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Risk Factors Affecting Multi-Drug Resistant Tuberculosis in Surakarta and Ngawi, Indonesia

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ABSTRACT

Background: The success rate of Tuberculosis treatment in Indonesia decreased by 81.3% in 2014, which below the 85% target. The current increasing problem in the developing world is multidrug resistance of Tuberculosis (MDR-TB). Many factors may contribute to MDR-TB. At the individual level these factors may include adherence to medication, perception of vulnerability, seriousness, benefit, barrier, and nutritional status. At the institutional level these factors may include the availability of drugs and implementation of DOTS program. This study aimed to analyze factors that affect MDR-TB in Surakarta and Ngawi, Indonesia.
Subjects and Method: This was an observasional analytic study with case control design. It was carried out in August-October 2016 in Surakarta and Ngawi, Indonesia. A total of 120 patients were selected by fixed disease sampling. Another sample of 44 health workers was also selected for the study. The endogenous variables: adherence, nutritional status, and implementation of the treatment of DOTS. The exogenous variables: perception of vulnerability, seriousness, benefits, barriers, the availability of anti Tuberculosis drugs. The data was collected by questionnaire and analyzed by path analysis.
Results: Nutritional status (b=-2.98; 95% CI=-5.31 to -0.64; p=0.012), adherence to anti Tuberculosis drugs (b=-3.38; 95% CI =-5.94 to -0.82; p=0.010), treatment with DOTS for MDR TB (b=-0.88; 95% CI=1.43 to 3.18; p=0.456) were associated with MDR-TB. Perceived vulnerability (b= 2.81; 95% CI= 0.99 to 4.64; p=0.003), seriousness (b=4.47; 95% CI= 2.38 to 6.57; p 0.001), benefits (b= 3.4; 95% CI=1.52 to 5.18; p=0.001), barriers (b =-1.81; 95% CI=-3.48 to -1.39; p=0.034), as well as availability of DOTS treatment (b = 3.14; 95% CI= 0.95 to 5.32; p=0.002), were associated with adherence to treatment.
Conclusion: Nutritional status, adherence to treatment, implementation of DOTS strategy for MDR-TB affect the risk of MDR TB. Perceived vulnerability, seriousness, benefit, and barrier, as well as availability of DOTS treatment, affect adherence to treatment. Partnership between patients and health care personnel is recommended to increase the success of TB treatment.

Keywords: tuberculosis, risk factor, MDR-TB, adherence to treatment

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BACKGROUND

Pulmonary tuberculosis (TB) is still one of the world's health problems although control efforts with the Direct Observed Treatment Shortcourse (DOTS) strategy have been applied in many countries since 1995 (Erah and Ojieabu, 2009). In 2012, pulmonary tuberculosis cases in the world were 8.6 million (Kemenkes RI, 2015). Based on World Health Organization (WHO) data in 2013 there were 9 million people of the world have been infected with

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TB germs (WHO, 2014). While in 2014 increased to 9.6 million (WHO, 2015).

One effort to control TB is by treatment. Indonesia experienced a decrease in treatment success rate in 2014 compared to the previous 6 years. In 2014, success rate was 81.3%. WHO set the standard of treatment success rate of 85%. Thus, in 2014 Indonesia did not reach those standards (Ministry of Health RI, 2015).

Pulmonary TB drugs should be taken by the patient routinely for six consecutive months without stopping. If the treatment is discontinued for up to six months, the patient will recur at any time and the bacterium *Mycobacterium tuberculosis* is resistant again and therefore it will cost a great deal of money (Faustini et al., 2006). In addition, a low nutritional status factor in most TB patients will slow the healing process and reduce the body's immunity that result in increasing the risk of bacteria becoming more dangerous or resistant (Budiyanto, 2014). The bacteria resistant to treatment is known as Multi Drug Resistant (MDR).

The prevalence of MDR TB cases in 2010 was 290,000 cases. While Indonesia is on 9 level with the number of cases 6,100 (Ministry of Health RI, 2011). In 2013 WHO estimates that in Indonesia there are 6,800 new TB cases with MDR TB in each year. An estimated 2% of new TB cases and 12% of cases of TB treatment are MDR TB cases (Kemenkes RI, 2015).

