Model of Risk Factors of Multidrug-Resistant Tuberculosis (MDR-TB) in RSUD Dok II Jayapura

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Abstract

Multidrug-Resistant Tuberculosis (MDR-TB) is the biggest problem in the prevention and eradication of TB world. Indonesia is ranked eighth out of 27 countries with the highest incidence of MDR-TB in the world. MDR-TB is a disease caused by Mycobacterium tuberculosis that at least resistant to rifampicin and ionized. This study is aimed to develop model base on various risk factors of MDR-TB in RSUD Dok II Jayapura. This study was conducted in RSUD Dok II Jayapura. The method used is observational case control study design. The population of the case is resistant positive and population control is resistant negative. Data were analyzed using chi-square test and multiple logistic regression. Out of 19 variables analyzed, there were 13 variables prove as risk factors that associated to the incidence of *Multidrug-Resistant (MDR-TB)* that is (1) the family expenses (OR = 4.297; 95% CI: 1.1413 to 13.068), (2) the difficulty of transportation costs (OR = 4.000; 95% CI: 1.272 to 12.578), (3) difficulty related to the distance of residence (OR = 4.000; 95% CI: 1.272 to 12.578), (4) no fixed residence (OR = 8.636; 95% CI: 2.566 to 29.073), (5) a companion to take medication (OR = 6.000; 95% CI: 1.172 to 30.725), (6) treatment compliance (OR = 67.667; 95% CI: 7.954 to 575.677), (7) the side effects of drugs (OR = 2.500; 95% CI: 1.780 to 3.511), (8) contact history (OR = 20,000; 95% CI: 5.384 to 74.298), (9) a history of smoking (OR = 3.500; 95% CI: 1.201 to 10.196), (10) a history of drinking alcohol (OR = 10.266; 95% CI: 2.557 to 41.372), (11) the knowledge about the causes of disease (OR = 7.000; 95% CI: 1.381 to 35.478), (12) the knowledge of the consequences if not treated with complete (OR = 8.105; 95% CI: 1.612 to 40.766), (13) the knowledge of the duration of treatment (OR = 6.000; 95% CI: 1.482 to 24.299).

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And the dominant factor affecting the incidence of MDR-TB were treatment adherence (OR = 48.495; 95% CI: 3.105 to 757.515), contact history (OR = 47.540; 95% CI: 3.657 to 617.986), and no fixed residence (OR = 20.795; 95% CI: 1.589 to 272.068). In conclusion, model building in this study were Risk Factor Model based on OR, Risk Factors Model based on Subject probability, and Scoring Card Model. Risk factors of MDR-TB in RSUD Dok II Jayapura were the family expenses, difficulties in transportation costs, the difficulty of the distance residence, no fixed residence, a companion to take medication, treatment compliance, drug side effects, contact history, history of smoking, alcohol drinking history, knowledge about the causes of disease, knowledge about the consequences if not treated thoroughly, and knowledge of the long treatment of disease. It is recommended that the need for increased understanding of the dangers of disease transmission of Tuberculosis and Multidrug-resistant Tuberculosis (MDR-TB), both to patients and healthcare workers.

Keywords: Tuberculosis; Multidrug-resistant; MDR-TB; risk factors; Jayapura.

1. Introduction

Tuberculosis (TB) is a chronic infectious disease caused by the bacterium Mycobacterium tuberculosis (M. tuberculosis), but also sometimes caused by Mycobacterium bovis, Mycobacterium canettii and Mycobacterium africanum [1,2]. All tissues in the body can be infected by M. tuberculosis except for hair, teeth, and nails but most commonly affects the lungs (David, 2004). In 2014, it is estimated there are about 9.6 million new cases of pulmonary tuberculosis (5.4 million men, 3.2 million women and 1 million children), but only about 6 million were reported to the World Health Organization. There are an estimated 1.5 million deaths from TB, 0.4 million were due to co-infection of HIV-positive [2]. TB is preventable and curable, therefore early detection and effective treatment is necessary to break the chain of transmission [1,3]. Although anti-TB drugs have been available for the past 50 years, TB remains a major cause of death worldwide [4]. Poor health systems, HIV / AIDS pandemic and the emergence of M. tuberculosis strains that are resistant to conventional drugs used in the treatment of TB threaten global TB control [3,4].

