

EVALUATION OF THE CHARACTERISTICS OF MULTI-DRUG RESISTANT TUBERCULOSIS (MDR-TB) PATIENTS IN RSUD dr. LOEKMONO HADI KUDUS

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Abstract. It is estimated that there are 630,000 cases of Multidrug-Resistant Tuberculosis (MDR-TB) globally and the situation is increasing. MDR-TB is Mycobacterium tuberculosis resistance to at least two types of first-line anti-TB drugs. It is necessary to know the characteristics of groups at risk for MDR TB to increase case detection rates and provide early treatment. The purpose of this research is to find out the characteristics of MDR TB patients at RSUD dr. Loekmono Hadi Kudus. This study uses a descriptive quantitative method by design Cross-Sectional approach. Data collection was carried out retrospectively from medical records of MDR TB patients at dr. Loekmono Hadi Kudus in 2019. Data analysis used Univariate Analysis and Spearman Correlation Analysis. The sample used in this study was 51 MDR TB inpatients at RSUD dr. Loekmono Hadi Kudus in 2019. The p-value of each MDR TB patient shows results > 0.05 with a correlation coefficient (r) of 0.00 - 0.20. These results show no significant relationship with a very weak correlation level between the characteristics of MDR TB patients and the therapeutic regimen.

Key words: [Patient Characteristics, Multidrug-Resistant Tuberculosis, Therapy Regimen]

INTRODUCTION

Health development is one of the main government missions in economic development and improving people's welfare. The nutritional and health status of the community is a description of the main priority as the target and realization of health development in Indonesia. These targets were developed into more specific goals, such as efforts to control TB (infectious disease) in Indonesia which are included in the health development section (Ministry of Health RI, 2011a). Tuberculosis (TB) is an infectious disease caused by Mycobacterium Tuberculosis, this disease usually affects the lungs and other organs (Permenkes RI, 2016). One of the countries that has a high burden of tuberculosis is Indonesia among 5 countries, namely India, Indonesia, China, the Philippines and Pakistan (WHO, 2017).

MDR tuberculosis (Multidrug-Resistant Tuberculosis) is a problem with new drugs related to the dual immunity of Mycobacterium tuberculosis bacilli against at least two types of first-line anti-tuberculosis (OAT), namely Rifampicin and Isoniazid (Widiastuti, Subronto, & Promono, 2017). It is estimated that there are 630,000 cases of Multidrug-Resistant Tuberculosis (MDR-TB) globally and the situation is increasing. In 2011 there were 260 cases of MDR-TB reported in Indonesia and 2013 there were 1,800 cases of MDR-TB detected (Reviono et al., 2014). RR-TB treatment is different from fixed-dose combination treatment for 6 months given to TB patients. Drugs used for the treatment of RR-TB or multi-drug resistant TB (MDR-TB) are treated with variable combinations of first- and second-line anti-TB drugs. Treatment is usually for 18 months or more (Ndjeka & Kock, 2018). It is necessary to know the characteristics of groups at risk for MDR TB to increase case detection rates and provide early treatment (Ismah & Novita, 2017). Therefore, it is important to conduct a study to explore the characteristics of MDR TB sufferers, in addition to facilitating the success of treatment it is also useful to increase case detection rates in groups at risk of MDR TB.

METHODS

The subjects of this study were inpatient MDR TB patients dr. Loekmono Hadi Kudus in 2019 with a population of all MDR TB patients at RSUD dr. Loekmono Hadi Kudus in 2019 there were 60 patients. Samples were obtained based on total sampling based on inclusion criteria. The independent variables in this study were age, gender, length of stay, and diagnosis of disease with the dependent variable being the therapeutic regimen. This study uses a descriptive quantitative method with a cross-sectional approach design. Data collection was carried out retrospectively from medical records of MDR TB patients at dr. Loekmono Hadi Kudus in 2019. The analysis used was Univariate Analysis and Spearman's Correlation Analysis.

