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The Relationship of Drug Therapy Problems and Outcome Therapy in Tuberculosis Patients in Surabaya Health Center

I Nyoman Wijaya[1]*, Luthfia Andini Nathaneila[1], Yuni Priyandani[1]
1. Pharmacy Practice Department, Faculty of Pharmacy, Airlangga University, Surabaya, East Java, Indonesia

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Corresponding Author:
I Nyoman Wijaya

Corresponding Author Email:
i-nyoman-w@ff.unair.ac.id

ABSTRACT

Background: Tuberculosis (TB) is a highly contagious disease and is difficult to eradicate in Indonesia. Indonesia ranks second in the number of TB sufferers in the world. Generally, TB patients use more than two types of drug therapy, it can affect the drug therapy problems that arise and can affect the success of treatment.

Objectives: This study aims to see the effect of the number of drugs used by TB patients on the number of drug therapy problems (DTP) and therapy outcomes in tuberculosis patients.

Methods: This study was a cross-sectional study with purposive sampling conducted at health centers in the Surabaya area in January-June 2024. The sample inclusion criteria included pulmonary tuberculosis patients who had undergone treatment for over one month, were at least 17 years old, and could communicate well using a guided interview method.

Results: The results showed that out of 110 patients, 30.0% used 4 types of drugs and 30.0% had two DTPs. Spearman's correlation test between the number of drugs and the number of DTPs with a p-value = 0.000 and a correlation coefficient of 0.472. Spearman's correlation test between the number of DTPs and therapy results with a p-value = 0.430 and a correlation coefficient of -0.076.

Conclusion: From this study, it can be concluded that there is a significant relationship between the number of drugs and the number of DTPs in TB patients and there is no relationship between DTP and the results of therapy in TB patients. Therefore, pharmacists at health centers need to keep helping patients understand how to follow their TB treatment correctly, including the right dose, timing, intervals, and length of the treatment.

Keywords: DTPs; Health centers; Outcome therapy; Tuberculosis

INTRODUCTION

Tuberculosis (TB) disease is an infectious disease caused by the bacteria *Mycobacterium tuberculosis*. The TB bacteria are easily spread through the air when TB patients cough, sneeze, and talk without wearing a mask [1]. Data from the Global Tuberculosis Report 2022, reports that there are 10.6 million tuberculosis (TB) cases in the world, 6.4 million (60.3%) people who have undergone treatment, and 4.2 million (39.7%) who have not been diagnosed. The number of TB cases in Indonesia in 2021 was 9.2% of world TB cases, making it the country with the second most cases after India. The number of TB death cases in Indonesia is high, reaching 93,000 per year or the equivalent of 11 deaths per hour [2].

The country's location on the equator causes Indonesia to receive large amounts of sunlight, as a result of which evaporation occurs in Indonesia so that the high humidity level in the air causes TB transmission to occur easily. In 2021, the number of TB cases found was 397,377 cases. East Java 44.6%, and Central Java 44.6% are the provinces with the highest number of TB cases in Indonesia [3]. Surabaya, with a total of 10,382 TB cases, is the city with the highest number of TB cases in East Java. The recovery rate of TB patients in Surabaya reached 56.8%, which is still below the minimum figure that must be achieved, namely 85.0% [4].