An estimated 32% of the world's population is infected with M. tuberculosis [5]. M. tuberculosis infection is a condition where a person carries mycobacterium in a small amount of inactivity because endurance is good, only about 10% of people infected with TB will become sick with signs and symptoms of active TB in the course of his life. Each case of TB is a risk factor for TB disease if not treated appropriately, any cases of active TB infects 10 to 15 people every year. People with HIV / AIDS have a higher risk to have active TB disease due to damage to the immune system [6]. Indonesia now is in the rank of the two countries with the highest TB burden in the world, after India. Estimates of the prevalence of TB cases amounted to 1,600,000 cases and incidence estimates totaled 1,000,000 new cases per year. The number of TB deaths estimated 100,000 deaths per year [2]. In 2014 found the number of new cases BTA + as many as 176 677 cases, declined compared BTA + new cases were discovered in 2013 that amounted to 196 310 cases. The highest number of cases were reported in provinces with large populations, namely West Java, East Java and Central Java. BTA + new cases in three provinces for 40% of the total number of new cases in Indonesia. Based on gender, BTA + cases in men is higher than women are 1.5 times compared to the case of BTA + in women. In each province throughout Indonesia case BTA + is more common in men than women. Highest Disparities between men and women

occurs in Bangka Belitung island, cases in men is almost double that of the cases in women. By age group, most new cases are found in the age group of 25- 34 years in the amount of 20.76%, followed by the age group of 45-54 years amounted to 19.57% and in the age group 35-44 years amounted to 19.24% [7].

In the province of Papua, since the enactment of Dok II Jayapura Hospital Referral Hospital as MDR-TB, there have been an increasing number of cases of MDR-TB. In 2013, of suspected MDR-TB by 51 people checked there were 10 people (19.61%) positive MDR-TB. In 2014, 150 people were examined suspect there were 20 (13.33) the positive MDR-TB. In 2015, out of 178 people examined suspect that there are 18 people (10,11%) were positive MDR-TB. And by 2016, from 143 examined suspect there are 12 people (8.39%) were positive MDR-TB [8]. Regional General Hospital (Hospital) Dok II Jayapura is the only Referral Hospital MDR-TB in the region of Papua and West Papua since 2013. There have been many MDR-TB suspect patients referred and treated at the hospital with good results, Therefore it will be in doing research related to factors that affect the incidence of MDR-TB in hospitals Dok II Jayapura.

2. Materials and Methods

2.1 Types of Research

The study design is a study design that consists of elements that are attached to each other and bind together to obtain the data in answering research questions [9]. This type of research used in this study was observational analytic with case control design, where the risk factors studied using retrospective approach. Case is characteristic of subjects with a positive effect, while the control is subject to the characteristics of the negative effects. A case-control study is the type of research design that is widely used, often in epidemiology. This is the kind of observational study in which two groups were no different in the results were identified and compared on the basis of some attribute causal. Case-control studies are often used to identify the factors that can lead to a medical condition by comparing subjects who have the condition / disease (the 'cases') with patients who did not have the condition / disease but is otherwise similar ('controls'). In this study, the cases are patients with MDR-TB who have tested positive based on test results of resistance and susceptibility test listed in Poli MDR-TB RSUD Dok II Jayapura, while controls were patients not people with MDR-TB that is also based on the results of resistance tests and the susceptibility test lung registered MDR-TB Hospital Poly Dok II Jayapura.

The risk factors that will be influence by the incidence of MDR-TB are gender, age, ethnicity, education, household expenditures, knowledge of (the causes, modes of transmission, consequences if not treated thoroughly, and duration of treatment) nutritional status, smoking habits, habits drinking alcoholic beverages, treatment compliance, the difficulty of transportation costs, the difficulty of the distance of residence, move to move residence, history of DM disease, companion to take medicine, history of contact with people with TB / MDR-TB.

The samples in this study were divided into two parts, namely samples for cases and samples for control. For a sample of the "case" will be taken throughout the MDR-TB patients were enrolled on the register MDR-TB patients in the MDR-TB Hospital Poly Dok II Jayapura, as many as 30 people. Next to the "control" will be

drawn at random sampling of TB patients other than MDR-TB by comparing cases and controls was 1: 1 and in the absence of matching as many as 30 people.

as the criteria for inclusion and exclusion of subjects. All of the selected sample included in this study except that reject or do not sign the informed consent.

2.2 Ethical research and data collection

Each respondent was asked to sign a consent Informed consent. Primary data was collected by conducting interviews directly to the sample using interview guideline (questionnaire).

