



Risk Factors of Multidrug-resistant Tuberculosis (MDR-TB) at Serui Regional General Hospital, Kepulauan Yapen Regency, Papua Province

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Abstract

Background: Tuberculosis, often known as TB, is a disease caused by an infection with the bacteria *Mycobacterium tuberculosis*. Patients who are not obedient and do not take their medicine on a regular basis will develop drug resistance, including Multidrug-resistant Tuberculosis (MDR-TB: resistant to INH and RIF), as well as concomitant illnesses. These variables can be modified by TB patients' characteristics like as age, gender, ethnicity, education, profession, side effects, medication supervisors, and co-morbidities. **Objectives:** The goal of this study is to identify the factors influencing MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022. **Methods:** This type of research is an observational study with a case control approach. The population consisted of 52 TB patients consisting of 26 cases and 26 controls by purposive sampling. Data were obtained from medical record data, and analyzed using chi square, odds ratio and binary logistic regression. **Result:** The results showed that the factors that had a significant effect on MDR-TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 were age (p-value = 0.002; OR = 8.8(2.336-33.152), gender (p-value = 0.049, OR = 3.701(1.156-11.861), ethnicity (p-value= 0.001 ; OR = 9.450(2.621-34.073), education (p-value= 0.002; OR = 12(2.340-61.520), occupation (p-value= 0.046; OR = 3.889 (1.178-12.841), side effects (p-value= 0.021; OR = 4.9(1.413-16.988), co-morbidity (p-value= 0.003; OR = 18.33(2.147-156.583). Factors that are not influence on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 was the drug taking supervisor (p-value = 0.771; OR = 0.711 (0.226-2.241).

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The dominant factors influencing MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 were age, gender, education, occupation and co-morbidity, while education was the most dominant risk factors.

Keywords: Multidrug-resistant; Tuberculosis.

1. Introduction

Tuberculosis (TB) is an infection caused by the bacteria *Mycobacterium tuberculosis*. Bacteria that enter and accumulate in the lungs may thrive, especially in those with weakened immune systems, and will spread through blood vessels or lymph nodes. Tuberculosis may infect practically every organ in the body, including the lungs, digestive system, bones, brain, kidneys, lymph nodes, and others, although the lungs are the most usually afflicted. If it is not treated quickly, it can lead to medication resistance and death [1].

According to the World Health Organization (WHO, 2022) report in 2021, an estimated 10.6 million increased previously from 2020 as many as 9.9 million people had tuberculosis (TB). The death rate was 1.6 million (including 187,000 people living with HIV). Tuberculosis is the 13th leading cause of death and the second infectious killer after COVID-19 (behind HIV/AIDS). Thirty countries with a high burden of TB account for 87% of new TB cases. Multidrug-resistant TB (MDR-TB) will increase between 2020 and 2021 by 450,000 cases. MDR TB cases in Indonesia are ranked the 5th highest in the world with as many as 24,000 RO-TB cases [2].

Data from the Indonesian Ministry of Health (2022), in 2021 the number of tuberculosis cases found was 397,377 cases, an increase when compared to all tuberculosis cases found in 2020, namely 351,936 cases. Nationally, the number of cases in men was 57.5% and 42.5% in women, most were found in the age group 45-54 years, which was 17.5%, followed by the age group 25-34 years, which was 17.1% and 15 – 24 years 16.9%. The treatment success rate is 86% [1].

Drug-resistant tuberculosis is a condition where the TB germ (*Mycobacterium tuberculosis*) is already resistant to OAT (Anti-Tuberculosis Drugs), namely Rifampicin-Resistant Tuberculosis (RR-TB: resistant to RIF), Multidrug-resistant Tuberculosis (MDR-TB: resistant to INH and RIF) and Extensive-resistant Tuberculosis (XDR), an MDR strain that is resistant to Quinolone and one of the group A drugs (Levofloxacin/ Moxifloxacin, Bedaquiline, Linezolid) [2].

