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Profile of Multi Drug Resistant Tuberculosis (MDR-TB) Patients Using Anti-TB Drugs in the Outpatient Unit of RSUD Poso Year 2022

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A B S T R A C T

The purpose of this study was to determine and further examine the description of Multi Drug Resistant Tuberculosis (MDR-TB) patients who have used anti-tuberculosis drugs in the Poso Regional General Hospital outpatient unit. This type of research is a non-experimental descriptive study (retrospective in nature) using research instruments in the form of data collection (prescriptions or medical records) of outpatient MDR-TB patients at the Poso Regional General Hospital, Central Sulawesi in 2022. Based on the results of research that has been conducted in the period January - December 2022, it can be concluded that the characteristics of treatment in Tuberculosis patients as a whole are 226 people, there are patients with MDR-TB drugs 16 people (7.08%), with a total of 127 prescription sheets (11.28%), the potential for drug interactions 36 prescriptions (28.35%) and no interactions 91 prescriptions (71.65%). Types of opportunistic infections are with a history of diabetes mellitus (DM) 6 people (37.50%), comorbid kidney and liver disease 2 people (12.50%), HIV-AIDS disease 2 people (12.50%), pneumonia 5 people (31.25%), fungal infection 1 person (6.25%). The average use of MDR-TB drugs with more than 1 type of drug will produce drug side effects on initial therapy and continued therapy with a total of 14 cases (87.50%) with different drug side effects and 2 people (12.50%) who did not experience drug side effects

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INTRODUCTION

Tuberculosis or in this case often called TB is an infectious disease caused by *Mycrobacterium tubercolulosis* (Somasundaram et al., 2014). The bacteria can invade the lungs and cause pulmonary tuberculosis (TB *pulmonary*), but it can also invade other parts of the body called extrapulmonary TB. Transmission of Mycrobacterium tuberculosis occurs when a person inhales airborne "droplet nuclei" when a person with TB coughs or sneezes. The occurrence of infection depends on the number of microorganisms inhaled or entering the body, the virulence of the microorganisms and the immune system of the patient (Tiffany, 2016; WHO, 2014).

Indonesia is in the list of 30 countries with the highest tuberculosis burden in the world and has the third highest tuberculosis cases in the world. In 2018, the incidence of tuberculosis in Indonesia in 2018 was 316 per 100,000 population, or an estimated 845,000 people who contracted tuberculosis in 2018. The WHO report also estimated the death rate from tuberculosis in Indonesia to be 35 per 100,000 population, or approximately 93,000 people died from tuberculosis in 2018. The estimated prevalence of 753 per 100,000 population due to tuberculosis is in the young and productive age group of 25 to 34 years (Kementerian Kesehatan RI, 2020).

Efforts to reduce the frequency of tuberculosis are carried out with ATDs therapy (Kementerian Kesehatan RI, 2011). Tuberculosis treatment regimen is a combination of several ATDs drugs, namely isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin given in sufficient quantities and correct doses with a treatment duration of 6 - 8 months. Treatment is carried out through 2 stages, namely the intensive stage and the advanced stage (Khutsiyah et al., 2018).

Resistance of *Mycobacterium tuberculosis* to Anti-Tuberculosis Drugs (ATDs) is one of the most common problems in curing tuberculosis. One of the forms of resistance is *Multi Drug Resistant* (MDR). MDR-TB is currently a major concern for the prevention and eradication of MDR-TB cases worldwide. Drug resistance occurs due to the use of inappropriate doses of ATDs for patients who are still sensitive to ATDs therapy. Treatment of ATDs-resistant tuberculosis is more complicated than treatment of non-resistant tuberculosis and requires more attention (Komalasari, 2020).

Multidrug resistant tuberculosis (MDR-TB) is a case of tuberculosis caused by *Mycobacterium tuberculosis* with minimal resistance to rifampicin and isoniazid together with or without other first-line Anti-Tuberculosis Drugs (ATDs) (WHO, 2010). Patients with MDR-TB need a lot of drugs in treatment, this will increase the possibility of problems related to *Drug Related Problems* (DRPs) in the categories of excessive doses, too low doses and drug interactions. Therefore, the role of pharmacy and pharmacists is very important for the success of treatment, ensuring optimal treatment efficacy, providing information, monitoring side effects of drugs, and evaluating rational drug use (Handayani et al., 2006; Musthofa, 2018).

