

RISK FACTORS FOR THE INCIDENCE OF DRUG-RESISTANT TUBERCULOSIS AT MARSRAM REGIONAL GENERAL HOSPITAL, SUPIORI REGENCY, PAPUA PROVINCE

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Abstract

Tuberculosis (TB) remains a serious global health challenge, with Indonesia occupying the second-highest case burden in the world. The emergence of Drug-Resistant Tuberculosis (TB-RO) further complicates countermeasures because it reduces the effectiveness of treatment and increases treatment costs. This study aims to analyze the relationship between various risk factors to the incidence of TB-RO at Masram Supiori Hospital. This study is a quantitative study with an analytical observational design using a case-control approach. The research will be carried out at Masram Supiori Hospital, Papua, in 2026 using secondary data from medical records and the Tuberculosis Information System (SITB). The total sample was 81 respondents, with a ratio of 1:2. Data analysis used *Chi-Square test* for bivariate and multiple logistic regression for multivariate analysis. The results of bivariate analysis showed a significant relationship between the incidence of TB-RO and the result of BTA sputum ($p=0.039$), nutritional status ($p=0.026$), previous treatment history ($p=0.000$), and drug side effects ($p=0.004$). Meanwhile, the variables of age, sex, occupation, and comorbidity factors showed no significant association ($p > 0.05$). The results of multivariate analysis showed that previous medical history was the most dominant factor related to the incidence of TB-RO at Masram Supiori Hospital ($p=0.000$).

Keywords: Tuberculosis, Successful Therapy, Failed Treatment

Introduction

In Indonesia, tuberculosis is still a serious public health problem. Based on the Global TB Report 2024, Indonesia occupies the second position in the world in terms of the burden of TB cases after India. There are an estimated 1,090,000 cases of TB and 125,000 deaths each year, which means there are about 14 deaths every hour. In 2024, around 885 thousand cases of tuberculosis were found, with a distribution showing that 496 thousand cases occurred in men, 359 thousand in women, and 135 thousand cases in children aged 0-14 years. These statistics confirm the urgency of increasing prevention and treatment efforts throughout Indonesia ⁽¹⁾.

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* ⁽²⁾. TB is still a major challenge in the global health sector. Globally, around 10 million people have TB, which puts TB as the 13th leading cause of death in the world and the second leading cause of death after COVID-19 ⁽³⁾.

Drug-resistant tuberculosis (TB RO) causes treatment effectiveness to decrease. Resistance occurs due to spontaneous mutations in the *M. tuberculosis* chromosome, so that the bacterial strain becomes unresponsive to first-line drugs ⁽⁴⁾. Indonesia ranks 27th in the country with the highest burden

of RO TB, with around 6,800 new cases annually; 2.8% came from new cases and 16% from retreatment cases ⁽⁵⁾.

Cases of drug-resistant tuberculosis can hinder the success of treatment. This condition demands an evaluation of the effectiveness of various treatment combinations used to treat RR/DR TB. Currently used regimens include 9-month therapy, and long-term therapy ⁽⁵⁾. The management of RR/MDR TB currently uses three main regimens, namely BPAL/M (bedaquiline, pretomanid, linezolid, and levofloxacin or moxifloxacin), 9-month therapy, and long-term therapy ⁽⁶⁾.

Indonesia is one of the countries with the highest burden of tuberculosis (TB) and Drug-Resistant Tuberculosis (TB RO) in the world. The notification of TB RR/MDR in Indonesia is 7,876 patients, with 392 pre-XDR/XDR patients. The number of notifications of this case is still far below the national estimate of 28,000 cases. In addition to the low number of RO TB notifications, Indonesia also still has challenges in the achievement of initiating treatment of RO TB patients. Of the total 12,531 patients with RO tuberculosis found in 2022, only 8,089 patients (65%) started second-line TB treatment ⁽⁶⁾.

The Papua Provincial Health Office noted that there were 215 cases of drug-resistant tuberculosis (Tb-RO) according to data from the Tb information system (SITB) from January to September 2024, so it is necessary to handle it as soon as possible. Head of the Center for AIDS, Tuberculosis, and Malaria Prevention and Control (BP2 ATM) of the Papua Health Office, Berri Wopari in Jayapura, Wednesday, said that out of 215 cases, 16 cases were cases of Tb-RO in childhood. Children who are included in Tb-RO range from 0-14 years old, therefore there needs to be more comprehensive treatment. Of these, 8 percent died in treatment ⁽⁷⁾.

