ORIGINAL ARTICLE

Two-years Biannual Evaluation of Drug-resistant Tuberculosis Patients Completing Their Treatment at Persahabatan General Hospital Jakarta

Murniati*, Diah Handayani, Fathiyah Isbaniah

Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia - Persahabatan Hospital, Jakarta

ABSTRACT

Background: Drug-resistant tuberculosis (DR-TB) is a worldwide threat, including in Indonesia, which course of treatments are time consuming and are expensive. Recent findings suggest trends in recurrence of DR-TB, while no data is available to summarize the recurrence of DR-TB in Indonesia. This study aimed to evaluate DR-TB patients which was biannually performed for two-years (e.g. at the 6th, 12th, 18th, and 24th mos) after treatment completion.

Methods: This cross-sectional study involved DR-TB patients completing their treatment at Persahabatan General Hospital Jakarta, Indonesia, between April and December 2017. The post-treatment evaluation during the 6th, 12th, 18th, and 24th mos included clinical, chest x-ray (CXR) and sputum culture examination.

Results: Sixty patients were observed in this study, 31 (51.7%) were males and 29 (48.3%) were females. The mean age was 42.3 ± 12.5 yo and the mean body mass index was 21.75 ± 4.34. Fourty nine (81.7%) patients showed extensive lesions per CXR and none of the patient showed *Mycobacterium tuberculosis* growth per sputum culture.

Conclusion: There was no recurrence of DR-TB from patients completing their treatment at Persahabatan General Hospital Jakarta, Indonesia during two-years post-treatment evaluation.

Keywords: drug-resistant tuberculosis evaluation, drug-resistant tuberculosis recurrence, radiological and microbiological tuberculosis evaluation

INTRODUCTION

Globally in 2017, it is estimated that the incidence of tuberculosis (TB) cases are 10 million (9.0-1 1.1 million) or the equivalent of 133 cases/100,000 population, the highest number in the Southeast Asia Region (44%). The top three countries are India (27%), China (9%) and Indonesia (8%). It is estimated that 3.5% of cases are multidrug-resistant tuberculosis (MDR-TB) and rifampicin-resistant tuberculosis (RR-TB) and 19% of these are cases previously treated with anti-tuberculosis drugs.[1]

Drug resistance research data indicate that an estimated 558,000 (483,000-639,000) MDR-TB/RR-TB, the highest number in China, India and the Russian Federation. There were 230,000 (140,000-310,000) people who died due to MDR-TB/RR-TB in 2017. At the end of 2017, it was reported from 127 countries that 8.5% of MDR-TB cases were accompanied by resistance to the fluoroquinolone class and the second-line injectable drug class (XDR-TB).[1]

Drug-resistant tuberculosis (DR-TB) has been treated well. However, it is still a global concern because, over the past few years, several studies have started to appear, showing that there has been a recurrence after DR-TB treatment. Reported recurrence rates varied across the globe from 0% after two years followed after recovery to 8.5% after eight years followed after recovery. DR-TB management currently available in the world requires too long a time (minimum 20 months), requires a large amount of money, both for the program and the patient. The program and the patient are factors that affect the success of DR-TB patient treatment.[2]

Worldwide DR-TB surveillance data also show unsatisfactory results in the long-term standard combination treatment success rate, which is around 50%. The management of DR-TB patients is a challenge for medical and public health professionals because drug options for treatment are limited and the threat of transmission will continue through contact with DR-TB patients.[2]

Disease recurrence is an important indicator of successful anti-tuberculosis treatment. Several studies have reported recurrencee rates after successful completion of DR-TB treatment. The study revealed that DR-TB recurrence could still occur, even in the condition of patients who received a combination of therapy individually. Recurrence rate was 0% after two years following in Nigeria, 3% after 4.8 years followed in Taiwan, 4.3% after 5.7 years in Hong Kong, 4.4% after two

years in South Korea, recurrence 5.2 % after two years followed in Peru and 8.5% after eight years in Estonia.[2–5] Examination of DR-TB patients who have recovered is considered very important to find the recurrence rate using sputum culture examinations every six months, done at least within the first two years after being declared cured.

