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To cite this article: M P F Manurung *et al* 2018 *IOP Conf. Ser.: Earth Environ. Sci.* **125** 012148

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Factors related to successful treatment of drug-resistance tuberculosis in H. Adam Malik hospital, Medan, Indonesia

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Abstract. The number of drug-resistant TB cases keeps increasing for over the years. Drug-resistant TB is a difficult case because of the treatment, many side effects, more expensive, and less satisfactory results. This study is a retrospective cohort design aimed to determine the factors influencing the success of TB drug resistance treatment at H. Adam Malik Hospital during 2012–2015. The number of confirmed patients with drug-resistant TB was 223 people, 153 male, and 70 female. Two factors have been found to affect the treatment outcomes significantly, age and resistance pattern ($P < 0.05$). Patients aged < 50 years old have 2.73 times greater chance of recovery than patients aged ≥ 50 years old. Based on resistance pattern, patients with rifampicin resistant or poly-resistant would be 6.4 times more likely to recover compared with pre-XDR patients. There was no significant difference in the success rate of treatment among MDR patients compared with rifampicin resistant or poly-resistant cases. Age and resistance pattern has been proved to influence the success of drug-resistant TB treatment.

1. Introduction

Multidrug-resistant tuberculosis (MDR-TB) is a growing problem that threatens public health worldwide.[1] And tuberculosis (TB) become a leading cause of morbidity and ranks among the ten most common causes of death worldwide.[2] According to World Health Organization (WHO) report in 2014, globally 5% of TB cases are thought to become MDR-TB. The drug resistance surveillance data shows an estimated 480,000 MDR-TB patients with 210,000 deaths.[3]

The management of MDR-TB is more complicated and requires more attention than non-resistant TB management. The treated TB patients are four times more likely to develop resistance and ten times being the incidence of MDR-TB. Although in the five most countries with MDR-TB patients have a successful treatment rate of $\geq 70\%$ but globally only 52%.[2,4,5]

According to data at H. Adam Malik Hospital, Medan, in 2015 there were 142 patients with drug-resistant TB and in 2016 were 219 patients. While the number of MDR-TB patients in Indonesia in 2015 was 1896 cases and in 2016 were 2,731 cases. It shows an increase and shows that the problem of drug-resistant TB in Indonesia remains a serious problem.[6,7]

Therefore, we are interested in identifying factors affecting the success rate of drug-resistant TB treatment.



2. Method

It was an analytic study with a retrospective cohort design aimed to determine the factors that influence the success of TB drug resistance treatment at H. Adam Malik Hospital. Data collection is done retrospectively, starting from April to August 2017. The population in this study was the data of all drug-resistant TB patients who had received MDR-TB treatment from 2012–2015.

The inclusion criteria were tuberculosis patients with a complete medical record, which has been stated as a case of drug resistance as evidenced by the results of the GeneXpert and or drug sensitivity test (DST) and patients who had received the MDR drugs. While the exclusion criteria were patients, who do not want to continue the treatment. Data collection was in total sampling from all medical records of patients treated at MDR-TB Clinic H. Adam Malik Hospital year 2012–2015. To identify factors that influence the success of treatment was by chi-square test and logistic regression. Factors studied include gender, age, resistance pattern, comorbid, and conversion time.

3. Results

This study involved 223 drug-resistant TB patients. The demographic characteristics of the patients can be seen in table 1. Based on gender, the majority of patients were 153 male (68.6%). The youngest age is 14 years old, and the oldest was 73 years old. The mean age was 42.1 ± 11.9 years old.

Table 1. Characteristic demographic of the study.

		Sample	
		n	%
Sex	Male	153	68.6
	Female	70	31.4
Age	< 20 years	1	0.44
	20 - 29 years	37	16.6
	30 - 39 years	59	26.5
	40 - 49 years	59	26.5
	50 - 59 years	51	22.9
	60 - 69 years	15	6.7
	≥ 70 years	1	0.4

All patients were examined by GeneXpert MTB/Rif first with MTB (+) rifampicin resistant results. Then patients examined sputum culture and drug sensitivity test (DST) to determine other types of drug resistance, classified into rifampicin resistant (RR), poly-resistant, MDR, pre-XDR, and XDR-resistant. Table 2 shows that of the 223 patients, the majority of patients were MDR-TB patients, 168 patients (75.3%), 31 patients (13.9%) were rifampicin resistant (RR), and 19 patients (8.5%) pre-XDR. As for the characteristics of the subjects based on the predicted criteria of MDR, found that the most were 6th criteria (recurrent cases of TB patients) are 46 patients (20.6%). Of all the subjects, 39 patients (17.5%) were MDR-TB patients with comorbid diabetes mellitus, and only one patient is a TB patient with HIV comorbid. All patients received treatment of drug-resistant TB in according to the guidelines for the treatment of drug-resistant TB that prepared by the Ministry of Health of Indonesia.

Table 2. Characteristics of research samples based on resistance patterns.

		Sample	
		n	%
Type of Resistance	RR	31	13.9
	Poly-resistance	5	2.2
	MDR	168	75.3
	Pre XDR	19	8.5

MDR Criteria	1 st Criteria	30	13.5
	2 nd Criteria	43	19.3
	3 rd Criteria	7	3.1
	4 th Criteria	43	19.3
	5 th Criteria	23	10.3
	6 th Criteria	46	20.6
	7 th Criteria	31	13.9
Comorbid	Without comorbid	183	82.1
	Diabetes	39	17.5
	HIV	1	0.4

Table 3. Characteristics of research samples based on successful treatment.

