Evaluation of Potential Drug Interaction in Advanced Phase Tuberculosis Patients at Jember Pulmonary Hospital

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Pulmonary TB is a disease caused by infection from the bacteria Mycobacterium tuberculosis that attacks the lungs. Based on WHO data in Indonesia, the total number of TB cases in 2023 was 1,060,000 cases, the prevalence of TB in the city of Jember was 5,244 cases, and nationally, East Java was in second place based on the estimated incidence of TB with a total of 107,547. From the results of a preliminary study at the Jember Pulmonary Hospital, there were 1,803 cases. This study was to evaluate the interaction of antituberculosis drugs in TB patients at Jember Lung Hospital. The method that will be used by researchers in this study is observation. This type of research is descriptive research with the number of samples used as many as 95 samples using the solvin formula. This study uses random sampling techniques. Data analysis uses univariate analysis, data is displayed in the form of frequency and percentage. Based on the results of the study, the number of men diagnosed with TB was 65%, women were 35%, the results showed that out of 95 tuberculosis patients, 100% of patients experienced potential drug interactions. Based on the severity, major was (65%), moderate was (32%), and minor was (3%), the age range that was more often diagnosed with TB was 17-25, namely 20% and age 55-60 was 28%. Based on the research results that most of the potential drug interactions occur in major interactions. The role of pharmacy in terms of drug interactions is to monitor drug use and regulate drug use scheduling, to avoid drug interactions.
Keywords: Drug Interactions, Tuberculosis, Potential, Advanced Phase, Hospital

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1. Introduction

Pulmonary TB is a disease caused by infection of Mycobacterium tuberculosis bacteria in the lungs and is a public health problem because it infects one-third of the world's population, especially in developing countries, including Indonesia. Pulmonary TB is the 9th leading cause of death worldwide, with the main cause being a single infectious agent (Wulandari et al, 2020). In 2023, Indonesia recorded a total of 1.060.000 TB cases, with the number of deaths reaching 134,000 per year and 820,789 TB patients. Nationally, East Java ranks second based on the estimated incidence of TB, with a total of 107.547 people diagnosed in 2023 (Dirjen p2p et al., 2023). In Jember Regency, there were 5.244 cases (Dinas Kesehatan Jawa Timur, 2023). Based on a preliminary study conducted at Jember Pulmonary Hospital, the number of inpatients was 1.803.

TB has many drugs because its treatment involves a combination of several types of drugs that work to kill, sterilize, and prevent resistance. In the continuation phase, patients receive fewer types of drugs but for a longer period. In this continuation phase, it is also important to kill persister bacteria to prevent relapse (Rahmat et a., 2021).

If TB patients also have comorbidities such as DM, HIV, and Pneumonia, then TB patients will receive additional drug therapy to treat the comorbidities. The concurrent use of anti-TB drugs (OAT) with drugs for comorbidities can potentially cause drug interactions. The effect of this drug interaction can cause

changes in the concentration of the comorbidity drug or the anti-TB drug. This can lead to toxicity or reduced efficacy of the anti-TB drugs and the comorbidity drugs. Reduced efficacy of anti-TB drugs can result in medical problems such as Multi-Drug Resistance (MDR), which ultimately leads to failure of tuberculosis therapy (Rika et al., 2019)

Drug interaction is a pharmacological or clinical response to the administration of drugs in combination or concurrently that can alter the effectiveness of one drug with another. This effect can be dangerous if the drug interaction causes increased toxicity or decreased therapeutic effectiveness of a drug (Ainaya et al., 2022)

Drug interactions change the way drugs work in the body when they interact with other substances such as drugs, food, drinks, or supplements. There are several types of drug interactions: minor interaction, moderate interaction, and major interaction. Minor interactions have limited clinical effects that may lead to increased severity of side effects but do not require major changes in therapy. Moderate interactions can cause exacerbation of the patient's condition or require changes in patient therapy. Major interactions are likely to be life-threatening or require medical intervention to prevent ADEs (Dai et al., 2017; Sasindi et al., 2024; Sigalingging et al., 2019).