RESULTS AND DISCUSSION

Subject overview

This research was conducted at the MDR TB Clinic RSUD dr. Loekmono Hadi Kudus with a population of 60 MDR TB patients in 2019. Samples were obtained based on a total sampling of inpatient MDR TB patients at RSUD dr. Loekmono Hadi Kudus in 2019, 9 samples did not meet the inclusion criteria because they were not included as inpatients, so the sample used in this study was 51 patients.

Characteristics of respondents

Based on Table 1, it can be seen that the most age group in patients with Multidrug-Resistant Tuberculosis (MDR TB) is the elderly, namely the age group of 46-65 years, totaling 23 people (45.1%). At this age, there is a decrease in immune function and an increase in the frequency of adverse drug reactions. Acute or chronic illness, malnutrition, and physiological changes associated with aging can also interfere with the body's immunity, and impair the mechanism for freeing bacteria (Moharana et al., 2017).

In terms of gender, the majority of respondents were female, 26 patients (51%). This is possible because women are more often late for health services than men, and may be related to shame, so they often experience fears of being ostracized from their families and the environment due to their illness (Azzahro, Safitri, & Huda, 2015). This study is in line with the research of Kasron, Rahayu, & Sobirin (2019). The characteristics of patients based on gender show that the majority of MDR-TB patients are women, namely 58.8%. This result can be caused because women are more susceptible to infection or disease due to a heavy workload, as well as financial burdens.

Length of stay refers to the duration of the patient's stay in the hospital. The most distribution of the duration of hospitalization for MDR TB patients was 4-10 days as many as 33 MDR TB patients (64.7 %). Based on research by Burgos et al. (2005) the average length of stay in the hospital from a study conducted in San Francisco was 14 days. Tamirat (2020) states that there is no specific reference regarding the length of stay of MDR TB patients that must be lived. This may be caused by differences in health care systems, clinical conditions of patients such as disease severity, adverse side effects, and the presence of co-morbidities, such as HIV and other co-morbidities that aggravate the patient's condition. There are considerations regarding the management of hospital patients the longer the patient stays in the hospital there will be increased the risk of nosocomial infection transmission which affects the quality of care outcomes and the patient care process (Bantubani et al., 2014)

The distribution of cure rates was higher in 94.1% of patients compared. The mortality rate of 5.9% of patients in MDR TB care. In this study, the researchers did not know the discharge criteria for patients who were considered cured at RSUD dr. Loekmono Hadi Kudus. The indicator of recovery here is not measured by the release of patients from MDR TB disease, but the indicator of recovery in this study is recovery from indications that endanger the patient or reduce the severity of the TB patient's disease. MDR and patients no longer require hospitalization and are allowed to go home to be able to undergo further therapy on an outpatient basis according to the duration of the therapy regimen used.

Table 1. Respondent characteristics of Multidrug-Resistant Tuberculosis (MDR TB) Dr. Loekmono Hadi Kudus Hospital in 2019

No.	Characteristics of respondents	Frequency	Percentage (%)
1	Age	-	-
	0-11 years (Infancy and childhood)	2	3,9%
	12-25 years (Adolescence)	20	39,2%
	26-45 years (Adults)	23	45,1%
	46-65 years (Elderly years)	6	11,8%
	>65 years (Elderly age)		
2	Type sex	25	49%
	Man	26	51%
	Women		
3	Long Maintenance		
	≤3 days	4	7,8%
	4-10 days	33	64,7%
	11-20 days	11	21,6%
	>20 days	3	5,9%
4	Status circumstances	48	94,1%
	Can go home-Heal	3	5,9%
	Died in care		
5	Diagnosis disease		
	Destroyed Lung/tuberculosis Bacterial Bta [+] (A15.0)	43	84,3%
	Respiratory tuberculosis Unspecified (A15.9)	8	15,7%
6	Regimen Therapy		
	Long treatment regimens	39	76,5%
	Short treatment regimens	12	23,5%

Source: Primary data (2020)

The death rate is influenced by the severity of the disease, damage to the lungs (destroyed lung), and second-line anti-tuberculosis toxicity is higher than first-line anti-tuberculosis which often causes life-threatening side effects (Pratiwi, Yowani, & Sajinadiyasa, 2016).

