

Evaluation of side effects of anti-tuberculosis drugs at Sungai Penuh General Hospital

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Abstract

Background: Tuberculosis (TB) remains a major public health problem worldwide. Anti-tuberculosis drug (ATD) therapy, though effective, often causes adverse drug reactions that may affect patient adherence and treatment success. This study aimed to evaluate the incidence and determinants of ATD-related side effects among TB patients.

Method: A retrospective cross-sectional study was conducted using secondary medical record data of 128 drug-sensitive TB patients receiving first category treatment at Mayjend H.A. Thalib General Hospital, Sungai Penuh, during 2023–2024. Data were analyzed using SPSS version 20 through univariate analysis and bivariate analysis using the Chi-square test to assess associations between variables.

Results: Of the 128 patients, 53.6% were male, 72.7% were aged <60 years, and 88.3% had pulmonary TB. ATD side effects occurred in 57.0% of patients, predominantly nausea (63.0%), itching (57.5%), and vomiting (27.4%). Significant associations were observed between adverse effects and drug type ($p = 0.037$), comorbidities ($p = 0.043$), treatment duration ($p = 0.010$), and treatment outcomes ($p = 0.015$).

Conclusions: More than half of TB patients experienced ATD-related side effects. These findings highlight the need for early detection, routine monitoring, and individualized management of adverse drug reactions, particularly in patients with comorbidities and prolonged treatment durations.

Keywords: Anti-tuberculosis drugs; Evaluation; Referral Hospital; Side Effects; Tuberculosis.

INTRODUCTION

Tuberculosis (TB) remains a global health problem, including in Indonesia. This disease is contagious and caused by infection with the bacterium *Mycobacterium tuberculosis* (1). In 2022, TB became the second-leading cause of death worldwide due to infectious agents after COVID-19, with more than 10 million patients contracting TB annually (2). In Indonesia, the number of diagnosed cases in 2023 reached 877,531, with the highest prevalence in Central Papua and the lowest in Bali (3).

Based on the 2022 Jambi Province Health Profile, 5,308 TB cases were detected. This figure increased compared to 3,682 cases in 2021. Data obtained showed that the case notification rate (CNR) for all TB cases by district/city in 2022 was highest in Jambi City at 209 per 100,000 residents, followed by

Sungai Penuh City with a CNR of 190 per 100,000 residents (4).

Recognizing the global impact of disorganized TB and variability in TB control programs, WHO developed the DOTS (Directly Observed Treatment Short-Course) strategy (5). TB treatment through the DOTS strategy requires patient adherence to anti-tuberculosis drugs (ATD) for at least six months. Failure to comply can lead to a recurrence of the disease and the development of multidrug-resistant (MDR) (6). Treatment is successful if patients adhere to their medication.

In general, ATD use can cause side effects, ranging from mild to severe, such as liver dysfunction, visual disturbances, peripheral neuropathy, seizures, allergic reactions, and gastrointestinal symptoms (7). These side effects can reduce quality of life and be a reason for unilateral discontinuation

of therapy (8). There is limited local evidence evaluating the incidence and determinants of ATD-related side effects among TB patients, particularly in referral hospital settings.

This study aimed to measure the incidence of ATD-related side effects and to analyze their association with patient was conducted to determine the incidence of ATD side effects so that appropriate treatment characteristics, treatment-related factors, and treatment outcomes among drug-sensitive TB patients receiving category I therapy at Mayjend H.A. Thalib General Hospital in Sungai Penuh City, during 2023-2024. By integrating side-effect profiles with potential clinical and treatment-related factors in an underrepresented referral-care setting, this study provides real-world evidence that may inform risk-based monitoring and early management of treatment-related toxicity during TB therapy.

METHOD

This was an observational study with a retrospective cross-sectional design. The data used were secondary data obtained from the medical records of tuberculosis patients at Mayjend H.A. Thalib General Hospital, Sungai Penuh City, during the period 2023–2024. The study population consisted of all TB-SO patients treated at the hospital, and the sample included patients who met the predetermined inclusion and exclusion criteria. The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, Universitas Jambi (approval No.2053/UN21.8/PT.01.04/2025).

The inclusion criteria included outpatients diagnosed with TB-SO and comorbidities, who had completed at least two months of treatment, were over 18 years of age, and received anti-tuberculosis therapy (ATD) according to the 2021 PDPI guidelines. A total of 128 patients met these inclusion criteria. Patients with incomplete medical records, including missing data on patients characteristics, ATD therapy, or laboratory results, as well as patients who died during the treatment period, were excluded from the study.