The World Health Organization (WHO) reported in 2016 that Indonesia is one of the 27 countries with the highest number of Multidrug Resistant

Tuberculosis (MDR-TB) cases globally, with an estimated 6,800 new cases each year. The national MDR-TB estimates are 2.8% of new tuberculosis cases and 16% of treated tuberculosis cases. The success rate of treatment for MDR or *Rifampicin Resistant Tuberculosis* patients registered in Indonesia is 51%, and the success rate of treatment for MDR-TB/RR-TB patients registered in Indonesia is 40% (WHO, 2016). Currently, for rifampicin-resistant TB and MDR-TB, the priority is to implement integrated management to control drug-resistant TB (Kementerian Kesehatan RI, 2014).

Resistance to antituberculosis drugs is basically an anthropogenic phenomenon which is mainly caused by lack of treatment in tuberculosis patients and transmission from tuberculosis patients who are resistant to many of these drugs. Munir (2010: 1) points out that inadequate treatment is generally the result of one or more of the following conditions: inappropriate regimen, ATDs dose, dose and method of use, patient drug intake, ATDs deviations and non-compliance, ATDs discontinuation, and poor drug quality (Kementerian Kesehatan RI, 2014; Munir et al., 2010).

MDR-TB treatment still uses first-line ATDs and second-line ATDs that are still sensitive, thus carrying the risk of more severe side effects, longer treatment duration, more expensive treatment costs compared to tuberculosis treatment, as well as the possibility of the emergence of resistance to ATDs which will complicate treatment therapy (Munir et al., 2010; Sarwani et al., 2013). Management of MDR-TB therapy uses at least five drugs and takes 18 to 24 months. Treatment of MDR-TB cases is often associated with the occurrence of side effects ranging from mild to severe (Reviono et al., 2014).

Poso District General Hospital is one of the hospitals owned by the Poso district government which is a regional referral hospital with extensive referral health service facilities and will continue to improve the quality of services to the community (BLUD Poso, 2021). One example of efforts to improve the quality of hospital services carried out by RSUD Poso is the handling of TB patients through better treatment therapy through a standardized treatment strategy program.

The purpose of this study was to determine and further examine the description of Multi Drug Resistant Tuberculosis (MDR-TB) patients who have used anti-tuberculosis drugs in the Poso Regional General Hospital outpatient unit so that the results of this study can be a reference for Poso Regional General Hospital in improving the quality of health services to the community, especially in the treatment of MDR-TB patients.

LITERATURE REVIEW

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, which can damage the lungs and other organs (Menteri Kesehatan RI, 2016). Tuberculosis is an infectious disease that mainly affects the lung parenchyma. Pulmonary tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, which is a disease of the lower respiratory tract. Most tuberculosis bacilli enter the lung tissue through airborne transmission (*airbone infection*) which then undergoes a process known as primary infection (*primary focus*) (Wijaya & Putri, 2013).

It is called tuberculosis because it is a microbacterium, where this disease forms lumps or tubercles and is accompanied by calcification, especially in lung tissue, caused by Mycobacterium tuberculosis, classified as actinomycetes, Mycobactericeace family, genus Mycobaterium which is acid resistant, and has a size between 0.2-0.6 x 1.5-4 microns, has granules that contain a lot of metachromatic (Yuniar et al., 2017). The natural course of the disease has four stages. These stages include exposure, infection, disease, and death (Fitriani et al., 2020).

The goal of tuberculosis treatment is to cure the patient, prevent death, avoid relapse, reduce infection in others, and avoid drug resistance. The treatment lasts 6-8 months to kill bacteria that were previously dormant and can come back to life (Dormant germs). There are three anti-tuberculosis activities, the first with bactericidal drugs including isoniazid (INH), rifampicin, spiranamide. Second with drugs with sterilization ability such as ripampicin, PZA, and the third with drugs that have the ability to prevent resistance such as rifampicin and INH, while ethambutol is less effective with streptomycin. The treatment consists of two phases, namely the initial and intensive phase (2 months), in this phase the germs are killed quickly, infected patients are free of infection within 2 weeks with improved clinical symptoms and BTA positive will become negative within 2 months. The continuation phase (4-6 months), in this phase kills germs that still exist and prevents relapse. This therapy (phases I and II) in the treatment of TB requires a Supervisor of Taking Medicine. The goal is to cure the patient, prevent death, prevent relapse, break the chain of transmission and avoid germ resistance to ATDs (Fitriani et al., 2020).

