

# Factors Affecting the Side Effects of Anti-Tuberculosis Drugs

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## ABSTRACT

Side effects of Anti-Tuberculosis Drugs is a problem in the treatment of tuberculosis patients. In Barru Regency, the number of pulmonary TB patient visits in the outpatient and inpatient units in 2014-2016 was still high. Based on these data, it is deemed necessary to conduct research on the causes of cure rates in only 73% of the total users of pulmonary TB drugs, in terms of the side effects of anti-tuberculosis drugs, pulmonary disorders and gastric disorders. This study was conducted on Agustus, 2017 to January, 2018; using cross sectional approach. Subject of this study were 75 tuberculosis patients with BTA+ and side effects of Anti-Tuberculosis Drugs on the lungs and stomach, selected by total sampling. Data were obtained through interview, then analyzed by using path analysis. It is known that the pathways of influence were significant ( $T\text{-value} > 1.96$ ) were knowledge on immune system, type of drug on immune system, knowledge on side effect of drug and type of drug on side effect of drug. Thus, the level of knowledge and types of drugs directly affect the immune system, as well as the side effects of drugs. Several factors that directly affect the side effects of anti-tuberculosis drugs are the level of knowledge and type of drug. Increased knowledge will reduce the side effects of the drug, because the patient makes an effort to neutralize the effect.

**Keywords:** Side effects, Anti-tuberculosis drug, Tuberculosis, Knowledge

## INTRODUCTION

Tuberculosis (TB) is a chronic granulomatous infectious disease caused by the bacillus *Mycobacterium tuberculosis bacilli* (Mtb) which was discovered by Robert Koch in 1882.<sup>(1),(2)</sup> TB is an age old dreadful disease and globally, there were an estimated 10.4 million new TB cases with 1.8 million TB deaths in 2015.<sup>(1)</sup> Twenty five percent of all deaths caused by pulmonary tuberculosis disease and it has become the leading cause of death on infectious diseases.<sup>3</sup>

The high incidence of pulmonary TB is a major problem for many countries in the world. WHO (2015) explains that 9.6 million of the world's population

are infected with TB bacteria and the most cases of pulmonary TB are in Africa (37%), Southeast Asia (28%), and the Eastern Mediterranean (17%). Indonesia ranks fifth in the world as a contributor to TB sufferers after India, China, Nigeria and Pakistan<sup>(4)</sup>.

TB prevalence in Indonesia in 2013 (297 / 100,000 population) was higher than in 2010 (289 / 100,000 population). regions with the highest TB cases were West Java, East Java and Central Java, with smear positive cases of almost 40% of the total cases in Indonesia<sup>(5)</sup>. Morbidity and mortality due to TB are serious problems, especially due to the emergence of side effects of anti-tuberculosis drugs and most The patient felt unable to resist the side effects of the drug<sup>(6-8)</sup>. It was noted that 69.01% of patients experienced side effects of the drug<sup>(8)</sup>. Side effects that often arise are stomach disorders (loss of appetite, nausea, stomach ache). Other disorders include joint pain, tingling and burning in the legs and redness of the urine. More severe side effects include tightness, severe hemoptysis, collapse, bronchiectasis, pneumothorax, and cardio pulmonary insufficiency,

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itching and redness of the skin, deafness, balance disorders, visual disturbances, confusion and vomiting, purpura and shock<sup>(9)</sup>.

The number of TB patients with smear + is 8.470%, the Case Notification Rate (CNR) of new cases of TB with smear + per 100,000 population is 97.98%, while the total number of TB cases in South Sulawesi is 12.625%<sup>(10)</sup>. The partnership effort to reduce TB prevalence is an effort to eliminate pulmonary TB. Pulmonary TB prevention strategy is Directly Observed Treatment Shortcourse (DOTS) and has been implemented thoroughly in Indonesia since March 24, 1999. The impact or side effects of anti-tuberculosis drugs is one of the risk factors for default<sup>(11-12)</sup>.

Pulmonary TB treatment aims to cure patients and improve productivity and quality of life, prevent death, prevent recurrence, break the chain of transmission and prevent the transmission of drug-resistant pulmonary TB. Handling of the high prevalence of pulmonary TB must be done to control this disease, one of which is treatment. Drug therapy problems in pulmonary TB patients require special attention because patients consume a lot of drugs and in large doses. In one study, the incidence of drug therapy problems in the category of unwanted drug reactions or adverse drug reaction (ADR) was quite high<sup>(13)</sup>.