Sampling was performed using a consecutive sampling technique, whereby all eligible patients during the study period were included until the minimum required sample size was achieved. This technique was selected to reduce selection bias and is appropriate for retrospective studies using secondary data. The minimum sample size was calculated using the Lemeshow formula, and the final sample size met the calculated requirement.

Data analysis in this study was performed using SPSS version 20 and included both univariate and bivariate analyses. The univariate analysis was conducted to describe the sociodemographic characteristics and clinical characteristics of patients. This analysis aimed to provide an overview of the data distribution. Furthermore, bivariate analysis was carried out to determine the relationship between the studied variables using the Chi-Square test, with results reported as p-values and considered statistically significant when p-value < 0.05.

RESULTS

This study involved 128 drug-sensitive TB patients at Mayjend H.A. Thalib Gneral Hospital, Sungai Penuh, Jambi, during the 2023–2024 period. The sociodemographic and clinical data of TB patients as seen in table 1 and table 2.

Tabel 1. Sociodemographic Characteristics of TB Patients

No. Characteristics	Total n (%)
1 Gender	
Male	68 (53.1)
Female	60 (46.9)
2 Age	
<60 years	93 (72.7)
≥60 years	35 (27.3)
3 Employment Status	
Employed	80 (62.5)
Unemployed	48 (37.5)
4 Education	
Primary-secondary education (elementary, middle, high school)	93 (72.7)
Higher education (university)	35 (27.3)

Tabel 2. Clinical Characteristics of TB Patients

No.	Characteristics	Total n (%)
1 TB Diagnosis		
	Pulmonary TB	113 (88.3)
	Extrapulmonary TB	15 (11.7)
2 Type of ATD		
	Fixed-dose combination (FDC)	122 (95.3)
	Combipak	6 (4.7)
3 BMI		
	<23 kg/m ²	121 (94.5)
	≥23 kg/m ²	7 (5.5)
4 Smoking Status		
	Smoker	44 (34.4)
	Non-smoker	84 (65.6)
5 Comorbidities		
	Yes	10 (7.8)
	None	118 (92.2)
6 Duration of Treatment		
	<6 months	9 (7.0)
	≥6 months	119 (93.0)
7 Treatment Outcome		
	Cured	44 (34.4)

Completed Treatment	75 (58.6)
Discontinued Treatment (lost to follow-up)	9 (7.0)
8 Adverse Events	
Yes	73 (57.0)
None	55 (43.0)

Tabel 3. Types of ATD Side Effects

Types of Anti-Tuberculosis Drug Side Effects	Total n (%)
Nausea	46 (63.0)
Itching	42 (57.5)
Vomiting	20 (27.4)
Decreased appetite	16 (21.9)
Malaise	15 (20.5)
Reddish urine	12 (16.4)
Joint pain	8 (11.0)
Headache	7 (9.6)
Fever	6 (8.2)
Elevated liver enzymes	5 (6.8)
Tingling	4 (5.5)

Tabel 4. Factors related to Incidence of ATD Side Effects

Variables	Anti-TB Drug Side Effects		P value	OR	CI 95%
	Yes	No			
Type of Anti-TB Drug					
Fixed-Dose Combination (FDC)	67 (54.9)	55 (45.1)	0.037	-	-
Combipak	6 (100.0)	0 (0.0)			
Gender					
Male	38 (55.9)	30 (44.1)	0.920	0.905	(0.448-1.825)
Female	35 (58.3)	25 (41.7)			
Age					
<60 Years	51 (54.8)	42 (45.2)	0.538	0.718	(0.323-1.594)
≥60 Years	22 (62.9)	13 (37.1)			
Employment Status					
Employed	44 (55.0)	36 (45.0)	0.678	0.801	(0.387-1.657)
Unemployed	29 (60.4)	19 (39.6)			
Education					
Primary-secondary education (elementary, middle, high school)	52 (55.9)	41 (44.1)	0.829	0.846	(0.384-1.864)
Higher education (university)	21 (60.0)	14 (40.0)			
TB Diagnosis					
Pulmonary TB	65 (57.5)	48 (42.5)	0.976	1.185	(0.402-3.492)
Extrapulmonary TB	8 (53.3)	7 (46.7)			
BMI					
<23 kg/m ²	68 (56.2)	53 (43.8)	0.698	0.513	(0.096-2.750)
≥23 kg/m ²	5 (71.4)	2 (28.6)			
Smoking Status					
Smoker	21 (47.7)	23 (52.3)	0.177	0.562	(0.269-1.175)
Non-smoker	52 (61.9)	32 (38.1)			
Comorbidities					
Yes	9 (90.0)	1 (10.0)	0.043	7.594	(0.932-61.856)

