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Analysis of Risk Factors for Comorbidities in Tuberculosis Patients and Resistance Patterns of *Mycobacterium Tuberculosis* at Gunung Jati Regional Hospital

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ABSTRACT
Tuberculosis (TB) treatment is complicated by drug resistance (especially MDR-TB) and comorbidities like diabetes, HIV, hypertension, kidney disease, cancer, lung diseases, psychiatric conditions, and malnutrition, all of which worsen outcomes and increase resistance risk. The purpose of the research was to find out and analyze the risk factors for tuberculosis patient comorbidities and the resistance pattern of *Mycobacterium tuberculosis* at the Gunung Jati Regional Hospital. The observational research method was analyzed with a *crosssectional approach* with univariate analysis, bivariate analysis (fisher's exact test) and multivariate analysis with logistic regression test with the backward method using medical record data of tuberculosis patients from January-November 2024 at the Gunung Jati Regional Hospital. The results of the comorbid results showed that the most tuberculosis patients were malnourished 75 (32.9%). The results of the characteristics of the most types of resistance were two drug combinations, namely INH and RIF Resistant, as many as 33 (14.5%). The results of fisher's exact test showed a significant relationship between DM and (p-value<0.001;OR= 4.42, 95% CI= 1.95-9.98) HIV (p-value=0.0.00;OR=4.19, 95% CI=1.67-10.5), kidney disease (p-value= <0.001;OR=4.81, 95% CI= 2.21-10.4), other lung diseases (p-value=0.015;OR= 2.52, 95% CI= 1.17-5.44), chronic hepatitis (p-value=0.005;OR= 2.86, 95% CI= 1.33-6.13), psychiatric conditions (p-value 0.004;OR=2.94, 95% CI= 1.37-6.32) and malnutrition (p-value=<0.001;OR= 5.35, 95% CI= 2.43-11.8) with *Mycobacterium tuberculosis resistance*. Conclusions: There is a significant association between DM, HIV, kidney disease, other lung diseases, chronic hepatitis, psychiatric conditions and malnutrition with *Mycobacterium tuberculosis resistance patterns*

Keywords: Tuberculosis; Drug Resistance; Comorbidities

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* and remains a global health problem (Chakaya et al., 2021; Organization, 2020). The disease spreads through inhaled airborne droplets when an infected individual coughs or sneezes (World Health Organization, 2023; Tobin & Tristam, 2024). According to the Global Tuberculosis Report 2023, the number of active TB cases worldwide reached 10.6 million, with a relatively high mortality rate, especially in developing countries such as Indonesia (World Health Organization, 2023).

Indonesia ranks third among the countries with the highest TB burden in the world, after India and China (Tobin & Tristam, 2024). Based on a report by the Ministry of Health, the incidence of TB in Indonesia increased significantly from 824 cases per 100,000 population in 2021 to 969 cases per 100,000 population in 2022 (World Health Organization, 2023). West Java, as the most populous province in Indonesia, recorded the highest number of TB cases, reaching 627,464 cases (RI DPK, 2020; Ministry of Health, 2024). A similar trend was also observed in Cirebon City, where pulmonary TB cases increased from 1,224 cases in 2020 to 1,908 cases in 2021 and reached 2,209 cases in 2022 (Hidayati et al., 2023). Furthermore, data from the Ministry of Health's Tuberculosis Information System (SITB) showed that examinations using the Molecular Rapid Test (TCM) at Gunung Jati Regional General Hospital in 2024 detected 1,476 TB cases (Ministry of Health, 2024).

The TB problem has become increasingly complex with the emergence of resistance to anti-tuberculosis drugs (ATDs), such as multidrug-resistant tuberculosis (MDR-TB), which poses a major challenge in TB treatment (Chidambaram et al., 2021). This resistance arises because of incomplete treatment, poor adherence, and comorbidity factors that reduce the effectiveness of therapy (Chidambaram et al., 2021). This condition requires serious attention because TB resistance decreases the likelihood of successful treatment and increases the economic burden on health services (Hidayati et al., 2023).