Factors affecting MDR rates are the availability of sufficient and qualified OAT or the OAT availability used for TB therapy (Sihombing, 2012). In addition, factors contributing to drug resistance in developing countries include the patient's ignorance of his illness, poor adherence, inadequate monotherapy or drug regimens, inadequate doses, poor instructions, poor treatment regimens, less patient motivations, drug supply irregularity, drug availability and drug quality contribute to secondary drug resistance (Masniari et al., 2007).

One of the models developed to look at the factors that influence a person's actions to seek a healthy lifestyle is the Health Belief Model (HBM) (Safri et al., 2014). Judging from HBM theory, individual health behavior is influenced the perception of susceptibility to a disease, perception to seriousness caused by disease, gain to conduct suggested health behavior and amount of obstacles encountered.

In 2010, MDR TB treatment program was started in Dr. Moewardi, Surakarta. Based on preliminary study conducted by studyers, MDR TB case in dr. Moewardi Surakarta has increased. In 2013 there were 40 cases and in 2016 there were 100 cases. OAT-resistant TB is essentially a result of inadequate TB patient's treatment leading to transmission to MDR TB patients to the community. The purpose of this study is to know the factors that influence MDR TB.

SUBJECTS AND METHOD

This study is a quantitative study using observational analytic design with case control approach. The population in this study wasTB and MDR TB patients in Surakarta and Ngawi. The number of study subjects was 164 subjects. The number of study subjects for patients was 120 subjects, while the number of study subjects for health workers was 44 subjects with fixed disease sampling sample techniques.

Endogenous variables included medication adherence, implementation of DOTS treatment, MDR TB. Exogenous variables included perceptions of vulnerability, perceptions of seriousness, perception of benefits, perception of barriers, availability

of OAT and nutritional status. Drug compliance was the patient's willingness to obey the rules of medical treatment routine and complete. The perception of vulnerability was a positive or negative assessment of the risk of experiencing MDR TB. The perception of seriousness was the individual's subjective perception of how severe the physical and social consequences of the illness were. Perceiving benefit was the patient's perceived belief in the benefits of treatment to reduce the risk of MDR TB. Perception of barriers was a belief that was a constraint or hindrance of patients to undergo treatment. The implementation of DOTS treatment was a strategy implemented in basic health services to detect and cure TB patients. Nutritional status was the assessment of the patient's nutritional status based on anthropometric assessment. All variables used a dichotomy scale. Data collection techniques used questionnaires. Data analysis used path analysis.

RESULT

1. Characteristics of Study Subjects

Characteristics of study subjects can be seen in Table 1.

Table 1.The Distribution of MDR TB study subjects

Characteristic	Case		Control	
	n	%	n	%
Gender				
Man	37	61.7	33	55.0
Woman	23	38.3	27	45.0
Age				
< 35 years old	31	51.7	23	38.3
≥ 35 years old	29	48.3	37	61.7
Last Education				
Low/Basic (Elementary,Junior)	30	50.0	31	51.7
High/Continuity (Senior, academic,university)	30	50.0	29	49.3
Family Income (Rp)				
< 1,500,000/month	53	88.3	45	75.0
≥1,500,000/month	7	11.7	15	25.0
Smoking Habit				
Smoking	15	25.0	20	33.3
Not Smoking	45	75.0	40	66.7
Alcohol Drinking Habit				
Drinking	5	8.30	3	5.00
Not Drinking	55	91.7	57	95.0
History of contact with TB patients				
Ever	20	33.3	17	28.3
Never	40	66.7	43	71.7
Long Suffering from TB				
<a year	17	28.3	44	73.3
≥ a year	43	71.7	16	26.7
TB Treatment History				
New	16	26.7	50	83.3
Has Recurred	44	73.3	10	26.7
Other Diseases Suffered				
No	46	76.7	42	70.0
Others (HIV, cancer, DM)	14	23.3	18	30.0

Characteristics of the study subjects showed that male's study subjects were more than women in the case and control group of 61.7% and 55%. Majority case group less than 35 years old was 51.7%,

while majority control group over the age of 35 years was 61.7%.