Resistance of Mycobacterium tuberculosis germs to ATDs is the state or inability of ATDs to kill germs or bacteria. There are five categories of anti-tuberculosis drug resistance, namely *Monoresistant*, *Polyresistant*, *Multi Drug Resistant* (MDR), *Extensively Drug Resistant* (XDR), and *Total Drug Resistant* (Total DR) (Komalasari, 2020).

The main factor causing germ resistance to ATDs is man-made as a result of poor management of TB patients. Inadequate management of TB patients can be viewed from the perspective of service providers or health workers, patients and the TB control program. Inadequate management in terms of service providers or health workers is caused by improper diagnosis, treatment that does not use the right combination, insufficient dose, type, amount of drugs and treatment period, and inadequate counseling to patients. Management from the patient's perspective was caused by the patient not complying with the doctor's

or health worker's recommendations, irregular swallowing of antituberculosis drugs (ATDs), unilaterally stopping treatment prematurely and interference with drug absorption. Management in terms of the TB control program is due to insufficient ATDs supply and low quality of ATDs provided (*Pharmaco-vigilance*) (Komalasari, 2020; Nugrahaeni & Malik, 2015).

On the other hand, the category of causes of resistance to antituberculosis drugs (ATDs) is based on not enough drug use, irregular drug administration, insufficient evaluation and coverage, irregular drug supply, and unimplemented programs and lack of organization in the program. Recently, TB treatment has encountered a number of obstacles, one of which is the emergence of cases of resistant TB germs to first-line ATDs. Providing therapy for MDR-TB patients is more difficult, the cost of therapy is expensive and provides less than optimal results. A WHO working group called the *Green Light Committee* (GLC) has developed a strategy to treat MDR-TB by promoting the rational use of second-line drugs and improving the quality of second-line drugs. So far, no new ATDs has been found to overcome the problem of MDR-TB treatment (Munir et al., 2010).

The current MDR-TB program in Indonesia uses a standardized treatment strategy. The classification of anti-tuberculosis drugs is divided into five groups based on their potency and efficacy, namely group 1 is used for first-line ATDs that is still sensitive, used because this group is the most effective and well tolerated (for example, pyrazinamide and ethambutol); group 2 is injectable ATDs that is bactericidal (in the form of Kanamycin or Capreomycin if allergic to Kanamycin); Group 3 are fluoroquinolone drugs with strong bactericidal activity (such as Levofloxacin or Moxifloxacin); Group 4 are second-line ATDs that are highly bacteriostatic (such as Para Amino Salicylate (PAS), Ethionamide, and Cycloserine) and finally Group 5 are drugs with unclear efficacy, including new TB agents or new ATDs (such as Bedaquiline, Clofazimine, Imipenem, Amoxicillin or clavulanate and Meropenem) (Munir et al., 2010; WHO, 2014).

METHODOLOGY

Type of Research

This type of research is a non-experimental descriptive study (retrospective in nature) using research instruments in the form of data collection (prescriptions or medical records) of outpatient MDR-TB patients at the Poso Regional General Hospital, Central Sulawesi in 2022.

Research Population and Sample

The population in this study were all data and medical records or prescriptions of tuberculosis patients admitted to Poso Regional General Hospital, Central Sulawesi. The samples taken in this study were data and medical records or prescriptions of outpatient Multi Drug Resistant TB (MDR-TB) patients who used Anti Tuberculosis Drugs (ATDs) from January to December 2022.

Data Capture and Collection

Data collection and collection used is a retrospective non-experimental descriptive method, namely taking, collecting and recording prescription numbers or medical records of patients who have a history of Multi Drug

Resistant TB (MDR-TB) from the registration book, the cases taken in this study are the period January-December 2022.

Data Processing Technique

Data obtained from prescriptions or medical records of each Multi Drug Resistant TB (MDR-TB) patient based on the prescription number or medical record that has been recorded previously in the registration book. Selection of prescription data or medical records based on the study or profile of Multi Drug Resistant Tuberculosis (MDR-TB) patients using anti-tuberculosis treatment (ATDs) in the Poso Regional General Hospital outpatient unit.