Head of the Center for AIDS, Tuberculosis, and Malaria Prevention and Control (BP2 ATM) of the Papua Health Office, Berri Wopari, revealed that the overall number of TB cases in Papua until September 2024 reached 5,046 cases, this was recorded through the discovery of cases by health workers or the public who reported to health facilities. Of these, 8 percent died in treatment ⁽⁸⁾.

Masram Supiori Hospital is one of the TB-RO referral hospitals in Supiori. Based on data from the Tuberculosis Information System (SITB) of Masram Supiori Hospital, the number of suspected TB-RO patients in 2022 was recorded at 13 cases, in 2023 the number of suspected TB-RO cases was 37 cases, in 2024 the number of suspected TB-RO cases was 25 cases, 5 cases were treated, in 2025 the number of suspected TB-RO cases was 19 cases and those receiving treatment were 8 cases, and in 2026 the number of suspected TB-RO cases will be 14 cases and there will be 28 cases, then decrease in 2024 by 5 cases, in 2025 it will increase again to 8 cases ⁽⁹⁾.

By 2025, the national targets that must be achieved include 90% case detection, 100% treatment initiation, and treatment success rate above 80%. The achievement of this target is expected to significantly reduce the number of TB cases and deaths. The WHO has set a target for TB elimination by reducing its incidence to less than 1 case per 1 million population by 2050. To achieve this target, various strategies are needed, one of which is the development and adoption of better vaccines for TB prevention ⁽¹⁰⁾.

TB-RO is a heavy burden on the health care system because it is a complicit in healing efforts that hinder TB control programs and requires the cost of 6 treatments that are worth more than TB that requires treatment. TB-RO is associated with a higher rate of therapy failure and case mortality compared to TB in general ⁽¹¹⁾.

Identification of risk factors is essential as a foundation for the development of disease prevention and control strategy programs. According to Trajman et al., there are 5 (five) factors of drug resistance in TB-RO patients, namely sociodemographic factors, lifestyle factors, health factors, environmental factors and knowledge and stigma factors. Sociodemographic factors include age, gender, marital status, education level, employment status, family income history. Lifestyle factors include smoking history, number of cigarettes/day, alcohol consumption, sleep duration, travel history and type of transportation used. Health factors include previous TB treatment history, medication side effects, contact history of

TB cases, BCG vaccine status, and access to health services. Environmental factors include the history of residential areas, frequency of crossing borders, residential neighborhoods, type of house, number of rooms, frequency of visiting crowded areas ⁽¹²⁾.

Research conducted by Dafrosia Darmi Manggasa and Dewi Nurviana Suharto (2022) proves that there is a relationship between previous treatment history and the presence of comorbidities of Diabetes Mellitus and the incidence of drug-resistant tuberculosis in Poso Regency ⁽¹³⁾.

Drug-Resistant Tuberculosis (TB RO) is still a public health problem, posing major challenges for patients, health workers, communities and health care systems. The increase in RO TB cases can threaten global and national progress. In order to achieve the elimination of tuberculosis by 2030, it is appropriate for all components of the nation to better interpret the values of mutual cooperation and jointly carry out efforts to prevent and control tuberculosis ⁽⁶⁾.

Method

This study is a quantitative research with an analytical observational design using a case-control study approach. Control case design, often referred to as *case comparison*, *case compeer study*, *case referent study*, or *retrospective study*, is an observational analytical epidemiological study that examines the relationship between certain effects (diseases or health conditions) and certain risk factors ⁽¹⁴⁾.