Drug-resistant TB cases in Indonesia are estimated to account for 2.4% of all new TB cases and 13% of treated TB cases. The estimated incidence of drug-resistant TB cases in Indonesia in 2019 was 24,000, but only around 9180 RR TB patients were identified in 2019, and only 49% of RR TB patients were confirmed starting second-line TB treatment. In 2019, it showed a decrease in the number of cases of drug-resistant TB in children and adults in the 1st-2nd quarter, namely 5,398 cases and increased again in 2021 to 5,632 cases of drug-resistant TB in the 1st-2nd quarter. Likewise, the number of drug-resistant TB registrations in children and adults in weeks 1-2 of 2021 is 2,618, compared to 2,637 in weeks 1-2 of 2021 [1].

A new problem related to TB is the dual immunity of germs to TB drugs (DR/MDR/XDR). MDR-TB transmission can be seen in several ways, including an inadequate control system and the services of health workers. The incidence of MDR-TB is influenced by several risk factors, including history, non-adherence to treatment, age, gender, side effects, anti-tuberculosis drugs (OAT), unsupervised, length of treatment, knowledge about MDR TB and DOTS plus, family income, endurance, and socioeconomic factors of the patient. Interrupted or inappropriate treatment with DOTS also contributes to MDR-TB cases. The management of TBMDR is more complex and requires more attention than the management of non-drug-resistant TB [3].

MDR-TB therapy side effects include the use of anti-inflammatory medications, one of which is Rifampicin, which can induce gastrointestinal side effects, nausea, itching, lack of appetite, and fever, among other things. The usage of vitamin B6 can help to minimize the nausea and vomiting caused by rifampicin. Hand cramping and tingling are adverse effects of isoniazid. OAT Adverse Effects This might be one of the reasons individuals are not taking their prescription on a regular basis. One of the causes for patient noncompliance in taking medicine till the end is the influence of anti-TB drug side effects [4].

The risk factors for causing multidrug resistant tuberculosis in Indonesia were obtained by dividing the risk factors for MDR-TB into three groups, namely respondent characteristics, history of TB and treatment, and comorbidities. Respondent characteristics that significantly influence the occurrence of MDR TB are family support, knowledge, age, and access to health facilities. Non-adherence to taking medication, history of TB treatment, inactive supervisor taking medication, medication side effects and the presence of comorbidities are also risk factors for MDR-TB. Identification of risk factors for MDR TB needs to be done properly. TB patients who have risk factors need to be given more comprehensive education and stricter supervision of taking medication to prevent the occurrence of MDR TB [5].

In 2022, secondary data from the Kepulauan Yapendi Regency Health Office revealed 622 TB cases and 26 drug-resistant or MDR TB patients (4.18%) [6].

Based on the case above, the researcher is interested in conducting research on the Factors Influencing MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

2. Methods

This is an observational study in which two separate groups in the findings are identified and compared based on many alleged causal factors. Case-control studies contrast with cohort studies, which follow both exposed and non-exposed study individuals until they provide the desired research findings. The case-control research was first examined to see if there was a statistically significant difference in the proportion of exposed patients between cases and controls. Case-control research approach, in which the investigation begins by identifying individuals with particular effects or diseases (referred to as cases) and those without effects (referred to as controls), then examines risk variables that might explain why cases are affected while controls are not. A case-control study compares a group of cases (those who have the effects or condition being examined) to a control group (those who do not have the disease) [7].

This research was conducted in November 2022, starting from research planning, research implementation, to writing research reports. The location of this research was Serui Regional General Hospital, Kepulauan Yapen Regency.

The term "population" refers to all of the study's elements/subjects [8].

In this study, the population consisted of all pulmonary tuberculosis patients at Serui Regional General Hospital, with a total of 622 cases and 26 instances of MDR TB in 2022. The sample size in this study was a 1:1 ratio of 26 MDR TB patients and 26 controls, for a total sample of 52 samples.

Data were analyzing using chi-square and binary logistic regression test with a 5% significant level.

3. Results

3.1. Effect of Age on MDR-TB

Table 1: Effect of Age on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Age	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
25 - 34 years old	16	61.5	4	15.4	20	38.5
< 25 or > 34 years old	10	38.5	22	84.6	32	61.5
TOTAL	26	100	26	100	52	100

P-value = 0.002; OR=8.8; CI 95% (2.336-33.152)

Source: Primary data, 2022

Table 1 shows that in the MDR TB case group there were 16 people (61.5%) aged 25-34 years and as many as 10 people (38.5%) aged <25 years and > 34 years.

