



REVEALING MDR RISK FACTORS AT THE JAYAPURA DISTRICT HEALTH OFFICE

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Abstract

The proportion of MDR TB in Jayapura Regency in 2022 is 2.32% and the figure is higher than MDR TB in Papua Province, which is 151 cases. Treatment of MDR TB is more complex than drug-sensitive TB. The purpose of this study was to determine the factors associated with the incidence of multidrug resistant tuberculosis (MDR TB) in patients with Pulmonary TB in the Health Office of Jayapura District, Papua Province. The type of case control study on the population of tuberculosis patients in the Jayapura Regency Health Office was 1,162 patients and samples were 27 cases and 54 controls. Data were obtained using medical record data and analyzed using chi square and logistic binary regression. The results showed that factors that were significantly associated with the incidence of MDR TB in patients with Pulmonary TB were side effects (p -value 0.000; OR = 9.1; CI95% (3.07 – 26.93), medication adherence (p -value 0.000; OR = 136; CI95% (25.45-724.06), duration of treatment (p -value 0.000; OR = 7.273; CI95% (2,546-20,773), treatment history in patients with Pulmonary TB in the Department (p -value 0.000; OR = 4.2; CI95% (8.801-21.991) and history of comorbidities (p -value 0.000; OR = 19.6; CI95% (5.79-66.34). Adherence to medication was the dominant factor in the incidence of MDR TB (p -value 0.000; OR = 36; CI95% (25,545 – 724,068). Conclusion: Adherence to taking medication is the dominant risk factor for MDR so it is recommended that in addition to PMO from Puskesmas need assistance from family. Studies have shown that TB patients who adhere to treatment are more likely to recover quickly and are no longer susceptible to other diseases than patients who do not adhere to treatment.

Keywords: Tuberculosis, Multidrug Resistant, Risk

Introduction

Tuberculosis is one of the infectious diseases that cause death. The number of people newly diagnosed with TB worldwide was reported at 7.5 million in 2022 compared to 7.1 million in 2019 and 6.4 million in 2020. India, Indonesia and the Philippines accounted for a large share ($\geq 60\%$) of the world's decline in the number of people newly diagnosed with TB in 2020 and 2021, all recovering to exceed 2019 figures in 2022. Globally in 2022, TB caused about 1.30 million deaths. This figure fell by 1.4 million in 2020 and 2021 and almost returned to 2019 figures ^[1].

At the same time, there is a dual immunity of TB germs to anti-TB drugs, causing drug resistant (RO) problems, consisting of *multidrug resistant tuberculosis* (MDR TB), *rifampicin-resistant tuberculosis* (RR TB), *rifampicin-resistant tuberculosis and extensively drug-resistant TB*. Globally, an estimated 410,000 - 450,000 suffer from multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) by 2022. The number of people diagnosed and starting treatment is much lower: 175,650 people in

2022, equivalent to about two in five of those in need and still below the pre-pandemic level of 181,533 people in 2019 [2].

Drug-resistant tuberculosis is a public health threat. Which is the main case in handling this case.[3][2]

Indonesia is one of the countries with the second highest cases of pulmonary TB in the world. In 2021, there were 360,565 tuberculosis cases with a total cure of 49.01%, complete treatment of 50.99% of people where the success of treatment reached 77.57%. Data on MDR TB patients as many as 8,268 patients. This is still far from the target of achieving the success of TB treatment in the strategic plan of the Indonesian Ministry of Health in TB control by 85%. [2]

The prevalence of pulmonary TB in Papua Province in 2020 was 2,721 (64.3%) and in 2021 it reached 2,772 (64.9%). Currently, Papua has 14 RO TB referral facilities, with the number of MDR TB patients in 2021 – July 2023 found to be 537 confirmed patients based on the results of the rapid molecular test [4].

Patient motivation, previous treatment history, medication adherence, duration of TB treatment and drug side effect status are associated with MDR TB incidence, family support, knowledge, age, and access to health facilities. Non-adherence to taking medication, history of TB treatment, inactive drug control, drug side effects and comorbidities are also risk factors for MDR TB [4] [5]

The number of TB cases in Jayapura Regency in 2021 was 654 cases and MDR TB was 19 cases and in 2022 the number of TB cases increased by 1,162 cases and MDR TB cases by 27 cases spread across Puskesmas Harapan, Sentani, Komba, Walianuw, Ebungfauw, Waibhu, Depapre, Genyem and Unurumguay [6].

Identifying the current MDR TB risk factors is very high, so it can help in prevention efforts. Based on this description, the author is interested in knowing and analyzing the "Factors Associated with the Incidence of *Multidrug Resistant* Tuberculosis (MDR TB) in the Jayapura District Health Office of Papua Province".