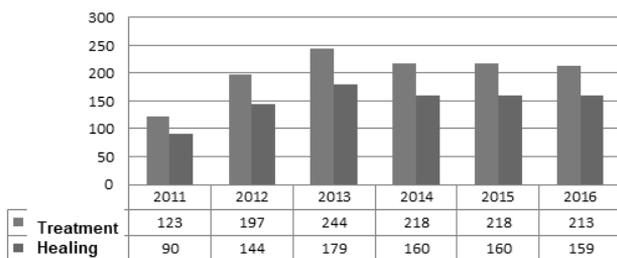


Figure 1. Trend of New Pulmonary TB Patient in Barru Regency 2011-2016<sup>(14)</sup>

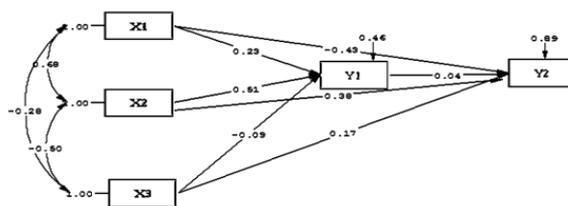
The number of pulmonary TB patient visits in the outpatient and inpatient units in 2014-2016 was still high. Based on these data, it is deemed necessary to conduct research on the causes of cure rates in only 73% of the total users of pulmonary TB drugs, in terms of the side effects of anti-tuberculosis drugs, pulmonary disorders and gastric disorders.

**METHOD**

This study was conducted on Agustus, 2017 to January, 2018; using cross sectional approach. Subject of this study were 75 tuberculosis patients with BTA+ and

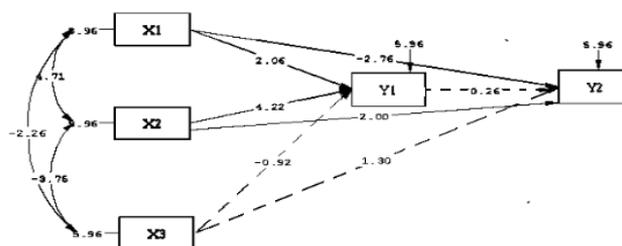
side effects of Anti-Tuberculosis Drugs on the lungs and stomach, selected by total sampling. Data were obtained through interview, then analyzed by using path analysis.

**RESULTS**



Note: X1 = knowledge, X2 = type of drug, X3 = dose of drug, Y1 = immune system, Y2 = drug side effects

Figure 2. Path coefficient of path analysis



Note: X1 = knowledge, X2 = type of drug, X3 = dose of drug, Y1 = immune system, Y2 = drug side effects

Figure 3. T-value of path analysis

Based on Figures 2 and Figure 3 it is known that the pathways of influence were significant (T-value > 1.96) were X1→Y1, X2→Y1, X1→Y2 and X2→Y2. Thus, the level of knowledge and types of drugs directly affect the immune system, as well as the side effects of drugs.

**DISCUSSION**

The results of data analysis showed that the level of knowledge directly affects the side effects of TB drugs on the lungs and stomach. The effect given is a negative influence, which means that if the level of knowledge increases then the side effects of the drug will decrease. In this regard, Handarini reports that respondents with good knowledge are more likely to be more obedient to taking medication<sup>(15)</sup>.

This research is also in accordance with Notoatmodjo's (2010) statement that one's actions about a health problem will basically be influenced by one's knowledge of the problem. In this case, the higher the level of knowledge possessed by TB patients, the higher the patient's compliance with treatment<sup>(16)</sup>.

The results showed that the type of drug did not affect the side effects of the drug. This is because most patients stop taking the drug because they cannot stand the side effects of the drug.

The anti-TB drug exhibits greater level of efficacy with a satisfactory degree of toxicity; however combination treatment, especially during the intensive phase of therapy may produce severe adverse events<sup>(17)</sup>. There may be considerable morbidity, even mortality, particularly with drug-induced hepatitis. These events may include substantial costs due to added visits, tests, and in more serious instances of hospitalizations<sup>(18)</sup>.