Drug interactions can occur when the effect of a drug is altered by the presence of another drug (which can be an herbal medicine or chemical), food, and drink. Drug-Related Problems (DRPs) are conditions that involve actual or potential drug therapy that interferes with desired health outcomes or to prevent toxicity in the body. If patients take two or more drugs simultaneously, there is a potential for drug interactions that can affect the drugs being taken. The interaction between these two drugs can decrease or increase the mechanism of action of the drugs consumed. According to research by Nurhikma 2017, the prevalence data of drug interactions showed 68% in Banjarmasin (Perdani dan Susilawati, 2023).

The main symptoms of TB are coughing for two weeks or more, coughing with additional symptoms such as sputum production, blood-streaked sputum, shortness of breath, fatigue, decreased appetite, weight loss, night sweats without physical activity, and fever for more than one month (Rika et al., 2019)

2. Method

This research was conducted from May to June 2025 in the medical records department of Jember Lung Hospital. This research received ethical approval with No. 893/KEPK/UDS/III/2025. The method that the researcher will use in this study is observation. Observation is a technique for collecting data and recording the conditions of a target object or research subject. The population in this study includes all inpatients diagnosed with advanced phase tuberculosis at Jember Lung Hospital from January to December 2024 who meet the inclusion criteria. The sample in this study consists of medical record data of advanced phase tuberculosis patients with comorbidities. The number of samples taken in this study is 95 patients, and the sampling was done using random sampling with the Slovin formula.

The research instrument used for data collection is a data recap sheet. The medical record data that meet the inclusion criteria are observed to note the patient's identity, the medications used by the patient, and the diagnoses the patient has. Next, the medications used by the patient are checked on Medscape to see if there are any drug interactions between OAT and comorbidities (DM, HIV, Pneumonia). If there are drug interactions, these are categorized as major, moderate, or minor. In this study, univariate analysis is used, with data presented in the form of frequency and percentage, and the data is processed using Microsoft Excel.

3. Results and Discussion

The research with the title Evaluation of the Potential for Drug Interactions in Advanced Phase Tuberculosis Patients at Jember Lung Hospital aims to identify the potential drug interactions of the use of tuberculosis drugs in tuberculosis patients and the use of other drugs in advanced phase tuberculosis patients. This research was conducted in May – June 2025 at Jember Lung Hospital. The sample in this study is medical record data of tuberculosis patients with comorbidities such as DM, HIV and pneumonia at Jember Lung Hospital for the period January – December 2024. This research received ethical approval with No. 893/KEPK/UDS/III/2025. The following are the characteristics of patients based on gender, age, and comorbidities in tuberculosis patients.

The following is a profile of patient characteristics by age and gender can be seen in table 1.

Table 1. Characteristics of patients by age and gender

Characteristics	Total (n)	Percentage (%)
Gender		
Male	62	65%
Female	33	35%
Total	95	100 %
Age		
17 – 25	19	20%
26 – 44	20	21%
45 – 54	29	31%
55 – 60	27	28%
Total	95	100 %
Diagnosis Disease		
TB	65	69%
TB Peumonia	16	17%
TB DM	9	9%
TB HIV	5	5%
Total	95	100 %

Source from : Jember Pulmonary Hospital

Based on table 1, in gender characteristics, the number of TB cases is more in men, which is as much as 65% compared to women, which is 35%. Based on the results of the survey on the prevalence of tuberculosis in men, the prevalence is higher than in women. It is likely that because of this, men are more exposed to TB risk factors such as smoking, and lack of knowledge about the disease (Kurniawati dan Sunarmi, 2022). In addition to smoking, the causes of men suffering more from TB include biological differences in men and women, such as differences in immunity levels, men reported consuming alcohol more often and differences in exposure to Mycobacterium tuberculosis which are associated with differences in lifestyle or social interaction activities where men do more daily activities and social interactions outside compared to Female (Pertiwi, 2020). According to the researchers, TB disease It can affect both men and women, but because men smoke more often, consume alcohol and have a less maintained lifestyle, men are more susceptible to tuberculosis.