The last educational proportions of patient study subjects were the same for case and control groups. Family income for a month in case group and control were more than the family income which have <Rp 1,500,000/ month that were 88.3% and 75%. Most of patients in the case and control group had no smoking habits (75% and 66.7%) and alcohol consumption of 91.7% and 95%. Case and control groups were largely never in contact with patients with previous tuberculosis, 66.7% and 71.7%. Case groups had tuberculosis disease ≥ 1 year that is 71.7% and most control groups had suffered from tuberculosis <1 year that is 73.3%. Case group, having previous history of tuberculosis treatment was more dominant that is 73.3%, while control group patients mostly getting tuberculosis treatment was 83.3%. Most case and control groups did not suffer from other illness than tuberculosis of 76.7% and 70%. Most case and control groups lived in a clean environment of 95% and 80%.

Table 2.The Distribution of study subjects (health workers)

Characteristic	Case		Control	
	n	%	n	%
Gender				
Man	6	27.3	1	4.5
Woman	16	72.7	21	95.5
Age				
< 35 years old	7	31.8	5	22.7
≥ 35 years old	15	68.2	17	77.3
Last Education				
Diploma	4	18.2	12	54.5
S1	3	13.6	2	9.1
S1+Profesion	13	59.1	8	35.4
Spesialist	2	9.10	0	0
Work Duration				
< 5 years	5	22.7	2	9.1
≥ 5 years	17	77.3	20	90.9

The result of study subject characteristic showed that health worker giving tuberculosis treatment was more female workers in case and control group that was 72.7% and 95.5%. Most of the age of health workers were over 35 years old in both case and control group, 68.2% and 77.3%. The most recent education owned by case group was mostly S1 + Profession was 59.1% and the proportion control group was almost the same studysubject as diploma III and S1 + Profession, 54.5% and 35.4%. Most of case and control groups had worked in health care institutions for ≥5 years, 77.3% and 90.9%.

2. Path Analysis

The results of path analysis data process used STATA 13, as follows:

a. Model Specification

The initial model in path analysis can be seen in Figure 1.

b. Model Identification

The measured variable was 9, the endogenous variable was 3, the exogenous variable was 6, and the parameter number was 9. Degree of freedom (df) = (measured variable number x (measured variable number + 1) / 2 (endogen variable+ exogenous varia-

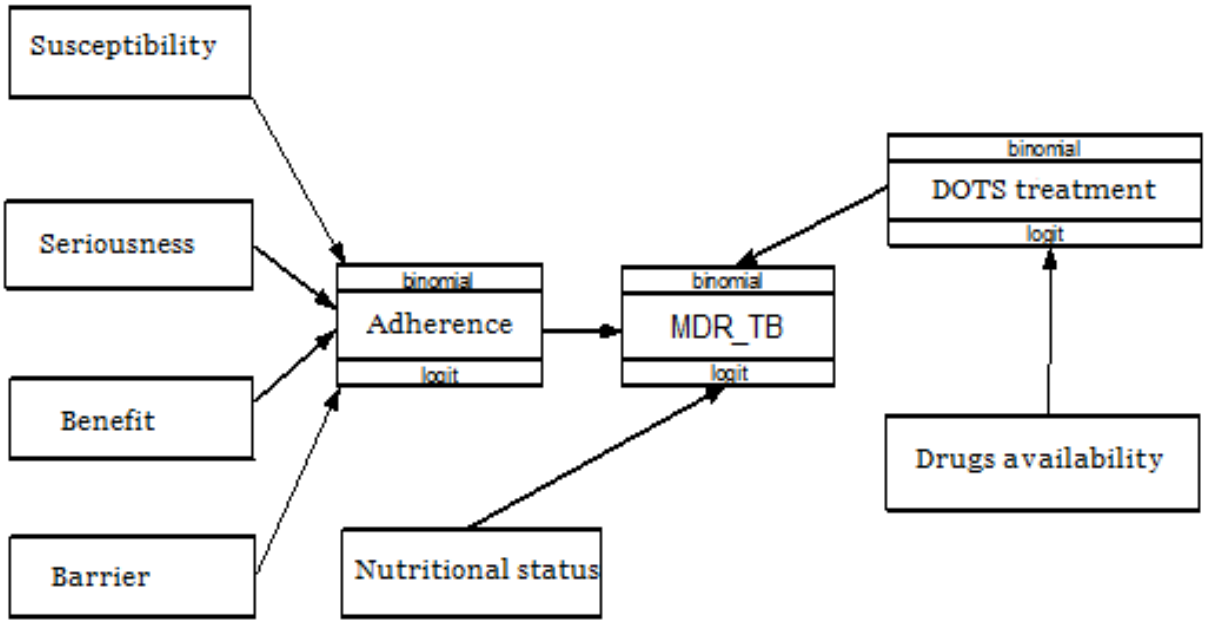
ble+ parameters)= (9x10) / 2 - (3+6+9) =27.