In the control group there were 4 people (15.4%) aged 25-34 years and as many as 32 people (61.5%) aged < 25 years or > 34 years.

The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.002 or $p < \alpha$ (0.05). This means that the effect of age on MDR TB in the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant.

The results of OR = 8.8 (2.336-33.152) which are interpreted that respondents aged 25-34 years are at risk of MDR TB 8.8 times higher than respondents aged < 25 years or > 34 years.

3.2. Effect of Gender on MDR-TB

Table 2: Effect of Gender on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Gender	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Male	19	73.1	11	42.3	30	57.7
Female	7	26.9	15	57.7	22	42.3
TOTAL	26	100	26	100	52	100

P-value = 0.048; OR=3.701; CI 95% (1.156-11.861)

Source: Primary data, 2022

Table 2 shows that in the MDR TB case group there were 19 people (73.1%) men and as many as 7 people (26.9%) women. In the control group there were 11 (42.3%) men and 15 (57.7%) women. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.048 or $p < \alpha$ (0.05). This means that the effect of gender on MDR TB in Serui Hospital, Yapen Islands Regency, in 2022 is significant. The results of OR = 3.701 (1.156-11.861) are interpreted that male respondents are at risk of MDR TB 3.701 times higher than female respondents.

3.3. Effect of Ethnic on MDR-TB

Table 3: Effect of Ethnic on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Ethnic group	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Papuan	21	80.8	8	30.8	29	55.8
Non-Papuan	5	19.2	18	69.2	23	44.2
TOTAL	26	100	26	100	52	100

P-value = 0.001; OR=9.450; CI 95% (2.621-34.073)

Source: Primary data, 2022

Table 3 shows that in the MDR TB case group there were 21 people (80.8%) from the Papuan ethnic group and as many as 5 people (19.2%) from non-Papuans. In the control group, 8 people (30.8%) came from Papua and 18 people (69.2%) were non-Papuan. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.001 or $p < \alpha$ (0.05). This means that the influence of ethnicity on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant. The results of the OR value

= 9.450 (2.621-34.073) which is interpreted that respondents from Papua are at risk of developing MDR TB by 9.450 times higher than respondents from non-Papuan ethnic groups.

3.4. Effect of Education on MDR-TB

Table 4: Effect of Education on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Education	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Low	13	50.0	2	7.7	15	28.8
High	13	50.0	24	92.3	37	71.2
TOTAL	26	100	26	100	52	100

P-value = 0.002; OR=12; CI 95% (2.340-61.520)

Source: Primary data, 2022

Table 4. shows that in the MDR TB case group there were 13 people (50%) with low education and as many as 13 people (50%) with higher education. In the control group, there were 2 people (7.7%) with low education and 24 people (92.3%) with high education. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.002 or $p < \alpha$ (0.05). This means that the effect of education on MDR TB in Serui Hospital, Yapen Islands Regency in 2022 is significant. The results of the OR value = 12 (2,340-61,520) which is interpreted that respondents with low education are at risk of developing MDR TB by 12 times higher than respondents with higher education.

3.5. Effect of Occupation on MDR-TB

Table 5: Effect of Occupation on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Occupation	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Doesn't work	20	76.9	12	46.2	32	61.5
Work	6	23.1	14	53.8	20	38.5
TOTAL	26	100	26	100	52	100

P-value = 0.046; OR=3.889; CI 95% (1.178-12.841)

Source: Primary data, 2022

Table 5 shows that in the MDR TB case group there were 20 people (76.9%) not working and as many as 6 people (23.1%) working. In the control group there were 12 people (46.2%) not working and as many as 14 people (53.8%) working. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.046 or $p < \alpha$ (0.05). This means that the effect of work on MDR TB in Serui Hospital, Yapen Islands Regency in 2022 is significant. The results of the OR = 3.889 (1.178-12.841) are interpreted that respondents who do not work are at risk of developing MDR TB by 3.889 times higher than respondents who work.