Based on the Indonesian Ministry of Health (2017) the diagnosis of disease in this study referred to the International Classification of Diseases (ICD-10) which is an international standard diagnostic classification for general epidemiological purposes and various health management. The distribution of MDR TB patients was based on the most disease diagnoses with a diagnosis of destroyed lung/smear (+) bacterial tuberculosis of 43 patients and 8 patients diagnosed with respiratory tuberculosis unspecified.

The code number following the terminology refers to the category and sub-category in which the terminology should be classified. If the code only has 3 characters, it can be assumed that the category has not been subdivided (Kemenkes RI, 2017a). So the diagnosis of diseases as in Table 1 has not been subdivided into MDR TB, it is still in the form of a large group diagnosis category, namely tuberculosis with the ICD 10 diagnosis code A15.0 (Ministry of Health RI, 2017a).

The distribution of MDR TB patients with the most treatment regimens was in the Long Treatment Regimen, namely 39 patients (76.5%) because according to a statement from the RSUD, the availability of second-line OAT for the treatment of the Short Treatment Regimen in Indonesia was limited, so the number of RSUD dr. Loekmono Hadi provides a Short Treatment Regimen only for certain conditions such as HIV and Children. In this study, the individual patient circumstances were not known with certainty. In lower-middle-income countries, most of them still use the Long Treatment Regimen and require patients to carry out therapy with a minimum duration of 18 months (Matambo et al., 2020).

Correlation between characteristics and therapy regimens for MDR TB patients at RSUD dr. Loekmono Hadi Kudus in 2019

Table 2 shows the results of the p-value of the Spearman correlation test for each characteristic of MDR TB patients, the results were > 0.05 , which means that statistically, there is no significant correlation between the characteristics of MDR TB patients and the therapeutic regimen. Based on the r value for each characteristic of MDR TB patients, the results obtained are susceptible to 0.00 – 0.20 which can be interpreted that the strength of the correlation between the characteristics of MDR TB patients and the therapeutic regimen is very weak with a negative correlation direction which can be interpreted between the 2 variables not in the same direction or contradict each other. Only in the age group variable that has a positive correlation direction can it be interpreted that there is a good relationship between age and therapeutic regimen.

Age group is not significantly related to the therapeutic regimen and it can be interpreted that age is not a benchmark in determining the regimen. Similarly, the sex of MDR TB patients also does not significantly influence or correlate. The length of stay in the hospital is the long duration of the patient's stay in the hospital due to the worsening clinical condition of the patient due to the MDR TB disease itself and does not determine the choice of a therapy regimen for the patient (Tamirat, 2020).

The diagnosis of disease in this study is the initial diagnosis of tuberculosis which refers to the International Classification of Diseases (ICD-10). It can be interpreted that the diagnosis of disease in this study is not an identification category of forms of OAT resistance but rather a classification of tuberculosis diagnoses (Kemenkes RI, 2017a). So, age, sex, length of stay, and diagnosis of MDR TB patients are not related to the qualifications for choosing a therapeutic regimen.

Table 2. Correlation between characteristics and therapy regimens for MDR TB patients at RSUD dr. Loekmono Hadi Kudus in 2019

No Patients	Characteristics of MDR-TB		Therapeutic Regimen		p.s Value	coefficient correlation (r)	Information
			LTR	STR			
1	Age	12-25 years	1	1	0.502	0.046	No connection and correlation level very weak with correlation direction (+)
		26-45 years	17	3			
		46-65 years	16	7			
		> 65	5	1			
2	Gender	Man	18	7	0.460	-0.103	No connection and correlation level very weak with correlation direction (-)
		Woman	21	5			
3	Length of treatment	≤ 3 days	3	1	0.477	-0.102	No there is a relationship and the level of correlation is very weak with the direction of correlation (-)
		4-10 days	24	9			
4	Disease Diagnosis	Destroyed Lung/tuberculosis Bacteria Bta [+]	32	11	0.423	-0.112	There is no relationship and the level of correlation is very weak with the direction of correlation (-)

respiratory tuberculosis Unspecified	7	1
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There are several factors related to the selection of the MDR TB regimen, namely the results of the patient's chest x-ray, pregnancy, M. tuberculosis drug susceptibility testing (DST) of MDR TB drugs, previous treatment history, and the availability of OAT, especially second line (Anjani & Soedarsono, 2019; Mitnick, 2016). There is some evidence that chest X-ray influences or is related to the determination of regimens in MDR TB patients. Several studies have reported different features as the most common in MDR-TB patients, including cavities and bilateral involvement (He et al., 2017; Zhang et al., 2016).