Evaluation within 2 years after the patient is declared cured, meaning that patients who have recovered are re-evaluated for 2 years, are there any patients who have recurrence and relapsed within 2 years after recovering. Recurrence means that tuberculosis has recurred due to reactivation of the germs that have calmed down, meaning that the germs that have calmed down (dormant) are active again. While relapse means being infected again with a different germ or new germs entering. We were evaluating post-treatment drug-resistant TB (DR-TB) patients who came to control at months 6, 12, 18 and 24 to look for the recurrence and relapsed rate at the Persahabatan General Hospital Jakarta, Indonesia

METHOD

The research design was cross-sectional, conducted at the MDR pulmonary clinic of the Persahabatan General Hospital Jakarta from April 2017 - December 2017. The sample of the study was DR-TB patients who had been declared cured and had complete treatment in the last two years at the Persahabatan General Hospital Jakarta, who came to control at month 6,12,18 and 24. The sampling technique was *consecutive sampling*.
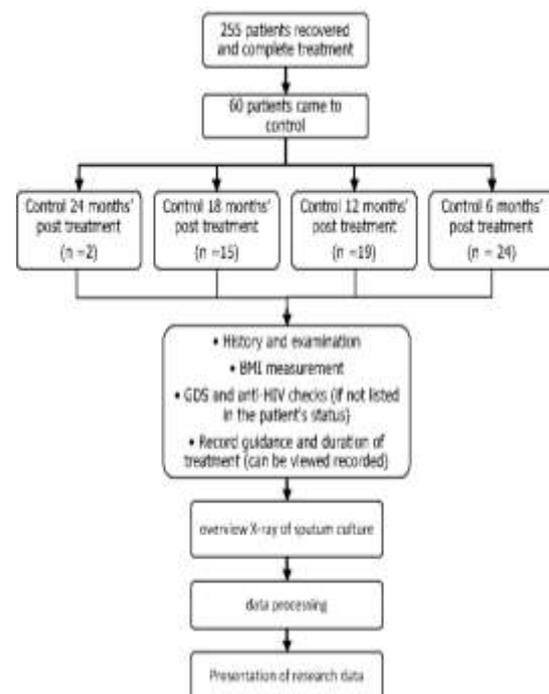

Figure 3.1. Research Flow

Acceptance criteria were patients are willing to participate in the study and sign informed consent and DR-TB patients who have been declared cured and patients who have completed treatment can undergo the research procedure. Rejection Criteria was DR-TB patients who had completed complete treatment and patients recovered but were unable to expel sputum, despite sputum induction.

This research procedure starts from DR-TB patients who have been declared cured and have complete treatment come to the Persahabatan Hospital pulmonary clinic, then screened whether they meet the criteria for acceptance and rejection. If the patient meets the admission criteria, the patient will be recorded as a participant and explained about the aims and procedures of the study. If the patient agreed, the patient signed informed consent to participate in the study.

Anamnesis was carried out regarding current complaints, measurements of body weight and height to calculate BMI. Doing a blood sugar check at a time and record the results of the anti-HIV examination listed in the patient's medical record. Records of the combination of drugs and duration of drug administration at the time of treatment are recorded. This data can also be seen in the patient's medical record.

The patient is asked to expel sputum, if the sputum cannot come out spontaneously then sputum induction is carried out, the sputum that has been accommodated is taken to the microbiology laboratory of the Friendship Hospital for culture and drug sensitivity testing using Ogawa 3% media and MGIT. Patients are asked to do a chest X-ray examination at the radiology department of Friendship Hospital. When there are results, the patient comes back with the results of the examination and is recorded as the results of the study.

RESULT

The research data collection was carried out at the MDR TB polyclinic Persahabatan General Hospital Jakarta from April to December 2017. The sample collection was carried out consecutively on DR-TB patients who had been declared cured and had complete treatment who came back for control at the Persahabatan Hospital in the first two years after recovering.

Sixty patients had been declared cured were included in this study. All patients who participated in the study met the inclusion criteria. The variables assessed in this study were characteristics which included age, sex, marital status, body mass index (BMI), final status of treatment, comorbid in the form of Diabetes Mellitus (DM) and Human Immunodeficiency Virus (HIV) infection, duration of DR-TB treatment, type of drug alloy given, lesion shape on chest X-ray at the time of control, clinical symptoms at control, type of resistance and sputum culture results taken at control.