Anti-TB drugs that are included in the first line are isoniazid, ethambutol, pyrazinamide, rifampicin and streptomycin. The administration of anti-TB drugs must be in the form of a combination of several types of drugs to prevent resistance, given in sufficient quantities, and in the right dose according to the treatment category [5]. Therefore, tuberculosis patients must use medications correctly, following the five rights: the right medication, right dosage, right timing, right intervals, and right duration. Patient compliance with TB treatment is crucial for achieving recovery, preventing transmission, and avoiding drug resistance. Patient recovery can be achieved through effective collaboration between patients, health care professional, health service providers, and the community [6]. A study at the Pegirian Health Center revealed that out of 44 TB patients, 42 experienced Drug Therapy Problems (DTP), with 13.5% having too low a dose, 73.1% experiencing unwanted drug reactions, 1.9% receiving too high a dose, and 11.5% being non-compliant [7]. DTP refers to problems related to drug therapy that can interfere with treatment goals, requiring assessment by health care professional or pharmacists to resolve [8]. In 2022, Indonesia's national TB treatment success rate was 86.0%, with success rates per province ranging from 72.1% to 96.2%. East Java Province achieved a success rate of 89.0% [3]. TB treatment faces challenges related to patient compliance, which can be influenced by factors such as the long duration of treatment, patients prematurely stopping medication due to feeling cured, lack of knowledge, reluctance to seek treatment, lack of family support, low self-motivation, and low levels of education [9].

Due to the lengthy TB treatment, the high incidence of DTPs in TB patients, and the low rates of successful therapy, this study seeks to investigate the possible correlation between the number of DTPs in patients and the outcomes of TB treatment and research like this has never been conducted on TB patients in Surabaya.

METHODS

Study design

This research is a descriptive study with a cross-sectional approach with accidental sampling carried out in four community health centers in the Surabaya region (Dr. Soetomo Health Center, Perak Timur Health Center, Pacar Keling Health Center, and Sidotopo Wetan Health Center) in January-June 2024.

Population and samples

The study sample included patients who had been diagnosed with pulmonary tuberculosis and had undergone treatment for more than one month, were at least 17 years old, and could communicate effectively. The research sample excluded patients with multidrug-resistant or drug-resistant TB. The researchers used the Slovin formula to calculate the sample size from a population of 573 cases, resulting in an initial estimate of 85 samples. However, the researchers later increased the sample size to 110 [4].

Study instruments and Data collection

Data collection was conducted using a structured interview method. It included gathering demographic data, patient lifestyle, disease history, treatment history, patient compliance with treatment, and observe the results of the acid-fast bacillus test in the patient's medical records.

Data Analysis

The determination of DTP is based on the existing standards in the textbook Pharmaceutical Care Practice 3rd Edition. Unnecessary drug therapy DTP occurs when a patient receives a drug that is not indicated. Additional drug therapy DTP occurs when a patient requires additional drug therapy to treat other complaints and achieve therapeutic targets. Ineffective drug therapy DTP occurs when the drug used by the patient does not provide a therapeutic effect. Too low a dose DTP occurs when the dose of the drug used is too low from the standard and does not reach the desired target. Too high a dose of DTP occurs when the dose of the drug used exceeds the standard and causes toxic effects. Adverse drug reactions DTP happen when there is an undesirable drug reaction to the therapeutic dose of the drug. Non-compliance DTP occurs when the patient does not comply with using the drug according to the doctor's instructions [8].

The treatment progress is assessed based on the results of the acid-fast bacillus test in the patient's medical record. The research findings, presented in tabular form, include descriptive data, and correlation tests are performed using statistical analysis software.

RESULTS AND DISCUSSION

In Table I the demographic profile of 110 research participants is presented. The sample consisted of 60.0% males, and 72.7% of the participants were aged between 19 and 59 years. 42.7% of the participants had an elementary school education, and 40.0% were unemployed. According to the World Health Organization (2022), the prevalence of tuberculosis is higher in men compared to women [2]. This is attributed to factors such as higher mobility of men outside the home, heavier workloads, and unhealthy lifestyles including smoking and alcohol consumption, which can weaken the immune system [10]. These findings align with the health data profile of the City of Surabaya in 2020, which also indicates a higher incidence of tuberculosis among men compared to women [4].