Standard anti-TB therapy typically continues for six months. For the first 2 months, three to four drugs receive patients, namely rifampin (R), isoniazid (H), pyrazinamide (Z), and, in some cases, ethambutol (E). During the final 4 months, they continue with rifampin and isoniazid<sup>(19)</sup>.

Tuberculosis is considered a serious disease, it can even be fatal if not treated properly. The treatment step given is the administration of antibiotics that must be spent by tuberculosis patients for a certain period of time according to a doctor's prescription. Common types of antibiotics are isoniazid, rifampicin, pyrazinamide and ethambutol. Like other antibiotics, antibiotics for tuberculosis also have side effects, especially rifampicin, isoniazid, and ethambutol. Rifampicin can reduce the effectiveness of hormonal contraceptives, ethambutol can interfere with the function of vision and isoniazid has the potential to damage nerves. A number of other side effects of anti-tuberculosis drugs are nausea, vomiting, decreased appetite, jaundice, dark urine, fever, rash, and skin itching<sup>(9,20)</sup>.

The healing period for tuberculosis varies depending on the patient's health condition and the severity of the disease. The condition of the patient generally starts to improve and stop contagious after taking antibiotics for 2 weeks. To ensure complete recovery, TB patients must use antibiotics given by doctors for 6 months. If the patient does not take the medicine as recommended or stops taking it before the recommended time, the bacteria may not be able to completely disappear, even though the patient feels that his condition has improved. Patients with tuberculosis have the potential to become resistant to antibiotics. If this happens, the condition becomes more dangerous and difficult to treat. Thus, the

healing period also becomes much longer.

The results showed that the dose of the drug had no effect on the side effects of the drug, either directly or indirectly, because the number of tuberculosis patients who stopped taking the drug due to the occurrence of disturbing side effects, so that many patients felt that they did not fit the drug<sup>(21-22)</sup>. This causes a healing failure so the patient must repeat the treatment. Another thing that causes no side effects of drugs when taking anti-tuberculosis drugs is because the dosage of tuberculosis medication is adjusted to the patient's weight, and there is prevention to using a single drug. The immune system does not play a role in resistance and side effects of anti-tuberculosis drugs<sup>(21-24)</sup>.

Treatment with anti-tuberculosis drugs also concerns the suitability of the number of tablets swallowed by the patient's body weight, which consists of 4 groups, namely 30-37 kg, 38-54 kg, 55-70 kg, and  $\geq 71$  kg. The more weight the patient has, the more tablets must be swallowed and the higher the dose. The administration of anti-tuberculosis drug dosage is seen from the presence or absence of the patient's physiological and pathological conditions that prevent the use of drugs (contraindications)<sup>(25-26)</sup>.

The results showed that the immune system had no effect on the side effects of the drug. The results of this study are different from the results of research conducted by Inez Clarasanti, Marthen CP Wongkar, Bradley J. Waleleng (2016) that in the use of anti-tuberculosis drugs (rifampicin, isoniazid, pyrazinamide and ethambutol / streptomycin) side effects complicate treatment targets. Common liver function tests include aspartate transaminase (AST) or more commonly referred to as serum glutamic-oxaloacetic transaminase (SGOT), and alanine transaminase (ALT) which is usually referred to as serum glutamic-pyruvic transaminase (SGPT). SGOT and SGPT show improvement if damage or inflammation occurs in liver tissue. SGPT is more specific to liver damage than SGOT. A slight increase (up to twice the normal rate) of SGOT and SGPT concentrations is often found. If the concentration of SGOT and SGPT is more than twice the normal number, it is considered meaningful and requires further examination. If there is an increase in transaminase enzyme concentration, there is an indication of malnutrition<sup>(27)</sup>.

## CONCLUSION

Several factors that directly affect the side effects of anti-tuberculosis drugs are the level of knowledge and type of drug. Increased knowledge will reduce the side effects of the drug, because the patient makes an effort to neutralize the effect.

## ADDITIONAL INFORMATIONS

**Ethical Clearance:** from Ethics Committee of Institute of Health Science “Maluku Husada”

**Funding Source:** authors

**Conflict of Interest:** None

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