Comorbidity factors, such as diabetes mellitus (DM), HIV/AIDS, hypertension, chronic kidney disease (CKD), and cancer, are known to be significantly associated with an increased incidence of TB drug resistance (Wang et al., 2024a; Luczynski et al., 2023). Previous research has shown that TB patients with DM have a 6.8-times higher risk of developing drug resistance than patients without DM (Rehman et al., 2023). HIV infection also worsens TB conditions, as individuals with HIV have a 26–31-times higher risk of developing active TB because of weakened immunity (Tobin & Tristam, 2024). Other comorbidities, such as cancer and CKD, also contribute to the development of TB resistance through metabolic disturbances and drug interactions (Wang et al., 2024a; Luczynski et al., 2023). Chronic obstructive pulmonary disease (COPD) further exacerbates the progression of TB. Respiratory damage caused by COPD impairs the body's immune response, allowing TB bacteria to proliferate more rapidly and increasing the risk of resistance (Shuu Lee et al., 2021). In addition, patients with other chronic diseases, such as epilepsy, psychiatric disorders, and malnutrition, often experience difficulties adhering to TB treatment. Antiepileptic drugs can interfere with ATD metabolism through the induction of liver enzymes, thereby reducing the effectiveness of TB treatment (Nikmawati, 2024; Samudra et al., 2024). Meanwhile, mental disorders such as depression and anxiety may also lead to medication nonadherence, thereby increasing the risk of drug resistance (Samudra et al., 2024).

Given the complexity of this problem, this study aims to provide an overview of comorbidity risk factors that influence TB resistance, particularly at Gunung Jati Regional Hospital. This research is expected to provide both theoretical and practical benefits. Theoretically, this study enriches the literature regarding comorbidity risk factors associated with *Mycobacterium tuberculosis* resistance patterns, especially in referral hospitals such as Gunung Jati Regional Hospital. The findings of this study may serve as the basis for developing a TB resistance prediction model based on comorbidities. Practically, the results of this study may be used by healthcare workers at Gunung Jati Regional Hospital and other healthcare facilities to identify TB patients with high-risk comorbidities, thereby enabling early intervention, improving treatment adherence, and preventing drug resistance. For policymakers, this study provides empirical evidence to support the development of TB treatment programs that are better integrated with the management of comorbidities such as DM, HIV, kidney disease, and malnutrition.

METHOD

This study used an observational analytical method with a cross-sectional research design, conducted in November 2024-June 2025.The sampling technique used was total sampling on secondary data (medical records) on tuberculosis patients at Gunung Jati Regional Hospital during the January-November 2024 period with a population of 229 patients. The

research was approved and received ethical clearance at Gunung Jati Hospital with number No.025/LAIKETIK/KEPPKRSGJ/II/2025. In carrying out research ethics, researchers respect and maintain the confidentiality of medical records.

RESULTS AND DISCUSSION

Table 1. Frequency and distribution of characteristics of tuberculosis patients

Characteristics	Frequency	Percentage (%)
Gender		
Male	138	60,5
Women	90	39,5
Age		
1-5	1	4
5-6	1	4
6-10	2	9
10-19	13	5,7
19-44	107	46,9
45-59	65	28,5
≥60	39	17,1
Diabetes Mellitus		
Yes	38	16,7
No	190	83,3
Hypertension		
Yes	19	8,3
No	209	91,7
Cancer		
Yes	21	9,2
No	207	90,8
HIV		
Yes	25	11
No	208	89
Kidney Disease		
Yes	73	32
No	155	68
Other Lung Diseases		
Yes	58	25,4
No	170	74,6
Chronic Hepatitis		
Yes	59	25,9
No	169	74,6
Epilepsy		
Yes	5	2,2
No	223	97,8
Psychiatric Conditions		
Yes	58	25,4
No	170	74,6
Malnutrition		

Characteristics	Frequency	Percentage (%)
Yes	75	32,9
No	153	67,1
Diagnosis		
TB SO	195	85,5
TB MDR	33	14,5
Types of Resistance		
INH Res, RIF Res	33	14,5
SO	195	85,5

Source: Medical records data of TB patients at Gunung Jati Hospital (January-November 2024) processed by researchers, 2025

Based on table 1, the gender of tuberculosis patients was obtained as many as men with a percentage (39.5%), while for characteristics based on age, 65 patients (28.5) aged 45-59 years were obtained. The data on the results of comorbid variables showed that tuberculosis patients had the most malnutrition, namely malnutrition as many as 75 (32.9%) patients. 138 patients with a percentage (60.5%) and the fewest were women as many as 90 respondents. The results of the diagnostic characteristics data showed that most patients had MDR TB, namely 33 (14.5%) patients. The most characteristics obtained for the type of resistance were INH Resistant, RIF Resistant, which was 33 (14.5%).