Research Conceptual Framework

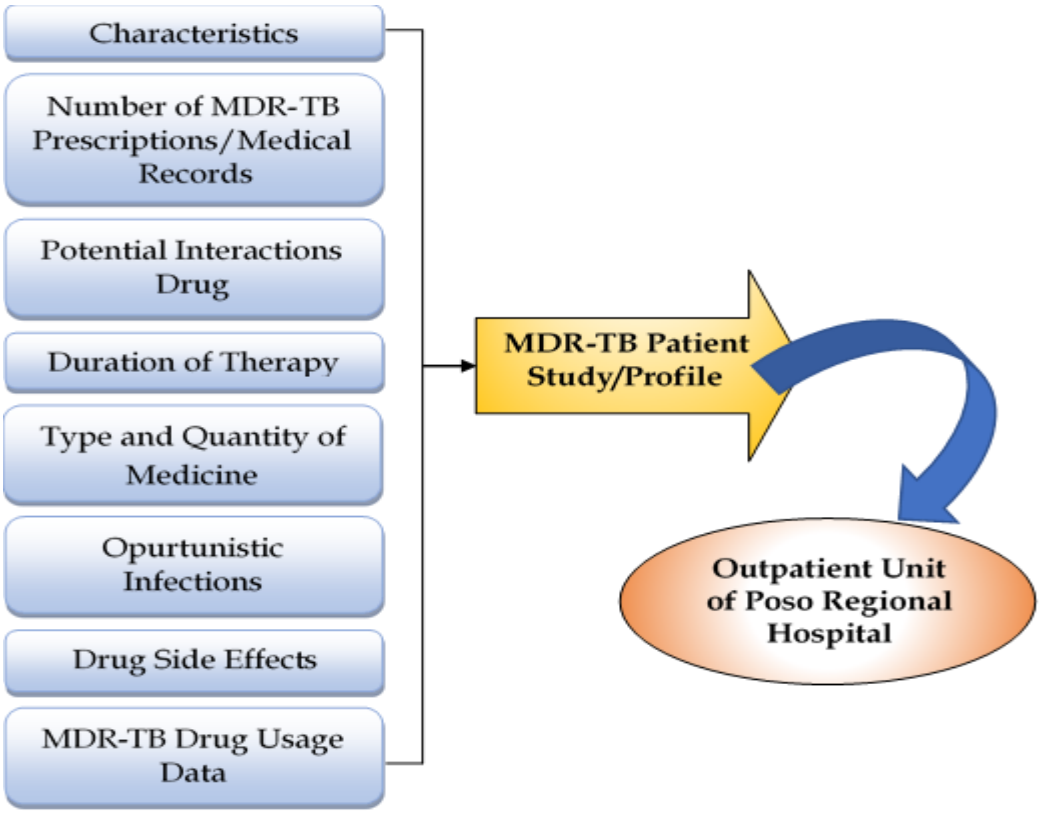

Figure 1. Research Conceptual Framework

RESULTS

Based on Gender

Table 1. Data on the Percentage of Characteristics of Tuberculosis Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022 Based on Gender

No	Gender	n (Person)	Percentage (%)
1	Male	127	56,20
2	Female	99	43,80
Total		**226**	**100%**

Based on Age

Table 2. Percentage Data on the Characteristics of Tuberculosis Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022 Based on Age

No	Patient Age (year)	n (Person)	Percentage (%)
1	1 – 9	28	12,39
2	10 – 17	8	3,53
3	18 – 25	20	8,84
4	26 – 35	28	12,39
5	36 – 45	25	11,10
6	46 – 55	43	19,02
7	56 – 65	42	18,58
8	66 – 75	21	9,29
9	76 – 84	9	3,98
10	85 – 89	2	0,88
Total		**226**	**100%**

Based on Patient

Table 3. Data on the Percentage of Tuberculosis Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022 Based on Patients

No	Type of Patient	n (Person)	Percentage (%)
1	Drug-Sensitive TB Patients	210	92,92
2	MDR-TB Patients	16	7,08
Total		**226**	**100%**

Based on Number of Prescriptions

Table 4. Data on the Percentage of Tuberculosis Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022 Based on the Number of Prescriptions

No	Type of Patient	n (recipe sheet)	Percentage (%)
1	Drug-Sensitive TB Patients	999	88,72
2	MDR-TB Patients	127	11,28
Total		**Total**	**100**