Results

1. Univariate analysis

Table 1. Independent variable distribution

Variable	Category	Frequency (n)	Percentage (%)
Age	Productif	61	75.3
	Unproductif	20	24.7
Gender	Female	43	53.1
	Male	38	46.9
Jobs	Doesn't Work	50	61.7
	Work	31	38.3
Acid-fast Bacillus (AFB) sputum	AFB 3+	35	43.2
	AFB <3+	46	56.8
Nutritional status	BMI < 18.5	46	56.8
	BMI ≥ 18.5	35	43.2
Previous medical history	Never	49	60.5
	Once	32	39.5
Side Effect	High	48	59.3
	Low	33	40.7
Comorbidities	Yes	22	27.2
	None	59	72.8
Total		81	100

Based on table 1, it is known that of the 81 respondents, most of them are in the productive age group (15-65) years (%) and in the gender variable the highest proportion is women, which is 43 people (53.1%). The highest proportion of work variables were respondents who did not work, which was 50 people (61.7%), while the variable of the results of the BTA sputum examination, the highest proportion was respondents with AFB < 3+ sputum results, which was 46 people (56.8%), while the lowest

proportion were respondents with AFB 3+ sputum results, which was 35 people (43.2%). This suggests that most respondents have lower AFB positivity rates (<3+). In the respondents' nutritional status variables, the highest proportion was respondents with a BMI <18.5, which was 46 people (56.8%), while the lowest proportion was respondents with a BMI ≥18.5, which was 35 people (43.2%). In the previous treatment history variable, the highest proportion was respondents who had never undergone treatment before, which was 49 people (60.5%), while the lowest proportion was respondents who had undergone previous treatment, which was 32 people (39.5%). In the drug side effect variable, the highest proportion was respondents who experienced severe drug side effects, which was 48 people (59.3%), while the lowest proportion was respondents who experienced mild drug side effects, which was 33 people (40.7%). In the comorbidity factor variable, the highest proportion was respondents who did not have comorbidities, which was 59 people (72.8%), while the lowest proportion was respondents who had comorbidities, which was 22 people (27.2%).

2. Bivariate Analysis

Table 2. Risk Attribute, Chi-Square Analysis, and Prevalence Ratio

No	Variable	drug resistance				P value	OR	Lower-Upper
		Case		Control				
		n	%	n	%			
1	Age							
	Productive	18	29.5	43	70.5	0.316	0.512	0.18-1.44
	Unproductive	9	45	11	55			
2	Gender							
	Male	11	40.7	27	50	0.582	0.6	0.2-1.7
	Female	16	59.3	27	50			
4	Jobs							
	Doesn't Work	20	74.1	30	55.6	0.169	2.2	0.82-6.80
	Worker	7	25.9	24	44.4			
5	Acid-fast Bacillus (AFB) sputum							
	AFB 3+	16	59.3	19	35.2	0.068	2.6	1.03-6.92
	AFB <3+	11	40.7	35	64.8			
6	Nutritional status							
	BMI < 18.5	20	74.1	26	48.1	0.047	3.07	1.11-8.47
	BMI > 18.5	7	25.9	28	51.9			
7	Previous medical history							
	Never	22	81.5	10	18.5	0.000	19.3	5.89-63.5
	Once	5	18.5	44	81.5			
8	Side Effect							
	High	22	81.5	26	48.1	0.008	4.73	1.56-14.3
	Low	5	18.5	28	51.9			
9	Comorbidities							
	Yes	6	22.2	16	29.6	0.659	0.67	0.23-1.99
	None	21	77.8	38	70.4			

Based on table 2 above, it is known that significant variables with the incidence of drug-resistant tuberculosis are nutritional status (p value; 0.047), there is a history of previous treatment (p value;

0.000), side effects (p value ; 0.008) . Meanwhile, variables that are not significant with the incidence of drug-resistant tuberculosis are age, sex, occupation, Acid-fast Bacillus (AFB) sputum and comorbidities because the p value is > 0.05.

Multivariat

Tabel 3. Candidates for Multivariate Analysis variables

Variable	p-value	RP
Jobs	0.169	2.2
Acid-fast Bacillus (AFB) sputum	0.068	2.6
Nutritional Status	0.047	3.07
Previous medical history	0.000	19.3
Side Effect	0.008	4.73

Based on the table above, it is known that there are 5 variables that are eligible to proceed to multivariate analysis because the p value < 0.25. After multivariate analysis with logistic regression of the enter method, the results are as follows:

Table 4. Multiple Logistic Regression Variable Analysis

Variable	p-value	RP	CI 95%
			Lower-upper
Previous medical history	0.000	23.6	5.5-100.2
Side Effect	0.003	16.2	2.6-99.9

Based on the table above, it is known that the dominant variable related to drug resistance is a history of previous treatment and drug side effects, and the most dominant variable is a history of treatment with a P value of 0.000 and RP; 23.6 CI 95% (5.5-100.2) or interpreted that TB patients who have a previous history of TB treatment are 23.6 times more likely to develop drug resistance compared to those who have no treatment history.