Bivariate Analysis

This analysis was carried out to test the influence of the free variable on the related variable, using fisher's exact test.

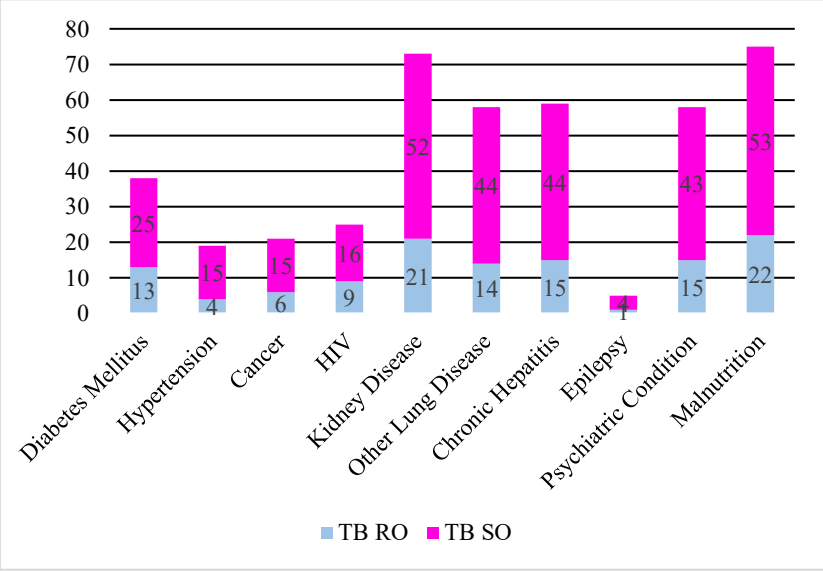

Figure 1. Frequency of comorbidities in patients with RO TB and TB SO

Source: Medical records data of TB patients at Gunung Jati Hospital (January-November 2024) processed by researchers, 2025

Bivariate Analysis and Multivariate Analysis

Table 2. Results of bivariate analysis (fisher's exact) and results of multivariate analysis (logistic regression with backward method) on comorbidity factors of patients with TB RO and TB SO

Comorbidities	Bivariate Analysis			Multivariate Analysis			
	p-value	OR	95% CI	Sig.	Exp (B)	95% C.I. for EXP (B)	
						Lower	Upper
Diabetes Mellitus	<0.001	4,42	1,95-9,98	.062	.273	.070	1.065
Hypertension	0,049	1,65	0,15-5,33	.659	.708	.152	3.284
Cancer	0,094	2,66	0,95-7,46	.115	12.388	.544	282.279
HIV	0,004	4,19	1,67-10,5	.038	.052	.003	.852
Kidney Disease	<0.001	4,81	2,21-10,4	<.001	.181	.072	.454
Other Lung Diseases	0,029	2,52	1,17-5,44	.373	3.886	.196	77.231
Chronic Hepatitis	0,009	2,86	1,33-6,13	.767	1.540	.094	25.283
Epilepsy	0,054	1,49	0,16-13,7	.993	1.013	.061	16.845
Psychiatric Conditions	0,008	2,94	1,37-6,32	.372	.186	.005	7.495
Malnutrition	<0.001	5,35	2,43-11,8	<.001	.199	.080	.493

Source: Medical records data of TB patients at Gunung Jati Hospital (January-November 2024) processed by researchers, 2025

Based on figures 1 and 2, it was obtained that the results of bivariate analysis using fisher's exact test found that there was a significant relationship between the comorbid factor diabetes mellitus p-value = <0.001 which means that there is a very significant relationship between diabetes mellitus in tuberculosis patients and *the Mycobacterium tuberculosis* resistance pattern. The results of the analysis obtained OR= 4.42 (95% CI= 1.95-9.98), meaning that tuberculosis patients with comorbid diabetes mellitus have a 4.42 chance of experiencing TB RO. Hypertension with p-value = 0.49 which means that there is an insignificant relationship between hypertension in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern*. The results of the analysis obtained OR= 1.65 (95% CI= 0.51-5.33), meaning that tuberculosis patients with comorbidities of hypertension have a 1.65 chance of experiencing TB RO.