The model identification was obtained in df value is over identified which means path analysis can be done.

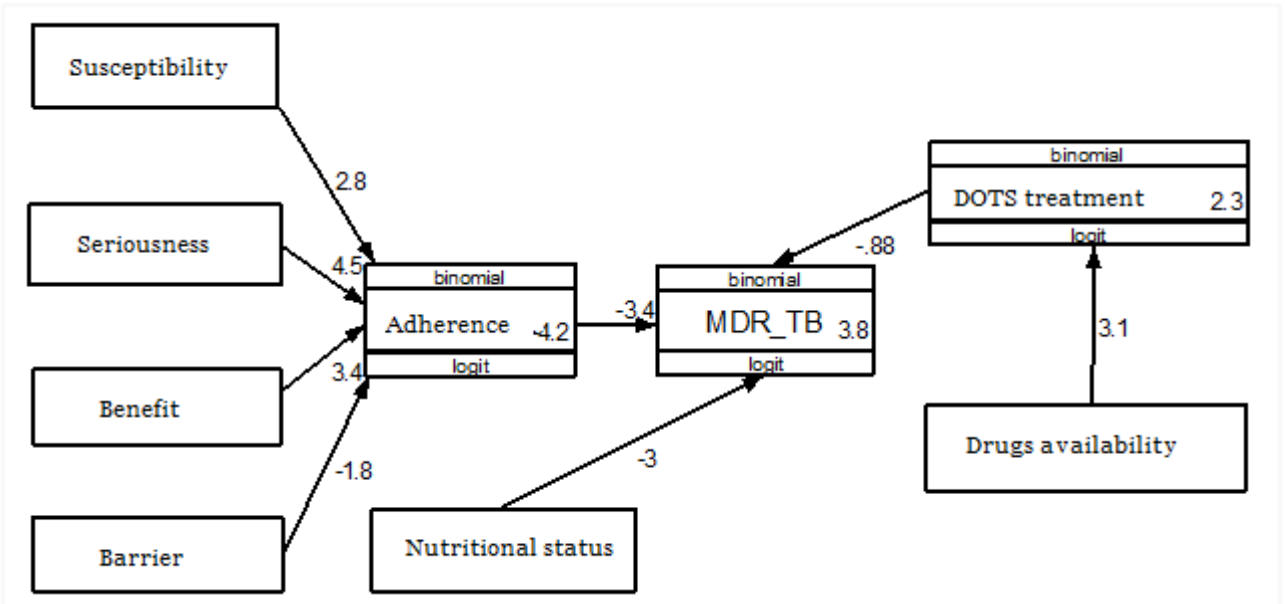
c. Model and parameter estimation compatibility

Path analysis model made by the researcher based on the theory checked its compatibility with the best variable relation model based on sample data collected by the researcher.

Picture 2 showed that the results of path analysis with STATA 13 resulted in the relationship between MDR TB and its risk factors.