Table 1. Profiles of DR-TB patients who recover/complete treatment who are controls over a specific period

Control Time	The number of patients come to control	The number of patients who recovered	Relative percentage of patients come to control
6th month	24	88	27.2 %
12th month	19	60	31.6 %
18th month	15	70	21.4 %
24th month	2	37	5.4 %
Total	60	255	23.5 %

The number of patients who have recovered and have complete treatment in the last two years is 255. It consists of 88 people who have recovered in the previous six months, 60 people who have recovered in the previous 12 months, 70 people who have recovered in the last 18 months, and 37 people who have recovered in the last 24 months.

Of these, we found 60 people who could be included in the study, consisting of 24 (27.2%) people who came to control at the sixth month, 19 (31.6%) people who came to control at month 12, 15 (21, 4%) people who came to control at month 18 and 2 (5.4%) who came to control at month 24. More details can be seen in Table 1. The number of patients who had been declared cured and had complete treatment was the same as the population, and the number of patients who came to control was the same as the number of samples.

The research subjects consisted of 31 males (51.7%) subjects and 29 (48.3%) female subjects with a mean age of 42.3 + 12.5 years. The research subjects were divided into three groups of age categories, namely 1 (1.7%) age <20 years, 41 (68.3%) subjects aged 20-50 years and 18 (30.0%) age> 50 years subject. Assessment of nutritional status with body mass index (BMI) obtained the nutritional status of underweight as much as 15 (25.0%), normal weight as much as 31 (51.7%), overweight as much as 11 (18.3%), and obesity as much as 3 (5.0%). There were 47 (78.3%) married patients, and 13 (21.7%) unmarried patients.

There were two patient statuses at the end of treatment, namely the recovered status of 58 (96.7%) subjects and the complete treatment status of 2 (3.3%) subjects. Recover in question is a patient who have completed treatment and ended up having a negative sputum test. If complete, the sputum was not checked when the treatment was finished at the end of the 6th month.

Table 2. Basic characteristics of subjects

Basic Characteristics	Number of Subjects (n=60)	
	n	%
Age		
<20 years old	1	1.7
20-50 years old	41	68.3
50 years old	18	30.0
Gender		
Male	31	51.7
Female	29	48.3
Nutritional Status		
Less weight	15	25.0
Normal weight	31	51.7
More weight	11	18.3
Obesity	3	5.0
Married Status		
Married	47	78.3
Unmarried	13	21.7
End of Treatment Status		
Recover	58	96.7
Complete Treatment	2	3.3
Diabetes mellitus		
Yes	16	26.7
No	44	73.3
HIV		
Yes	0	0.0
No	60	100.0
Treatment Regimen		
Conventional standard regimen	50	83.3
Individual regimen	10	16.7
Resistance type		
Rifampin resistant	15	25.0
Poli-resistant	1	1.7
MDR	36	60
Pre-XDR	7	11.7
XDR	1	1.7

There are 16 (26.7%) of patients with DM disease and 44 (73.3%) patients who did not have DM. All patients did not suffer from Human Immunodeficiency Virus (HIV) infection. Patients who received conventional standard anti-tuberculosis drug combination were 50 (83.3%) subjects, and 10 (16.7%) subjects received individual anti-tuberculosis drug combinations. Subjects consisted of several resistance patterns, namely rifampicin resistance (RR) 15 (25.0%), poly-resistance 1 (1.7%), multidrug-resistant (MDR) 36 (60%), pre-extensively drug-resistant (pre-XDR). 7 (11.7%) and extensively drug-resistant (XDR) 1 (1.7%) subjects. The description of patient characteristics in this study can be seen in Table 2.

An overview of body mass index (BMI) changes at the time of recovery compared to BMI at the time of control can be seen in Table 3. The mean BMI, when declared cured, was 20.75 + 4.06. Meanwhile, the average BMI at the time of control was 21.75 + 4.34. There was an increase in the mean BMI of patients after recovering from drug-resistant tuberculosis. By using the paired t-test, there was a significant difference between the mean BMI at recovery and the mean BMI at the arrival of control.

The median duration of treatment in months at the initial stage was 7.0 months, with a minimum duration of 5.7 months and a maximum of 10.4

months. The median duration of advanced treatment was 13.0, with a minimum duration of 10.8 months and a maximum of 20.1 months. The median total duration of treatment was 20.0 months, with a minimum duration of 18.9 months and a maximum duration of 29.2 months. An overview

of the duration of treatment can be seen in Table 4.