Cancer with a p-value of 0.094 means that there is no statistically significant relationship between cancer in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern*. The results of the analysis obtained OR= 2.66 (95% CI= 0.95-7.46), meaning that tuberculosis patients with comorbidities of cancer have a 2.66 chance of developing TB RO.

HIV (p-value = 0.004 which means that there is a significant relationship between HIV in tuberculosis patients and resistance patterns *Mycobacterium tuberculosis*. The results of the

analysis obtained OR= 4.19, 95% CI= 1.67-10.53), meaning that tuberculosis patients with HIV comorbidities have a 4.19 chance of experiencing RO TB. Kidney disease with p-value = <0.001 means that there is a significant relationship between kidney disease in tuberculosis patients and resistance patterns *Mycobacterium tuberculosis.* The results of the analysis obtained an OR= 4.81 (95% CI= 2.21-10.4), meaning that tuberculosis patients with comorbid kidney disease have a 4.83 chance of experiencing RO TB.

Other lung diseases (p-value = 0.029 There was a significant association between lung disease in tuberculosis patients and resistance patterns *Mycobacterium tuberculosis*. The results of the analysis obtained OR= 2.52, 95% CI= 1.17-5.44). The results of the analysis obtained OR= 2.52 (95% CI= 1.17-5.44), meaning that tuberculosis patients with comorbidities of other lung diseases have a 2.52 chance of experiencing TB RO.

Chronic hepatitis (p-value = 0.009 which means that there is a significant relationship between chronic hepatitis in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern*. The results of the analysis obtained OR= 2.86, 95% CI= 1.33-6.13, meaning that tuberculosis patients with chronic hepatitis comorbidities have a 2.86 chance of experiencing RO TB.

Epilepsy with a p-value of 0.546 means that there is no statistically significant relationship between epilepsy in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern*. The results of the analysis obtained an OR= 1.655 (95% CI= 0.16-13.7), meaning that tuberculosis patients with comorbid epilepsy are 1.65 times more likely to experience RO TB.

Psychiatric condition p-value = 0.008 which means that there is a significant relationship between chronic hepatitis in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern*. The results of the analysis obtained OR= 2.94, 95% CI= 1.37-6.32). The results of the analysis obtained OR= 2.94 (95% CI= 1.37-6.32), meaning that tuberculosis patients with comorbid psychiatric conditions have a 2.94 chance of experiencing RO TB.

Malnutrition p-value = <0.001 which means that there is a very significant relationship between malnutrition in tuberculosis patients and *Mycobacterium tuberculosis resistance pattern.* The results of the analysis OR= 5, 35, 95% CI= 2.43-11.8 The results of the analysis obtained OR= 5.35 (95% CI= 2.43-11.8), meaning that tuberculosis patients with comorbid malnutrition have a 5.35 chance of experiencing RO TB.

Based on the results of the multivariate analysis, the results of the table logistics regression test with the backward method of table 2 were obtained a pattern *of resistance of Mycobacterium tuberculosis*, namely malnutrition with a p value of <0.001; OR = 199 and an aOR of 199 (95% CI: 0.080-0.493 which shows that it is affected by malnutrition with a significant value of <0.001 with an OR value of Exp(B) of 1.99 which means that the resistance pattern of *Mycobacterium tuberculosis* is affected by malnutrition with a risk of incidence of 1.99 times greater than that of those who are not affected by malnutrition.

Univariate Analysis

Characteristics of Tuberculosis Patients at Gunung Jati Regional Hospital

The overall sample in this study, most of the male sex was male with a total of 168 (60.5%) while the rest were female sex 90 (39.5%). Based on the distribution of age characteristics, in this study 107 years old to 44 years old (46.9%) were 107 (46.9%).