Method

This study is an observational study with a case control study *design*. A case-control study is an epidemiological study design that studies the relationship between exposure (risk factors) to a disease or health status by comparing a group of cases with a control group based on their exposure status. In case-control studies, effects (health status) were identified on these seats, while risk factors were identified as occurring retrospectively [7]. The research was conducted at the Jayapura District Health Office which will be carried out in November 2023.

The population in this study is all Pulmonary TB patients in January - September 2023 at the Jayapura Regency Health Office as many as 1,162 people and as many as 27 MDR TB patients. The sample size used in this study is *purposive sampling* where researchers determine sampling in a 1: 2 way, namely the proportion of cases as many as 27 and the proportion of control as many as 54 cases. Data were analyzed using chi square, odds ratio and logistic binary regression.

Result

The results of the study on the Independent variable showed that of 81 respondents, most experienced mild side effects as many as 45 people (55.6%), adherence to taking medication as many as 54 people (66.7%), duration of treatment < 6 months as many as 56 people (69.1%), history of treatment that was not at risk as many as 62 people (76.5%), no history of comorbidities as many as 58 people (71.6%) and MDR TB as many as 27 people (33.3%).

Variabel	Kejadian TB MDR				n	%	p-value	OR CI95% (L-U)
	TB MDR		Non TB MDR					
	n	%	n	%				
Side Effects	21	77,8	15	27,8	36	44,4	0,000	9,1 (3,07-26,93)
Heavy	6	22,2	39	72,2	45	55,6		
Light								
Adherence to taking medication	24	88,9	3	5,6	27	33,3	0,000	13 (25,45-724,06)
Disobedient	3	11,1	51	94,4	54	66,7		
Obedient								
Duration of Treatment	16	59,3	9	16,7	25	30,9	0,000	7,273 (2,546-20,773)
> 6 months	11	40,7	45	83,3	56	69,1		
≤ 6 months								
Total	27	100	54	100	81	100		
Treatment History	17	63	2	3,7	19	23,5	0,000	4,200 (8,801-21,991)
Risk	10	37	52	96,3	62	76,5		
No risk								
Total	27	100	54	100	81	100		
History of Comorbidities	18	66,7	5	9,3	23	28,4	0,000	19,6 (5,79-66,34)
Exist	9	33,3	49	90,7	58	71,6		
None								
Total	27	100	54	100	81	100		

The results on the relationship of side effects with the incidence of MDR TB in patients with pulmonary TB showed that in the group of MDR TB cases who experienced severe side effects as many as 21 people (77.8%) were lower in experiencing mild side effects as many as 6 people (22.2%). The results of the chi square statistical test at a meaning value of 95% ($\alpha = 0.05$) obtained a p-value of 0.000 or $p < \alpha$ (0.05), thus there is a significant side effect relationship with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province. When viewed from the value of OR = 9.1; CI95% (3.07 – 26.93) includes a number of > 1 which interprets that respondents who experience significant severe side effects with an incidence of MDR TB is 9.1 times higher than respondents who experience mild side effects.

The results of adherence to taking medication with MDR TB patients showed that in the group of MDR TB cases who were not adherent to taking medication as many as 24 people (88.9%) lower who were adherent as many as 3 people (11.1%). The results of the chi square statistical test at a meaning value of 95% ($\alpha = 0.05$) obtained a p-value of 0.000 or $p < \alpha$ (0.05), thus there is a significant relationship between medication adherence to the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province. When viewed from the value of OR = 13; CI95% (25.45-724.06) includes a number of > 1 which interprets that respondents who do not comply with taking medication are at risk with an incidence of MDR TB 13 times higher than respondents who experience non-adherence to taking medication.

The results on the duration of treatment with MDR TB events showed that in the group of MDR TB cases the duration of treatment > 6 months as many as 16 people (59.3%) was lower than the duration of treatment < 6 months as many as 11 people (40.7%). The results of the chi square statistical test at a meaning value of 95% ($\alpha = 0.05$) obtained a p-value of 0.000 or $p < \alpha$ (0.05), thus there is a significant relationship between the duration of treatment and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province. When viewed from the value of OR = 7.273; CI95% (2,546-20,773) includes a number of > 1 which is interpreted that respondents who have a long treatment of > 6 months are at risk of MDR TB incidence of 7.27 times higher than respondents who have a long treatment < 6 months.

The results on the relationship of treatment history with the incidence of MDR TB showed that in the group of MDR TB cases with a history of treatment the risk was 17 people (63%) lower the history of treatment was not at risk as many as 10 people (37%). The results of the chi square statistical test at a meaning value of 95% ($\alpha = 0.05$) obtained a p-value of 0.000 or $p < \alpha$ (0.05), thus there is a significant relationship between treatment history and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province. When viewed from the value of OR = 4,200; CI95% (8,801-21,991) includes a number of > 1 which interprets that the treatment history of TB patients at risk with MDR TB incidence is 4.2 times higher than respondents with a history of non-risk treatment.