Table 4. Overview of treatment duration

Duration of treatment	Median (min-max)
Early stage	7,0 (5,7 - 10,4)
Advanced stage	13,0 (10,8 - 20,1)
Total treatment	20,0 (18,9 – 29,2)

Table 3. An Overview of Changes in Body Mass Index

BMI	Average±SD	SD	95% CI	P
BMI healed	20,75±4,06	0,99±1,67	0,56-1,42	<0,001*
BMI control	21,75±4,34			

Note: *Paired t test

Table 5. Description of Clinical Symptoms Based on Time of Control, X-ray image on the arrival of the control

Variables	Time of Control			
	6 months (n=24)	12 months (n=19)	18 months (n=15)	24 months (n=2)
Clinical Symptoms				
There is no symptom	13 (54,1%)	16 (84,2%)	10 (66,7%)	2 (100%)
Cough	6 (25%)	1 (5,2%)	4 (26,6%)	0 (0%)
Cough + Tightness	3 (12,5%)	1 (5,2%)	1 (6,6%)	0 (0%)
Cough + chest pain	2 (8,4%)	1 (5,2%0	0 (0%)	0 (0%)
X-ray images				
Normal	0 (0%)	1 (5,2%)	2 (13,3%)	0 (0%)
Fibroin filtrates+calcification	12 (50%)	9 (47,3%)	8 (53%)	1 (50%)
Bronchiectasis	3 (12,5%)	3 (15,7%)	0 (0%)	0 (0%)
Atelectasis	4 (16,6%)	0 (0%)	1 (6,7%)	1 (50%)
Cavity	0 (0%)	2 (10,5%)	1 (6,7%)	0 (0%)
Bulla	2 (8,3%)	1 (5,2%)	1 (6,7%)	0 (0%)
Destroyed Lung	2 (8,3%)	3 (15,7%)	2 (13,3%)	0 (0%)
Nodules	1 (4,1%)	0 (0%)	0 (0%)	0 (0%)
X-ray category overview				
Normal	0 (0%)	1 (5,6%)	2 (13,3%)	0 (0%)
Minimal Lesions	3 (12,5%)	5 (15,8%)	1 (6,7%)	1 (50%)
Extensive Lesions	21 (87,5%)	15 (78,8%)	12 (80%)	1 (50%)
Culture Results				
Positive	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Negative	24 (100%)	19 (100%)	15 (100%)	2 (100%)

Patients who came to control in the sixth month mostly had no symptoms, namely 13 (54.3%), 6 (25%) cough symptoms, 3 (12.5%) coughs accompanied by chest pain, and 2 (8), 3%). In the group of patients who came to control at the twelfth month, 16 (84.2%) had no symptoms, 1 (5.2%) cough, 1 (5.2%) cough accompanied by pain, and 1 (5.2%) cough accompanied by pain. The chest is 1 (5.2%). In the group of patients who came to control in the eighteenth month, there were 10 (66.7%) patients who did not complain of symptoms, 4 (26.6%) coughed, 1 (6.6%) cough with shortness. Patients who came to control at the twenty-fourth month, as much as 2 (100%) had no clinical symptoms. The clinical symptoms complained of by patients when they came to control can be seen in Table 5.

In the group of patients who came to control at the sixth month, there was no normal chest X-ray, 12 (50%) fibroinfiltrates and classification, 3 (12.5%) bronchiectasis, 4 (16.7%) atelectasis, 0 cavities (0 %), bullae as much as 2 (8.3%), lung yield as much as 2 (8.3%) and nodule appearance as much as 1 (4.1%). In the group of patients who came to control at the twelfth month, there was a normal chest X-ray image of 1 (5.2%), 9 (47.3%) fibroinfiltrates and

calcifications, 3 (15.7%) bronchiectasis, 0 (0) atelectasis. %), cavities as much as 2 (10.5%), bulla as much as 1 (5.2%), lung yield as much as 3 (15.7%), and nodule appearance 0 (0%).