According to the data of this study, out of the total number of 228 tuberculosis patients, most of the patients had comorbid malnutrition, namely 75 (32.9%) patients. The results of *Mycobacterium tuberculosis* resistance data or those who experienced MDR TB were 33 (14.5%) patients. The results of the type of TB resistance were obtained that most of the patients experienced INH Res, RIF Res as many as 33 (14.5%) patients. The results of this study data are in line with Nikmawati's 2024 research on the description of MDR TB patients undergoing treatment at M. Natsir Hospital, showing that the majority of TB patients are men as many as 32 (51.6%) (Nikmawati, 2024). The results of the study are similar to the Samudra research in 2024 show that the majority of patients with TB are male (55.3%) (Samudra et al., 2024).

The high rate of TB-MDR in men can be caused by a combination of several factors. These factors include lifestyle, high mobility, dense physical activity, and lack of rest time. The combination of these factors is suspected to increase the likelihood of TB transmission in men. In addition, men's tendency to spend more time outside the home also increases the risk of exposure. The results of the 2022 study by Rizal are in line with the results of this study, reporting male patients (74.5%) of the TB cases studied (Rizal et al., 2021; Nikmawati, 2024). In this study, the age group of 19-44 years showed the highest prevalence of MDR-TB, with 107 patients (46.9%) of the total cases. These findings highlight that individuals of productive age face a significant risk of exposure to MDR-TB. In line with the views of the World Health Organization (WHO), the high incidence of drug-resistant pulmonary TB in developing countries is often found in productive age. This is most likely due to the high mobility of this age group, which includes frequent outdoor activities and interaction with MDR-TB patients without adequate protection such as personal protective equipment (PPE). In this age range, individuals are often at the peak of social and economic involvement. Extensive social engagement, whether in offices, campuses, public transportation, or crowded areas, significantly increases the likelihood of exposure to MTB bacteria. Closed and congested environments are the optimal means of airborne TB transmission, so anyone who is regularly in them has a greater risk of infection (Nikmawati, 2024).

This study shows that malnutrition is the most common comorbid found in tuberculosis patients, namely 75 patients (32.9%). Regarding drug resistance, as many as 33 patients (14.5%) were identified as having MDR TB. This result is similar to Nikmawati's 2024 research that the most common comorbidities are malnutrition (54.6%) with the most type of resistance, namely 59.6% of patients experiencing MDR TB (TB RO) (Nikmawati, 2024). The results of the study are in line with Samudra's research in 2024 showing that the majority of patients with TB with comorbidities are malnourished as much as (46.1%) (Samudra et al., 2024). Adequate nutrition significantly contributes to the improvement of symptoms and clinical manifestations of pulmonary TB as a whole. Conversely, poor nutritional conditions increase a person's susceptibility to pulmonary TB, and even the disease itself can worsen nutritional status due to the impact on the body's immune system. In addition, malnutrition or malnutrition weakens immunity, thus triggering drug resistance (Nikmawati, 2024). At the cellular level, malnutrition inhibits the proliferation of T cells and weakens the immunity mediated by T cells, making it susceptible to MDR TB infection (Samudra et al., 2024).

The results of this study show that the majority of cases of TB resistance are found in patients with resistance to isoniazid (INH) and rifampicin (RIF), as many as 33 (14.5%) patients from all identified resistances. The results are in line with the results of the research of

Wahidah et al. (2024) showing that the majority of the types of resistance of the two drugs, namely isoniazid and rifampicin, were obtained at dr. Soebandi as many as 28 (43.8%) patients and at Jember Lung Hospital as many as 26 (27.7%) patients, making the total total of 54 (34.2%) patients. Patient resistance to the combination of Isoniazid (H) and Rifampicin (R) drugs often occurs because these two agents are an integral part of first-line therapy for TB (Baluku et al., 2021). The high effectiveness of H and R in eradicating TB bacteria also encourages their use as monotherapy or in short therapeutic regimens, which, without close supervision, can contribute to the development of resistance (Rizal et al., 2021).