3.6. Effect of Drug side effects on MDR-TB

Table 6: Effect of drug side effects on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Drug side effects	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Yes	14	53.8	5	19.2	19	36.5
No	12	46.2	21	80.8	33	63.5
TOTAL	26	100	26	100	52	100

P-value = 0.021; OR=4.9; CI 95% (1.413-16.988)

Source: Primary data, 2022

Table 6 shows that in the MDR TB case group there were 14 people (53.8%) who had side effects and as many as 12 people (46.2%) had no side effects. In the control group, 5 people (19.2%) had side effects and 21 people (80.8%) had no side effects. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.021 or $p < \alpha$ (0.05). This means that the effect of side effects on MDR TB in Serui Hospital, Yapen Islands Regency, in 2022 is significant. The results of the OR value = 4.9 (1.413-16.988) which is interpreted that respondents who have side effects are at risk of MDR TB by 4.9 times higher than respondents who have no side effects.

3.7. Effect of co-morbidity on MDR-TB

Table 7: Effect of co-morbidity on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Co-morbidity	MDR-TB				Total	%
	Cases		Controls			
	n	%	n	%		
Yes	11	42.3	1	3.8	12	23.1
No	15	57.7	25	96.2	40	76.9
TOTAL	26	100	26	100	52	100

P-value = 0.003; OR=18.33; CI 95% (2.147-156.543)

Table 7 shows that in the MDR TB case group there were 11 people (42.3%) who had co-morbidities and as many as 15 people (57.7%) had no co-morbidities. In the control group, 1 person (3.8%) had co-morbidities and 25 people (96.2%) had no co-morbidities. The results of the chi square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained a p-value of 0.003 or $p < \alpha$ (0.05). This means that the effect of co-morbidities on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant. The results of OR = 18.33 (2.147-156.583) were interpreted that respondents with co-morbidities were at risk of MDR TB 18.33 times higher than respondents who had no co-morbidities.

3.8. Effect of drug taking supervisor on MDR-TB

Table 8: Effect of drug taking supervisor (PMO) on MDR TB at the Serui Regional General Hospital, Kepulauan Yapen Regency in 2022.

Drug supervisor	taking	MDR-TB				Total	%
		Cases		Controls			
		n	%	n	%		
No		8	30.8	10	38.5	18	34.6
Yes		18	69.2	16	61.4	34	65.4
TOTAL		26	100	26	100	52	100

P-value = 0.771; OR=0.711; CI 95% (0.226-2.241)

Source: Primary data, 2022

Table 8 shows that in the MDR TB case group, there were 8 people (30.8%) there were no PMOs and as many as 18 people (69.2%) were PMOs. In the control group there were 10 people (38.5%) there were no PMOs and as many as 16 people (61.4%) were PMOs. The results of the Chi Square statistical test at a significance value of 95% ($\alpha = 0.05$) obtained P-value 0.771 or $P > \alpha$ (0.05). This means that the influence of PMO is not significant on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022. Results of the value of OR = 0.711 (0.226-2,241) which includes a value of 1, so that PMO is not a risk factor for MDR TB in TB patients.

3.9. Multivariate Analysis

Multivariate analysis is used to obtain the dominant risk factors related to the incidence MDR-TB, so it is necessary to carry out bivariate analysis and proceed to multivariate tests.

The independent variables that meet the requirements to be included in the multivariate analysis are age, gender, education, occupation, drug side effects, and co-morbidity. Backward LR method was used in the multiple logistic regression multivariate tests. The result of the analysis can be seen in Table 9.

Table 9: Analysis of Multiple Logistics Regression Variables on the incidence of MDR-TB.

Variables	B	p-value	OR	95% C. I. for Exp (B)	
				Lower	Upper
Age	4.673	0,026	107.071	1.728	6633.460
Gender	3.877	0,039	48.269	1.211	1923.861
Education	5.793	0,016	328.138	2.926	36801.069
Occupation	3.292	0,041	26.885	1.144	631.996
Drug side effects	3.422	0,052	30.620	.971	965.324
Co-morbidity	4.263	0,018	71.057	2.102	2402.549
Constant	-40.684	0,004	0,000		

Source: Primary Data, 2022

Table 9 above shows the dominant risk factors that influence the incidence of MDR-TB, namely age, gender, education, occupation, and co-morbidity, and the most dominant risk factor affecting MDR-TB was education.