Discussion

Based on the results of the study, it was shown that there was no significant relationship between age and the incidence of Drug-Resistant Tuberculosis (TB-RO). Descriptively, the productive age group was the largest group, 61 (75.3%), but the distribution of TB-RO cases did not show a clear pattern based on age.

The results of this study are in line with several previous studies that stated that age is not the main risk factor for drug-resistant TB. Research by Wahyuni et al. In 2020, it was found that there was no significant relationship between age and the incidence of TB-RO ($p > 0.05$), but rather the dominant factors were previous TB treatment history and adherence to therapy ⁽¹⁵⁾. In addition, research by Putra et al., in 2025 also shows that drug resistance is more influenced by treatment irregularities than by the age factor of the patient ⁽¹⁰⁾.

However, there are studies that show a tendency for TB-RO cases to be more in the productive age group (15–50 years), which is thought to be related to high mobility and social interaction in that age group, as reported by ⁽¹⁶⁾. Nonetheless, the WHO also affirms that TB-RO can occur in all age groups without biologically significant differences. Thus, the results of this study reinforce that age is not the main determinant factor in the incidence of TB-RO, but is more influenced by clinical factors and treatment behavior.

Based on the results of the study, it is known that there is no significant relationship between sex and the incidence of Drug-Resistant Tuberculosis (TB-RO). Descriptively, the number of female respondents was higher (53.1%) than the number of men (46.9%). However, the distribution of TB-RO cases shows that women have 16 cases (37.2% in their group), while men have 11 cases (28.9%). The insignificance of the relationship between sex and RO TB can be caused by other factors that are more dominant in influencing the occurrence of drug resistance, such as previous TB treatment history, medication adherence, access to health services, and the patient's immunological condition. These factors play a greater role in determining the success of TB therapy than demographic characteristics such as gender.

The results of this study are in line with the study conducted by Putri et al., which showed that there was no significant relationship between sex and the incidence of drug-resistant TB ($p > 0.05$). The study explains that both men and women have the same risk of developing TB-RO if they have an incomplete treatment history ⁽¹⁷⁾.

In addition, research by Wahyuni et al. (2020) also found that gender is not the main risk factor for TB-MDR (Multidrug Resistant Tuberculosis), but is more influenced by treatment adherence factors and previous therapy history ⁽¹⁵⁾.

However, several reports from the World Health Organization (WHO) state that globally TB cases are more commonly found in men, which is associated with behavioral factors such as smoking, exposure to the work environment, and delays in seeking treatment. Nonetheless, the WHO also affirms that TB-RO can occur in all sexes without significant biological differences. Thus, the results of this study strengthen the evidence that gender is not the main determinant factor in the incidence of TB-RO, but rather is more influenced by clinical factors and treatment behavior ⁽¹⁸⁾.

Based on the results of the study, it is known that there is no significant relationship between work and the incidence of Drug-Resistant Tuberculosis (TB-RO). Descriptively, respondents who did not work amounted to 50 people (61.7%), while those who worked amounted to 31 people (38.3%). The insignificance of this relationship can be caused by other factors that are more dominant in influencing the incidence of TB-RO, such as previous treatment history, medication adherence, socioeconomic conditions, and access to health services. Employment status alone does not necessarily reflect a person's exposure or risk to TB drug resistance.

The results of this study are in line with the research of Sari et al. (2022) which showed that employment status was not significantly related to the incidence of MDR-TB ($p > 0.05$). The study

explained that both working and non-working patients have the same risk if they do not comply with TB treatment ⁽¹⁹⁾.

In addition, research by Nurdin et al. (2020) also found that work is not the main risk factor for drug-resistant TB, but a more influential factor is incomplete treatment history and regularity of medication ⁽²⁰⁾. This shows that the treatment behavior factor has a greater role than the occupational factor.

However, theoretically, work can have an indirect effect on the incidence of TB because it is related to economic conditions, access to health services, and the work environment. The WHO also mentions that socioeconomic factors are an important determinant in the incidence of TB in general, although they are not directly specific to drug resistance.