Secondary data was collected in Poly MDR-TB Hospital Dok II Jayapura and Papua Provincial Health Office. Data processing was performed using a computer with the help of program packages and SPSS Epidata

3. Results and Discussion

3.1 Univariate Analysis

Univariate analysis is an analysis of each variable to describe the results of the research. This analysis only displays the frequency and percentage of each variable. Results of univariate analysis of variables as follows:

a. Characteristics of Respondents base on sex

Respondents in this study of 60 people consisting of 30 cases and 30 controls. Characteristics of respondents by sex can be seen in Table 4.1:

Table 1: Distribution of Cases and Controls Respondents by Gender in hospitals Dok II Jayapura 2016

Sex	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Male	15	50,0	17	56,7	32	53,3
Female	15	50,0	13	43,3	28	46,7
Total	30	100	30	100	60	100

Table 1 shows that out of 30 patients with MDR-TB, sex men and women are comparable, respectively as many as 15 people (50%). Meanwhile, of the 30 patients with non-MDR-TB, the largest gender is male as many as 17 people (56.7%) and women were 13 (43.3%).

b. Characteristics of Respondents by Ethnicity

Table 4.2 shows that out of 30 patients with MDR-TB, the highest rate was Papua as many as 23 people (76.7%), and Non Papua 7 people (23.3%). Meanwhile, of the 30 patients with non-MDR-TB, the highest rate was Papua as many as 17 people (56.7%) and non-Papuan many as 13 people (43.3%).

Table 2: Distribution of respondents Cases and Controls According to Tribe in hospitals Dok II Jayapura 2016

Tribe	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Papua	23	76,7	17	56,7	40	66,7
Non Papua	7	23,3	13	43,3	20	33,3
Total	30	100	30	100	60	100

c. Characteristics of Respondents by Age Group

Characteristics of respondents by age group are shown in Table 3.

Table 3: Distribution of respondents Cases and Controls According to Age Group in hospitals Dok II Jayapura 2016

Age	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
19 – 49 year	25	83,3	23	76,7	48	80,0
> 49 year	5	16,7	7	23,3	12	20,0
Total	30	100	30	100	60	100

Table 3. shows that out of 30 patients with MDR-TB, the largest age group is aged 19-49 years as many as 25 people (83.3%), and the age group> 49 years as many as five people (16.7%).

Meanwhile, of the 30 patients with non-MDR-TB, the largest age group is aged 19-49 years as many as 23 people (76.7%) and the age group> 49 years of 7 people (23.3%).

d. Characteristics of Respondents by Education Level

Characteristics of respondents by level of education can be seen in Table 4.4:

Table 4: Distribution of respondents Cases and Controls According to Education in RSUD Dok II Jayapura 2016

Education level	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	N	%
Non school	3	10,0	0	0,0	3	5,0
Basic school	3	10,0	4	13,3	7	11,0
Junior H. School	0	0,0	0	0,0	0	0,0
Senior H. School	12	40,0	11	36,7	23	38,3
Higher education	12	40,0	15	50,0	27	45,0
Total	30	100	30	100	60	100

Table 4 shows that of the 30 patients with MDR-TB, education level was graduated from high school and Graduated PT respectively 12 people (40.0%), and the lowest is the End SMP 0 votes (0.0%). Meanwhile, of the 30 patients with non-MDR-TB, education level is Graduated PT as many as 15 people (50.0%) and the lowest is Not The End school and SMP respectively 0 votes (0.0%).

e. Characteristics of Respondents base on Jobs

Table 5 shows that out of 30 patients with MDR-TB, most jobs are Private many as 11 people (36.7%) and the lowest is a farmer as much as 1 (3.3%). Meanwhile, of the 30 patients with non-MDR-TB, most jobs are civil / military / Plori many as 17 people (56.7%) and the lowest is as much Labour 2 (6.7%).

Table 5: Distribution of respondents Cases and Controls According to Work in hospitals Dok II Jayapura 2016

Occupation	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Not work	8	26,7	5	16,7	13	21,7
Private	11	36,7	3	10,0	14	23,3
PNS/TNI/Polri	8	26,7	17	56,7	25	41,7
Labor	2	6,7	2	6,7	4	6,7
Farmer	1	3,3	3	10,0	4	6,7
Total	30	100	30	100	60	100

f. Characteristics of Respondents by Marital Status

Characteristics of respondents by marital status can be seen in Table.6:

Table 6: Distribution of respondents Cases and Controls According to Marital Status in hospitals Dok II Jayapura 2016

Marital status	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Marriage	7	23,3	12	40,0	19	31,7
Single	11	36,7	11	36,7	22	36,7
Widow	8	26,7	5	16,7	13	21,7
Widower	4	13,3	2	6,7	6	10,0
Total	30	100	30	100	60	100

Table 6 shows that out of 30 patients with MDR-TB, most marital status is Single as many as 11 people (36.7%) and the lowest is the widower of 4 people (13.3%).