4. Discussion

4.1. Effect of Age on MDR-TB

The results showed that there was an effect of age on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR value were interpreted that respondents aged 25-34 years had a risk of developing MDR TB by 8.8 times higher than respondents aged <25 years and > 34 years.

In line with Nunkaidah's research (2017) found that age is related to MDR TB. Patients of productive age generally have quite high daily activities so they sometimes forget to take medication regularly [9].

Age is a risk factor for MDR TB. The study also found that living in a household with only one room and a history of previous treatment were factors that influenced the occurrence of MDR TB. High MDR TB in the productive age ranges from 25-34 years [10].

Age of a person can affect exposure to a disease. The more mature a person's age, the more in the act of prevention of a disease. However, TB cases can attack anyone without knowing age restrictions [11].

In the MDR TB case group there were 61.5% aged 25-34 years compared to 38.5% aged < 25 years and > 34 years. it is clear that MDR-TB patients who are taking this treatment are still classified as of a high productive age, but there are also quite a number of patients who are still younger than their age group who have taken treatment 6 months before, but due to busyness and lack of follow the direction of health workers to continue taking the drug even though they feel healthy.

MDR TB patients aged 25-34 years have a higher risk of MDR TB when compared to > 25 years and > 34 years because a lot of activity can be a cause of failure in undergoing treatment and easy interaction with other people which makes it easy to contract TB and also transmit TB.

4.2. Effect of Gender on MDR-TB

The results showed that there was an effect of gender on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR = 3.701 (1.156-11.861) were interpreted as male respondents who were at risk of developing MDR TB by 3.701 times higher than respondents who female.

This is supported by research conducted by Bijawati (2018) epidemiologically the number of sufferers at risk of MDR-TB is greater in men because they have high mobility, where a lot of activity is coupled with less rest, allowing wider transmission to occur. In addition, the frequency of leaving the house for men is also higher than for women, so that men are more at risk than women [12].

According to Nugroho (2018) most male respondents are at risk of MDR TB because it is caused by workload, lack of rest, high mobilization, and unhealthy lifestyles including smoking and drinking alcohol. These behaviors can be risk factors that can reduce the body's immunity so that it is susceptible to MDR TB. In addition, there are differences in activities outside the home, especially for work and exposure to air pollution [13].

The high number of male patients at productive age allows for wider transmission. This is because the male group mostly leaves the house to earn a living at a productive age, with frequent leaving the house it is possible for transmission to occur [14].

Researchers assume that the male sex is more likely to experience MDR-TB due to the large number of activities and the large number of male interactions outside the home with high activity which results in a lack of rest which results in a decrease in one's immune system and unsupportive workplace conditions which results in patients have a risk of getting TB disease and also cause the occurrence of MDR-TB patients which occur due to being too busy at work so that they are negligent in taking medication.

4.3. Effect of Ethnic on MDR-TB

The results showed that there was an influence of ethnicity on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR value = 9.450 (2.621-34.073) which were interpreted that respondents from Papua were at risk of developing MDR TB by 9.450 times higher than respondents from non-Papuan ethnic groups. In the MDR TB case group (80.8%) came from Papuan ethnic groups and 19.2% came from non-Papuans. This is due to the poor living environment and also no self-monitoring. One of the causes of the outbreak of these diseases is the attitude of society in general who do not care about their health [15]. In addition, people's knowledge of this disease is still low and TB sufferers who come from Papua are generally disobedient to treatment until they are fully recovered [16].

4.4. Effect of Education on MDR-TB

The results of the study showed that there was an effect of education on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR value indicated that respondents with low education were at risk

of developing MDR TB 12 times higher than respondents with higher education. In the MDR TB case group, 50% had low education, and as much as 50% are highly educated. In the control group, 92.3% did not experience MDR TB and were highly educated.

Education is the process of changing the attitude and behavior of a person or group of people in an effort to mature humans through teaching and training. Education means guidance given by someone to other people in order to understand something, it cannot be denied that the higher a person's education, the easier it is for them to receive information and in the end the more knowledge they will have [17].