The group of MDR TB cases with a history of comorbidities as many as 18 people (66.7%) had a lower history of comorbidities as many as 9 people (33.3%). The results of the chi square statistical test at a meaning value of 95% ($\alpha = 0.05$) obtained a p-value of 0.000 or $p < \alpha$ (0.05), thus there is a significant relationship with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province. When viewed from the value of OR = 19.6; CI95% (5.79-66.34) includes a number of > 1 which is interpreted that a history of comorbidities with TB patients is at risk with an incidence of MDR TB is 19.6 times higher than respondents with no history of comorbidities.

This study shows that the p value is 0.000; OR = 36; CI95% (25,545 – 724,068) which is interpreted that medication adherence is the dominant factor in the incidence of MDR TB in the Jayapura District Health Office.

Discussion

The results of the study obtained pulmonary TB patients suffering from MDR TB at the Jayapura Regency Health Office were women, but those who experienced MDR TB were mostly men as many as 19 people (70.4%). In line with Wahyuni's research in 2020, it found that MDR TB sufferers were more in men as much as 69.7% [4]

1. The relationship of side effects with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office, Papua Province

The results of the study obtained a group of MDR TB cases that experienced severe side effects as many as 21 people (77.8%) lower experienced mild side effects as many as 6 people (22.2%). The results of statistical tests have a significant relationship of side effects with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province, where side effects are at risk of 9.1 times the incidence of MDR TB. In line with Wahyuni's research in 2020 at the Semarang City Health Center, it was found that drug side effects were 5,333 times more likely to experience MDR TB than respondents who did not experience OAT side effects. [4]

In general, the symptoms of drug side effects found in patients are frequent headaches, feeling nauseous, feeling vomiting, and bone joint pain. Symptoms are usually due to side effects of RHZE drugs (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol). [15], [16].

Overcoming the side effects felt by patients, the action taken by health workers at the Puskesmas is to provide counseling about temporary side effects of drugs and mild side effects, so it is recommended to remain obedient to taking drugs.

2. The Relationship between Adherence to Taking Medication with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office, Papua Province

The results of the study obtained a group of MDR TB cases who were not adherent to taking medication as many as 24 people (88.9%) lower who were obedient as many as 3 people (11.1%). The

results of statistical tests obtained a significant relationship between medication adherence to the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province with an OR value interpreted that respondents who did not take medication were at risk of MDR TB by 13 times compared to respondents who were adherent to taking medication.

In line with Nurdin's research in 2020, patient adherence to taking medication is very influential on the emergence of MDR-TB. Respondents who did not comply with taking medication had a risk of MDR TB 16 times compared to respondents who regularly took medication ^[20].

Regular medication adherence behavior is also very important for tuberculosis patients. Non-compliant respondents took medication. Respondents of tuberculosis patients who did not work and did not comply with treatment because they were based on income because they had to pay transportation costs and focused on meeting daily needs rather than for treatment. Vice versa, respondents who work because they have a need to meet needs so sometimes forget to take medicine, but this is influenced by the patient's motivation factor that is lacking. Because if the motivation is high, pulmonary TB patients who already know the schedule to take the drug will take the time to come take the drug.

Barriers experienced by respondents to medication adherence can be caused by being saturated with treatment for a long time, drug side effects, or feeling better after the beginning (first 2 months) of treatment. Other causes such as economic factors and transportation barriers to health services.

3. The relationship between the length of treatment and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office, Papua Province

The results of the study in the group of MDR TB cases with a long treatment of > 6 months as many as 16 people (59.3%) were lower than the duration of treatment \leq 6 months as many as 11 people (40.7%). The results of statistical tests obtained that the significant duration of treatment with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province with an OR value was interpreted that the duration of treatment > 6 months was at risk with the incidence of MDR TB.

found that the duration of previous TB treatment > 6 months was 25,714 times the risk of MDR TB compared to respondents who had a previous TB treatment < 6 months. Treatment of TB takes longer than treating other bacterial infections. If TB treatment is not completed, drug resistance will develop ^{[4], [17] [8]}

The results of searching for medical documents for MDR TB patients at the Jayapura Regency Health Office obtained a history of treatment by administering TB drugs in accordance with the guidelines. However, the duration of treatment is more than 6 months, the stage of intensive treatment is more than 2 months because some patients delay treatment. This shows that TB treatment is inadequate, even though the Puskesmas already has operational standards for TB services, but in reality it does not work as expected. Seeking alternative treatments and delaying conventional treatment will lead to inadequate treatment and will have an impact on germ sensitivity to drugs.

