Tarumanagara Medical Journal
Vol. 3, No. 2, 238-248, Oktober 2021

Factors influenced of drug-resistant tuberculosis and non-drug-resistant tuberculosis patients in Pulmonary Hospital Dr. M. Goenawan Partowidigdo, Bogor district

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ABSTRAK

Tuberculosis is one cause of death, the ninth of all diseases in the world. The increasing cases of antimicrobial-resistant tuberculosis is a global challenge especially multi-drug resistant TB (MDR-TB). Drug-resistant Tuberculosis is classified as a condition where Mycobacterium tuberculosis can't be treated with anti-tuberculosis drugs. The study aimed to determine the associated risk factors with drug-resistant Tuberculosis compared with second category tuberculosis (non-drug resistant Tuberculosis). A case-control study was undertaken — there were 40 cases (drug-resistant TB) and 80 controls (non-drug resistant TB) were conveniently sampled. Data we collected from medical records and direct interviews using questionnaires. The variables of interest were gender, age, occupation, income, medication history, side effects, regularity of taking medication, nutritional status, smoking, alcohol, contact history, treatment chronology, and health facility distance. The results showed majority of respondents were mostly men, age >41 years, low education, work, incomes >1.00,000 IDR, failed/discontinued treatment, no side effects, adherence treatment, BMI> 18.5, no smoking, no alcohol consumption, no contact history, lack of knowledge, drug swallowing supervisor (DSS), health services distance <3 km. Final model adherence of treatment p-value 0.0001, OR 6.460, 95% CI 2.384-17.504; contact history p-value 0.004, OR 4.549, 95% CI 1.623-12.748; side effects p-value 0.017, OR 3.580, 95% CI 1.260-10.17; health service distance p-value 0.061, OR 2.627, 95% CI 0.955-7.226. These four factors have contributed to the occurrence of drug-resistance TB.

Kata kunci: side effects, distance, adherence, drug resistant TB

INTRODUCTION

Tuberculosis (TB) is one of the top ten causes of death in the world. The current global challenges related to tuberculosis include increased drug resistance. In drug-resistant Tuberculosis (DR-TB), Mycobacterium tuberculosis bacteria cannot be eradicated by anti-Tuberculosis drugs used previously. In the world, about 3.3% of Tuberculosis cases in 2014 are multidrug-resistant (MDR), 480.000 people in 2015 were estimated to suffer from DR-TB and in 2016 an estimated 600.000 people suffer from DR-TB. Three countries with the highest cases of DR-TB were China, India, and the Russian Federation.[1]

In Indonesia, the incidence of DR-TB cases trends was increased from 2013 to 2015. Data in 2013 estimated 3.833 new cases of DR-TB. There were 1.094 cases

of positive DR-TB and 819 were treated. In 2014, there were 9.399 new suspected DR-TB cases, and 1.752 positive DR-TB, 1.287 were treated. In 2015 there were 15.380 new cases of DR-TB, in which 1.860 were confirmed and 1,566 were treated.[2]

Data of DR-TB in Pulmonary Hospital Dr. M. Goenawan Partowidigdo from 2015- 2017 showed increasing trends. In 2015 positive cases of DR-TB were 147 (17.8 %), 236 (24.6%) cases in 2016 and 233 (l7.9%) cases in 2017. Positive drug-resistant cases from January to March 2018 were 64. Based on the data presented above, it is important to identify risk factors of DR-TB. The objectives of this study are to identify the key associative factors with the occurrence of DR-TB and produce a multivariate model to identify those factors. The risk factors are a socio-economic factor; presence and effect of common co-morbidities (human immunodeficiency virus (HIV), acquired immune deficiency syndrome (AIDS), and diabetes mellitus; environment-associated risk factors, such as the contact history, availability of Drug Swallowing Supervisor (DSS), and the distance of health facilities.