Research conducted by Nurdin (2020) found that those with a basic education level have a 13 times greater risk of developing TBMDR compared to those with a higher education level [18]. This is likely because low knowledge makes it difficult to obtain information to understand TBMDR services and treatment.

It is understood that MDR TB in TB patients with low educational status will experience more difficulties in receiving information provided by health workers. This will result in the cessation of the program to continue OAT treatment which should be consumed regularly [19].

Knowledge about tuberculosis and its treatment should increase along with the level of education obtained. The level of education of respondents is a determining factor in all processes of health education. In addition, these patients have a better chance to find enough knowledge about tuberculosis from various existing media.

4.5. Effect of Occupation on MDR-TB

The results of the study showed that there was an effect of education on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR value indicated that respondents with low education were at risk of developing MDR TB 12 times higher than respondents with higher education. In the MDR TB case group, 50% had low education. and as much as 50% are highly educated. In the control group, 92.3% did not experience MDR TB and were highly educated.

Education is the process of changing the attitude and behavior of a person or group of people in an effort to mature humans through teaching and training. Education means guidance given by someone to other people in order to understand something, it cannot be denied that the higher a person's education, the easier it is for them to receive information and in the end the more knowledge they will have [17].

It is understood that MDR TB in TB patients with low educational status will experience more difficulties in receiving information provided by health workers. This will result in the cessation of the program to continue OAT treatment which should be consumed regularly [19].

Knowledge about tuberculosis and its treatment should increase along with the level of education obtained. The level of education of respondents is a determining factor in all processes of health education. In addition, these patients have a better chance to find enough knowledge about tuberculosis from various existing media.

4.6. Effect of Drug side effects on MDR-TB

The results showed that there were side effects on MDR TB at Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR value were interpreted that respondents who had side effects were at risk of developing MDR TB by 4.9 times higher than respondents who had no side effects. In the group There were 14 cases of MDR TB (53.8%) who had side effects and 46.2% had no side effects.

This is in line with Widiastuti's research (2017), that the side effects of these drugs also cause patients not to want to take medication. From these several reasons, TB resistance to anti-TB drugs or MDR (Multidrug Resistant) emerges [20].

Side effects of MDR-TB treatment are side effects of using anti-inflammatory drugs, one of which is the drug Rifampicin, which can cause gastrointestinal side effects, nausea, itching, loss of appetite and fever, among others. The use of vitamin B6 can reduce the side effects of nausea and vomiting of rifampicin. Isoniazid side effects hand cramps and tingling. Side Effects of Oatmeal This may be one of the reasons patients are not regular and cause laziness to take medication. The effect of side effects of anti-TB drugs is one of the reasons for patient non-compliance in taking medication until the end [21].

TB patients who experience drug side effects are caused by the patient's body is in the process of adapting to the drug the patient is taking.

Based on the results of research by Nugroho and his colleagues 2018 most respondents (75%) experienced many side effects. All respondents stated that they felt side effects every day after taking the drug. The most common side effects experienced by respondents were nausea and vomiting. The existence of drug side effects is one of the causes of failure in the treatment of MDR TB [13].

Researchers are of the opinion that the side effects of TB drugs are one of the factors causing MDR TB because the side effects of drugs cause patients to feel uncomfortable and want to stop treatment, causing many treatment failures.

4.7. Effect of co-morbidity on MDR-TB

The results of the study showed that there was an effect of co-morbidities on MDR TB at Serui Hospital, Kepulauan Yapen Regency in 2022. The results of the OR values were obtained by respondents with a co-morbidity at risk of developing MDR TB by 18.33 times higher than respondents who had no co-morbidities. In this study, patients who had a history of co-morbidities were diabetes mellitus and HIV/AIDS.

In line with Anisah's research (2021) found that DM and HIV co-morbid factors are diseases that have an impact on MDR TB [11]. Approximately 75% of TB-RO patients have co-morbidities with drugs that are taken together. In addition, the results of a meta-analysis found that diabetes mellitus, HIV and kidney disorders were the co-morbidities that most often appeared in TB-RO patients [22].