	Parameter	Total	
		n	%
Results	Cured	107	48.0
	Stop treatment	66	29.6
	Complete treatment	2	0.9
	Death	42	18.8
	Failed	2	0.9
	Not evaluated/ moved	4	1.8
Conversion Time	0-2 month	103	46.2
	3-4 month	54	24.2
	5-6 month	10	4.5
	7-8 month	2	0.9
	Failed conversion	2	0.9
	Death before conversion	52	23.3
Death	0-2 month	14	33.3
	3-6 month	15	35.7
	7-12 month	8	19.0
	13 month – end treatment	5	11.9

In table 3 above, out of 223 subjects, 107 people (48%) completed medication until the end and were stated cured. A total of 66 patients (29.6%) did not complete treatment and loss to follow up. Overall only 2 (0.9%) patients who did not experience acid-fast bacilli (AFB) smear conversion at the end of treatment, and declared failed case.

Characteristics of the study subjects based on conversion time, 103 patients (46.2%) had undergone conversion within the first two months of treatment, and a total of 52 patients (23.3%) had died before the patient experienced sputum smear conversion.

The highest mortality rate found in the first six months of treatment. In general, the number of subjects that died in this study was 42 patients (18.8%).

To identify any factors contributing to the success of drug-resistant TB treatment, a statistical analysis of the results in table 4.

Table 4. Factors that affect the success of treatment.

	Parameter	Failed/Death		Healed		p-value	OR	95% CI
		n	%	n	%			
Sex	Man	34	77.3	71	65.1	0.14 ^a	0.55	0.24-1.23
	Woman	10	22.7	38	34.9			
Age	< 50	26	59.1	87	79.8	0.008 ^a	2.73	1.27-5.86
	≥ 50	18	40.9	22	20.2			

Resistance Type	RR/Poly-resistant	3	6.8	17	15.6	0.04 ^b	1	1	
	MDR	33	75.0	85	78.0		2.2	0.60-8.01	
Comorbid	Pre-XDR	8	18.2	7	6.4	0.53 ^a	6.4	1.31-31.8	
	Without comorbid	38	86.4	88	80.7		0.73	0.27-1.97	
Conversion Time	With comorbid	6	13.6	19	17.4	1 ^b	1	1	
	1-2 month	10	22.7	67	61.5		1	1	
	3-4 month	6	13.6	35	32.1		0.804	1.14	0.38-3.42
	5-6 month	2	4.5	6	5.5		0.363	2.23	0.39 - 12.63
	No conversions	26	59.1	1	0.9	<0.001	174.2	21.2-1429.5	

^aChi-Square Test

^bLogistic Regression Test

Table 4 shows two things that significantly affect the treatment outcome, i.e., age and resistance type ($P < 0.05$). While the gender, comorbid disease, and conversion time variables were not proven to affect the success of treatment.

Patients with aged < 50 years old will have 2.73 times greater chance of recovery than patients aged ≥ 50 years old.

Based on resistance pattern, rifampicin resistant or poly-resistant patients would be 6.4 times more likely to be cured compared to pre-XDR patients. However, there was no significant difference in the success rate of treatment among MDR patients compared with rifampicin resistant and poly-resistant cases.

4. Discussion

This study found the factors that have been shown to influence the success of treatment are age and resistance pattern. While gender, comorbid disease and conversion time were not proven to affect the success of treatment.

The amount of success rate treatment in this study reached 48%. Means that the number of patients declared cured is not up to half of the total number of patients. This result shows that not too different from other centers as listed in table 5.[5,8,9]

Table 5. Comparison of the success rate of drug-resistant TB treatment.

Researchers	Place	Year	Successful Rate
Manurung et al	Medan, Indonesia	2012-2015	48%
Tirtana	Semarang, Indonesia	2011	40%
Marais et al	South Africa	2013-2014	48,8%
WHO	Global	2016	52%

Marais et al. found that poly-resistant and rifampicin resistant had no significant difference in success rates. Additional resistance to Ethambutol and streptomycin does no effect on the success of MDR-TB treatment compared with patients who are resistant only to rifampicin and isoniazid.[8]

Means that as long as the drug-resistant TB patients obtain the appropriate therapeutic regimen, the success rate is not much different from that of patients diagnosed with rifampicin resistant and poly-resistant. However, patients with pre-XDR TB still have a risk of treatment failure when compared with rifampicin resistant and poly-resistant patients.

This study also revealed that comorbid disease (DM and HIV) did not affect the success rate of drug-resistant TB patients ($p > 0.05$). It also found by research conducted by Marais et al., who stated that HIV incidence did not have a significant effect on the success rate of drug-resistant TB patients.[8]

5. Conclusion

The success rate of drug-resistant TB treatment in H. Adam Malik Hospital from 2012–2015 is 48%. Age and resistance pattern proved to influence the success of drug-resistant TB treatment ($p < 0.05$), while gender, comorbidity and conversion time did not significantly ($p > 0.05$).

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