Based on the results of the study, the Pearson Chi-Square value was obtained of 4.251 with a p-value of 0.039 (<0.05), so it can be concluded that there is a significant relationship between the results of the BTA phlegm test and the incidence of Drug-Resistant Tuberculosis (TB-RO). Descriptively, respondents with Phlegm BTA 3+ amounted to 35 people (43.2%), consisting of 16 cases of TB-RO (45.7% in the BTA 3+ group) and 19 controls (54.3).

Epidemiologically, the high BTA results reflect the high burden of *Mycobacterium tuberculosis* germs in the patient's body. This condition is often associated with delayed diagnosis, failure of previous therapy, or poor adherence to medication, which is a major factor in the occurrence of drug resistance in TB. Thus, patients with high BTA tend to have a greater risk of developing drug-resistant TB.

The results of this study are in line with the research of Kurniawati et al. (2020) which showed that patients with high BTA results have a greater risk of TB treatment failure, which can develop into drug-resistant TB. This is because the high number of bacilli indicates a more severe infection and the possibility of inadequate treatment.

Research by Zhang et al. 2022 also states that high-positive smears ($\geq 2+$ or $3+$) are associated with an increased risk of MDR-TB, especially in patients with a history of irregular medication. This suggests that a high bacterial load is an important indicator in the development of drug resistance.

In addition, the World Health Organization explains that the BTA test is used to assess the rate of TB infection, but high BTA results are often found in patients with delayed diagnosis or treatment failure, which is an important factor in the emergence of drug-resistant TB. WHO also emphasized that TB-RO is more influenced by treatment factors than only the BTA positivity rate ⁽²¹⁾.

There was a significant relationship between the results of BTA phlegm and the incidence of Drug-Resistant Tuberculosis (TB-RO). Patients with BTA 3+ have a higher proportion of TB-RO compared to BTA $<3+$, so it can be concluded that the higher the BTA outcome, the more likely it is to develop drug-resistant TB.

In the context of research conducted at Marsram Supiori Hospital, this finding is very relevant considering the geographical conditions and access to health services in the Supiori area which is still limited. Limited access to adequate diagnostic facilities, patient delays in seeking treatment, and the possibility of low therapeutic adherence due to social and economic factors may contribute to the high rate of positive BTA and the incidence of TB-RO. This shows that environmental factors and local health care systems play a role in the interaction of epidemiological triangles, especially in the host and environment components.

Thus, efforts are needed to strengthen the TB control program at Marsram Supiori Hospital, such as increasing early detection, monitoring treatment compliance, and educating the public about the importance of complete TB treatment. This intervention can reduce the incidence of drug-resistant TB in the region.

Thus, it can be concluded that there is a significant relationship between BTA sputum results and the incidence of TB-RO. Patients with BTA 3+ have a higher proportion of TB-RO compared to BTA

<3+, so the higher the BTA result, the greater the likelihood of drug-resistant TB, especially in the context of health services at Marsram Supiori Hospital.

Based on the results of the study, the Pearson Chi-Square value was obtained of 4.930 with a p-value of 0.026 (<0.05), so it can be concluded that there is a significant relationship between nutritional status and the incidence of Drug-Resistant Tuberculosis (TB-RO). These results show that nutritional status is one of the factors related to the incidence of TB-RO in the study respondents.

Descriptively, respondents with poor nutritional status (BMI <18.5) had a proportion of TB-RO incidence of 20 people (43.5%), while respondents with normal nutritional status (BMI ≥18.5) were only 7 people (20.0%). This shows that respondents with poor nutritional status have a higher tendency to experience TB-RO compared to respondents with normal nutritional status.

Biologically, nutritional status has an important role in the immune system. Malnutrition, especially lack of energy and protein, can decrease the function of the cellular immune system which plays a role in fighting *Mycobacterium tuberculosis* infection. This condition makes the body more susceptible to more severe infections, slows down the healing process, and increases the risk of treatment failure. Failure of treatment is one of the main factors that contribute to the occurrence of drug resistance in TB.

The results of this study are in line with the research of Lestari et al. (2021) which showed that there is a significant relationship between nutritional status and the incidence of MDR-TB, where patients with low BMI have a higher risk of developing drug resistance. The study states that malnutrition can worsen the course of TB disease and interfere with the effectiveness of therapy ⁽²²⁾.