None	64 (54.2)	54 (45.8)			
Duration of Treatment					
<6 months	9 (100.0)	0 (0.0)	0.010	-	-
≥6 months	64 (53.8)	55 (46.2)			
Treatment Outcome					
Cured	21 (47.7)	23 (52.3)			
Completed Treatment	43 (57.3)	32 (42.7)	0.015	-	-
Discontinued Treatment (lost to follow-up)	9 (100.0)	0 (0.0)			

DISCUSSIONS

Based on the table 1, the majority of TB patients were male, totaling 68 patients (53.1%), while females accounted for 60 patients (46.9%). This finding is consistent with the 2023 WHO report and the study by Humayun et al. (2022), which stated that men are more frequently diagnosed with TB than women (2)(9). One of the possible reasons is that men tend to have more outdoor activities, such as working or socializing, which increases the likelihood of TB exposure (9). Compared to women, men are also more likely to experience a decrease in immune system function due to fatigue or unhealthy habits, making them more susceptible to this disease (10).

In terms of age, most TB patients were under 60 years old (72.7%). This aligns with the study by Aida et al. (2022), which indicated that individuals of productive age are closely associated with high levels of social activity and mobility, increasing the likelihood of contact with TB patients and exposure to *Mycobacterium tuberculosis* bacilli in workplaces, public transportation, or other public places (11).

Regarding employment status, the majority of TB patients were employed, totaling 80 patients (62.5%), while 48 patients (37.5%) were unemployed. The most common occupations were self-employed workers and farmers. The study by Arisandi and Muhajir (2024) also reported that the majority of TB patients in Nglipar District (63.64%) were workers, where occupations such as self-employment—which involve frequent interaction with many people or working in dusty environments—increase the risk of TB transmission (12). Talarima et al. (2021) stated that the prevalence of pulmonary TB was higher among farmers or

fishermen (42.8%) due to lower educational levels, poor working environments, and smoking habits triggered by heavy workloads (13). Workers with heavy workloads, such as drivers, construction workers, laborers, and civil servants, are also at higher risk of developing TB due to lack of rest and unhealthy lifestyles (14).

In terms of educational level, 93 patients (72.7%) had primary to secondary education, while 35 patients (27.3%) had higher education. Education plays an important role in decision-making related to adopting healthy living behaviors and influences patients' understanding of TB transmission and treatment (15). The higher the educational level, the better the knowledge regarding TB prevention, although a higher level of education does not always guarantee the formation of attitudes or actions consistent with the intended goals (16).

The clinical characteristics data as seen in table 2 shows that the majority of patients had pulmonary TB, totaling 113 patients (88.3%), while extrapulmonary TB occurred in only 15 patients (11.7%). This is because *Mycobacterium tuberculosis* is transmitted through the air contaminated by droplets from an infected person when coughing or sneezing, allowing the bacteria to first enter and settle in the lungs. This condition makes the lungs the most frequently infected organ, although in some cases, the bacteria may spread through the bloodstream or lymphatic system to other organs such as the brain, kidneys, bones, or digestive tract, which is referred to as extrapulmonary TB (17).

Regarding the type of anti-tuberculosis drugs (ATD), the majority of patients, 122 (95.3%), used fixed-dose combinations (FDC), while 6 patients (4.7%)

used combipacks. FDC is a medication package for one treatment period with doses adjusted according to the patient's body weight, thereby minimizing dosing errors, reducing the number of tablets, and improving adherence and therapeutic effectiveness (18). FDC-TB drugs contain 2–4 types of medications in a single tablet administered during both the intensive and continuation phases (19). Meanwhile, combipack refers to loose-packaged drugs containing isoniazid, rifampicin, pyrazinamide, and ethambutol in blister form, intended for patients who cannot tolerate FDC (20).

Based on Body Mass Index (BMI) status, the distribution showed that 121 patients (94.5%) had a BMI <23 kg/m², while 7 patients (5.5%) had a BMI ≥23 kg/m². Patients with low nutritional status are more susceptible to TB infection due to reduced immune defense, as reported by Risanti et al. (2025), who found a correlation between low body weight and poor TB treatment outcomes. Low BMI may also affect drug pharmacokinetics, such as lowering plasma drug concentrations, increasing renal elimination, and impairing absorption due to intestinal morphology and enzyme function changes. These conditions contribute to suboptimal therapy and may lead to treatment failure and TB recurrence (21).

