HRCT, MMP-9, TCM, HbA1c and patient quality of life was carried out to understand the relationship between the degree of lung damage and related clinical factors. An analytical observational study with a cross-sectional approach was conducted on TB patients who had been declared cured (after 6 months of treatment) and quality of life assessment using the WHOQOL-BREF instrument. Correlation analysis was performed to determine the relationship between these parameters and the degree of lung sequelae assessed radiologically. Results: The most significant HRCT images were fibrosis in TB- DM: 26 (86.7%), TB without DM: 10 (33.3%), p: 0.00, then followed by opacity in TB-DM: 21 (70.0%), TB without DM: 11 (36.7%), p: 0.01. While cavities were only found in TB-DM: 12 (40.0%), TB without DM: 8 (26.7%), p: 0.02. MMP-9 in TB-DM patients: 171.33 ± 50.49 TB without DM: 63.90 ± 37.98, p: 0.00. TCM in TB-DM patients: 30 (100%), TB without DM: 17 (56.7%). HbA1c in TB-DM patients: 7.12 ± 0.94 TB without DM: 4.19 ± 0.71, p: 0.00. Quality of life (WHOQOL-BREF): Physical TB-DM patients: 48.30 ± 5.79, TB without DM: 81.50 ± 6.15, p: 0.00. Psychological of TB-DM patients: 45.15 ± 4.95 TB without DM: 80.90 ± 4.48, p: 0.00. Social of TB-DM patients: 45.63 ± 5.29, TB without DM: 79.60 ± 5.90, p: 0.00. Environment of TB-DM patients: 44.83 ± 4.78 TB without DM: 81.50 ± 6.37, p: 0.00. Quality of Life score of TB-DM patients:

183.90 ± 11.94 TB without DM: 317.83 ± 25.758, p: 0.00. The combination of HRCT, MMP-9, TCM, and HbA1c, can be used as a prognostic indicator to assess the degree of sequelae in TB-DM patients. Early and proper diagnosis can improve quality of life and reduce long-term complications.

KEYWORDS: Tuberculosis, Diabetes Melitus, HRCT, MMP-9, TCM, Sequelae, Quality of life.

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INTRODUCTION

Tuberculosis (TB) is an infectious disease that is a global health problem, especially in developing countries. According to data from the World Health Organization (WHO) (2021), 10.6 million people worldwide are affected by TB, with Indonesia contributing the second-third of cases after India (WHO, 2022). According to data from the Indonesian Ministry of Health (Kemenkes RI), the prevalence of TB in Indonesia is quite high, with figures reaching 300,000 new cases annually (Kemenkes RI, 2022). Diabetes mellitus (DM) increases the risk of TB infection, worsens disease progression, and increases the risk of long-term sequelae, such as pulmonary fibrosis and impaired respiratory function. TB infection can worsen glycemic control in DM patients, leading to increased glycated hemoglobin (HbA1c) levels and diabetes-related complications (Jung et al., 2023).

High-Resolution Computed Tomography (HRCT) is a sensitive imaging modality for assessing the degree of lung damage caused by TB. HRCT images of TB-DM patients show more fibrosis, bronchiectasis, and cavitation than TB patients without DM. Data from Adlanta et al. (2022) show that DM patients hospitalized for TB have a higher incidence (Adlanta et al., 2022). Individuals with DM are at higher risk of developing active TB, as high glucose levels can reduce the body's immune response to infection (Gonzalez et al., 2024).

Matrix Metalloproteinase-9 (MMP-9) is a proteolytic enzyme that plays a role in lung tissue degradation in TB. MMP-9 levels are an important biomarker in the inflammatory process and tissue remodeling. Increased MMP-9 levels correlate with HRCT findings showing fibrosis and lung cavities, supporting the hypothesis that MMP-9 is a key mediator in the pathogenesis of secondary TB, this is in line with the study of Messah et al. (2024). In DM patients, high MMP-9 levels affect the progression of

diabetes complications, such as retinopathy and neuropathy (Mastari, 2022). Recent research shows that high MMP-9 levels are associated with the severity of TB infection and serve as an indicator of response to therapy to assess the pulmonary inflammatory reaction in TB patients, especially those with comorbidities such as DM (Qu et al., 2025).