The study results revealed that the majority (72.7%) of respondents were aged 19-59 years. Tuberculosis is often found in the 19-59 age group because the immune system generally begins to decline in this range, making people more susceptible to contracting tuberculosis [11]. This correlates with the findings of Andayani's research in 2017, which showed that individuals in the productive age group are highly active outside the home, frequently interacting with others, including tuberculosis sufferers [12]. Elementary school graduates represent the largest percentage of education levels in this study, at 42.7% of respondents. This finding is consistent with Mientarini's (2018) research, which reported that 33.0% had an elementary school education, the highest percentage [13]. Education plays a crucial role in enhancing knowledge, attitudes, and behaviors related to understanding tuberculosis. The level of education among tuberculosis patients can impact their understanding of tuberculosis treatment and prevention [14].

Based on Table II, it is known that the largest number of drug items obtained by each respondent was a combination of 4 drugs (30.0%). The combination of 4 drugs obtained by patients consisted of variations of anti-TB, anti-nausea, antiplatelet, antihistamine, anti-asthma, antidiabetic, antipyretic, analgesic, cough medicine, and vitamins. TB patients, in addition to receiving anti-TB, also received other drugs to treat symptoms that appear together with tuberculosis infection [15]. These results are in line with research by Fortuna et al. (2022), which stated that in addition to anti-TB, patients also received many other drugs such as cough medicine, bronchodilators, antipyretics, vitamins and minerals, and others [16].

In Table III, it was observed that out of 110 respondents, there were numerous cases of Drug Therapy Problems (DTPs). The DTP analysis was based on the drugs used, the complaints reported by the respondents, and the behavior or experiences of the patients during treatment. A total of 202 DTPs cases were identified from the 110 respondents, with the highest number of DTPs (81 cases, 40.1%) being related to adverse drug reactions.

Unnecessary drug therapy DTP can occur when the drugs prescribed to a patient are compared with the doctor's diagnosis or the patient's complaints, and it's found that the patient doesn't actually need to take those drugs. In a recent study, 3 cases (1.5%) of unnecessary drug therapy DTP were identified. These cases involved patients who were using antacids, Na diclofenac, and simvastatin without indicating their use of these drugs. Additionally, some patients were given domperidone therapy even though they didn't experience nausea and vomiting. These findings contrast with those of other researchers who reported a 0.0% rate of unnecessary drug therapy DTP [7,17]. This disparity might be due to differences in the methods of collecting data in the field, such as how patient information is gathered. If information collection is thorough and detailed, including laboratory data and careful observation of patient symptoms and complaints, the study results are likely to be more accurate.

The need for additional drug therapy DTP can be determined by evaluating any new complaints or conditions experienced by the patient. In this study, 3.9% of patient complaints required additional drug therapy, including cases of diarrhea, high cholesterol, and itching. Research conducted by Khotimah et al. in 2023 showed that 12.0% of patients required additional drug therapy DTP [17]. In this study, there was 1 case (0.5%) of ineffective drug DTP. This DTP occurred in TB patients with comorbid DM who consumed dexamethasone tablets. Dexamethasone is used to treat sore throat and needs close monitoring of blood glucose in patients with DM, because it can cause increased gluconeogenesis in the liver and insulin resistance [18]. Therefore, dexamethasone is not effective in curing sore throats, and the risks outweigh the benefits.

Too high a drug dose is caused by the patient taking more medicine than the recommended dosage based on their weight. This exceeds the guidelines for the management of tuberculosis in Indonesia and the regulation of the Minister of Health No. 67 of 2016 [5]. Additionally, a high dose of DTP can also result from drug interactions, leading to increased drug levels in the blood and toxic effects. In a recent study, 15 cases (7.4%) of drug doses DTP were found to be too high. For example, a patient weighing 45 kg should have taken 3 tablets but took 4 tablets, and a patient weighing 32 kg should have taken 2 tablets but took 3 tablets. There is a drug interaction

Table I. Demographic data of respondents

Characteristics of respondents	N (%)
Sex	
Man	66 (60.0)
Woman	44 (40.0)
Age (years)	
17-18	8 (7.3)
19-59	80 (72.7)
60-80	22 (20.0)
Education	
No Educated	6 (5.5)
Elementary School	47 (42.7)
Junior High School	18 (16.4)
High School	36 (32.7)
Bachelor's Degree	3 (2.7)
Occupation	
Not Working	44 (40.0)
Students	9 (8.2)
Self-Employed	25 (22.7)
Private Employee	32 (29.1)