In the group of patients who came to control at the eighteenth month, 2 (13.3%) normal chest radiographs, 8 (53.3%) fibroinfiltrates and calcifications, 0 (0%) bronchiectasis, 1 (6,7%) atelectasis %), cavities, bulla as much as 1 (6.7%), lung yield as much as 2 (13.3%) and nodule appearance 0 (0%). In the group of patients who came to control at the twenty-fourth month, there was a normal chest X-ray image of 0 (0%), fibroinfiltrates and calcifications as much as 1 (50%), bronchiectasis 0 (0%), atelectasis as much as 1 (50%), cavity 0 (0%), bulla 0 (0%), lung yield 0 (0%) and nodule appearance 0 (0%). The description X-ray images are summarized in Table 5.

The description X-ray images we categorize into standard description X-ray images, minimal lesions, and extensive lesions, can be seen in Table 4.7. Chest X-ray image at the time of sixth-month control was normal picture 0 (0%), minimal lesions were 3 (12.5%), extensive lesions were 21 (87.5%). Chest X-ray image at the time of arrival at the twelfth month of control was normal, as much as 1 (5.6%),

minimum lesions were 3 (15.8%), extensive lesions were 15 (78.8%).

The description X-ray at the eighteenth-month control time was normal, as much as 2 (13.3%). And the minimal lesions as much as 1 (6.7%) and extensive lesions as much as 12 (80%). The description X-ray image at the arrival time at the twenty-fourth-month control was no normal photo image, the minimum lesion picture was 1 (50%), and the extensive lesion picture was 1 (50%).

An overview of the culture results of *Mycobacterium tuberculosis* can be seen in table 4.8. The *M.tb* culture results in the sixth month of control were positive 0 (0%), 24 negative results (100%). The result of *M.tb* culture when the control came in the twelfth month was positive 0 (0%), negative results 19 (100%), the result of *M.tb* culture when the control came in the eighteenth month was positive 0 (0%), negative 15 (100%), the result of *M.tb* culture when the control came in the twenty-fourth month was positive 0 (0%), negative 2 (100%).

DISCUSSION

Based on the guidelines for the administration of drug-resistant tuberculosis known as Programmatic Management of Drug-Resistant Tuberculosis (PMDT) that patients who have undergone treatment of drug-resistant tuberculosis should remain evaluated at least 2 years after completing treatment. Evaluation is carried out every six months by conducting an examination of sputum breeding in patients who have been declared cured or complete treatment. This is important for early detection of recurrence in patients so that it can be given quick and precise treatment. Previously, the patients have been educated about the importance of regaining control after recovery.[6]

Researchers took data on when patients came to control in the sixth, twelfth, eighteenth and twenty-fourth months. All patients who control come with their awareness following a control schedule that has been determined by the officer. From the data, it obtained by four groups of patients based on the time the patient came to control. The largest group of patients were patients who came under control in the sixth month, and the least was the group of patients who were in control in the twenty-fourth month.

This study is a cross-sectional study so that the patients studied are different people in each group based on the control time. This data showed that the longer the distance between time healed and control time, the lower percentage of patients who came to

control. Control declared cured, and complete treatment aims to track recurrence so that when the patients found a recurrenced, it can be treated immediately.

In this study, the most age group was the productive age group of 20-50 years old, which is 41 (68%) Patients. This finding is similar to Librianty N et al. 's research that the age of drug-resistant TB patients in Persahabatan Hospital is 18-40 years old by 58.5% and age 41-60 years old as much as 36.7%. The findings are similar to the TB-RO recurrence study conducted by Chen MY et al. in Taiwan. They found that most subjects in the study were aged 35-60 years, which was 55.8%. Lee J et al. research in Korea found the study subjects' median age was 33.0 (26-50) years. This finding corresponds to the literature that the most suffering from tuberculosis disease is the productive age group.[2,7,8]

This study found that men were more found to be 31 (51.7%) Patients. These findings are similar to research conducted by Librianty N et al., they found that the most drug-resistant TB sufferers were men by 56.9%. The same things were also found in the research conducted by Chen MY et al., finding that the number of men was 77.2%, and research conducted by Lee J et al. found that male subjects were

56.7%. These findings correspond to the results of previous studies that number is more men than women. This is because men are more active outdoors than women, so men are more likely to get infections from outdoor environments. Besides, men also smoke more than women. Smoking is one of the factors that can cause tuberculosis infection.[2,7,8]

In this study, the married status was obtained for 47 (78.3%) people. A spouse or husband can become supervisors for taking medication in accordance with the government policy that a person who is currently taking anti-tuberculosis drugs must be supervised by the Drug Administration or Pengawas Minum Obat (PMO). In drug-resistant TB treatment, the PMO is a health worker, but the success of treatment cannot be separated from the role of family members, who will always remind patients to come to a health facility to get treatment according to the specified time.