Molecular Rapid Testing (TCM) is a Polymerase Chain Reaction (PCR)-based diagnostic method that has improved the detection of Mycobacterium tuberculosis (MTB) with high sensitivity and specificity. However, the relationship between TCM results and the severity of pulmonary sequelae in TB-DM patients has not been widely studied. A positive TCM result at the time of initial diagnosis has not been shown to directly correlate with the degree of sequelae at the end of treatment. Previous research has shown that false-positive results are more common in DM patients (Rejito et al., 2024). However, TCM remains important in ensuring successful therapy and preventing resistance (Rahman et al., 2023). Therefore, TCM test results must be interpreted in light of the patient's clinical condition, including diabetes status.

HbA1c is used as an indicator of long-term glycemic control and has been associated with disease severity in TB-DM patients. In this study, high HbA1c values were associated with more severe lung damage and poor quality of life. TB infection can worsen glycemic control in DM patients, which in turn can increase the risk of diabetes complications such as neuropathy, retinopathy, and cardiovascular disease (IDF, 2021). Economically, TB treatment in DM patients can also pose a greater financial burden. Increased treatment costs, coupled with lost productivity due to the disease, can negatively impact the family and community economy (Vaquero et al., 2021).

Quality of life is an important indicator for assessing the impact of the disease on patient well-being. Post-TB patients, especially in the physical and psychological domains, show sequelae impacts on the patient's daily life, including physical health, mental health, and social interactions. Patients with TB-DM experience a more significant decline in quality of life compared to TB patients without DM (Murlistyarini and Dani, 2022; Chowdhury et al., 2024). Research by Febriana et al. (2025) showed that patients with TB-DM experience more severe symptoms, such as fatigue, pain, and difficulty breathing, compared to TB patients without DM (Febriana et al., 2025; Hadi et al., 2025). This study used the WHOQOL-BREF instrument. There was a significant decrease in quality of life scores in TB-DM patients compared to TB without DM.

To date, there has been no comprehensive study linking HRCT, MMP-9, Molecular Rapid Test, HbA1c, and Quality of Life (QoL) in the TB-DM sequelae population. Against this backdrop, research is needed to analyze the correlation between HRCT, MMP-9, TCM, HbA1c, and QoL in patients with and without TB-DM sequelae. The results of this study are expected to provide new insights into TB-DM management and support the development of more effective management strategies. The novelty of this study lies in its multidimensional approach in evaluating the interaction between biomarkers, diagnostic methods, and patient clinical conditions, a practice that has not been widely studied before.

RESEARCH METHODS

Types of research

The type of research used is descriptive quantitative with an approach cross-sectional, conducted systematically and placing more emphasis on facts than conclusions. This type of research emphasizes the measurement/observation time of independent and dependent variable data only once at a time.

Time and Place of Research

The research was conducted from March 2025 to July 2025 at Syafira Hospital, Pekanbaru

Population and Sample

The target population was patients who had been declared cured of TB or had received complete treatment, with or without DM. Subject selection was based on polyclinic data and medical records of TB-DM and non-DM patients from the Lung Clinic, Internal Medicine Clinic of Syafira Hospital, and several Community Health Centers in the Pekanbaru-Riau region. The study sample was a subset of the population that met inclusion and exclusion criteria, with TB patients without DM as controls.

Research Subject Criteria

Inclusion criteria

1. The research subjects were diagnosed with TB with DM and without DM who had been declared cured or had received complete treatment.
2. Age between 20 years to 60 years, not experiencing mental retardation
3. The research subjects agreed to participate in this research, signed Informed Consent

Exclusion Criteria

1. Active pulmonary TB or TB with MDR
2. Research subjects are alcoholics or have a history of drug use
3. Have cardiovascular disease (angina, heart failure, acute myocardial infarction) based on anamnesis and evaluation of status.
4. Subject refused to participate

Sample Size

The sample size in this study was obtained using the total sampling technique, where all members of the population were used as samples.

Determining the number of samples using the Slovin formula:

$$n = \frac{N}{1+N(d)^2}$$

$$n = \frac{70}{1+68(0,05)^2}$$

$$n = \frac{70}{1+64(0,05)^2}$$

$$n = \frac{70}{1+0,175}$$

$$n = \frac{70}{1,175}$$

$$n = 59,57$$

$$n = 60$$

Information:
n = Number of samples required
N = Population size = 70 respondents
e = Level of error in the study = 0,05 (5%)
So the minimum number of samples used is 60 research subjects.