In table 1, according to WHO, TB disease is more susceptible to attack the age of 55-60 years, which is as much as 28%. Pulmonary tuberculosis is most often found at productive age because at this age many people spend time and energy working. Where a lot of energy is drained, the rest time is reduced, so that the body's immunity decreases. Danusiatua from 55 – 60 years old with a total of 27 and a percentage of 28% this is because at productive age the body's immune system during old age decreases so that it is very

susceptible to diseases, especially pulmonary tuberculosis. For 17-25 years of age with a total of 19 and a percentage of 20% are least affected by tuberculosis infection (Achmad et al., 2023). Based on the results and theories above, researchers believe that as we age, the function and capacity of some of our body organs decrease, such as the function of pancreatic beta cells that produce insulin, thereby causing an increase in immunity. The age of 17-25 years and above is the age where a person is at risk of developing TB and comorbidities due to lack of immunity, TB mainly affects people over 17 years old and increases in people over 60 years old.

Based on the results of the research conducted, it showed that as many as 9 patients with a percentage of 9% of people were positive for TB and DM, the majority of TB patients were non-DM, the relationship between TB infection and DM was interdependent. Increased risk of diabetes mellitus in people with TB can be done with screening and treatment of tuberculosis infection. This screening stage can help with early detection of DM. The risk is also greater in DM with independent insulin or type 2 diabetes mellitus. Diabetes is a cormobid disease of TB, at the age of more than 50 years can increase the likelihood of morbidity simultaneously (Kahar et al., 2022). Patient diagnosis shows that TB patients with comorbidities with DM at Jember Lung Hospital are one risk factor for tuberculosis, diabetes mellitus. Patients with DM will have a low immune system so that it can cause TB to develop to be more active and high. Patients with DM will tend to have 2 to 3 times the risk of developing TB than people without DM. The World Health Organization (WHO) said that in 2025, Indonesia will be estimated to be ranked number 5 in the world. Eight of the ten countries with the highest incidence of DM in the world are grouped into countries with the highest cases of pulmonary TB (Yunita, 2018). The clinical symptoms of DM and TB have similarities such as weight loss and weakness. Respiratory clinical symptoms such as coughing can be clinically inconspicuous in TB patients with DM. This is due to a disturbance of cilia motility which reduces the cough reflex. People with TB with DM usually have fever complaints with a longer duration and greater weight loss than TB patients without DM (Rakhmandani et al., 2024). According to researchers, TB and DM are two diseases that have a complex and mutually affecting relationship, at the age of more than 50 years patients with DM will be more likely to have a lower immune system so that it can lead to the development of TB disease.

In table 1, the diagnosis of TB patients with HIV comorbidities at Jember Lung Hospital is 5% of cases. According to the Center for Disease Control and Prevention (CDC), tuberculosis is an infectious disease caused by Mycobacterium tuberculosis. Tuberculosis is a serious disease that must be treated immediately because this disease is very risky for people with HIV. This disease will be more dangerous in people with HIV and is the cause of most cases of death in

people with HIV. People with untreated TB infection and HIV infection make it possible that the patient will suffer from TB disease for the rest of his life compared to patients with TB infected without HIV (Rakhmandani et al., 2024) . In these cases of TB-HIV coinfection, knowing the characteristics of the patient with this coinfection is essential for effective treatment. Patients suffering from both TB and HIV often show unusual or unusual symptoms, which can lead to delays in TB diagnosis. This delay has the potential to lead to delayed treatment, increasing the risk of complications and death from such coinfection (Laksono, 2024). Tuberculosis and HIV are two infectious diseases that have received special attention from health practitioners due to their increasing prevalence. This also happens in the incidence of TB-HIV coinfection. This is because these two diseases and their causes can interact with each other and affect their respective epidemiology (Nl'mal & Cahyati, 2016). According to researchers, TB and HIV are interrelated diseases and often appear together. Patients who suffer from TB are also very susceptible to HIV disease and show unusual symptoms, so the patient needs to undergo routine treatment so that unwanted things do not happen.

Based on table 1, TB and Pneumonia diseases are as much as 17%. The incidence of pneumonia increases in people with comorbid diseases including diabetes mellitus and tuberculosis. Tuberculosis is a chronic infectious disease caused by the bacterium Mycobacterium tuberculosis. This bacterium is rod-shaped and acid-resistant, so it is often known as Acid-Resistant Bacillus (BTA). Most TB germs are often found to infect the pulmonary parenchyma and cause pulmonary TB, but these bacteria also have the ability to infect other organs of the body (extrapulmonary TB) such as pleura, lymph nodes, bones, and other extra-pulmonary organs (Sari dan Sinaga, 2022). According to researchers, pneumonia can attacks on patients with TB, due to an unhealthy lifestyle and lack of exercise. Therefore, pneumonia patients are susceptible to TB disease. The following is the profile of the distribution data table of potential drug interactions can be seen in table 2.