Based on smoking status, 44 patients (34.4%) were smokers, while 84 patients (64.6%) were non-smokers. This finding is similar to Atira (2020), who reported that 38 patients (45.2%) were active smokers and 46 patients (54.8%) were non-smokers or passive smokers (22). Smoking can reduce the effectiveness of the respiratory defense mechanism because cigarette smoke inhibits ciliary movement and stimulates mucus production. This condition causes mucus buildup, facilitating bacterial growth, including *Mycobacterium tuberculosis*, the causative agent of pulmonary TB. Not only active smokers but also passive smokers are at risk due to exposure to cigarette smoke containing harmful chemicals. The more frequent the exposure, the higher the risk of developing pulmonary TB (23).

Comorbidity characteristics showed that only 10 patients (7.8%) had comorbid diseases, while 118 patients (92.2%) did not. According to Adawiyah et al. (2023), in a study involving 340 patients, the most common comorbidity among TB patients was diabetes mellitus (17.1%). In TB patients with diabetes, hyperglycemia can disrupt body metabolism, reduce cellular immunity, and weaken phagocytic and macrophage functions, leading to slower bacterial clearance (24).

In terms of treatment duration, most patients, 119 (93%), had undergone therapy for ≥6 months, while 9 patients (7%) had been treated for less than 6 months. The duration of TB treatment refers to the time required to prevent relapse, drug resistance, transmission, and death. Generally, TB treatment lasts for 6–8 months (25). The results are consistent with Adawiyah et al. (2023), who reported that most TB patients (93.2%) underwent treatment for more than 6 months, compared to only 6.8% who were treated for less than 6 months (24).

Treatment outcomes showed that 44 patients (34.4%) were cured, 75 patients (58.6%) completed the entire therapy, and 9 patients (7%) defaulted on treatment. A study by Saefina et al. (2025) reported similar results, where most patients completed therapy, but a small proportion defaulted. This highlights the need for strict monitoring to ensure patients remain adherent until treatment completion (26).

Adverse drug reactions (ADRs) related to anti-tuberculosis drugs were observed in 73 patients (57%), while 55 patients (42%) did not experience them. The high rate of adverse effects may be due to prolonged drug use, type of combination regimen, or individual variations in response to therapy. ADRs require special attention as they may affect treatment adherence and increase the risk of treatment interruption. Therefore, continuous monitoring and patient counseling are essential to ensure therapeutic success without compromising patients' quality of life (27).

Several common TB regimens include Isoniazid, Rifampicin, Pyrazinamide, and

Ethambutol. According to *Pharmacotherapy Handbook* (9th edition) by Dipro (2015), Isoniazid may cause adverse effects such as elevated liver enzyme levels often without clinical symptoms clinical hepatitis, and even fatal hepatitis. It may also lead to peripheral neuropathy, hypersensitivity reactions, and diarrhea. Rifampicin commonly causes skin and gastrointestinal reactions such as nausea, loss of appetite, and abdominal pain. Some patients may also develop flu-like symptoms, hepatotoxicity, severe immunologic reactions, and discoloration of body fluids such as sputum, urine, sweat, and tears to a reddish color. Pyrazinamide can cause hepatic dysfunction, gastrointestinal symptoms (nausea, vomiting), and joint pain. It may also lead to asymptomatic hyperuricemia, acute gout attacks, transient skin rash, and dermatitis. Meanwhile, Ethambutol can cause retrobulbar neuritis characterized by visual disturbances, particularly decreased visual acuity and red-green color discrimination difficulty, as well as peripheral neuropathy and skin reactions (28)(29).

Based on the table 3, the results of the study showed that most patients experienced adverse effects of anti-tuberculosis drugs in the form of gastrointestinal disorders, with the most common complaints being nausea (63%), vomiting (27.4%), and loss of appetite (21.9%). This finding is consistent with the study by Maulitha et al. (2020), which also reported nausea, vomiting, and loss of appetite as the most frequent complaints (30). These disorders are generally triggered by the use of rifampicin, isoniazid, and pyrazinamide (31). Symptoms of nausea and vomiting can be reduced by drinking warm water, taking the medication before bedtime, or administration of vitamin B6, omeprazole, or metoclopramide. Meanwhile, the side effect of loss of appetite can be managed by giving vitamin B complex (32).