Picture 1. Path analysis with specification model



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Picture 2. Model with parameter estimation

The result of coefficient value on each variable in each path was a positive relationship between perception of susceptibility to adherence to medication compliance, which was 2.8, there was a positive relationship between perceptions of seriousness with medication adherence of 4.5, there was a positive relationship between the perception of benefits with compliance of 3.4, there was a negative relationship between the perception of obstacles with compliance of drinking drug of -1.8. The path coefficient value between medication adherences and MDR TB was negative at -3.4. The path coefficient value between drug availability and MDR of TB was positive value at -3.1. The path coefficient value between the treatment of DOTS and MDR TB was negative at -8.8, there was a negative relationship between nutritional status and MDR TB at -3.

Table 3.The results of risk factor analysis path of *Multi Drug Resistant Tuberculosis* (MDR TB)

Dependent Variable		Independent Variable	b	95% CI Lower Limit	95% CI Upper Limit	p
Direct effect						
MDR TB	←	Nutritional status (normal)	-2.98	-5.31	-0.64	0.012
MDR TB	←	Benefit (high)	-3.38	-5.94	-0.82	0.010
MDR TB	←	DOTS treatment (DOTS)	-0.88	-3.18	1.43	0.456
Indirect effect						
Adherence	←	Susceptibility (high)	2.81	-0.99	4.64	0.003
Adherence	←	Seriousness (high)	4.47	2.38	6.57	<0.001
Adherence	←	Benefit (high)	3.35	1.52	5.18	<0.001
Adherence	←	Barrier (high)	-1.81	-3.48	-0.14	0.034
DOTS treatment	←	Drug availability (available)	3.14	0.95	5.32	0.005
N Observation = 120						
Log likelihood =-56.73						
AIC = 135.46						
BIC = 166.13						

Table 3 showed that the results of calculations using computer software program STATA 13, there was a relationship between nutritional status of tuberculosis patients and decreased risk logit for MDR TB and the relationship was statistically significant. Tuberculosis patients with good or normal nutritional status had a 2.98 risk *logit* lower than in patients with abnormal nutritional status (b = -2.98; 95% CI = -5.31 to -0.64; p = 0.012).

There was a relationship between patient adherence in taking medication and decreased risk logit for MDR TB occurrence and the relationship was statistically significant. Patients who were obedient in taking tuberculosis medication had a 3.38 lower risk logit than patients who did not adhere to taking tuberculosis medication (b = -3.38; 95% CI = -5.94 to -0.82; p = 0.010).

There was a relationship between treatment with the DOTS strategy and decreased risk logit for MDR TB occurrence and the relationship was not statistically significant. Medicines who performed treatment using the DOTS treatment strategy had a 0.88 lower risk logit than the non-performing medical personnel using the DOTS treatment strategy (b = -0.88; 95% CI = -3.18 to 1.43; p = 0.456).

There was a relationship between susceptibility perceptions and increased logit to have patient adherence in taking tuberculosis medication and the relationship was statistically significant. Patients with high perceptual tuberculosis had a 2.81 logit risk higher than tuberculosis patients with low susceptibility perception (b= 2.81; 95% CI= 0.99 to 4.64; p = 0.003).

There was a relationship between perception of seriousness and increased logit to have adherence in taking tuberculosis drugs and the relationship was statistically significant. Patients with severe perception of seriousness had a 4.47 logit risk higher than those with a low seriousness perception (b = 4.47; 95% CI = 2.38 to 6.57; p <0.001).

There was a relationship between beneficial perceptions and increased logit to have adherence to tuberculosis drug treatment and the relationship was statistically significant. Tuberculosis patients with high benefit perceptions had a 3.35 higher risk logit than tuberculosis patients with low benefit perceptions (b = 3.35; 95% CI = 1.52 to 5.18; p <0.001).

There was a relationship between perception of barriers and decreased logit to have adherence in taking tuberculosis drugs and the relationship was statistically significant. Highly perceptual tuberculosis patients had a logit risk of 1.81 lower than in low-perception tuberculosis patients (b = -1.81; 95% CI = -3.48 to -1.39; p = 0.034).

There was a relationship between drug availability and increased logit in the implementation of treatment with the DOTS strategy and the relationship was statistically significant. Health workers providing drugs suitable with the DOTS logit risk strategy were 3.14 times higher than the health professionals who did not provide the medication according to the DOTS treatment strategy (b = 3.14; 95% CI = 0.95 to 5.32; p = 0.002).

d. Model Respesification

The model in this study was due to the sample data as indicated by the saturation model and also the regression coefficient which was more than zero and statistically significant, it was not necessary to recreate the path analysis model.