Based on the Potential Occurrence of Drug Interactions

Table 5. Data on the Percentage of Potential Drug Interactions in Tuberculosis-Multi Drug Resistant (MDR-TB) Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022

No	Potential Drug Interactions	n (recipe sheet)	Percentage (%)
1	Interaction Occurs	36	28,35
2	No Interaction	91	71,65
	Total	**127**	**100**

Based on Length of Patient Therapy

Table 6. Data on the Percentage of Length of Therapy in Tuberculosis-Multi Drug Resistant (MDR-TB) Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022

No	Conversion Month	Initial Stage Duration (a)	Length of Treatment (b)	Advanced Stage Duration (b-a)	n (person)	Percentage (%)
1	0-2 months	12 months	24 months	12 months	8	50,00
2	3-4 months	+ 13 months from the month of conversion	+ 22 months from the month of conversion	12 months	5	31,25
3	5-8 months	+ 10 months from the month of conversion	+ 22 months from the month of conversion	12 months	3	18,75
		Total			**16**	**100%**

Based on Type and Quantity of Medicine

Table 7. Percentage Data on the Type and Amount of Drugs in Tuberculosis-Multi Drug Resistant (MDR-TB) Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022

No	Type of medicine	n (Total)	Percentage (%)
1	Levofloxacin 250 mg	23040	18,18
2	Ethionamide 250 mg	17280	13,63
3	Pyrazinamide 500 mg	17280	13,63
4	Ethambutol 400 mg	17280	13,63
5	Isoniazid 300 mg	11520	9,10
6	Bedaquiline 100 mg	23040	18,18
7	Clofazimine 100 mg	5760	4,54
8	Vitamin B6 25 mg	11520	9,15
	Total	**126720**	**100%**

Opportunistic Infections in MDR-TB Patients

Table 8. Data on the Percentage of Opportunistic Infections in Tuberculosis-Multi Drug Resistant (MDR-TB) Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022

No	Types of MDR-TB Opportunistic Infections	n (person)	Percentage (%)
1	Diabetes Melitus (DM)	6	37,50
2	Comorbid kidney and liver disease	2	12,50
3	HIV-AIDS Disease	2	12,50
4	Pneumonia	5	31,25
5	Fungal Infection	1	6,25
	Total	**16**	**100**

Data on Drug Side Effects in MDR-TB Patients

Table 9. Data on the Percentage of Drug Side Effects in Tuberculosis-Multi Drug Resistant (MDR-TB) Patients in the Outpatient Unit of RSUD Poso for the Period January - December 2022

No.	Drug Side Effects	n (Number of Cases)	Persentase (%)
1	Gastrointestinal disorders (nausea, vomiting, gastritis, diarrhea), impaired liver function, gouty arthritis, peripheral neuropathy, icteric with or without vomiting	5	31,25
2	Peripheral neuropathy (Peripheral nerve disorders), Visual impairment, color blindness, toxic psychosis, impaired liver function, seizures	2	12,50
3	Cardiac distress, nausea, headache, dizziness, reddish color of urine, feces and other body fluids, brown-black color of lesions and skin	3	18,75
4	Renal function abnormalities, visual impairment, color blindness, peripheral neuritis (peripheral nerve disorders), gastrointestinal disorders	1	6,25
5	Hearing loss, numbness or tingling of the skin, seizures	0	0
6	Depression, peripheral neuropathy (peripheral nerve disorders), insomnia	0	0
7	Sleep disturbance, weakness, nausea and diarrhea	3	18,75
8	Seizures, allergic reactions (difficulty breathing, throat closure), swelling	0	0
9	Did not experience any drug side effects	2	12,50
	Total	**16**	**100**

DISCUSSION

Multidrug Resistant Tuberculosis (MDR-TB) is a case of tuberculosis caused by *Mycobacterium tuberculosis* that is minimally resistant to multiple drugs (rifampicin and isoniazid) simultaneously, with or without other first-line antituberculosis drugs (ATDs). Antituberculosis drug resistance tuberculosis is essentially a man-made phenomenon due to inadequate treatment of tuberculosis patients as well as the result of one or more of the conditions of inappropriate ATDs regimen, dosage, and usage, irregularity or non-compliance of patients in taking drugs, interruption of ATDs availability, and very low drug quality.