The next most frequently reported adverse effect was allergic reactions in the form of itching (57.5%). This condition can be caused by all types of anti-tuberculosis drugs and generally occurs due to skin allergic reactions to the active drug substances such

as monoacetylhydrazine metabolite from isoniazid and desacetyl rifampicin from rifampicin. In mild cases, the complaints can be relieved with antihistamines or vitamin B6, while in severe reactions, temporary discontinuation of anti-tuberculosis drugs is necessary (33).

Treatment with rifampicin can cause renal failure and interstitial nephritis, which are usually preceded by symptoms of fever and flu-like syndrome, such as fatigue, headache, and bone pain(32). In this study, several patients experienced symptoms of malaise (20%), headache (9.6%), and fever (6.8%), which are generally related to the use of rifampicin. These complaints are usually mild and can be treated with symptomatic therapy such as the administration of antipyretics (34).

Based on the data obtained, it was found that 12 patients (16.4%) reported red-colored urine. The red color of urine is a common side effect of rifampicin use. This condition is not dangerous because it is caused by drug metabolic residues. Considering that this side effect is harmless, management can be carried out by providing Communication, Information, and Education (CIE) to patients (27). This is in line with the study by Putri et al. (2024), which recorded 20 out of 30 patients experienced red-colored urine. This indicates that the side effect is commonly found (27).

Joint pain was recorded in 11% of patients, which is mainly related to the use of pyrazinamide through the mechanism of increased uric acid levels. Management can be carried out by giving anti-inflammatory drugs. Management is given according to the symptoms, namely anti-inflammatory drugs such as aspirin (33). The study by Tri Siwi et al. (2020) showed similar results, with 14.1% of patients experiencing muscle pain symptoms (35).

An increase in liver enzymes (ALT/AST) was found in 8.2% of patients, indicating a risk of hepatotoxicity due to pyrazinamide or a combination of other anti-tuberculosis drugs. This side effect requires special attention because it can lead to liver injury, so periodic monitoring of liver function

is highly recommended (35). If drug-induced hepatotoxicity occurs during TB treatment, therapy should be temporarily discontinued until clinical symptoms improve for two weeks and liver function returns to normal. After that, pyrazinamide is no longer used in the treatment regimen (36).

Another symptom reported was tingling (5.5%) due to the use of isoniazid. Tingling or burning sensations in the palms and soles can occur due to isoniazid use. To overcome these complaints, patients are usually given vitamin B6 (pyridoxine) as adjunct therapy to prevent peripheral neuropathy, which is commonly caused by isoniazid (37).

Based on the table 4, the analysis results show that among the types of ATD used, the FDC group had 54.9% of patients experiencing side effects and 45.1% without, while the Kombipak group showed all patients (100%) experiencing side effects, with a p-value of 0.037, indicating a significant difference between the type of ATD and the occurrence of side effects. This finding is consistent with the study by Maharani et al. (2024), which reported that the FDC formulation caused more side effects, with a p-value of 0.022 (<0.05) (18). The use of FDC ATD potentially causes more side effects because the dosage is determined based on weight groupings, whereas the Kombipak dosage is more specifically calculated according to the patient's body weight (18). The higher side-effect rate in the Combipak group may reflect confounding by indication, as separate-drug regimens are often used in patients with prior intolerance or need for dose adjustment. The retrospective design also prevents establishing temporal relationships, making this association hypothesis-generating only. Gastrointestinal symptoms (nausea, vomiting, decreased appetite) were most common, likely related to isoniazid, rifampicin, and pyrazinamide. Although usually non-severe, these effects can impair nutrition and adherence, highlighting the need for early recognition and management in TB patients.

The male group showed 55.9% experiencing side effects, while 35 female

patients (58.3%) experienced side effects, with a p-value of 0.92; OR=0.905 (0.448–1.825), indicating no significant difference. This result aligns with Pratiwi et al. (2018), who reported no significant relationship between gender and side effects ($p>0.05$) (38). However, Shareef et al. (2018) reported that women tend to experience side effects more frequently due to physiological factors such as pregnancy, menstruation, and smaller body size (39).

In the age variable, the group aged <60 years showed 54.8% with side effects, while those aged ≥ 60 years had 62.9% with side effects, with a p-value of 0.538; OR=0.718 (0.323–1.594). There was no significant difference between age and side effects. However, Lee et al. (2022) and Resende et al. (2015) stated that elderly individuals are at higher risk of hepatotoxicity due to decreased metabolism and enzymatic activity (40)(41).