Table 2. Drug Interaction Potential Distribution Data

Potential Drug Interactions	Total (n)	Percentage (%)
Drug interactions occur	147	100 %
Total	147	100 %

Source from: Jember Pulmonary Hospital

Based on table 2, it was obtained that the percentage of patients who were TB and had a history of comorbidities in the inpatient facility at Jember Lung Hospital, more than 147 patients (100%) had the potential for drug interactions.

Drug interactions change the way drugs work in the body that occur when they interact with other substances such as edible, drinking, or supplements. There are several types of drug interactions, namely minor interactions, moderate interactions, and major interactions. Minor interactions have limited clinical effects that allow for increased severity of side effects but do not require major changes in therapy. Moderate interactions may cause exacerbations in the patient's condition or require a change in therapy in the patient. Major interactions may be life-threatening or require medical intervention to prevent ADE from occurring (Dai et al., 2017; Sasindi et al., 2024; Sigalingging et al., 2019).

Drug interactions can occur when the effects of a drug change in the presence of other drugs (can be herbal medicines, chemicals), food, and drinks. Drug Related Problem (DRP) is a condition that involves actual or potentially disruptive drug therapy or to prevent toxicity in the body. If the patient takes two or more drugs at the same time, there is a potential for drug interactions which have an effect on the drugs consumed. The interaction between the two drugs can decrease or increase the working mechanism of the drugs consumed (Perdani et al., 2023).

Of the many potential drug interactions that occur, it is important to know in advance all the drugs that the patient consumes, including prescription drugs, over-the-counter drugs, and supplements. Furthermore, it is necessary to know whether there is a possibility of interaction between TB drugs and pernyerta disease drugs or not, if it is known that there is a drug interaction, it can be adjusted. By adjusting the dosage of the drug, changing the time to take the drug, or choosing another drug that will not interact with it. The following is a profile of drug interaction data based on the level of clinical significance can be seen in table 3.

Table 3. Identification of TB + TB drugs and TB drugs + other drugs.

Category	Total (n)	Percentage (%)
TB With TB	95	65%
TB With Other Medications	52	35%
Overall Total	147	100%

Source from: Jember Pulmonary Hospital

The use of TB drugs with TB drugs has the potential for drug interactions, in table 3 it was found as many as 47 (26%). The use of tuberculosis drugs is divided into two phases, namely the intensive phase (2-3 months) and the advanced phase (4-6 months). Anti-tuberculosis drugs (OATs) are an important component in the treatment of tuberculosis because they are the most efficient in preventing the further spread of tuberculosis germs. The types of OATs used in the first line are rifampicin, isoniazid, Pyrazinade and etambutol (Fernadya et al., 2018).

The use of OAT drugs with OAT can cause potential drug interactions if consumed at the same time such as rifampicin and pyrazinamid, rifampicin and isoniazid can cause major interactions, while examples of moderate interactions are the use of etambutol drugs with isoniazid and rifampicin with etambutol. Major and moderate interactions have clinical effects that have the potential to cause serious side effects. Therefore, the role of a pharmacist is to ensure safe drug administration therapy, consult a doctor if the combined drugs cause potential clinical effects on the patient's body.

The use of tuberculosis drugs with other drugs in table 2 had 134 interactions (74%). In the use of TB drugs with comorbidities such as DM, HIV and pneumonia, it is a disease that is very susceptible to lowering the immune system so that it is very susceptible to tuberculosis and on the other hand, tuberculosis also causes the body's inability to control the patient's blood sugar so that it will be easy to experience TB-DM (Fortuna et al., 2022). The use of TB with other drugs can also have the potential for drug interactions and the treatment of TB with comorbidities is a difficult thing compared to the treatment of TB without comorbidities, therefore the role of a pharmacist is to ensure safe drug administration therapy, consult a doctor if the combined drugs cause potential clinical effects on the patient's body. The following is the data on TB and TB drugs can be seen in table 4.