4. The relationship between treatment history and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office, Papua Province

The results showed that in the group of MDR TB cases with a history of treatment risk of 25 people (59.3%) lower history of treatment not at risk as many as 2 people (7.4%). The results of statistical tests obtained a significant relationship between treatment history and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province with the results of the OR value interpreted that previous treatment history had a 4.2 times higher risk of MDR TB.

The findings in this study found that, of those who suffer from MDR-TB including relapsing patients, patients failing treatment and patients dropping out of treatment. The average distance between

TB patients and MDR-TB patients is approximately 3 years. Based on data from the analysis of patient medical records, patients who relapse before being diagnosed with MDR-TB on average patients have been declared cured in 2020 but return to coughing for 3 months in the following year. In patients who failed in treatment, it was found that, patients were not adherent in taking OAT in the first 6 months of treatment. Meanwhile, in patients with dropout status in treatment, it was found that in the treatment patients dropped out of treatment for 3 months before being diagnosed with MDR-TB.

5. The relationship between the history of comorbidities and the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office, Papua Province

The results of the study were obtained in the group of MDR TB cases with a history of comorbidities as many as 18 people (66.7%) lower the history of comorbidities as many as 9 people (33.3%). Comorbidities experienced by patients are HIV / Aids, DM and COPD. The results of statistical tests obtained a significant relationship between the history of comorbidities with the incidence of MDR TB in patients with Pulmonary TB at the Jayapura District Health Office of Papua Province with an OR value which interpreted that a history of comorbidities had a risk of 19.6 times higher than the incidence of MDR TB.

Research by Nurdin in 2020 suggested that Diabetes Mellitus (DM) is one of the risk factors for drug resistance, because TB patients with comorbid DM must be given more OAT and control blood sugar. ^[20]

Comorbidities can have adverse effects related to the progress of treatment. The likelihood of increased germ resistance and treatment failure. Special monitoring should be done regarding patients with comorbidities This can certainly reduce the body's immune function so that it becomes more susceptible to RO-TB. Along with decreased immunity, HIV-AIDS is also an important risk factor for TBRO. Individuals with Chronic Obstructive Pulmonary Disease (COPD) have a 2.79 to 4.51 times greater risk of developing RO-TB ^{[27],[9]}.

6. Dominant Factors in MDR TB Incidence

The results of the study found that adherence to taking medication was the dominant factor in the incidence of MDR TB in the Jayapura District Health Office. In line with research with Almaini and Sutriyanti in 2022 in Rejang Lebong Regency, it was found that irregular treatment behavior and delaying treatment were the dominant factors in causing the incidence of MDR TB. ^[28]

Research conducted by Aristiana in 2018 ^[21] stated that TB patients with low medication adherence had a 10.73 times greater risk of becoming MDR TB than TB patients with high medication adherence. Previous research, found that irregularity in treatment is associated with the incidence of MDR TB, can occur due to the emergence of laziness in sufferers, forgetting to take medicine, and boredom because they have to take many drugs every day ^[29].

Adherence to taking medication is one of the factors that influence the occurrence of MDR TB. TB patients who do not comply with medication will have a 6.7 times greater risk of developing MDR TB than patients who are adherent to taking medication. Rifampicin causes side effects gastrointestinal disorders, nausea, itching, decreased appetite and fever. In addition, the use of vitamin B6 can minimize the side effects of nausea, vomiting from Rifampicin. While Isoniazid causes side effects of hand cramps and tingling. Side effects of OAT can be one of the causes of irregular sufferers and cause laziness in taking drugs. Side effects of TB drugs are one of the reasons for the patient's non-compliance with taking the drug completely ^{[25], [30]}

Conclusion

Factors that are significantly associated with the incidence of MDR TB in patients with Pulmonary TB are side effects (p-value 0.000; OR = 9.1; CI95% (3.07 – 26.93), medication adherence (p-value 0.000; OR = 136; CI95% (25.45-724.06), duration of treatment (p-value 0.000; OR = 7.273; CI95% (2,546-20,773), significant treatment history with MDR TB incidence in patients with Pulmonary TB in the Department (p-value 0.000; OR = 4.2; CI95% (8.801-21.991) and history of comorbidities (p-value 0.000; OR = 19.6; CI95% (5.79-66.34). The dominant factor in the incidence of MDR TB in the Jayapura District Health Office (p-value 0,000; OR = 36; CI95% (25,545 – 724,068).

For Puskesmas, it is expected to improve health services and health education for tuberculosis patients related to handling side effects, adherence to taking medication and risk factors for previous treatment accompanied by comorbidities. Increase self-motivation by adhering to taking medication even though it has side effects but still strive for medication adherence as one of the best ways to prevent MDR TB.

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