One example of efforts to improve the quality of hospital services carried out by RSUD Poso is handling tuberculosis patients through better treatment therapy with a standardized treatment strategy program. Further studies on multidrug resistant tuberculosis patients in the outpatient unit of Poso Regional General Hospital who used antituberculosis treatment during 2022 (January-December period) were very varied, this can be seen in terms of characteristics (gender, patient age, patient type), number of prescriptions, drug interactions, duration of therapy, opportunistic infections, adverse drug effects and evaluating the use of the type and amount of antituberculosis drugs in MDR-TB patients at Poso Regional General Hospital.

In the results of research that has been conducted in the outpatient unit of Poso Regional Hospital for the period January - December 2022, it can be seen that tuberculosis patients with male gender are 127 people (56.20%), and 99 people (43.80%) are female. From the results of these percentages, it is clear that male patients have the most history of tuberculosis disease both in drug-sensitive TB treatment therapy and drug-resistant TB treatment therapy. The results of the search that has been done, this is due to men having a heavy workload, mobility, and unhealthy lifestyles such as smoking and consuming alcohol. According to (Jiménez-Corona et al., 2006), tuberculosis (TB) cases in some countries are twice as common in men as in women, which is generally due to biological and epidemiological characteristics and socioeconomic and cultural barriers to accessing health services. In addition, this is also reinforced in the report of the Ministry of Health of the Republic of Indonesia in 2023, which states that the total number of tuberculosis cases, tuberculosis cases with male gender amounted to 57.7% in 2021 and 57.8% in 2022, while female gender amounted to 42.3% in 2021 and 42.2% in 2022 (Kementerian Kesehatan RI, 2023). The results of the study can be seen in table 1.

Characteristics of patients based on patient age with the period January - December 2022 in the outpatient unit of Poso Regional Hospital, it is clear that the age of patients who have a history of Tuberculosis is very varied starting with ages between 1 - 9 years with a total of 28 people (12.39%), ages between 10 - 17 years with a total of 8 patients (3.53%), ages between 18 - 25 years ranging from 20 people (8.84%), age 26 - 35 years ranged from 28 people (12.39%), age 36 - 45 years ranged from 25 people (11.10%), age 46 - 55 years with a total of 43 patients (19.02%), age 56 - 65 years ranged from 42 people (18.58%), age 66 - 75 years with a total of 21 patients (9.29%) and patient age 76 - 84 years with a total of 9 people

(3.98%) and patient age 85 - 89 years with a total of 2 people (0.88%). Patients with various ages in this study were patients with drug-sensitive TB treatment therapy and drug-resistant TB treatment therapy, but the highest tuberculosis cases were in the age range of 46-55 with a percentage of 19.02%, in second place in the age range of 56-65 years with a percentage of 18.58% of the total 226 people (patients) as a whole (Table 2). This is based on the age range that spends time and energy to work so that a lot of energy is drained, reduced rest time so that the immune system decreases. In theory, the group of tuberculosis patients is mostly in the age range of 15-55 years (in productive age). This is also reinforced in the report of the Indonesian Ministry of Health in 2023 that tuberculosis (TB) patients in 2021 or 2022 had the highest age group in the range of 45-54 years (male gender) and the range of 15-24 years (female gender) (Kementerian Kesehatan RI, 2023).

The results of the study described in table 3 show that the percentage of characteristics in Tuberculosis patients in the outpatient unit of Poso Hospital for the period January - December 2022 based on the type of patient is for Drug-Sensitive TB as many as 210 people (92.92%), and Drug-Resistant TB (MDR-TB) as many as 16 people (07.08%). Basically, patients with Drug-Resistant TB have a long treatment history because it is possible that there are several types of drugs that are resistant to *Mycobacterium tuberculosis*, thus increasing the possibility of *Drug Related Problems* (DRPs) in the categories of over-dose, subdose and risk, as well as more severe side effects, this is characterized by patients whose sputum examination results remain positive or become positive again in the 5th month or more throughout the healing period; or at any time during the healing period obtained from laboratory results that show the presence of ATDs resistance.