Research Variables
Independent variable : TB-DM
Intermediate variables : HRCT, MMP-9, TCM, HbA1c and Quality of Life as
Dependent Variables : Sequelae of TB-DM and Without DM

Research Procedures
Sampling was carried out using total sampling., in humans and the materials used for research samples were the results of HRCT thorax and venous blood. Before conducting the study, ethical approval was requested from the Research Ethics Committee of the Faculty of Medicine, University of Riau/Prima Indonesia Medan. Validity of Thoracic HRCT results reading was carried out by two Thoracic Consultant Radiology Specialists. Venous blood was taken to assess serum MMP-9 levels, then put into a plan tube at a standard temperature to be sent to the Lontar laboratory of FK Unri Pekanbaru.

Instrument reliability testing was conducted on the research protocol, including chest HRCT, HbA1C blood tests, TCM molecular tests, and MMP-9 immunohistochemical tests. Data were collected following agreed-upon steps as a procedure.

Data Processing and Analysis
Statistical analysis method using Statical Program for Social Science (SPSS) version 25.

Research Operational Framework

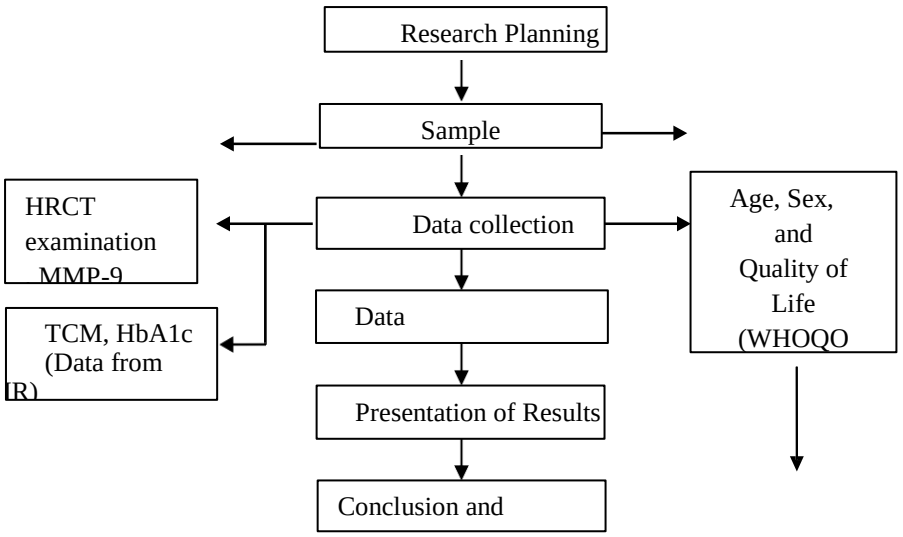

Figure 1 Research Flow

RESEARCH RESULTS AND DISCUSSION

Research result

This study was conducted at the Radiology Unit of Syafira Hospital, Pekanbaru, from March 2025 to July 2025. The study population consisted of patients who had been declared cured of TB or had received complete treatment, both with and without DM. Subject selection was based on polyclinic data and medical records of TB-DM patients and those without DM from the pulmonary and internal medicine polyclinics of Syafira Hospital and several community health centers in the Pekanbaru-Riau region.

Frequency Distribution by Age and Gender

Table 1 Frequency Distribution by Age and Gender

Demographic Characteristics of TB-DM (n=30) and Patient Clinical Variables		TB-DM (n=30)	*p-value*
Age (years)	43,80 ±10,34	48,40 ± 14,98	0,172
Gender			
Man	12 (40,0%)	12 (40,0%)	1
Woman	18 (60,0%)	1 60,0%)	

Table 1 shows no statistically significant differences between the TB-DM and TB-without-DM patient groups in terms of age or gender. The mean age of the TB-DM patients was 43.80 ± 10.34 years, while the TB-without-DM group was 48.40 ± 14.98 years. p: 0.172. This shows that the age difference between groups is not significant (p> 0.05). Gender distribution also did not show significant differences in the TB-DM and non-DM groups, with 12 men (40.0%) and 18 women (60.0%), respectively. p: 1.00. This finding indicates that patient characteristics based on age and gender were similar between the two groups, allowing for further analysis without significant demographic bias.