METHODS

This study used a case-control design, applied and quantitative research. The case study population was all DR-TB patients and the control population was all 2nd category of TB patients (non-DR-TB). Research samples were 120 respondents (40 DR-TB patients and 80 non-DR-TB patients). This study was conducted at the Pulmonary Hospital Dr. M. Goenawan Partowidigdo, Bogor in July 2018. The sampling technique used was convenience sampling for DR-TB cases and non-DR-TB cases in Pulmonary Hospital Dr. M. Goenawan Partowidigdo. Data collection was obtained from medical record information and direct interview using questionnaires. Data were analyzed using univariate, bivariate with chi-square and multivariate with multiple logistic regressions (SPSS software version 23).

RESULTS

The result from this study, from 120 patients, the majority of respondents were mostly men (61.7%), age >41 years (54.2%), low education (56.7%), work or have a job (63.3%), incomes >1.000.000 IDR (51,7%), failed/dropout of treatment (54,2%), no side effects from drugs (55%), adherence treatment (61,7%), BMI >18.5 (62.5%), no smoking (85%) and alcohol (90%) consumption, no contact history (60,8%), lack of knowledge (50,8%), DSS (56,7%), and

health services distance <3 km (53.3). (Tabel 1)

Table 1. Analysis of the independent variables (N=120)

Characteristics	n (%)
Gender	
Male	74 (61.7)
Female	46 (38.3)
Age	
>41 tahun	65 (54.2)
≤41 tahun	55 (45.8)
Education	
Low	68 (56.7)
High	52 (43.3)
Job	
Working	76 (63.3)
Not working	44 (36.7)
Income	
≤1.000.000 IDR	58 (48.3)
>1.000.000 IDR	62 (51.7)
Treatment history	
Dropout of treatment	65 (54.2)
Complete treatment	55 (45.8)
Side effect	
Positive side effect	54 (45)
Negative side effect	66 (55)
Adherence of treatment	
Non adherence	46 (38.3)
Adherence	74 (61.7)
Nutritional status	
BMI ≤ 18.5	45 (37.5)
BMI > 18.5	75 (62.5)
Smoking	
Yes	18 (15)
No	102 (85)
Alcohol consumption	
Yes	12 (10)
No	108 (90)
Contact history	
Yes	47 (39.2)
No	73 (60.8)
Knowledge of TB	
Not good	61 (50.8)
Good	59 (49.2)
Drug swallowing supervisor (DSS)	
No	52 (43.3)
Yes	68 (56.7)
Distance of health service	
≥ 3 km	56 (46.7)
< 3km	64 (53.3)

Variables that are significantly associated with the incidence of DR-TB are side effect of medication, regularity of treatment, contact history, and distance of health care facilities. While the variables that are not significant with the incidence of DR-TB are gender, age, education, occupation, income, nutritional status, smoking, alcohol consumption, knowledge, and DSS. (Table 2)

The most dominant variable associated with the incidence of DR-TB is the regularity of treatment because the OR value of 6.460, which means that patients who take medication irregularly will have 6,46 times higher risk of developing DR-TB compared to those who take medication regularly, after adjusting for side effects, contact history, treatment history and distance to health facilities. The four variables above such as regularity of medication, side effects of drugs, contact history and distance to health care facilities contribute to the occurrence of DR-TB. (Table 3)

Table 2. Analysis result of independents and dependent variables in Pulmonary Hospital Dr. M. Goenawan Partowidigdo (N=120)