Bivariate Analysis

The relationship between diabetes mellitus in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns

The results of fisher's exact test between diabetes mellitus in tuberculosis patients and *the Mycobacterium tuberculosis* resistance pattern in this study showed statistically significant results with p-value = <0.001 This study in accordance with the results of Rehman's research in 2023 found a significant relationship with p-value<0.001, that tuberculosis patients have a high risk of developing RO TB. Tuberculosis (TB) patients with comorbidities of diabetes mellitus (DM) have a higher risk of developing drug resistance, especially resistance to first-line drugs such as INH and RIF. Tuberculosis patients with DM cause the elimination of *Mycobacterium tuberculosis* to be suboptimal, thereby increasing the possibility of selection of resistant bacteria. In addition, DM also affects the pharmacokinetics of anti-TB drugs, causing the concentration of drugs in the blood to be lower than they should be. This can prolong the infection period and increase the risk of resistance Because in addition to experiencing a decrease in immunity, TB patients with DM also experience uncontrolled blood sugar, triggering drug resistance (Luczynski et al., 2023).

The relationship between hypertension in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns

Fisher's exact test results between hypertension in tuberculosis patients and resistance patterns *Mycobacterium tuberculosis*. In this study, it showed statistically insignificant results with a p-value = 0.491. This is different from the results of Hosu's research in 2024 found a significant relationship between hypertension and RO TB resistance with a p-value of 0.022 (Hosu et al., 2024). In this study, there was no significant relationship between hypertension and RO TB because RO TB is a serious condition in which bacteria *Mycobacterium tuberculosis* have developed the ability to no longer respond to one or more major anti-TB drugs. This resistance phenomenon arises as a result of genetic mutations in bacteria triggered by selection pressures from improper treatment. The main causes of resistance include several important factors such as the patient's non-compliance with the entire treatment regimen, inadequate use of drug doses, poor drug quality, or even direct transmission from other individuals already suffering from drug-resistant TB. In other words, TB drug resistance is a problem rooted in the microbiological characteristics of bacteria and their response to therapy, not in the patient's physiological conditions or comorbidities such as hypertension (Hosu et al., 2024). Hypertension is a comorbidity condition that may exist in TB patients, but is not a direct trigger for drug resistance (Seid et al., 2023).

The Relationship of Cancer in Tuberculosis Patients and *Mycobacterium Tuberculosis* Resistance Patterns

The results of fisher's exact test between cancer in tuberculosis patients and *the Mycobacterium tuberculosis* resistance pattern in this study showed statistically insignificant results with p-value = 0.094. This study in accordance with the results of Alhayani's research in 2021 obtained an insignificant relationship with a p-value of 0.744, meaning that there was no relationship between cancer and *Mycobacterium tuberculosis* resistance pattern. According to Shulee in 2021, factors associated with tuberculosis patients accompanied by cancer are incompleteness of TB treatment (in stages III and IV) and not using first-line TB drugs. Incompleteness of TB treatment in patients with cancer comorbidities, not in the mechanism by which the cancer itself will cause TB drug resistance. However, this association is the result of disruption of the treatment regimen, not due to the effects of cancer on MTB so that it can result in resistance (Shuu Lee et al., 2021).

The Relationship of HIV in Tuberculosis Patients and *Mycobacterium Tuberculosis* Resistance Patterns

The results of fisher's exact test between HIV in tuberculosis patients and the resistance pattern of *Mycobacterium tuberculosis* in this study showed statistically significant results with p-value = 0.004. This study is in accordance with the results of Arianti's research in 2024 obtained a significant relationship with a p-value of 0.009, meaning that there is a significant relationship between HIV and *Mycobacterium tuberculosis* resistance (Arianti et al., 2024). The results of the study are in line

Laili's 2024 study found a significant association between HIV and drug-resistant TB with p-value = <0.001 with COR = 1.8 times more likely to experience treatment failure than TB without HIV (Laili et al., 2024). This study is also in line with Montes in 2021 obtained significant results between HIV and *Mycobacterium tuberculosis* resistance with p-value = <0.001. HIV patients have impaired immunity, especially in CD4+ T cells, which function against TB infection. In addition, the high rate of progressive primary infection and TB reactivation in HIV-positive populations increases the likelihood of exposure to OAT-resistant bacteria (Seid et al., 2023). Immunocompromised conditions in HIV patients make them more susceptible to difficult-to-treat TB infections. In addition, delays in diagnosis and inadequate treatment in HIV patients can worsen the likelihood of developing drug resistance (Ngouama et al., 2025).