HRCT Frequency Distribution of TB-DM and Non-DM Patients

Table 2 HRCT Frequency Distribution of TB-DM and Non-DM Patients

HRCT findings	TB-DM (n=30)	TB without DM (n=30)	Total	*p-value*
Opacity				
Of	21(70%)	11(36.7%)	32 (53,3%)	0.01
No	9(30%)	19(63%)	28 (46,7%)	
Parous fibrosis				
Of	26 (86,7%)	10 (33,3%)	36 (60,0%)	0.00
No	4 (13,3%)	20 (66,7%)	24 (40,0%)	
Cavity				
Of	12 (40%)	8 (26,7%)	20 (33,3%)	0.02
No	18 (60%)	22 (73,3%)	40 (66,7)	
Pleural Effusion				
Of	12 (40%)	3 (10,0%)	15(25,0%)	0.00
No	18 (60,0%)	27 (90,0%)	45 (75,0%)	
Bronchiectasis				
Of	19 (63,3%)	4 (13,3%)	23 (38,3%)	0.00
No	11 (36,7%)	26 (86,7%)	37 (61,7%)	
Tram line				
Of	4 (13,3%)	6 (20,0%%)	10 (16,7%)	0.48
No	26 (86,7%)	24 (80,0%)	50 (83,3%)	
Tree in bud				
Of	7 (23,3%)	1 (3,3%)	8 (13,3%)	0,02
No	23 (76,7%)	29 (96,7%)	52 (86,7%)	
Lung nodules				
Of	21 (70,0%)	0 (0,0%)	21 (35,0%)	0.00
No	9 (30%)	30 (100%)	39 (65,0%)	

Table 2 shows significant differences in the appearance of opacities, cavities, fibrosis, pleural effusion, bronchiectasis, tree-in-bud, and nodules in TB-DM patients compared to TB without DM. However, the appearance of the threshold is not different in TB-DM compared to TB without DM.

HRCT Sequelae Score of TB-DM and Non-DM Patients

Table 3 HRCT Sequelae Score of TB-DM and Non-DM Patients

Variables	TB-DM (n=30)	without DM (n=30)	*p-value*
HRCT Sequelae Score	4,0 ± 1,94	1,43 ± 1,96	0.00

Distribution of MMP-9 in TB-DM and TB without DM Patients

Table 4 Distribution of MMP-9 in TB-DM and TB without DM Patients

Variable	TB-DM (n=30)	TB without DM (n=30)	p-value
MMP-9	171,33 ± 50,49	63,90±37,98	0.00

Table 4 shows a significant difference in MMP-9 in TB-DM patients compared to TB without DM, where the MMP-9 levels in TB-DM patients are higher than in TB without DM.

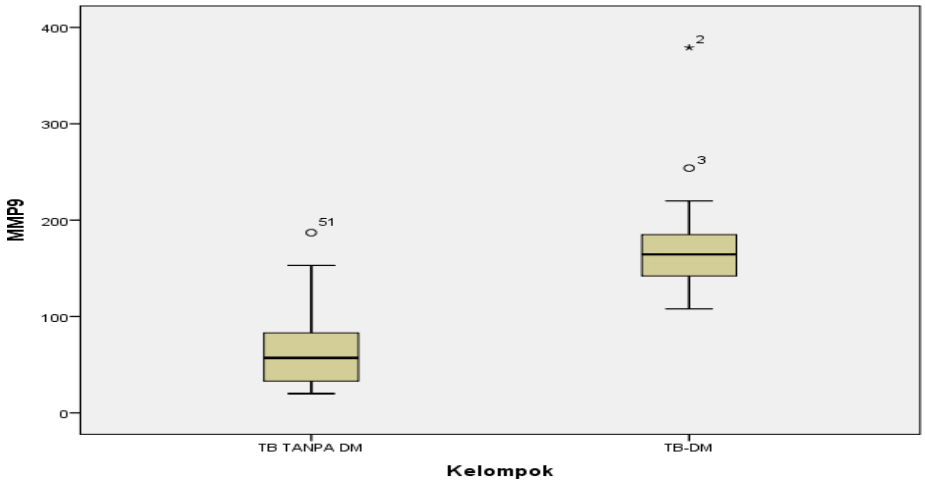

Diagram 1 MMP-9 in TB patients with and without DM

Frequency Distribution of TCM in TB-DM and Non-DM Patients

Table 5 Frequency Distribution of TCM in TB-DM and Non-DM Patients

TB-DM TCM Results	(n=30)	TB without DM (n=30)	*p-value*
Detection	30(100%)	17 (56,7%)	0.00
Non-Detection	0 (0,0%)	13 (43,3%)	0.00
Total	30	30	

Based on the data above, there are significant differences in TCM in TB-DM patients compared to TB without DM.