Variables	Drug resistant Tuberculosis		P value	OR (CI 95%)
	DR-TB (n=40)	Non-DR-TB (n=80)		
Gender				
Male	20 (50%)	54 (67.5%)	0.097	0.451 (0.221-1.047)
Female	20 (50%)	26 (32.5%)		
Age				
>41 tahun	22 (55%)	43 (53.7%)	1.000	1.052 (0.491-2.254)
≤41 tahun	18 (45%)	37 (46.3%)		
Education				
Low	23 (57.5%)	45 (56.3%)	1.000	1.052 (0.459-2.266)
High	17 (42.5%)	35 (4.7%)		
Job				
Working	23 (57.5%)	53 (66.3%)	0.461	0.659 (0.316-1.503)
Not working	17 (42.5%)	27 (33.7%)		
Income				
≤1.000.000 IDR	16 (40%)	42 (52.5%)	0.172	0.603 (0.279-1.303)
>1.000.000 IDR	24 (60%)	38 (47.5%)		
Treatment history				
Dropout of treatment	29 (72.5%)	36 (45%)	0.098	3.222 (1.416-7.331)
Complete treatment	11 (27.5%)	44 (55%)		
Side effect				
Positive side effect	30 (75%)	24 (30%)	0.0001*	7.000 (2.960-16.554)
Negative side effect	10 (25%)	56 (70%)		
Adherence of treatment				
Non adherence	29 (72.5%)	17 (21.3%)	0.0001*	9.770 (4.066-23.477)
Adherence	11 (27.5%)	63 (78.7%)		
Nutritional status				
BMI ≤ 18.5	20 (50%)	25 (31.3%)	0.072	2.200 91.009-4797)
BMI > 18.5	20 (50%)	55 (68.7%)		
Smoking				
Yes	9 (22.5%)	9 (11.3%)	0.175	2.290 (0.829-6.324)
No	31 (77.5%)	71 (88.7%)		
Alcohol consumption				
Yes	5 (12.5%)	7 (8.7%)	0.747	1.490 (0.441-5.025)
No	35 (87.5%)	73 (91.3%)		
Contact history				
Yes	28 (70%)	19 (23.7%)	0.0001*	7.491 (3.202-5.235)
No	12 (30%)	61 (76.3%)		
Knowledge of TB				
Not good	26 (65%)	35 (43.7%)	0.095	2.355 (1.055-5.235)
Good	14 (35%)	45 (56.3%)		
Drug swallowing supervisor (DSS)				
No	30 (75%)	22 (27.55)	0.099	7.909 (3.321-15.536)
Yes	10 (25%)	58 (72.5%)		
Distance of health service				
≥ 3 km	25 (62.5%)	31 (38.7%)	0.024*	2.634 (1.205-5.760)
< 3km	15 (37.5%)	49 (61.3%)		

***P value <0.05**

Tabel 3. The final model of risk factor of DR-TB and non-DR-TB in Pulmonary Hospital Dr. M. Goenawan Partowidigdo

Variable	P value	OR	95% CI		Nagelkerke R square
			Lower	Upper	
Side effect	0.017	3.580	1.26	10.173	0.237
Adherence treatment	0.0001	6.460	2.354	17.504	0.307
Contact person with TB	0.004	4.549	1.623	12.747	0.253
Health service distance	0.061	2.627	0.955	7.226	

DISCUSSION

Relationship of gender with DR-TB.

We found no significant difference in the distribution of men and women who suffer from DR-TB. This result was in line with the research conducted by Demile B et al., (2018), Lia Alfiana Fauziah (2013), Dorothea Ojo Linda (2012). The three studies with different samples, also showed that gender is not related to the incidence of DR-TB.[3-5]

Relationship of age with DR-TB.

In this study, there was no significant difference in the occurrence of drug-resistant tuberculosis in age groups (<4l years and >41 years). In theory, age affects drug absorption, so older age increases the risk of DR-TB, but in this study age does not contribute to the occurrence of DR-TB. Most respondents in this study were DR-TB because they did not take medication regularly, dropped out of treatment, and even failed treatment, causing respondents to experience DR-TB. Demile, Lia, and Dorothea also reported that age is not related to the incidence of DR-TB.[3-5]

Relationship of education to DR-TB.