In this study found 58 (96.7%) patients have recovered, then patients and complete treatment of 2 (3.3%) patients, namely one patient who came to control in his sixth month and one patient who came to control in the twelfth month. These two patients did not issue phlegm at the end of the treatment because there was no

phlegm production even though there had been sputum induction. Patients with complete treatment status are more at risk of recurrence than patients who are cured because, in those patients, it cannot be proven that the results of the sputum examination are negative at the end of treatment because there is no production of sputum.[2,8,9]

In this study, the relationship between the final status of treatment and recurrence could not be analyzed because none of the patients recurrenceed. A study conducted by Lee J et al. in Seoul found a recurrence rate of 4.4%, with four recurrenceed patients among the 90 patients studied. All patients who recurrencee are full of treating patients. The same research conducted by Chen MY et al. in Taiwan found that more patients with complete treatment were 7% more likely to experience recurrence than only 3% of patients who had a recurrence. The same was also found in research conducted by Cox H et al. in Uzbekistan that recurrencees were more common in patients with complete treatment status of 47% compared to patients with cured status of 31% with P=0.02.[2,8,9]

In this study, there were 16 (26.7%) patients who are suffering from DM but cannot be analyzed

because no patients that recurrencee. Diabetes Mellitus is a predictor factor for recurrence if not appropriately treated. Patients suffering from DM should have a blood sugar test and HbA1c every time they come under control to ensure the disease is well controlled so that recurrence can be avoided. In this study, blood sugar and HbA1c were not performed due to researchers' limitations and were not included in the research procedure. A study conducted by Chen MY et al. in Taiwan found that TB-RO patients suffering from DM had a higher recurrence rate of 5% compared to TB-RO patients who did not suffer from DM who had a recurrence rate of only 3%. Research conducted by Franke MF found that TB-RO patients suffering from DM were also an influential factor in the recurrence of the disease. According to research by Fisher-Hock, SP et al. found that TB-RO patients who had DM disease had low output. The results of some of these studies give an idea that DM can be an influential factor in TB-RO recurrence, but if DM can be adequately handled, then recurrence can be avoided.[2,10,11]

HIV infection increases the risk of tuberculosis recurrence. Based on e-TB manager data from 2013 to 2015, the number of people with HIV is estimated at 3.5%. Of these, patients who

recovered 1.3%, negligent patients had 1.5% treatment and patients who died 0.6%. In this study, there were no patients infected with HIV because of the small number, and this may be one of the factors that did not occur recurrence in the patients studied. Chen et al. concluded from the results of his study that the recurrence of common drug-resistant tuberculosis was 3.4% due to one of the factors because people with HIV lacked only 2% of all the study subjects. Gelmanova et al. concluded that the low recurrence rate of TB-MDR due to its study subjects was 99.7% HIV negative. According to research conducted by Marin et al. that tuberculosis patients infected with HIV have a 3.3 times risk of recurrence compared to tuberculosis patients without HIV infection.[2,4,12]

In this study, there were 45 (75 %) subjects who have normal nutritional status and more nutrition, 15 (25 %), which has malnutrition status. One of the factors that play a role in the recurrence is of low nutritional status. In this study, there was no recurrence because most subjects had good nutritional status. But there are 15 (25%) subjects that have malnutrition status but do not occur recurrence. It is because, despite the lack of nutritional status, the patient undergoes an improvement in nutritional status that can be assessed from a significant increase in average body mass index (BMI) after the patient recovers P<0.001. There is no recurrence in the malnourished subject group, and it can be explained that improving nutritional status can prevent a recurrence. According to Marin et al., the result showed that malnutrition status is less associated with recurrence risk. It fits the theory that an increase in body mass index can improve the body's ability to fight infection.[12,13]