Table 4. TB and TB drug data

Category	Drug Name	Total (n)	Percentage (%)
Tuberculosis Drugs	2FDC	58	62%
	Rifampisin & Isoniazid	37	19%
	Total	**95**	**100 %**

Source from : Jember Pulmonary Hospital

Based on the table above, this study examines the treatment of advanced phase tuberculosis. Based on the data, table 4 shows that the most widely used is the combination of 2FDC (2 Fixed Dose Combination). The WHO recommends the use of fixed dose combinations (FDCs) covering four important drugs designated as the first line, namely Isoniazid (H), Rifampicin (R). The administration of this drug is carried out for 6-12 months which is not only aimed at curing the sufferer, preventing recurrence, breaking the chain of transmission and preventing the occurrence of bacterial resistance to OAT (Varentika et al., 2022). The mechanism of action of isoniazid is to affect the biosynthesis process of lipids, proteins, nucleic acids and glycolysis. The main action of isoniazid inhibits the biosynthesis of mycolic acid which has an important constituent in the cell wall of microbacteria. Rifampicin is a macrocyclic antibiotic complex that inhibits the synthesis of ribonucleic acid in a broad spectrum against pathogenic germs. It has a potent bactericidal activity and sterilizing effect against tubercle bacilli at both local and extracellular locations (Widiyasusanti et al., 2022). Here are the data of other drugs can be seen in table 5.

Table 5. Other drug data

Category	Drug Name	Total (n)	Percentage (%)
Other Drugs	Metformin	9	18%
	Doxycycline	14	28%
	Rilpivirin	1	2%
	Sulfonilurea	1	2%

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Category	Drug Name	Total (n)	Percentage (%)
	Lamivudine	1	2%
	MetilPrednisolon	12	24%
	Contrimoxazole	5	10%
	Glimepiride	3	6%
	Nevirapine	1	2%
	Efavirenz	2	4%
	Arsitam	1	2%
	Total	**50**	**100%**

Source from: Jember Pulmonary Hospital

Based on the table of the 5 most drug classes, the most common opioid drug classes are prescribed to patients who experience coughing painfully. Tuberculosis patients can also experience infections in the respiratory tract and there is a relationship between tuberculosis and other respiratory problems that can trigger inflammation, as well as other factors, namely TB patients often experience a decrease in appetite and weight which can also trigger respiratory tract disorders. Neurosanbe drugs are vitamins that are used to treat deficiencies related to the health of the patient's body (Shintani dan Melyani, 2023). As well as the results of the research conducted by the researcher show that there is a potential drug interaction between tuberculosis, but it is better to re-check the dosage and patient's condition before giving it to the patient. The following is a profile of drug interaction data based on the level of clinical significance can be seen in table 6.

Table 6. Drug interactions based on levels of clinical significance

Level of Clinical Significance	Total (n)	Pescentage (%)
Mayor	95	65%
Minor	4	3%
Moderate	48	32%
Total	147	100 %

Source from: Jember Pulmonary Hospital

Based on the level of clinical significance, drug interactions are classified into three namely major, moderate and minor. This study aims to identify potential drug interactions based on the level of clinical significance on the prescribing pattern of inpatients at Jember Lung Hospital, knowing the possible impact on drug interactions.

Based on table 4, from the results of the research that has been carried out, there are the most drug interactions from the above cases, namely the moderate category with a percentage of 32% or as many as 48 potential interactions. Moderate interactions are clinically significant, usually to avoid combinations of medications taken at the same time and to use them only in special circumstances or as necessary. This is very important to note considering that the incidence of drug interactions occurs more in adult patients and elderly patients than in pediatric patients. Moderate interactions mostly occur in adult patients due to the use of one or more medications for specific chronic diseases or those caused by complications of a disease (Agustin dan Fitrianingsih, 2020). According to the researcher, patients should be monitored to monitor response to treatment and identify any interactions that may occur over time, patients should be educated about the medications they are taking, possible interactions, symptoms to look out for, and what to do if problems arise so that treatment management is organized.