Diabetes mellitus is a condition in which a person's blood sugar level is above normal limits (> 126 mg/dl), but the effect of diabetes on the severity of TB disease cannot be explained. However, it is certain that diabetes mellitus has a negative impact on treatment with OAT. This is proven by looking at the plasma concentration of rifampicin in TB-DM patients compared to TB patients who do not have DM [23].

The presence of HIV infection in tuberculosis sufferers can accelerate the development of tuberculosis and vice versa. In addition to weakening the immune system, HIV makes sufferers susceptible to opportunistic diseases, it is also known that OAT can directly interfere with antiretroviral treatment. Rifampicin has been shown to significantly reduce serum concentrations of protease and reverse transcriptase inhibitors found in antiretroviral drugs [24].

HIV infection has also been shown to cause malabsorption of most anti-TB drugs, especially rifampicin and ethambutol which cause treatment failure and resistance in MDRTB cases. The possibility that antiretroviral drugs can cause genetic mutations in tuberculosis bacteria that cause these bacteria to evolve into MDR-TB is not fully known [24].

According to the researchers, the research results have obtained data that co-morbidities can cause adverse effects related to progress treatment. Possibility of increased bacterial resistance and treatment failure. Special monitoring should be carried out in patients with co-morbidities.

4.8. Effect of drug taking supervisor on MDR-TB

The results of the study showed that there was no effect of PMO on MDR TB in Serui Hospital, Kepulauan Yapen Regency in 2022. The Medication Supervisor (PMO) is someone who oversees the regularity of medication or the regularity of taking medication for a tuberculosis patient. A PMO can be a health worker such as a midwife, TB control cadre at a public health center, a nurse, or can also be a close family member [25].

The Drug Swallowing Supervisor who played a role in this study was from the family (wife/husband/child/daughter-in-law/parents/relatives). Drug Swallowing Supervision is one of the success factors of the DOTS (Directly Observed Therapy Short-course) program and the success of therapy because it influences medication adherence so that sufferers are diligent and motivated to take medication. A PMO must be known, trusted and approved, both by health workers and patients, apart from that they must be respected and respected by patients, someone who lives close to the patient, is willing to help patients voluntarily and is willing to be trained and/or receive counseling [25]. The Medication Supervisor (PMO) is one of the success factors of the DOTS program and the success of therapy because it will affect the adherence of TB sufferers to taking OAT, so that sufferers are diligent and motivated to take medication. PMO is needed to determine whether the drug is actually taken or not. The role of the drug-taking supervisor in this study is not the cause of MDR-TB because the role of the medication-taking supervisor is to ensure that patients take medication regularly and provide support and motivation to accelerate healing but if they are supervised but the patient does not take the medication, this will cause the patient to experience failure to take medication so that it causes patients to develop drug resistance [10].

Researchers assume that the supervisor's role in taking medication in this study is not the cause of MDR-TB because the role of the supervisor taking medication is to ensure that patients take medication regularly and provide support and motivation to accelerate healing but if it has been supervised but the patient does not take the medication it which will cause the patient to experience failure in taking the drug so that it causes the patient to experience drug resistance

5. Conclusion

Based on the results of the discussion it can be concluded as follows:

- a. The effect of age on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value = 0.002; OR = 8.8 (2.336-33.152)).
- b. The effect of gender on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value = 0.049, OR = 3.701 (1.156-11.861)).
- c. The effect of ethnicity on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value = 0.001; OR = 9.450 (2.621-34.073)).
- d. The effect of education on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value= 0.002; OR = 12(2,340-61,520)).
- e. The effect of work on MDR TB in Serui Hospital, Yapen Islands Regency in 2022 is significant (p-value = 0.046; OR = 3.889 (1.178-12.841)).
- f. The effect of side effects on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value = 0.021; OR = 4.9 (1.413-16.988)).
- g. The effect of co-morbidities on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is significant (p-value = 0.003; OR = 18.33 (2.147-156.583)).
- h. The effect of drug taking supervisor on MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 is not significant (p-value = 0.771; OR = 0.711 (0.226-2.241)).
- i. The dominant factors influencing MDR TB in Serui Regional General Hospital, Kepulauan Yapen Regency in 2022 are age, sex, education, employment and co-morbidities, while education is the most dominant risk factors.

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