Another study by **Sari et al. (2020)** also found that poor nutritional status is a risk factor for TB treatment failure, which ultimately increases the likelihood of drug-resistant TB ⁽²⁰⁾. This shows that nutritional conditions play an important role in the success of TB therapy.

Based on the World Health Organization, malnutrition is one of the main determinants of TB incidence globally. The WHO asserts that malnutrition can increase susceptibility to TB infection as well as worsen treatment outcomes, including increasing the risk of drug resistance.

There is a significant relationship between nutritional status and the incidence of Drug-Resistant Tuberculosis (TB-RO). Respondents with under-nutrition status (BMI <18.5) had a higher proportion of TB-RO incidence compared to respondents with normal nutritional status (BMI ≥18.5). This shows that nutritional status is an important factor that can influence the incidence of TB-RO through mechanisms of immunity reduction and increased risk of treatment failure.

Research conducted at Marsram Supiori Hospital, the relationship between nutritional status and the incidence of TB-RO is very relevant. The Supiori region has its own challenges, such as limited access to nutritious food, socio-economic conditions of the community, and limited affordability of health services. These factors can cause a high prevalence of malnutrition status in TB patients. In addition, poor nutritional conditions can affect patients' adherence to long-term therapy, increasing the risk of treatment failure and the emergence of drug resistance.

From an epidemiological perspective, this condition shows the strong role of host and environmental components in the occurrence of TB-RO in the region. Nutritional status as a host factor interacts with environmental conditions such as food availability and access to health services, which ultimately affects the success of TB treatment.

Thus, it can be concluded that there is a significant relationship between nutritional status and the incidence of TB-RO. Respondents with under-nutrition status (BMI <18.5) had a higher proportion of TB-RO incidence compared to respondents with normal nutritional status (BMI ≥18.5), so nutritional status is an important factor that affects the incidence of RO TB through the mechanism of lowering immunity and increasing the risk of treatment failure, especially in the context of health services at Marsram Supiori Hospital.

Based on the results of the study, the Pearson Chi-Square value was obtained of 29.858 with a p-value of 0.000 (<0.05), so it can be concluded that there is a very significant relationship between the previous treatment history and the incidence of Drug-Resistant Tuberculosis (TB-RO). These results show that previous TB treatment history is a factor that greatly affects the incidence of TB-RO.

Descriptively, respondents who had a previous history of TB showed a much higher proportion of TB-RO incidence, namely 22 out of 32 respondents (68.8%), compared to respondents who had no previous treatment history, which was only 5 out of 49 respondents (10.2%). This difference is particularly striking and suggests that previous treatment history has a strong role in the occurrence of drug resistance.

Biologically and clinically, previous TB treatment history, especially if it is inadequate, incomplete, or not up to standard, can cause *Mycobacterium tuberculosis bacteria* to survive and undergo mutations so that they become resistant to anti-tuberculosis drugs (OAT). In addition, the patient's non-compliance in undergoing therapy can also increase the risk of selection of resistant germs, which eventually develop into TB-RO.

The results of this study are in line with various previous studies that stated that TB treatment history is the main risk factor for drug-resistant TB. Research by **Pradipta et al. (2018)** showed that patients with a previous history of TB treatment had a much higher risk of developing MDR-TB than new patients. This is due to the possibility of inadequate treatment or premature discontinuation of therapy.

The research of Zhang et al., 2022 also found that previous TB treatment history was the strongest determinant of the incidence of drug-resistant TB, especially in patients who experienced therapy failure or discontinuation ⁽²³⁾.

In addition, the World Health Organization confirms that most cases of drug-resistant TB occur in patients who have previously received TB treatment. WHO states that treatment history is a major global risk factor in the incidence of TB-RO, especially in retreatment cases ⁽²¹⁾.

There was a very significant relationship between previous treatment history and the incidence of drug-resistant tuberculosis (TB-RO). Respondents who had a previous history of TB treatment had a much higher risk of developing TB-RO compared to respondents who had no treatment history. This shows that treatment history is the main determinant factor in the incidence of TB-RO.

Based on the results of the study, it was concluded that there was a significant relationship between drug side effects and the incidence of Drug-Resistant Tuberculosis (TB-RO). These results show that drug side effects are one of the factors related to the incidence of TB-RO. Descriptively, respondents who experienced severe drug side effects had the proportion of TB-RO incidence of 22 out of 48 respondents (45.8%), while in the group with mild side effects only 5 out of 33 respondents (15.2%). This shows that respondents with more severe drug side effects have a higher tendency to experience RO TB compared to respondents with mild side effects.