In terms of the percentage of the number of prescriptions for Tuberculosis patients in the outpatient department of RSUD Poso for the period January - December 2022, the results were obtained in TB-Sensitive Drugs as many as 999 prescription sheets (88.72%), and TB-MDR Drugs as many as 127 prescription sheets (11.28%). Details of the number of prescriptions obtained for TB-Sensitive Drugs in January were 15 prescription sheets, February were 28 prescription sheets, March were 38 prescription sheets, April were 43 prescription sheets, May were 52 prescription sheets, June were 58 prescription sheets, July were 85 prescription sheets, August were 106 prescription sheets, September were 121 prescription sheets, October were 153 prescription sheets, November were 185 prescription sheets, and December were 226 prescription sheets. While the details of the number of prescriptions obtained for TB-MDR drugs in January were 2 prescription sheets, February 0 prescription sheets, March 2 prescription sheets, April 3 prescription sheets, May 5 prescription sheets, June 0 prescription sheets, July 1 prescription sheet, August 0 prescription sheets, September 1 prescription sheet, October 2 prescription sheets, November 0 prescription sheets, and December 0 prescription sheets. The research results can be seen in table 4.

The results of the research conducted as in table 5 show that the percentage of Potential Drug Interactions in outpatient Tuberculosis-Multi Drug Resistant (MDR-TB) patients at Poso Hospital for the period January - December 2022, namely in MDR-TB patients who experienced drug interactions as many as 36

sheets (28.35%) and in MDR-TB patients who did not experience drug interactions as many as 91 sheets (71.65%). The occurrence of drug interactions is based on several events in MDR-TB treatment such as Isoniazid (INH) drugs often cause hepatitis and hepatotoxic effects, INH sometimes increases when Rifampicin is used. At a moderate level of interaction is usually found with ethambutol and ethionamide, the usual symptoms are neuropathy in the form of numbness in the hands or feet, pain, tingling and burning, sometimes a dose reduction is made or the use of ethambutol and ethionamide is stopped. Dosage use sometimes does not exceed the prescribed dose in order to limit further damage. The use of levofloxacin, which is a floroquinolone class drug, can interact with vitamin B6 so that levofloxacin will reduce pyridoxine levels or effects by changing the intestinal flora. In addition, drug interactions occur due to the use of multiple drugs, resulting in resistance to Isoniazid and Rifampicin with or without resistance to other drugs.

The results of the research that has been done, obtained the results in the form of the length of special therapy for Tuberculosis-Multi Drug Resistant (MDR-TB) patients in the outpatient unit of Poso Regional Hospital for the period January - December 2022, where the length of therapy with a conversion month of 0 - 2 months with an initial stage of 12 months and a length of treatment of 24 months with an advanced stage for 12 months was obtained by 8 people (50.00%). Conversion month 3 - 4 months with the initial stage plus +13 months from the conversion month then plus +22 months from the conversion month for the length of treatment and advanced stage for 12 months obtained 5 people (31.25%). Conversion months of 5 - 8 months with the initial stage plus +10 months from the conversion month with the length of treatment plus +22 months from the conversion month with an advanced stage of 12 months were obtained by 3 people (18.75%). In addition, at Poso Hospital, treatment therapy was also obtained with a length of therapy ranging from 9 - 11 months depending on the complete treatment therapy both in first-line treatment and with second-line treatment. The results of the study can be seen in table 6.

In table 7 obtained from the recapitulation results in the study, it can be seen that the percentage of the number of drugs in Tuberculosis-Multi Drug Resistant (MDR-TB) patients in the outpatient unit of Poso Hospital in the period January - December 2022 was Levofloxacin 250 mg as much as 23040 (18. 18%), Ethionamide 250 mg 17280 (13.63%), Pyrazinamide 500 mg 17280 (13.63%), Etambutol 400 mg 17280 (13.63%), Isoniazid 300 mg 11520 (9.10%), Bedaquiline 100 mg 23040 (18.18%), Clofazimin 100 mg 5760 (4.54%) and Vitamin B6 25 mg 11520 (9.15%). With a total n = number of tablets ranging from 126720 (100%).

In the results of the study, it was found that the percentage of opportunistic infections in Tuberculosis-Multi Drug Resistant (MDR-TB) patients in the outpatient unit of RSUD Poso for the period January - December 2022 was with Diabetes Mellitus (DM) as many as 6 people (37.50%), with comorbid kidney and liver disease as many as 2 people (12.50%), with HIV-AIDS disease as many as 2 people (12.50%), with pneumonia as many as 5 people (31.25%), and with fungal infections as many as 1 person (6.25%). According to (Agarwal et al., 2015), suggested that opportunistic infections are manifestations by pathogens that are

more common in humans and are not invasive but when they enter the body can cause weak immunity. In 2005, the dominant opportunistic infections that usually appear in people with AIDS such as pulmonary tuberculosis (50%), hepatitis (30%), candidiasis (25%), pneumonia (33%), followed by chronic diarrhea, and extra-pulmonary tuberculosis (Framasari et al., 2020). The research data obtained can be assumed that MDR-TB patients at RSUD Poso are indeed patients who come with several comorbidities so that the treatment of Tuberculosis is basically accompanied by other treatments in accordance with the opportunistic diseases obtained.