DISCUSSION

1. Relationship between patient adherence on taking Tuberculosis Drugs and MDR TB

The analysis results showed that there was a direct correlation between patient adherence in taking tuberculosis medication on MDR TB incidence. Treatment adherence is important to avoid MDR TB and treatment failure. Patient compliance is highly demanded in this long-term treatment. Compliance taking this drug is needed in all diseases, especially tuberculosis disease that requires extra surveillance in its treatment (Nurismi, 2014).

The study results were consistent with Fauziah study (2013) indicates that MDR TB patients are more on the subjects of non-adherence in treatment than those who are obedient. Patients who are disobedient have a 10.8-fold chance of experiencing MDR TB compared with patients who are obedient to their treatment.

The result of this study was in line with Nurismistudy (2014) that there is a significant relationship between the level of treatment adherence with MDR TB incidence in RSUD Labuan Baji Makassar and the magnitude of risk can be seen from the value OR = 28.02 which means the studysubject with the level of adherence treatment is not good possibility with MDR TB occurred 28 times compared with the subjects with good adherence level.

Noncompliance in treatment becomes an important factor inresistance development. Non-compliance in treatment is often underestimated by health personnel and difficult to predict. This is probably due to many factors that affect it. Certain factors, such as morbidity, alcohol consumption, medication consumption and vagrants become a non-adherence factor to treatment. In addition, complex treatment, drug effects and treatment time that took a long time to make the patient decided to stop taking drugs (Jain and Dixit, 2008).

2. Relationship between perceptions of vulnerability and MDR TB through adherence variables

The results of the analysis indicated that there was an indirect relationship between susceptibility perception and MDR TB incidence through patient compliance variable in taking TB medication.

One of the models developed to look at the factors that influence a person's actions to seek a healthy lifestyle is the Health Belief Model. HBM was developed to explain the failure causes of a group of individuals in a disease prevention program and expanded to study the person behavior against a well-established diagnosis of medication adherence issues (Safri et al., 2014).

Vulnerability perception is the way a person acts to treat or prevent his illness; he must feel that he is susceptible to the disease. In other words, a precaution against a disease will arise when a person has felt that he or his family is susceptible to the disease (Nurhayati et al., 2015).

The results of Safri et al. (2014) showed that there was no relation between perception of susceptibility and tuberculosis drug adherence observed from p = 0.998. This means that the perception of vulnerability has no relationship with compliance if it is not shared with other variables. However, this variable will have a relationship if it is analyzed together as one unity with other variables that are perceived susceptibility, feeling seriousness (perceived seriousness), perceived benefit and perceived barrier.

Factors that affect individuals and families of tuberculosis patients in seeking health care and are adherent to medication are the level of education, knowledge, attitudes, occupations, income, distance of health services and support of drug conservers and supported by the role of health workers in motivating behavioral change (Safri et al ., 2014).

3. Relationship between Perceptions of seriousness and MDR TB through adherence variables

The results of the analysis indicated that there was an indirect correlation between the perception of seriousness and MDR TB incidence through patient compliance variable in taking TB medication.

The health-faith model is useful for estimating noncompliance, which beliefs about one's health and personality play a role in determining the patient's response to treatment recommendations. Individual actions for treatment and disease prevention will be driven by the seriousness of the disease against individuals or communities. In this case, the action taken by tuberculosis patients is compliant to take tuberculosis medication considering this disease is a serious disease and can cause death (Safri et al., 2014).

The results of Safri et al. (2014) showed that there was no correlation between the perception of seriousness of TB drug adherence observed from p = 0.998. This means the perception of seriousness has no relationship with compliance if it is not shared with other variables. However, this variable will have a relationship if it is analyzed together as a

whole with other variables of perceived susceptibility, perceived seriousness, perceived benefit and perceived barrier.