The results of this study are in line with the research of Fitriana et al. (2022) which showed that drug side effects are significantly related to TB treatment adherence, where severe side effects increase the risk of patients not completing therapy ⁽²⁴⁾.

The research of Tola et al. (2015) also found that drug side effects are one of the main factors influencing TB patients' non-compliance with therapy, which ultimately contributes to the occurrence of drug resistance ⁽²⁵⁾.

In addition, the World Health Organization (WHO, 2023) states that one of the main causes of drug-resistant TB is non-adherence to treatment, which is often triggered by poorly handled drug side effects. WHO emphasizes the importance of side effect management to improve the success of TB treatment ⁽²⁸⁾.

There is a significant association between drug side effects and the incidence of drug-resistant tuberculosis (TB-RO). Respondents who experienced severe drug side effects had a higher proportion

of TB-RO events compared to respondents who experienced mild side effects. This suggests that drug side effects play a role in increasing the risk of TB-RO through a mechanism of decreasing treatment adherence.

Based on the results of the study, it is known that there is no significant relationship between comorbidity factors and the incidence of Drug-Resistant Tuberculosis (TB-RO). These results show that the presence of comorbidities does not play a meaningful role in the incidence of TB-RO in the respondents of this study.

Descriptively, respondents who had comorbidities amounted to 22 people (27.2%), with 6 cases of TB-RO (27.3%). Meanwhile, respondents without comorbidities amounted to 59 people (72.8%), with 21 cases of TB-RO (35.6%). The results of this study are in line with the research of Molla et al. (2020) which showed that comorbidities did not have a significant relationship with the incidence of TB-MDR after controlling for treatment adherence factors and previous therapy history. This shows that treatment factors are more dominant than comorbidities ⁽²⁶⁾.

Research by Utomo et al. (2016) also found that although diabetes mellitus increases the risk of TB in general, it is not always directly related to the incidence of drug-resistant TB, especially if stronger medication adherence factors play a role ⁽²⁷⁾.

In addition, the World Health Organization (WHO, 2023) states that comorbidities such as HIV and diabetes do increase the risk of active TB, but are not always the main determinants of drug-resistant TB. The WHO emphasizes that the main causes of TB-RO remain related to inadequate treatment, discontinuation of medication, and previous treatment history ⁽²⁸⁾.

Comorbidity factors did not have a significant association with the incidence of drug-resistant tuberculosis (TB-RO) in this study. Although theoretically comorbidities can affect the body's immunity, in the context of drug resistance, other factors such as treatment history and therapeutic adherence are more dominant in determining the incidence of TB-RO.

The results of the multivariate analysis found that the dominant variable related to drug resistance was a history of previous treatment and drug side effects, and the most dominant variable was a treatment history with a P value of 0.000. The dominance of previous treatment history variables suggests that the main problem in TB control at Marsram Supiori Hospital may lie in the aspects of sustainability and success of treatment, such as patient adherence, regularity of therapy, and supervision of medication use. In addition, the significant influence of the nutritional status and side effects of the drug also reflects the importance of a comprehensive approach that focuses not only on pharmacological therapy, but also on nutritional support and management of side effects during treatment.

From an epidemiological perspective, these findings show that the interaction between host factors (nutritional status, adherence, response to medication) and environment (access to health services, treatment system) is more dominant in influencing the incidence of TB-RO than demographic factors alone. Therefore, advanced analysis through multivariate logistic regression is important to identify the most dominant factors, which can later be the basis for the development of more effective intervention strategies at Marsram Supiori Hospital.

Conclusion

1. Significant variables with the incidence of drug-resistant tuberculosis are nutritional status (p value; 0.047), there is a history of previous treatment (p value; 0.000), side effects (p value ; 0.008). Meanwhile, variables that are not significant with the incidence of drug-resistant tuberculosis are age, sex, occupation, Acid-fast Bacillus (AFB) sputum and comorbidities because the p value is > 0.05.
2. The dominant variable related to drug resistance is a history of previous treatment and drug side effects, and the most dominant variable is a history of treatment with a P value of 0.000 and RP; 23.6 CI 95% (5.5-100.2)

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