In this study, the average duration of early-stage treatment is 7 months 24 days + 1 month 14 days, the average duration of advanced treatment is 14 months 1 day + 2 months 29 days. The average total duration of treatment is 21 months, 25 days + 1 month, 7 days. This finding is following TB-RO treatment guidelines in Indonesia, which is at the initial stage at least 6 months or 4 months after the conversion of breeds, and the total duration of treatment is at least 18 months. There are 2 patients who underwent the initial treatment duration less than 6 months. This is because the patient has been converted in the first month, so the initial stage is only 5 months, which is 1 month plus 4 months, then continued to the advanced stage.[10]

All patients in this study underwent treatment for more than 18 months, which led to no recurrence because all patients had been given the right combination of medications and treatment length following TB-RO control guidelines. According to research conducted by Franke et al. in Peru states that patients receiving TB MDR treatment with a combination of aggressive treatment that is a treatment given at least 18 months after conversion can reduce the recurrence rate. In this study, some patients received treatment less than 18 months after conversion, but there was no recurrence, this was due to the combination of drugs given according to the results of the drug sensitivity test, and the alloy was significant enough to kill germs.[10]

RR patients and MDR TB patients get a mixture of conventional standard drugs. Polyresistic TB, pre-XDR TB, XDR TB, and 1 MDR TB patient who experienced intolerance to conventional standard drug alloys got individual drug alloys. Pre-XDR TB and TB XDR are possible factors that allow recurrence due to the lack of a drug alloy sensitive to germs M. Tuberculosis that causes pre-XDR TB and TB XDR. But in this study, there was no recurrence despite the cases of pre-XDR TB and TB XDR, it because the patient had been treated with an individual alloy that matched the results of the drug sensitivity test. But these patients are still at risk for recurrence, therefore having to keep monitoring once every six months in the first two years after being declared cured.[2,14]

In contrast to the research conducted by Chen, MY et al. revealed that among 15 TB XDR patients, there was 1 patient (7 %) recurrence. Among 43 pre-XDR TB patients, there was 3 patients (7%) recurrence compared to MDR recurrence patients only occurred in 4 patients (3 %) among the 157 patients. Research conducted by Blondal et al. in Estonia states that drug-resistant TB recurrence is associated with resistance to second-line injectable drugs (HR 2.27, 95% CI 1.16-5.06, p = 0.04) and resistance to some kinds of drugs (HR 2.16, 95% CI 1.11-1.64, p = 0.016).[2,14]

Most of the patients in each group did not complain of clinical symptoms. Among the 60 patients, only 19 (31.7) patients complained of respiratory symptoms after being declared cured. Symptoms that are still complained about are coughing, coughing accompanied by tightness, and cough accompanied by chest pain, especially new patients who just completed the treatment that came under control in the 6th month. Compared to the group

of patients who came to control in the 6th month with the group of patients who came in the 12th month, more symptoms were found in the group of patients in control in the 6th month; most symptoms were coughing.

This finding contrasts with research conducted by Singla N et al. in New Delhi found that among the 51 patients studied, 40 (78%) patients are still complaining of residual symptoms. The most common remaining symptoms were tightness of 53%, phlegm cough 43%, cough accompanied by tightness 31%, and who did not complain of symptoms as much as 22%. Meanwhile, Singla R et al. in New Delhi found that among 46 patients, 44 (95.7%) still have the most symptoms, and symptoms are tightness as much as 40 (87%).[15,16]

In this study, most of the thorax photos in the form of images of fibroinfiltrates and calcification. It is appropriate in the literature that the picture of fibrosis and calcification is a sign of inactive tuberculosis. There are 3 patients (5 %) with a thin-walled cavitation picture in the thorax photo, 2 were obtained in the group of patients who came under control in the 12th month, and 1 was obtained in the group patients who came to control in the 18th month. Chest X-ray image in the form of a cavity is a risk factor for recurrence of drug-resistant TB because it is associated with poor drug penetration into the cavity and the large number of germs in the cavity so that even though aggressive drugs have been given, the results achieved are not optimal. But in this study the relationship between cavity and recurrence could not be analyzed because none of the patients had recurrencees.