Individual actions to treat and prevent disease will also be encouraged by the seriousness of the disease against individuals or communities. In this case, the actions taken by TB patients are compiled to take TB medication, since tuberculosis is a serious disease that can cause death. The heavier the risk of disease, the more likely the individual feels threatened. This threat encourages individual action to take preventive and healing measures of disease (Safri et al., 2014).

4. Relationship between perceived of benefits and MDR TB through adherence variables

The results of the analysis indicated that there was an indirect relationship between beneficial perception and MDR TB incidence through patient compliance variable in taking TB medication.

If the individual feels himself vulnerable to serious diseases, he will take a certain action. This action depends on the perceived benefits. Perceiving need for action is influenced by variables that affect a person's perception and consequently indirectly affect his or her health behavior (Safri et al., 2014).

The results of Safri et al. (2014) showed that there was no correlation between perception of benefit and tuberculosis drug adherence observed from p = 0.998. This means that the perception of benefits has no relationship with compliance if it is not shared with other variables. However, this variable will have a relationship if it is analyzed together as a whole with other variables of perceived susceptibility, perceived seriousness, perceived benefit and perceived barrier.

The study results in line with Nurhayati study (2015) state that there is a relationship between the perception of benefits and the prevention of tuberculosis ($p < 0.05$), the more positive the perception of MDR TB patients about the usefulness, the better the tendency to take action and confidence in running the prevention of transmission of tuberculosis increasingly.

5. Relationship between perceived barrier and MDR TB through adherence

The analysis results indicated that there was an indirect correlation between barrier perception and the incidence of MDR TB through patient compliance variable in taking TB medication.

The last forming of HBM is the barrier perception to be faced from the action or health behavior. However, a person may not take anaction, even if the individual believes in the benefits of taking such action. This could be caused by obstacles. Barrier refers to the characteristics of a preventive measure such as inconvenient, expensive, unpleasant. This characteristic will cause the individual to move away from the action desired to be performed (Nurhayati, 2015).

The results of Safri et al. (2014) showed that there was no correlation between perception of obstacles and TB drug adherence observed from p = 0.998. This means the perception of obstacles has no relationship with compliance if it is not shared with other variables. However, this variable will have a relationship if it is analyzed together as one unity with other variables that are perceived susceptibility, perceived seriousness, perceived benefit, and perceived barrier.

One of the factors quite influential on compliance to take the drug is the personal experience of the studysubject. In this case, the personal experience is the experience of the side effect of OAT. The side effect itself felt by study subjects such as nausea

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vomiting becomes a person's obstacles in drinking OAT. This really affects the patient's adherence to take medication, as they feel traumatized by the side effects that arise after taking the drug (Safri et al., 2014).

6. Relationship between the implementation of DOTS treatment and MDR TB.

The analysis results showed that there was a direct relationship between the implementation of DOTS treatment and the incidence of MDR TB. The concept of DOTS is one of the important efforts in ensuring patient's treatment regularity and tackling MDR TB problem (Syahrini, 2008). Intermittent or non-DOTS treatment can also result in the emergence of multiple immune cases against anti-tuberculosis drugs that lead to a stronger type of tuberculosis germ known as MDR TB (Sarwani et al., 2012).

Lack of funding support and facilities such as for cultivation and unavailable sensitivity are often the main barriers to MDR TB control. In addition, guidelines, issued by WHO, are often filtered to reselect the treatment. Some of the program approaches used for the management of patient treatment failures may fail on some sides, as it can be seen after the recording (Fauziah, 2013).

The study results in line with study by Nurismi (2014) showed that there was no significant relationship between the perception of study subjects on tuberculosis treatment management and MDR TB incidence. Management of a good treatment program, half of the study subjects of tuberculosis and a small part of management of treatment programs, is not good on the subject of MDR TB study, because the information provided by health workers is very clear and the supervision of taking medication (PMO) plays a good role.