The relationship between kidney disease in Tuberculosis Patients and *Mycobacterium tuberculosis* Resistance Patterns

The results of fisher's exact test between kidney disease in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns in this study showed very statistically significant results with p-value = <0.001. This study is in accordance with the results of Arianti's research in 2021, a statistically significant relationship was obtained with a p-value of 0.024, meaning that there is a significant relationship between CKD and drug-resistant TB (MDR TB). Chronic kidney disease (CKD) is one of the comorbidities that has a significant impact on drug-resistant tuberculosis (MDR TB). CKD causes disruption in the metabolism

and elimination of anti-TB drugs, the accumulation of drugs in the body due to impaired kidney function can increase the risk of serious side effects, often necessitating dosage adjustments or discontinuation of certain medications. This often leads to non-adherence to the planned treatment regimen and as a result, suboptimal treatment outcomes and drug resistance (Ngouama et al., 2025).

Relationship between other lung diseases in Tuberculosis Patients and *Mycobacterium tuberculosis* Resistance Patterns

The results of fisher's exact test between other lung diseases in tuberculosis patients and the resistance pattern of *Mycobacterium tuberculosis* in this study showed statistically significant results with a p-value of 0.029. This study is in accordance with the results of Ngouama's research in 2025 obtained a significant relationship with a p-value of 0.003, meaning that there is a significant relationship between other lung diseases and TB RO. [16] The results of the study are in line with the results of Rupani's research in 2024 that other lung diseases are very significantly related to RO TB with a p-value of <0.001 (Ngouama et al., 2025). TB patients with comordibites of lung disease are very likely to have difficulty adhering to a long and complex TB treatment regimen. This can lead to incomplete treatment and increase the risk of drug resistance. Decreased immunity can allow bacteria to survive and replicate, even in the presence of medications, which ultimately triggers the development of resistance (Ngouama et al., 2025; Rupani, 2024).

The relationship between chronic hepatitis in Tuberculosis Patients and *Mycobacterium tuberculosis* Resistance Patterns

The results of fisher's exact test between other chronic hepatitis in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns in this study showed statistically significant results with p-value = 0.009. This study is in accordance with the results of Wang's research in 2024 obtained a significant relationship with a p value of 0.009, meaning that there is a significant relationship between chronic hepatitis and *Mycobacterium tuberculosis* resistance. Chronic hepatitis causes prolonged inflammation of the liver, which can interfere with the functioning of the immune system and worsen the body's response to TB infection. The affected hepatobiliary system causes one of the adverse events related to OAT therapy so that it can cause drug resistance (Rehman et al., 2023). According to Zheng in 2020, severe liver damage may require drug dose adjustments, temporary discontinuation of therapy, or even replacement of drugs with less hepatotoxic ones. All of this has the potential to prolong the duration of treatment or even reduce its effectiveness. and trigger drug resistance (Rehman et al., 2023; Zheng et al., 2020).

Other Epilepsy Associations in Tuberculosis Patients and *Mycobacterium Tuberculosis* Resistance Patterns

The results of fisher's exact test between epilepsy in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns in this study showed statistically insignificant results with p-value = 0.546. This is different from the results of Hosu's 2024 study that between epilepsy and *Mycobacterium tuberculosis* resistance showed significant results with a p-value of 0.022. In this study, there was no association between epilepsy and *Mycobacterium tuberculosis* resistance because the brain functions through a complex balance between excitation signals (spurring neuron activity, especially by neurotransmitters such as glutamate) and inhibition signals (inhibiting neuronal activity, especially by GABA/gamma-aminobutyric

acid). While TB drug resistance involves *the bacterium Mycobacterium tuberculosis.* The mechanism that causes dysfunction in human neurons will not cause genetic mutations in the bacteria, and vice versa (Hosu et al., 2024).