In the treatment of MDR-TB patients at Poso Hospital in the period January - December 2022, various side effects of drugs were obtained which can be seen from the use of drug combinations, found the incidence of Side Effects of Drugs in patients including gastrointestinal disorders (nausea, vomiting, gastritis, diarrhea), impaired liver function, gouty arthritis, peripheral neuropathy (peripheral nerve disorders), jaundice with or without vomiting with a total of 5 cases (31.25%). Peripheral neuropathy (peripheral nerve disorders), visual disturbances, color blindness, toxic psychosis, impaired liver function, seizures as many as 2 people (12.50%). Cardiac disorders, nausea, headache, dizziness, reddish color of urine, feces and other body fluids, brown-black color of lesions and skin as many as 3 people (18.75%). Kidney function abnormalities, visual disturbances, color blindness, peripheral neuritis (peripheral nerve disorders), gastrointestinal disorders as many as 1 person (6.25%). Sleep disorders, weakness, nausea and diarrhea as many as 3 people (18.75%). While those who did not experience Side Effects of Drugs were 2 people (12.50%).

Various results, data and direct interviews that have been conducted, Poso Regional General Hospital has succeeded in handling tuberculosis patients appropriately and efficiently both in Drug Sensitive-TB and in Drug MDR-TB, this can be seen from the results of providing regular treatment to patients as well as suppressing the spread and control of tuberculosis in the Poso area by involving all elements of the hospital through seminars on tuberculosis, IEC (Information, Education, Communication) activities on drugs by Pharmacists, involving Tuberculosis cadres according to their roles and duties through the delivery of information, counseling and training. In addition, Poso Regional Hospital and the local government are active in implementing the national strategy for tuberculosis control with various structured programs. The implementation of these strategies is monitored regularly and evaluated systematically to achieve success in tuberculosis management.

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of research that has been conducted in the period January - December 2022 on the profile of Multi Drug Resistant Tuberculosis (MDR-TB) patients using anti-TB drugs in the outpatient unit of Poso Hospital, it can be concluded that the characteristics of treatment in Tuberculosis patients as a whole are 226 people, there are patients with MDR-TB drugs as many as 16 people (7.08%), with a total of 127 prescription sheets (11.28%), the potential for drug interactions as many as 36 prescriptions (28.35%) and no interactions as many as 91 prescriptions (71.65%), with the length of therapy with months of conversion between 0-2 months as many as 8 people (50.00%), 3-4 months as many as 5 people (31.25%), 5-8 months as many as 3 people (18.75%) with a total of 16 patients with MDR-TB, and the use of the highest number of drugs is Levofloxacin 250 mg and Bedaquiline 100 mg with a total of 23040 (18.18%) each than other drugs. Types of opportunistic infections are with a history of diabetes mellitus (DM) as many as 6 people (37.50%), comorbid kidney and liver disease 2 people (12.50%), HIV-AIDS disease 2 people (12.50%), pneumonia 5 people (31.25%), and fungal infection 1 person (6.25%). The average use of MDR-TB drugs with more than 1 type of drug will produce drug side effects on initial therapy and continued therapy with a total of 14 cases (87.50%) with different drug side effects and 2 people (12.50%) who did not experience drug side effects.

The assessment and profile of the use of anti-tuberculosis drugs in MDR-TB patients in the outpatient unit of RSUD Poso should continue to be evaluated and monitored continuously in order to create success in the handling and control of tuberculosis with targets and strategies.

FURTHER STUDY

It is recommended to further study the treatment of MDR-TB with a combination of drugs in various lines of treatment (line 1 and 2) based on the classification of TB patients, as well as treatment of pediatric tuberculosis with a combination of drugs so that additional data can be obtained for further treatment of tuberculosis so as to create success in appropriate and efficient treatment, especially at Poso Hospital.

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