Distribution of HbA1c in TB-DM and TB without DM Patients

Table 6 Distribution of HbA1c in TB-DM and TB without DM Patients

Variable	TB-DM (n=30)	TB without DM (n=30)	p-value
HbA1c	7,12±0,94	4,19±0,71	0.00

Table 6, there is a significant difference in HbA1c in TB-DM sufferers compared to TB without DM, where the HbA1c levels of TB-DM sufferers are higher than those of TB without DM.

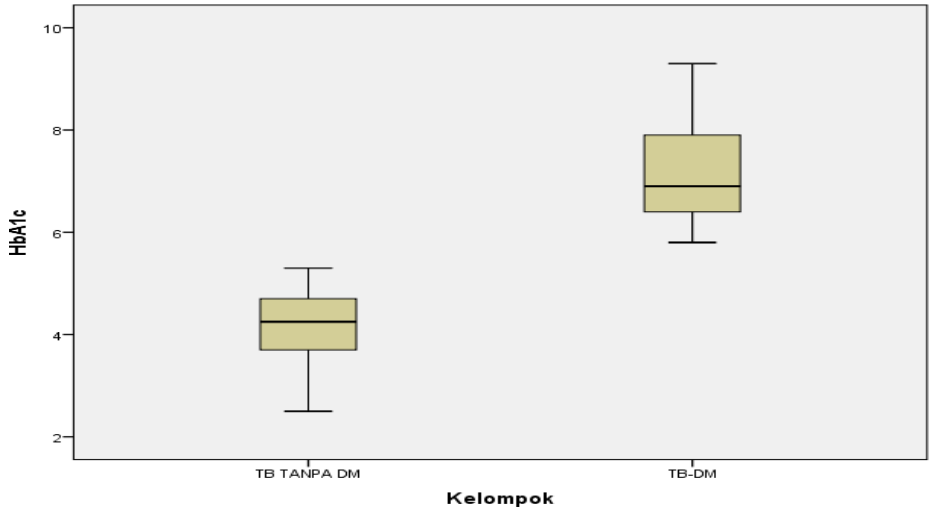

Diagram 2 HbA1c of TB patients with DM and without DM

Distribution of Quality of Life of TB-DM and Non-DM Patients

Table 7 Distribution of Quality of Life of TB-DM and Non-DM Patients

Quality of Life Domain (WHOQOL-BREF)	TB-DM (Mean ± SD)	TB without DM (Mean ± SD)	*p-value*
Physical health	48,30±5,79	81,50±6,15	0.00
Psychological health	45,13±4,95	80,90±4,48	0.00
Social relations	45,63±5,29	79,60±5,90	0.00
Environment	44,83±4,78	81,50±6,37	0.00
Quality of life score	183,90±11,94	317,83±25,758	0.00

Table 7, there are significant differences between physical, psychological, social, environmental health, quality of life scores in TB-DM sufferers compared to TB without DM, where the levels of physical, psychological, social, environmental health, and quality of life scores of TB-DM sufferers are lower than TB without DM.

DISCUSSION

Table 1 contains the demographic data of the study subjects. A total of 60 subjects participated in the study, consisting of 30 with TB-DM and 30 with TB without DM. Based on this study, there were no significant differences between age and gender groups in TB-DM and non-DM patients. This contrasts with data from the Indonesian Ministry of Health, 2021, which indicates that DM is more common in productive age groups, which has implications for community productivity. Although the prevalence of DM increases with age, older age groups do not dominate the cases.