From table 4 above, it can be seen that the incidence of major interactions is 65% or as many as 95 interaction events. Major drug interactions are interactions that can cause severe consequences for patients,

this interaction should be prioritized to be prevented or overcome immediately because of its life-threatening effects and may cause permanent damage to the body, the potential major interactions found in the study below are one of which is the interaction between isonoazid, rifampicin. Therefore, the use of isoniazid with rifampicin can cause serious side effects affecting the liver (Agustin dan Fitrianingsih, 2020). According to researchers, in major interactions, patients need to be given information or monitored in taking medication and must be given a gap of 1-2 hours so that serious interactions do not occur.

Next is drug interactions which are classified as minor categories where from the data that has been presented in table 4 minor interactions are obtained as much as 3% or 4 potential interactions. Minor interactions may cause less significant side effects and do not affect the outcome of therapy. Clinically, minor interactions are not very dangerous if used and should still be monitored during use. And minor interactions of INH and dexamethasone drugs can reduce the effectiveness of the drug (Agustin dan Fitrianingsih, 2020). According to researchers, the right patient treatment is to review all the drugs that the patient consumes, monitor the symptoms in the patient, if there is simultaneous use of the drug, then taking the drug must be paused. With a careful approach and proper monitoring, drug interactions can be controlled to achieve optimal treatment outcomes and reduce the likelihood of side effects.

The following is a data profile of drugs that interact based on their severity can be seen in table 7.

Table 7. Data on interacting drugs by severity

Severity	Interacting drugs	Total (n)	Percentage (%)
Mayor	1. Isoniazid + Rifampisin	95	64%
Minor	2. Isoniazid + MetilPrednisolon	4	3%
Moderate	3. Rifampisin + Metformin	6	4%
	4. Isoniazid + Metformin	3	2%
	5. Isoniazid + Tenovofir	1	1%
	6. Isoniazid + Doxycycline	12	8%
	7. Rifampisin + Doxycycline	12	8%
	8. Isoniazid + Rilpivirin	1	1%
	9. Rifampisin + MetilPrednisiolon	4	3%
	10. Isoniazid + Glimepiride	3	2%
	11. Rifampisin + Glimepiride	1	1%
	12. Isoniazid + Nevirapine	1	1%
	13. Isoniazid + Contrimoxazole	2	1%
	14. Rifampisin + Contrimoxazole	2	1%
	Total	147	100 %

Source from: Jember Pulmonary Hospital

From the data from the results of the research that has been carried out, it is found that the use of antituberculosis drugs that are often combined are two drugs, namely isoniazid and rifampicin, the combination of both isoniazid and rifampicin drugs is often used in TB patients who need treatment of bacteria that grow in the body. This combination has a synergistic effect because both contribute to the treatment of TB disease and can kill bacteria in the body.

The interaction of rifampicin and isoniazid, namely rifampicin, increases the tosicicity of isoniazid by accelerating metabolism. Rifampicin induces isoniazid hydrolase by increasing the production of hepatotoxic hydrazine when rifampicin is combined with isoniazid, resulting in a higher risk of hepatotoxicity when administered simultaneously than when administered individually (Afrianti et al., 2023). In the use of rifampicin and isoniazid, caution is strongly advised in patients with liver disorders, the

elderly and malnourished patients. Liver function tests should be routinely reviewed in patients taking a combination of rifampicin and isoniazid, whereas both drugs are also the same class of antibiotics for the treatment of TB (Afrianti et al., 2023).

Rifampicin and isoniazid are required by tuberculosis patients with higher benefit considerations when given in combination. Although rifampicin may increase the hepatotoxicity of isoniazid, this combination does not cause hepatotoxicity in most patients. However, strict monitoring must still be carried out, one of which is with liver function tests in case of liver function changes, especially for patients with liver function disorders and isoniazid slow acetylator disorders and consider discontinuation of one or both drugs in the event of an interaction between the two OATs (Veryanti et al., 2019).

From the above explanation, several steps can be taken to reduce the risk of potential drug interactions, including antituberculosis drugs such as isoniazid and rifampicin that may be used together, patients should be monitored regularly by a physician to monitor response to treatment and identify drug interactions that may occur frequently over time. Patients should be educated about the medications they are taking, possible interactions, symptoms to look out for, and what to do if interaction problems arise.