Meanwhile, of the 30 patients with non-MDR-TB, most marital status is Married as many as 11 people (40.0%) and the lowest is as much Duda 2 (6.7%).

g. Characteristics of Respondents by Home Reference

Characteristics of respondents by reference source can be seen in Table 7:

Table 7: Distribution of respondents Cases and Controls According to the Home Referral Hospital in Dok II Jayapura 2016

Reference source	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Health centre	21	70,0	16	53,3	37	61,7
Government hospital	3	10,0	6	20,0	9	15,0
Private hospital	3	10,0	7	23,3	10	16,7
Others	3	10,0	1	3,3	4	6,7
Total	30	100	30	100	60	100

Table 7 shows that out of 30 patients with MDR-TB, the largest referral source is Puskesmas many as 21 people (70.0%) and the lowest is the RS Government, Private Hospitals and Medical Practitioners respectively of three people (10.0%). Meanwhile, of the 30 patients with non-MDR-TB, the largest referral source is Puskesmas with 16 people (53.3%) and the lowest is the Physician Practice as much as 1 (3.3%).

3.2 Bivariat Analysis

The bivariate analysis describes the results of research on the relationship between the independent variables, namely gender, ethnicity, age, education level, family expenditure per month, the difficulty of transportation costs, the difficulty of the distance residence, place of residence is not fixed, a companion to take medication, treatment compliance, securities drug side, a history of contact with people with TB / MDR-TB, history of diabetes, smoking history, history of drinking alcoholic beverages, knowledge about the causes of TB / MDR-TB, knowledge about the modes of transmission of TB / MDR-TB, knowledge about the consequences if not treated with complete TB / MDR-TB, knowledge about the duration of treatment of TB / MDR-TB with MDR-TB incidence in RSUD Dok II Jayapura. To determine the relationship of the dependent and independent variables used chi-square test. The bivariate analysis done by the cross table (crosstab) two times two. The results of the bivariate analysis of research on factors related to the incidence of MDR-TB in hospitals DOK II Jayapura in 2016 are presented in the table - the table as follows:

1. Relationship Sex with MDR-TB incidence

Table 8 shows that out of 30 patients with MDR-TB, 15 (50%) sex male and 15 (50%) were female. Meanwhile, of the 30 patients with non-MDR-TB, 17 (56.7%) male sex and 13 people (43.3%) women. This shows that in the case group, the proportion of men and women equally, whereas in the control group, the proportion of men is more compared with women.

Table 8: Gender relations with MDR-TB incidence in hospitals Jayapura 2016

Sex	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Male	15	50,0	17	56,7	32	53,3
Female	15	50,0	13	43,3	28	46,7
Total	30	100	30	100	60	100
P-value = 0,796; OR = 0,765; 95%CI (0,277 – 2,144)						

Statistical test results obtained by OR of 0.765 and 95% CI (0.277 to 2.144) shows that gender is a protective factor to the incidence of MDR-TB. Therefore, the value OR 95% CI includes the value 1, then gender is not a significant protective factors with the incidence of MDR-TB in hospitals Dok II Jayapura.

2. Relations with the tribe incidence of MDR-TB

Table 9 shows that out of 30 patients with MDR-TB, 23 (76.7%) rate Papua and 7 (23.3%) Non-Papuan tribes. Meanwhile, of the 30 patients with non-MDR-TB, 17 (56.7%) Papua tribe and 13 patients (43.3%) Non-Papuan tribes. This shows that in the case group, the proportion of Papuan tribe more than the non-Papuan tribes, and in the control group, the proportion of Papuan tribe also much more compared with non-Papuan tribes.

Table 9: Tribe relationship with MDR-TB incidence in hospitals Jayapura 2016

Tribe	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
Papua	23	76,7	17	56,7	40	66,7
Non-Papua	7	23,3	13	43,3	20	33,3
Total	30	100	30	100	60	100
P-value = 0,171; OR = 2,513; 95%CI (0,826 – 7,642)						

Statistical test results obtained by OR of 2.513 and 95% CI (0.826 to 7.642) indicates that the rate is a risk factor to the incidence of MDR-TB. Therefore, the value OR 95% CI includes the value 1, then the rate is not significant risk factors with the incidence of MDR-TB in hospitals Dok II Jayapura

3. Relationship Age with MDR-TB incidence

Based on testing the relationship of age with the incidence of MDR-TB, the result as in Table 10 below:

Table 10: Age Relationship with MDR-TB incidence in hospitals Jayapura 2016

Age	MDR-TB Occurrence				Number	
	casus		control			
	n	%	n	%	n	%
19 – 49 year	25	83,3	23	76,7	48	80,0
> 49 year	5	16,7	7	23,3	12	20,0
Total	30	100	30	100	60	100
P-value = 0,747; OR = 1,522; 95%CI (0,423 – 5,472)						