Table II. Number of drugs used per patient

Number of drug Items per patient	N (%)
1 drug	9 (8.2)
2 drugs	25 (22.7)
3 drugs	21 (19.1)
4 drugs	33 (30.0)
5 drugs	16 (14.6)
≥6 drugs	6 (5.4)
Total	110 (100.0)

Table III. Types of DTP that occurred to respondents

Type of DTP	N (%)
Unnecessary drug therapy	3 (1.5)
Need additional drug therapy	8 (3.9)
Ineffective drug	1 (0.5)
Dosage too high	15 (7.4)
Dosage too low	50 (24.8)
Adverse drug reactions	81 (40.1)
Non-compliance	44 (21.8)
Total	202 (100.0)

between isoniazid and dexamethasone, with isoniazid influencing the inhibition of CYP3A4 enzyme metabolism, leading to increased dexamethasone levels, and consequently, increased side effects and toxicity of dexamethasone [19].

The text indicates that a low dose of a drug can result from using fewer tablets than necessary or from drug interactions reducing drug levels in the blood. For instance, 50 cases (24.8%) were found where the dose was too low DTP. One example given is for patients taking anti-TB drugs, where a patient weighing 58 kg should take 4 tablets but only took 3. Furthermore, dose reductions can occur due to drug interactions, such as rifampicin decreasing the concentration of glimepiride in the blood of TB patients with comorbid DM. This is

caused by the induction of the cytochrome p450 CYP2C9 enzyme by rifampicin, requiring monitoring of blood sugar levels and an increase in the dose of glimepiride [5,20].

The data on adverse drug reactions (ADR) related to DTP were collected through interviews and patient observations. Patients reported experiencing side effects from the drugs they were using, including nausea and vomiting from rifampicin, tingling in the feet from isoniazid, blurred vision from ethambutol, and joint pain from pyrazinamide [5]. Similarly, research by Tajudin et al. (2022) revealed that 31 respondents (39.2%) experienced nausea as a side effect [21]. It was found that taking rifampicin before bedtime can help reduce the nausea caused by its active metabolite, which acts as an emetogenic agent stimulating the vagus and releasing 5-hydroxy tryptamine (5-HT3) [22]. The study indicated a total of 81 cases (40.1%) of adverse drug reactions to DTP. Other studies mentioned even higher rates of ADR cases, with Priyandani et al. (2014) reporting 73.1% and Khotimah et al. (2023) mentioning 80.8% [7,17].

Treatment supervisors play an important role in improving TB patients' adherence to their anti-TB treatment. They remind patients to take their medication, directly supervise their medication intake at home, accompany them to health check-ups at health centers, and provide motivation [23]. In this study, patient non-compliance with treatment was 21.8%. Other studies found a non-compliance rate of 11.5% in a survey conducted by Priyandani et al in 2014 and 1.6% in a study conducted by Khotimah et al in 2023 [7,17].

In Table IV, it is noted that 11.8% of patients did not receive DTP, as they only used anti-TB drugs. The dosage of anti-TB drugs administered to patients adhered to guidelines, and no complaints of side effects were reported. Additionally, at most 30.0% of patients had 2 DTPs. The combinations of 2 DTPs varied, including the need for additional drugs, no necessity for drug therapy, ineffective drugs, too high or too low doses of drugs, and non-compliance.