Based on research Yeom et al. (2009) reported a significant correlation between bilateral and multiple findings with primary MDR-TB, and the area under the curve (AUC) reached 66%. This indicates that chest X-rays can be used to differentiate between MDR TB and drug-sensitive TB. From chest X-rays, it can also be used to consider selecting the right regimen for MDR TB patients because in the MDR TB treatment criteria bilateral disease and multiple cavities, it is not recommended to use the Short Treatment Regimen because it is entered in severe TB disease and has a high risk of treatment failure (MoHSS)., 2019).

Pregnancy is one of the most important factors in considering the selection of the right MDR TB therapy regimen. Management of MDR-TB in pregnancy is like a double-edged sword. On the one hand, second-line anti-TB drugs used for treatment are potentially teratogenic, less effective, and more dangerous, on the other hand, sub-optimal care of these patients may be dangerous. The regimen used in the treatment and the duration of therapy for patients usually use the Long Treatment Regimen with adjustments to the susceptibility pattern of the bacterial strain (Rohilla et al., 2016).

M. Tuberculosis Drug Susceptibility Testing (DST) MDR TB drugs are mandatory in the diagnostic phase of MDR TB treatment. DST is an isolate of Mycobacterium tuberculosis complex (MTBC) which is very important for the selection of effective treatment regimens and the prevention of further development of resistant forms of TB (Yakrus et al., 2016). DST can help identify the feasibility of an effective treatment regimen and full oral treatment for the majority of patients (WHO, 2018).

Drug resistance related to the history of previous treatment. The possibility of resistance occurring in patients with a history of previous treatment is 4 times, while for MDR TB it is 10 times or more compared to patients who have never been treated (Anjani & Soedarsono, 2019). In selecting the regimen, proper consideration is needed, in the use of the Short Treatment Regimen there are exclusion criteria which can mean that only patients with certain requirements can receive the regimen such as the patient is new, based on previous treatment history the patient has never been treated with second-line drugs for more than 1 month,

In lower-middle-income countries, most of them still use the Long Treatment Regimen and require patients to carry out therapy with a minimum duration of 18 months (Matambo et al., 2020). This is due to the unavailability of several second-line anti-TB drugs and substantial delays in receiving an adequate MDR-TB treatment regimen (Falzon et al., 2015). The quality of available second-line drugs can also be a problem. At present OAT producers, especially second-line, especially drugs in the Short Treatment Regimen treatment, whose quality is recognized internationally, are very limited (RI Ministry of Health, 2011b). These factors can be a high risk for MDR-TB among MDR-TB patients, where there is a shortage of second-line anti-TB drugs in a country (Falzon et al., 2015).

CONCLUSION

Based on the results of the research that has been done, it can be concluded that:

1. Based on the characteristics of MDR TB patients at Dr. Loekmono Hadi Kudus Hospital, the majority were aged 46-65 years as much as 45.1%, dominated by women as much as 51.0%, based on length of stay the average duration of patient stay was 4-10 days of 64.7 %, The status

of the patient's condition after being hospitalized 94.1% was in the status of being able to go home-Recovered and 5.9% was declared dead in treatment, based on the patient's diagnosis 83.3% of patients had Destroyed Lung / Bta Bacteria (+), the Long treatment regimen is the regimen most widely used by MDR TB patients at Dr.Loekmono Hadi Kudus General Hospital with 76.5%.

2. Age, gender, length of stay, and diagnosis of MDR TB patients did not have a significant relationship with the therapeutic regimen because the p-value results for each characteristic of MDR TB patients obtained results > 0.05 and based on the correlation coefficient (r) has a correlation that is very weak between the characteristics of MDR TB patients and the therapeutic regimen.

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