3.3 Multivariate Analysis

The results of the bivariate analyzes that have a probability value p≤0,25 continued its analysis by using statistical analysis multivariate logistic regression with LR Forward Stepwise method. All variables are risk factors incorporated into the process of interaction, the next most related variables included in the model one by one to obtain the estimated variables that play an important role in the incidence of MDR-TB in hospitals DOK II Jayapura.

a. Selection of Variable Multivariate

Multivariate analysis used in this research is the multiple logistic regression analysis is a mathematical model used to study the relationship between one or more independent variables with the dependent variable is dichotomous (Dahlan, 2012). This analysis is intended to determine the risk factors most associated with the incidence of MDR-TB in hospitals DOK II Jayapura.

Table 11: The results of the analysis as models multivariate analysis

No	Variabel	Categories	p-value	Conclusion
1	Sex	1. male	0,796	Not significant
		0. female		
2	Tribe	1. Papua	0,171	Not significant
		0. Non Papua		
3	Age	1. 19 – 49 year	0,747	Not significant
		0. > 49 year		
4	Education level	1. low (< graduate SMA)	0,729	Not significant
		0. high (≥ graduate SMA)		
5	Family expenditure	1. low (< UMP)	0,018	Significant
		0. high (≥ UMP)		

4. Conclusion

Based on the results of data analysis and hypothesis testing, it can be concluded as follows:

1. The socio-demographic factors associated with the incidence of MDR-TB in hospitals Dok II Jayapura is a family spending per month (p-value = 0.018; OR = 4.297). While unrelated factors are gender (p-value = 0.796 <0.05), ethnicity (p-value = 0.171), age (p-value = 0.747), and education level (p-value =

0.729).

2. Factors knowledge related to the occurrence of MDR-TB in hospitals Dok II Jayapura is knowledge about the causes of TB / MDR-TB (p-value = 0.024; OR = 7.000), knowledge about the consequences if not treated with due TB / MDR -TB (p-value = 0.012; OR = 8.105), and knowledge of the long treatment of TB / MDR-TB (p-value = 0.017; OR = 6.000). While the factors that are not related are the knowledge about modes of transmission of TB / MDR-TB (p-value = 0.267> 0.05).

3. Behavioral factors associated with the occurrence of MDR-TB in hospitals Dok II Jayapura is a history of smoking (p-value = 0.036; OR = 3.500), history of drinking alcoholic beverages (p-value = 0.001; OR = 10.286), treatment compliance (p-value <0.001; OR = 67.667), the difficulty of transportation costs (p-value = 0.030; OR = 4.000), the difficulty of the distance of residence (p-value = 0.030; OR = 4.000), often change residence (p Value-= 0.001; OR = 8.636).

4. Clinical factors associated with the incidence of MDR-TB in hospitals Dok II Jayapura is a companion to take medication (p-value = 0.045; OR = 6.000), side effects of medications (p-value = 0.002; OR = 2.500), history of contact with TB patients (p-value <0.001; OR = 20,000). While the factors that are not related is a history of diabetes (p-value = 1.000> 0.05).

5. The dominant factor of socio-demographic factors, knowledge, behavior and clinical jointly associated with the incidence of MDR-TB in hospitals Dok II Jayapura was successively a history of contact with TB patients (p-value = 0.003; OR = 47 , 54), medication adherence (p-value = 0.006; OR = 48.495), and place of residence do not settle (p-value = 0.021; OR = 20.795).

6. The best model is based on socio-demographic factors, knowledge, behavior and clinical together to predict the incidence of MDR-TB in hospitals Dok II Jayapura is based OR Model Risk Factors, Risk Factors Model based Probability Subject, and Model Scoring Card.

5. Suggestions

1. The need for increased understanding of the danger of infection of Tuberculosis and Multidrug Resistant Tuberculosis (MDR-TB) and losses, to prevent the emergence of drug resistance is higher in hospitals DOK II Jayapura.

2. The need for a policy on the increase in TB officers equipped with knowledge as a counselor for TB, especially MDR-TB could help patients understand illness and the consequences if it does not complete the treatment completely in hospitals Dok II Jayapura.

3. It needs continuous dissemination to all personnel handling the TB disease both in health centers, hospitals, clinics, doctors, and NGOs so if treating patients with symptoms of suspected MDR-TB to immediately refer to the MDR-TB Hospital Poly Dok II Jayapura for an immediate inspection of drug resistance.

4. The need for further research into the potential of Genesis Related Infections Health Service that is associated with the handling of MDR-TB patients in hospitals Dok II Jayapura.

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