We also found no significant difference in education level in DR-TB. The distribution of low educated or highly educated DR-TB patients in this study is similar. Low-educated patients, mostly are housewives and they contract TB disease from their families. The highly educated patients mostly work in the private sector, and they contract TB disease from other than their families, as well as their colleagues and workplaces people. This result is in line with research conducted by Lia Alfiana Fauziah (2013) and Ariska (2016), which states that there is no significant relationship between the level of education and the incidence of DR-TB, especially MDR-TB.[4,6]

Relationship between occupation with DR-TB

Substantial work has no meaningful relationship with the occurrence of DR-TB. There is no meaningful difference between working people and non-working people, they suffer DR-TB from their family or co-workers, in addition to being infected, treatment compliance, dropping out of treatment, and even failed treatment, also play some roles in DR-TB. Lia Alfiana Fauziah (2013) and Ariska (2016) also stated that there is no meaningful relationship between work with the incidence of DR-TB, especially MDR-TB.[4,6]

Based on statistical analysis there is no significant difference in proportion between income ≤1.000.000 IDR and > 1.000.000 in the incidence of DR-TB, so that it can be inferred that there is no relationship between DR-TB and income. The study by Ariska (2016) also stated that there is no influence between income and the incidence of DR-TB, especially MDR-TB.[6] On the contrary, a study in Serbia stated that income significantly influenced the incidence of DR-TB, (OR=3.71 ; 95% Cl= 1.22- 11.25).[7]

Relation of treatment history with DR-TB.

In this study, the history of previous treatment is very difficult to determine the occurrence of DR-TB because most patients who suffer from DR-TB have a history of dropping out of treatment and failing treatment so that not all TB germs are killed by drugs taken before that cause the TB germs to develop into tuberculosis germs drug resistant. The results of this study are in line with the research conducted by Ariska (2016) and Girum et al (2018) which explained that the history of previous treatment strongly determines the occurrence of DR-TB, especially MDR-TB.[6,8] Patients with TB who have previously failed or dropped out of TB treatment have a higher risk of (6.560 times) than TB patients who have cured or completed treatment outcomes.[6]

Relationship of side effects with DR-TB.

This study shows that most people who suffer from DR-TB are respondents who experience drug side effects. types of side effects felt by respondents were dizziness, nausea, vomiting, red urine, joint pain, lack of appetite, and others. Respondents who experienced drug side effects mostly stopped treatment, then most of them dropped out of treatment, so the condition contributed to TB RO. TB drugs have side effects that cause discomfort for those who consumed them. The results of this study are in line with the research

conducted by Andrianti (2014), which states that the side effects of tuberculosis treatment are risk factors for DR-TB, especially MDR-TB.[9]

Relationship between regular treatment with DR-TB.

We found a significant difference between patients who regularly taking medication and who did not, to the incidence of DR-TB, so that it could be stated that there was a relationship between regular treatment with DR-TB. Regular treatment or adherence to tuberculosis treatment determines the outcome of treatment. Patients often stop treatment before treatment is completed for the reason that the patient feels better so that he or she does not need to continue treatment. Patients are expected to adhere to recommendations for taking medication as prescribed by a doctor or pharmacist. Patients who have long been in treatment usually feel bored and do not take drugs as prescribed by a doctor. This often triggers the occurrence of resistant tuberculosis bacteria against anti-tuberculosis drugs.[10] The results of this study are in line with the results of research conducted by Girum et al in Ethiopia, and Ariska which explained that adherence to tuberculosis treatment greatly determines the occurrence of DR-TB, especially MDR-TB in Ethiopia.[6,8] People who do not regularly take medication will have 17.905 times higher risk developing MDR-TB compared to people who regularly take medication.[6]

Relationship of nutritional status with DR-TB.

There was no significant difference in the proportion between BMI ≤ 18.5and BMl > 18.5 for the incidence of DR-TB so that it could be stated that there was no correlation between nutritional status and DR-TB. The results are confirmed by a study conducted by Demile B et al, which states that body mass index is not related to the incidence of MDR-TB.[3]

The relationship between smoking and DR-TB

In this study there was no relationship between smoking with the incidence of DR-TB. Amount of respondents who had ahistory of smoking were very less, compared to those who did not smoke. Non-smokers are mostly women and students so that statistically it does not show a significant relationship between smoking and the incidence of DR-TB. The results of this study are in line with research conducted by Lia Alfiana Fauziah (2013), which states that there is no effect of smoking on the incidence of DR-TB, especially MDR-TB.[4]

The relationship of alcohol consumption with DR-TB

The results of this study there was no correlation between alcohol consumption and the incidence of DR-TB because respondents who had a history of alcohol consumption were very poor, compared to those who did not consume alcohol. Respondents who are not alcohol consumption are mostly from women and students so it does not statistically show a significant relationship between alcohol consumption and the incidence of DR-TB. The results of this study are in line with research conducted by Ariska (2016), which states that there is no effect of alcohol consumption with the incidence of DR-TB, especially MDR-TB.[6]

Relationship of contact history with DR-TB.