From the results of the study in Table V, data was obtained that 83.6% of patients experienced improvement in outcomes after receiving anti-TB treatment. Anti-TB drugs must be given for a sufficient period, including the early stage/intensive phase and advanced stage. In general, the duration of treatment for pulmonary TB without complications and comorbidities is 6 months [24]. In extra pulmonary TB and TB with comorbidities, treatment can last more than 6 months. Improvement in outcomes is assessed by reducing TB symptoms such as coughing, increased appetite, and weight gain. In addition, it can also be seen from the results of the acid-fast bacillus (AFB) test. A decrease in the number of TB bacterial colonies is indicated by a change from AFB (3+) to AFB (2+), from AFB (2+) to AFB (1+), and from AFB (1+) to AFB (-). AFB is a type of bacteria that causes tuberculosis and other types of mycobacterial infections, such as leprosy (Hansen's disease). The AFB test is usually performed for people with symptoms of active tuberculosis, commonly known as TB. 1-10 AFB per field in at least 50 fields is reported as “2+”. Note that a plus sign must appear after the number. This is a positive result. More than 10 AFB per field in at least 20 fields is reported as “3+”. Negative AFB means there is no infection, the symptoms are caused by something other than mycobacteria, or the mycobacteria are not numerous enough to be seen under the microscope [25].

In Table VI, Spearman's correlation test showed a strong relationship between the number of drugs used and the number of DTPs in TB patients. The test resulted in a p-value of 0.000 and a correlation coefficient of 0.472, indicating a significant positive correlation. This means that as the number of drugs used by patients increases, the number of DTPs also increases.

The Spearman's correlation test (Table VII) between the number of DTP and the results of therapy in TB patients obtained a p-value of 0.430 and a correlation coefficient of -0.076. A p-value greater than 0.05 indicates that there is no relationship between the number of DTPs occurring in patients and improvements in patient therapy results. Conflicting results were obtained from the study of Ayu et al. (2021), which showed a relationship between the occurrence of drug-related problems (DRPs) and patient treatment results (p-value < 0.05) [26]. This discrepancy may be due to the different types of DTPs experienced by patients. Despite experiencing various DTPs like drug side effects, patients must adhere to their medication as per the guidelines. Adhering to the doctor's instructions is crucial for patients to recover from TB. The results of therapy in TB patients are greatly influenced by patient compliance in using anti-TB drugs, including the right dose, interval, frequency, and duration of treatment.

The study has some limitations. Firstly, it was conducted cross-sectional, which means that researchers were unable to monitor the progress of patients during therapy and there was no follow-up after identifying the type of DTP. Additionally, the research samples were non-randomly selected, so the conclusions cannot be generalized.

Table IV. Number of DTP per patient

Number of DTP Per Patient	N (%)
0 DTP	13 (11.8)
1 DTP	31 (28.2)
2 DTPs	33 (30.0)
3 DTPs	25 (22.7)
4 DTPs	7 (6.4)
5 DTPs	1 (0.9)
Total	110 (100.0)

Table V. Patient Therapy Outcome

Patient Therapy Outcome	N (%)
Improved	92 (83.6)
Not Improved	18 (16.4)
Total	110 (100.0)

Table VI. Correlation test of drug amount and DTP amount

			Number of drugs	Number of DTPs
Spearman's rho	Number of drugs	Correlation Coefficient	1.000	0.472**
		Sig. (2- tailed)		0.000
		N	110	110

**) Correlation is significant at the 0.01 level (2-tailed)

VII. Correlation test of DTP and therapy outcome

			Number of drugs	Therapeutic outcomes
Spearman's rho	Number of drugs	Correlation Coefficient	1.000	-0.076**
		Sig. (2- tailed)		0.430
		N	110	110

P=0.430>0.05: There is no relationship between the number of DTPs and therapy outcome

CONCLUSION

Based on the study results, it can be concluded that there is a significant relationship between the number of drugs used by patients and the number of Drug Therapy Problems (DTPs) per patient. There is no relationship between the number of DTPs in patients and the success of TB treatment. Therefore, pharmacists at health centers should continue to strive to improve patient understanding and compliance with TB treatment, including adherence to dose, frequency, interval, and duration of anti-TB treatment.

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STATEMENT OF ETHICS

This research is accompanied by an ethical certificate from the Research Ethics Commission of the Faculty of Dentistry, Airlangga University Number 0161/HRECC.FODM/III/2024.

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