The study results is not in line with the study by Zhao et al., (2012) which stated that the implementation of ineffective tuberculosis treatment with DOTS may increase the risk of MDR TB incidence with OR = 1.84. In this study, the main risk factors of MDR TB in addition to poor implementation of DOTS, the bad factor of treatment and tuberculosis treatment also trigger the incidence of MDR TB. Studyby Jain and Dixit (2008) showed that a program for controlling tuberculosis with first-line therapy and DOTS was performed on 467 patients with AFB + in a prison. After observation, it was concluded that the effectiveness of the DOTS program with first-line therapy decreased from 85% of target set by WHO. The lack of TB infection control in health centers and the lack of training from staff is also a risk for MDR TB. Mistakes and disobedience in prescribing by health professionals are frequent and underestimated so that it is also difficult to precipitate.

7. Relation between OAT Availability and MDR TB through Variables between the Implementation of DOTS Treatment

The analysis results indicated that there was an indirect relationship between the availability of OAT and the incidence of MDR TB. Many factors cause MDR TB. Some analyzes focus on patient noncompliance. Non-compliance is more associated with treatment barriers such as lack of diagnostic, drug, transport, logistics and TB program control costs. One of the strategies contained in the DOTS treatment program is the availability of appropriate anti-tuberculosis drugs including the type, dose and time period appropriate to treatment therapy (Jain and Dixit, 2008).

The study results are in line with studies conducted by Zhao et al., (2012)

which suggest that poor quality of DOTS treatment is associated with poor quality of TB treatment (drug type and given dosage) that may cause TB patients to be resistant to give therapy which increases the risk of MDR TB occurrence (OR = 2.65).

The results of Mulu et al. (2015) showed that the poor treatment and inappropriate medication would increase the risk of MDR TB.This study also revealed that patients who undergo treatment in a non-intensive and continuous risk of MDR TB. This is related to bacterial death and developmental cycles, as it allows the bacteria within the individual to mutate and create new genes or bacteria.

Fauziah (2013) stated in an observation conducted among MDR TB patients, of 35 patients was a management error in 28 patients with an average error of 3.93 per patient. The most common mistakes are the addition of unsuccessful drugs, failure to identify the existing or existing drug resistance, initiation of inadequate primary regimens, failure to identify and recognize drug nonconformities and inaccurate preventive therapy with isoniazid.

8. Relationship between nutritional status with MDR TB

The results showed that there was a direct correlation between the nutritional status of tuberculosis patients and MDR TB incidence. Nutritional status is an important part in determining one's health level. Nutrition status in addition will affect the immune system directly also play a role in the healing process of disease including patients suffering from tuberculosis (Patiung, 2014). Nutritional status is one of the main factors causing increased morbidity and mortality rate in tuberculosis cases (Kumar, 2014).

Tuberculosis patients often experience a decrease in nutritional status, even it can be malnutrition status if it is not balanced with proper diet. The study results of Patiung et al. (2014) showed that people with nutritional status were less likely to have 3.7 times more risk to have more severe tuberculosis compared with those with enough or more nutritional status.

Tuberculosis and malnutrition are more likely to interact with each other (Patiung et al., 2014). Tuberculosis patients have poorer nutritional status than healthy ones. This can be caused by a decrease in appetite in patients with tuberculosis (Wokas et al., 2015).

The study results in line with the study by Muaz (2014) showed that there was a relationship between nutritional status and the incidence of tuberculosis with a value of p = 0.001 and OR = 2.513, which means poor nutritional status will increase the risk of 2.5 times exposed to tuberculosis compared with good nutritional status .

The study results in line with the studyby Fauziah (2013) which shows the studysubject suffering from MDR TB is more suffered by study subjects who have BMI <18.5. Jain (2008) stated that underweight TB patients have a higher risk for relapse after completion of treatment. The low nutritional status also increases the failure of TB treatment or develops into latent TB infection. Low nutritional status can cause germs that proliferate rapidly so that it inhibits conversion, but it also causes a low immune system making it difficult to heal and facilitate recurrence of tuberculosis having subsided (Nurismi, 2014).

Drug compliance, treatment with DOTS strategies and nutritional status of tuberculosis patients are directly related to MDR TB. Perceptions of vulnerability, seriousness, benefits and barriers are indirectly associated with MDR TB through medication adherence. So it can be

concluded that the perception of patients on MDR TB can affect the occurrence of MDR TB with the compliance of tuberculosis patients in taking the drug.

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