Relationship of Other Psychiatric Conditions in Tuberculosis Patients and *Mycobacterium Tuberculosis* Resistance Patterns

The results of fisher's exact test between psychiatric conditions in tuberculosis patients and *Mycobacterium tuberculosis* resistance patterns in this study showed very statistically significant results with p-value = <0.008. This study is in accordance with the results of Laxmeshwar's research in 2022 and obtained a significant relationship with p-value = 0.014, meaning that there is a significant relationship between psychiatric conditions and *Mycobacterium tuberculosis* resistance. Comorbid psychiatric conditions cause poorer TB treatment outcomes, leading to drug resistance. The mental state of patients affects their ability to successfully undergo TB treatment, which is very complex and challenging. Adherence to this long and complicated treatment regimen is disrupted by psychiatric conditions creating opportunities for *Mycobacterium tuberculosis* bacteria to survive, indirectly facilitating the selection and proliferation of resistant bacterial strains. So that when treatment does not work, drug resistance can continue or spread (Laxmeshwar et al., 2022).

Other Associations of Malnutrition in Tuberculosis Patients and *Mycobacterium tuberculosis* Resistance Patterns

The results of fisher's exact test between malnutrition in tuberculosis patients and the resistance pattern of *Mycobacterium tuberculosis* in this study showed very significant results with p-value = <0.001. This study in accordance with the results of Magassouba's research in 2021 obtained a significant relationship with a p-value of <0.001, meaning that there is a very significant relationship between malnutrition and *Mycobacterium tuberculosis* resistance. The results of the study showed a very high prevalence of malnutrition among RO TB patients, with 85.7% of patients experiencing malnutrition. This high prevalence indicates that malnutrition is a common and serious problem in patients facing this difficult-to-treat form of RO TB. It also indicates the presence of a worsening cycle in which chronic infections and severe medication worsen nutritional status and indicate its role as a factor that significantly worsens the course of the disease and the effectiveness of treatment (Magassouba et al., 2021; Baluku et al., 2021).

Multivariate Analysis

The results of multivariate analysis using a logistic regression test with the backward method in Table 2 identified that malnutrition was the most significant comorbid with the resistance pattern of *Mycobacterium tuberculosis*. The values obtained were $p < 0.001$ with an OR of 0.199 and an aOR of 0.199 (95% CI: 0.080–0.493). The interpretation of this result is that tuberculosis patients with malnutrition have a probability of about 80.1% to experience *Mycobacterium tuberculosis* resistance compared to patients without malnutrition, even after considering the influence of other comorbidities. These findings confirm the role of nutritional status as a significant protective factor in the development of *Mycobacterium tuberculosis* resistance. Malnutrition has a close relationship with tuberculosis (TB), where poor nutritional conditions can weaken the body's immune system. Nutritional deficiencies play a role in lowering innate and adaptive immunity through mechanisms of reducing phagocytosis, antigen presentation, and complement function. As a result, the body becomes more susceptible to

Mycobacterium tuberculosis infection and has an non-optimal immune response to treatment. This condition increases the risk of therapy failure and the emergence of drug-resistant strains of *Mycobacterium tuberculosis*. Thus, malnutrition not only increases susceptibility to TB, but can also worsen the course of the disease as well as the effectiveness of treatment (Baluku et al., 2021).

CONCLUSION

Based on the results of this study, it can be concluded that malnutrition was the most common and the most influential comorbidity associated with *Mycobacterium tuberculosis* resistance patterns among tuberculosis (TB) patients at Gunung Jati Hospital. The most frequently identified resistance pattern involved a combination of isoniazid (INH) and rifampicin (RIF). Significant associations were found between TB resistance patterns and comorbidities such as diabetes mellitus, HIV, kidney disease, other pulmonary diseases, chronic hepatitis, psychiatric disorders, and malnutrition, whereas hypertension, cancer, and epilepsy showed no significant association. These findings highlight the importance of strengthening nutritional screening and management, as well as implementing multidisciplinary monitoring for TB patients with high-risk comorbidities to improve treatment adherence and reduce the risk of drug resistance. In addition, healthcare workers should provide continuous education regarding medication adherence and comorbidity management. Future research is recommended to use prospective cohort designs to further investigate the causal relationship between malnutrition and TB drug resistance, as well as to evaluate the effectiveness of nutritional supplementation interventions in reducing resistance rates among malnourished TB patients.

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