We found a significant difference in contact history and incidence of DR-TB. In the analysis, we obtained OR value of 7.491 means, that people who have a contact history will be at risk of 7.491 times greater than no contact history. In this study, most respondents who suffer from drug-resistant tuberculosis had a contact history of family, neighbors, and co-workers who suffer from DR-TB. They were unaware of the risk of contracting drug-resistant tuberculosis. In line with the results, research conducted by Girum et al. and Lia Alfiana Fauziah also explained that people who had a history of contact with MDR TB patients strongly determined the occurrence of DR-TB, especially MDR-TB in Ethiopia.[8,4,11]

The Relationship of knowledge with DR-TB.

Based on the results of statistical analysis there is a significant difference in the projection between low knowledge and good knowledge of the incidence of DR-TB so that it can be stated that there is a relationship of knowledge with DR-TB. In the analysis, the OR value of 2.355 means that people who have less knowledge will have 2.355 times the risk of developing DR-TB compared to people who have good knowledge.

In this study, most respondents suffering from DR-TB were respondents who had less knowledge about tuberculosis because most of the respondents had low education, namely elementary school and even some people who did not complete primary school. Lack of information received by the community related to the prevention of tuberculosis transmission also plays some roles, so respondents do not know how to prevent DR-TB. The results of

this study are in line with research conducted by Marahatta et.al, concerning the factors of risk factors of MDR-TB in Central Nepal obtained results of a significant relationship between knowledge and the incidence of DR-TB, especially MDR-TB.[12]

Relationship between the presence of DSS with DR-TB.

Based on the results of statistical analysis there is a significant difference between the absence of DSS and the presence of DSS in the incidence of DR-TB. Chi-square statistical test results obtained p-value = 0,0001 (<0,05 so that it can be stated that there is a relationship between the existence of DSS and DR-TB. In the analysis OR value 7.909 means that people who do not have a person who monitored them when swallowing drugs will be at risk 7,909 times greater to suffer from TB. The results of this study are in line with the research conducted by Ariska, showing the relationship between drug swallowing supervisors (DSS) and the incidence of MDR-TB. Patients who do not have DSS have an 8.47 fold risk of experiencing MDR-TB compared to people who have DSS.[6]

The role and motivation of DOT and family are very important for the successful treatment of patients with pulmonary TB. The role of DSS is important to supervise patients in terms of swallowing drugs, remind patients for phlegm re-examination in accordance with the prescribed schedule, encourage patients to seek treatment regularly until complete, advise patients to continue to swallow medication regularly until finished.[13]

Relationship between the distance of health service and DR-TB.

Our results showed significant differences between the distances ≤ 3 km and > 3 km to health services facilities with the incidence of DR-TB. This analysis obtained OR value of 2.634, which means that people who live further than 3 Km from health services facilities have a greater risk of 2.634 times to suffer DR-TB. This can be explained by the effect of continuity in the regularity of treatment as well as the ability of people to walk to the place of service during TB treatment completion. Distance from the place of residence is also related to the costs incurred for the time spent, which will affect the disorder of patient treatment.[14] The results of this study are in line with research conducted by Putri et al showing a relationship between the distance of health services and the incidence of DR-TB, especially MDR-TB. The farther the distance of health

facilities, the more risk to suffer from MDR-TB.[15]

CONCLUSION

In conclusion, we found that age, education, occupation, income, BMI, lack of knowledge, alcohol, and smoking had no correlation with the development of DR-TB. Risk factors that increase the likeliness of developing DR-TB are treatment compliance, side effects, contact history, and the distance to health services facilities.

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