In terms of gender, there was no significant difference, where, previous studies showed that men tend to have riskier lifestyles, such as smoking habits and higher alcohol consumption, which can contribute to an increased risk of DM. This finding is in line with research by Adlanta et al. (2022) which showed that men are more susceptible to DM, this is caused by hormonal factors and different lifestyles between men and women (Adlanta et al., 2022). Table 2 In this study, almost all subjects had sequelae on HRCT examination. The most significant HRCT images were fibrosis TB-DM: 26 (86.7%), TB without DM: 10 (33.3%), p: 0.00, then followed by opacity TB-DM: 21 (70.0%), TB without DM

DM: 11 (36.7%), p: 0.01. Meanwhile, cavities were only found in TB-DM: 12 (40.0%), TB without DM: 8 (26.7%), p: 0.02. Similar results were also obtained in the study (Sukardi et al, 2023) which found that all their patients had sequelae in the form of fibrosis. Analysis of pulmonary fibrosis showed that most patients experienced fibrosis ranging from mild to severe, meaning there was a significant proportion of structural changes in the lungs. This is important to note because pulmonary fibrosis causes lung tissue to become stiff and thickened, so that the exchange of oxygen and carbon dioxide is disrupted, which ultimately affects the patient's quality of life significantly (Duarte et al., 2024).

Tramline appearance, an image like two parallel lines that indicate thickening of the bronchial walls due to chronic inflammation. In this study, the tramline appearance did not show a significant difference between TB-DM patients 4 (13.3%) compared to TB without DM 6 (20.0%). The incomplete healing process causes anatomical abnormalities in the lungs that lead to reduced lung volume. In this study, pulmonary nodules were not found in TB patients without DM. Similar results were obtained in the study

of Jung et al. (2023) in TB patients without DM with controlled HbA1c levels, pulmonary nodules were also not found (Jung et al., 2023). Bronchiectasis, is a permanent condition in the airways characterized by abnormal dilation of the bronchi. In this study, 19 (63.3%) patients with bronchiectasis in TB-DM patients, while in TB patients without DM, 4 patients (13.3%) were found. This is in line with the WHO report (2022) which states that good diabetes management can help reduce the risk of pulmonary complications (WHO, 2022).

Table 3 shows a significant difference between the HRCT sequelae scores in TB-DM patients compared to TB patients without DM, where the sequelae scores in TB-DM patients are higher than in TB patients without DM. This is because residual symptoms that appear after someone recovers from TB still leave scars from the infection, while this is not visible clinically but is visible radiologically (Messah et al., 2024). The HRCT score indicates the presence of lung abnormalities, mostly significant lung damage. Lung damage detected by HRCT can be associated with a decrease in physical and psychological quality of life. With a rapid and accurate diagnosis using HRCT, severe lung damage can be prevented. Thus, HRCT can provide a clear picture of lung morphology and can be linked to all measured parameters (biochemical factors and patient quality of life).

Table 4 shows a significant difference in serum MMP-9 levels between TB-DM patients (median 171.33) and TB without DM (median 63.90), where MMP-9 levels in TB-DM patients are higher than in TB without DM. As a proteolytic enzyme, MMP-9 functions to destroy extracellular matrix components (such as collagen elastin) and plays a vital role in tissue remodeling during inflammation and infection. Even at low levels, MMP-9 can still influence the formation of fibrosis, cavities, and bronchiectasis (Messah et al. 2024). Thus, serum MMP-9 has the potential to be a marker for predicting long-term lung damage in TB patients. Patients with lower MMP-9 levels tend to report a better quality of life in terms of mental health and emotional well-being (Nyirenda et al., 2023).

Table 5 shows that TCM results were positive in 30 (100%) TB-DM patients, while only 13 (43.3%) were undetectable in TB patients without DM. A positive TCM result at the time of initial diagnosis has not been shown to directly correlate with the degree of sequelae at the end of treatment. However, previous research has shown that false-positive results are more common in DM patients. This is because TCM detects the immune response to TB, so even though the infection has resolved and the patient has been treated, the result can remain positive. Therefore, a positive TCM result does not always indicate an active infection, but rather a previous exposure to TB (Rejito et al., 2024). However, TCM remains important in ensuring successful therapy and preventing resistance (Rahman et al., 2023). Therefore, the results of this TCM test must be interpreted in light of the patient's clinical condition, including diabetes status.