Furthermore, the second interaction is between the drug isoniazid and doxycycline, where the effect of isoniazid or commonly referred to as Isonicotinyl Hydrazid (INH). The drug is a *prodrug* activated by catalase - peroxide (KatG) of the microbacterium is tuberculostatic. The mechanism of action of INH inhibits the biosynthesis of mycolic acid, INH also prevents the prolongation of very long fatty acid chains which is the initial form of mycolic acid molecules. The absorption of the drug is impaired along with food, specifically carbohydrates, or with antacids containing aluminum. The most common and fairly mild side effects of the isoniazid type of drug are nausea, vomiting, and epigastric pain (Vellia et al., 2024). While doxycycline is one of the oldest classes of drugs used to treat asthma which is hypothesized to be the result of various mechanisms. Doxycycline has a direct bronchodilating effect through non-selective inhibition of phosphodiesterase, adenosine receptor antagonism, modulation of intracellular calcium release via ryanodine receptor agonists as well as stimulation of endogenous catecholamine release (Rahmawati et al., 2023). Doxycycline toxicity can present with symptoms of unbearable nausea and vomiting, seizures, cardiac arrhythmias, multifocal atrial tachycardia, heart failure, and death (Rahmawati et al., 2023). And the interaction of the two drugs then the use of isoniazid along with doxycycline can increase the effects of doxycycline, and the side effects of experiencing vomiting, diarrhea, headache, restlessness, insomnia, seizures, or irregular heartbeat (Maghfiroh, 2022).

From the explanation above, there are several steps that need to be taken by researchers to reduce the risk of potential drug interactions that occur, so patients need to be monitored to take medication and monitoring and time limits for taking medication must be needed so that unwanted things do not happen. The following is the profile of the drug interaction evaluation data can be seen in table 8.

Table 8. Drug interaction evaluation data

Types of Interactions	Evaluation Interaction	Total (n)	Percentage (%)
Mayor	Monitoring of patients' clinical conditions in medical records data or directly by monitoring clinical and lab data.	95	65%
Moderate	Provide *a timeline* of medication use	17	12%
	Monitoring of clinical conditions from drug use	31	21%
Minor	Provide *a timeline* of medication use	4	2%
	Total	147	100%

Source from: Jember Pulmonary Hospital

Based on table 8 of moderate and minor evaluations in medical record services, monitoring is used to monitor patients' clinical conditions directly by monitoring patient clinical data. Monitoring is also used to ensure that the work procedure system in the medical record unit has been implemented properly. Monitoring activities are intended to determine the clinical condition of patients from drug use. Monitoring is used to improve the use of drugs so that it can be monitored in consuming drugs and so that unwanted drug interactions do not occur (Poltekkes Kemenkes Yogyakarta, 2022). According to the researcher, it is necessary to monitor the patient's clinical condition in order to adjust the administration of drugs and so that unwanted drug interactions do not occur.

According to table 6, minor evaluations are very necessary for patients in the timeline or the use of drugs is very important in healthy living behaviors. Compliance with taking anti-tuberculosis drugs is consuming medications as prescribed and prescribed by a doctor. Treatment will be effective if the patient is compliant and consumes it (Kusmiyani et al., 2024). According to the Indonesian Ministry of Health, one of the causes of the failure to cure pulmonary TB patients is the patient's compliance in treatment. Treatment carried out by TB patients aims to cure the patient, prevent death and prevent drug resistance. However, due to the long treatment period (6-8 months), accompanied by the consumption of various drugs and also the side effects caused, it tends to make patients become non-compliant [30]. Non-compliance with this treatment is also often a problem globally, if this is left unchecked, the impact that will arise if the patient stops taking medication is the emergence of drug-resistant pulmonary TB germs if this continues to happen and the germs continue to spread and pulmonary TB control will be increasingly difficult to implement which has an impact on the increasing mortality rate due to Pulmonary TB disease (Kusmiyani et al., 2024). According to researchers, the evaluation of drug interactions is very important for patients who consume drugs and it is very important to monitor compliance or timeline of drug use so that patients are safer in taking drugs.

4. Conclusion

Based on the results of the study, the number of men diagnosed with TB was 65%, women were 35%, the results showed that out of 95 tuberculosis patients, 100% of patients experienced potential drug interactions. Based on the severity, major was (65%), moderate was (32%), and minor was (3%), the age range that was more often diagnosed with TB was 17-25, namely 20% and age 55-60 was 28%.

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