A study conducted by Chen MY et al. in Taiwan expressed the idea that the thorax photo's cavities are an essential factor in drug resistance. In the study revealed that of the 124 patients who found cavities in the thoracic, there are 8 (7%) patients who experienced recurrence, compared to 171 patients who did not have a picture of the cavities, there are only 2 (1%) patients experienced recurrence with a P=0,03. Chen MY's findings are similar to the results of research conducted by Marin et al., they state that cavitation in the photos of the thorax is closely related to the risk of tuberculosis recurrence.[2,17]

There are two thorax photos with an infiltrated image, obtained in the group of patients who came to control in the 6th month. The infiltrate image is a sign of active infection, but this picture is still obtained in patients who have been declared cured. A photo of

fibroinfiltrates and pulmonary damage found by patients who came under control in the 6th, 12th, and 18th months, this image shows a wide pulmonary abnormality. There is one picture of nodules found in the month of the patient that comes to control in the 6th month, a picture of nodules rarely found in pulmonary patients. This patient needs to be explained that the nodules seen in the thorax photo should be further examined, such as CT-scans of the thorax and Bronchoscopy, to find out the nodules the possibility of a tumor or abnormality due to tuberculosis infection.

The findings are similar to research conducted by Singla N et al. in New Delhi, and they found that among 45 patients, the normal thorax photo picture was only 1 (2%), a minimum lesion of 16 (36%) and 28 (46.7%). A cavities picture was found in 24 (53%). While according to Singla R et al. research reporting that 46 patients were studied, all patients had a picture of bilateral radiology abnormalities, 82.6% had a comprehensive view of pulmonary abnormalities, 17% had a broad pulmonary view, and no minimal lesion pulmonary abnormalities were found. Multiple cavities reported as many as 24 (52.2%).[15,16]

The standard in the diagnosis of tuberculosis is the culture of M. tuberculosis. There are two ways that can be used to breed *Mycobacterium tuberculosis*, namely using solid media for Lowenstein-Jensen (LJ) and Liquid Media Mycobacterium Growth Indicator Tube (MGIT). Conventionally bacterial cultures are carried out in Lowenstein-Jensen (LJ) media.

The advantage of this conventional culture is the low cost with a simple procedure. At the same time, the disadvantage is that it takes a long time. Culture using the LJ medium takes about 20-56 days for diagnosis and 4-6 weeks after culture for drug sensitivity tests. It has the effect of delaying therapy for patients who are positive for bacterial culture. BACTEC MGIT is a growing medium for *Mycobacterium sp* bacteria.

The advantage of MGIT is that the culture time is relatively shorter than the culture in LJ media. Based on Hanan et al. research in 2008, the average growth of Mycobacterium tuberculosis in BACTEC MGIT 960 was 4.6 days, while in LJ, it took 37 days. Besides, Setiarsih et al. research in 2010 stated the average time it takes to detect Mycobacterium tuberculosis in medium MGIT 960 is 16 days, while it takes an average of 32 days on medium LJ.

The disadvantage of BACTEC MGIT is the number of contaminant

bacteria that can grow because it is a liquid medium. Some studies say higher levels of contamination occur in liquid media than solid media. Contamination rates in Mycobacterium tuberculosis cultures were 8.5% for BACTEC MGIT and 3% for LJ.

This study has many limitations, this study is not a cohort study, so it does not follow the patients who come to control every 6 months. The distribution of evaluated patients is not the same between the four groups, especially in the group of patients who came to control in the 24th month; the number is minimal compared to the number in the group that came control in the 6th month. The patients evaluated are patients who come passively, i.e., These patients come because of their awareness for control. There is no active search of the subject, and the thorax photo does not compare to the previous photo.

CONCLUSION

The number of patients who come to control is getting less between recovering and the control schedule. In this study found that out of 60 patients evaluated, there was no recurrence. Factors that affect recurrence cannot be analyzed because, in the study, no patients recurrenceed.

Researcher suggest to evaluation at month 18 and month 24 needs to be improved by doing home visits all patients who have been declared cured to determine the condition of patients who have completed treatment; it is necessary to evaluate all patients who have to declare cured and complete treatment once every six months, at least the first 2 years after recovery, which is carried out actively by the program's officers and managers and in cooperation with health centers and health services; it is necessary to conduct cohort research on patients who have been declared cured and complete treatment with a longer research duration; It is necessary to provide a separate room between the patient who has been declared cured and the patient whose complete treatment comes control, and the patient is still undergoing treatment; and patient data recording should be filled completely in the patient status and in the program management computer.

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