Table 6 shows a significant difference between the HbA1c levels of TB-DM patients and those without DM. The HbA1c levels of TB-DM patients are higher than those without DM. This is in line with research by Jung et al. (2023), which states that glycemic status (HbA1c levels greater than 7) influences the occurrence of lung damage. In TB-DM patients, high HbA1c values indicate poor blood sugar control, which can reduce cellular immunity and increase lung tissue damage and worsen clinical manifestations (Jung et al., 2023). HbA1c shows the average blood sugar level in the last 2-3 months and, as an indicator of long-term glycemic control, has a significant correlation with various aspects of patient quality of life. Research shows that high HbA1c levels are associated with decreased quality of life, especially in TB-DM patients. Hadi et al. (2025)

Table 7 shows significant differences in quality of life: physical, psychological, social, and environmental health. The quality of life scores in TB-DM patients compared to TB without DM, where the levels of physical, psychological, social, and environmental health, the quality of life scores of TB-DM patients are lower than those of TB without DM. The most impaired quality of life is primarily in physical conditions (48.30%). The correlation with the social and environmental domains shows a positive direction, although it remains very weak. This may be due to the increased social support received by TB-DM patients, which can help them in facing life's challenges.

This is in line with research by Kodical et al. (2025) which showed that social support can improve the quality of life of TB patients, even though their physical condition may not be optimal. This demonstrates the importance of social interventions in improving the quality of life of TB-DM patients (Kodical et al., 2025). Research by Hadi et al. (2025) shows that TB patients, especially those with comorbidities such as DM, are more vulnerable to mental health problems. This is due to the psychological burden caused by a serious disease diagnosis and prolonged treatment (Hadi et al., 2025).

Patients with better social support and education are better able to perform physical and psychological activities. A study by Kodical et al. (2025) found that family and community support play a crucial role in the recovery of TB patients (Kodical et al., 2025). According to Purba et al. (2018), patients with diabetes often experience mental health problems that can worsen their quality of life. This suggests that good diabetes management is crucial for improving the quality of life of TB-DM patients (Purba et al., 2018).

The novelty of this study is the correlation between HRCT and MMP-9 in TB-DM patients, which can be used as a marker for predicting long-term lung damage in TB patients. The results showed that higher MMP-9 levels in TB-DM patients correlated with more severe lung damage on HRCT, such as fibrosis, cavities, and bronchiectasis. Higher MMP-9 levels in TB-DM patients can influence the formation of fibrosis, cavities, and bronchiectasis. HRCT results showed the presence of fibrosis, cavities, and bronchiectasis, which correlated with MMP-9 levels.

CONCLUSION

The average age of TB-DM patients was 43.80 ± 10.34 years, TB without DM was 48.40 ± 14.98 years, with a value of p: 0.172. The gender of the TB-DM and non-DM groups were 12 men each (40.0%), while the females each numbered 18 people (60.0%), with a value of p:1,00.

The most meaningful HRCT images are TB-DM fibrosis: 26 (86.7%), TB without DM: 10 (33.3%), p: 0.00, followed by TB-DM opacity:

21 (70.0%), TB without DM: 11 (36.7%), p: 0.01. While TB-DM cavity:

12 (40.0%), TB without DM: 8 (26.7%), p: 0,02.

There is a relationship between MMP-9 levels and the severity of pulmonary sequelae in TB-DM and TB patients without DM. MMP-9 in TB-DM patients: 171.33 ± 50.49 TB without DM: 63.90 ± 37.98, p: 0,00.

There is a correlation between Molecular Rapid Test results and TB-DM and TB without DM. TCM patients with TB-DM: 30 (100%), TB without DM: 17 (56.7%).

There is a relationship between HbA1c levels with TB-DM and TB without DM. HbA1c patients with TB-DM: 7.12±0.94, TB without DM: 4.19±0.71, p: 0,00.

There is a relationship between the quality of life of TB-DM patients compared to TB without DM. Quality of life (WHOQOL-BREF): Physical TB-DM: 48.30±5.79, TB without DM: 81.50 ± 6.15, p: 0.00. Psychological TB-DM: 45.15 ± 4.95 TB without DM: 80.90 ± 4.48, p: 0.00. Social TB-DM: 45.63 ± 5.29, TB without DM: 79.60 ± 5.90, p: 0.00. TB-DM environment: 44.83 ± 4.78 TB without DM: 81.50 ± 6.37, p: 0,00.

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