Employment status showed that 55% of working patients experienced side effects and 29 non-working patients (60.4%) did, with a p-value of 0.678; OR=0.801 (0.387–1.657), indicating no significant difference. These findings are similar to those of Amalba & Bugri (2021) and Djochie et al. (2023), who also found no direct relationship between employment and ATD side effects (42)(43).

Regarding education level, 55.9% of patients with primary–secondary education experienced side effects, while 60% of those with higher education did, with a p-value of 0.829; OR=0.846 (0.384–1.864), indicating no significant difference. According to Imam et al. (2021), side effects were more common among patients with primary–secondary education (44). Education plays an important role in improving patients' understanding of therapy, where good knowledge is associated with higher treatment adherence (45)(46). Although education contributes to patient awareness, ATD side effects may still occur across all educational levels.

Pulmonary TB patients showed 57.5% with side effects, while extrapulmonary TB patients showed 53.3%, with a p-value of 0.976; OR=1.185 (0.402–3.492), indicating no significant difference. Jorge et al. (2024)

reported that pulmonary TB had more side effects (78.3%) than extrapulmonary TB (21.7%) (46), while Shi et al. (2024) found the opposite, with extrapulmonary TB having a higher incidence (33.8%) (47). The difference in findings may be influenced by the smaller number of extrapulmonary TB samples.

Regarding BMI, the group with <23 kg/m² had 56.2% experiencing side effects, while ≥ 23 kg/m² had 71.4%, with a p-value of 0.379; OR=1.479 (0.718–3.047). There was no significant difference between BMI and side effects. Delgado et al. (2011) stated that BMI ≥ 25 kg/m² is associated with drug toxicity due to dosages calculated based on total body weight (48). Other studies also reported that higher doses in obese patients may increase the likelihood of side effects (49). Larsson et al. (2025) added that a decrease in BMI may reflect the early pathogenesis of TB through metabolic and immunological changes (50).

Based on smoking status, 47.7% of smoking patients experienced side effects, while 61.9% of non-smoking patients did, with a p-value of 0.177; OR=0.562 (0.269–1.175), indicating no significant difference. Shi et al. (2024) also reported similar results (p=0.975; OR=1.004) (51). However, Chumovarov et al. (2022) explained that chemicals in cigarette smoke can reduce immunity and increase the risk of liver toxicity (52).

Among patients with comorbidities, 9 patients (90%) experienced side effects and 1 patient (10%) did not, with a p-value of 0.043; OR=7.594 (0.932–61.865), showing a significant relationship. This result aligns with Teshome et al. (2022), who stated that patients with comorbidities were six times more likely to experience side effects (AOR=5.809; p=0.038) (53). Drug–drug interactions and the number of medications taken increase toxicity risk (54)(55). Handayani (2015) stated that patients taking more than five types of drugs are 10.278 times more likely to experience side effects (56).

Based on treatment duration, all patients treated for <6 months (100%) experienced side effects, while ≥ 6 months

showed 53.8% with side effects, with a p-value of 0.010, indicating a significant difference. This finding is consistent with Natalie et al. (2016) and Shi et al. (2024), who showed that treatment duration was significantly associated with side effects (57)(47). Side effects commonly appear in the early phase of therapy as the body adapts, as reported by Nurbiah (2018), where 96% of patients experienced complaints during the initial phase (51).

The final treatment outcomes showed that 47.7% of the cured group experienced side effects, 57.3% of the completed treatment group did, and 100% of those who defaulted on treatment had side effects, with a p-value of 0.015, indicating a significant difference. SKI (2023) mentioned that one reason for treatment interruption is intolerance to side effect (3). Patients experiencing side effects tend to be non-adherent and may discontinue therapy (58). In this study, all patients who defaulted on treatment experienced side effects, indicating the importance of early education on potential side effects so patients understand that such reactions can be managed and are not a reason to discontinue treatment (59).

A strength of this study is the provision of real-world pharmacovigilance evidence from a referral-care setting in Sumatra, an Indonesian region that remains underrepresented in the international literature on ATD-related toxicity. The study also evaluated a broad range of sociodemographic, clinical, and treatment-related characteristics rather than reporting the frequency of individual symptoms alone. This allows the findings to generate hypotheses regarding which patients or phases of treatment may warrant closer monitoring.

Therefore, this study has several limitations. The data were obtained retrospectively from medical records, so some important information, such as the severity of adverse effects and patient adherence, was not completely recorded. The study was also conducted in a single hospital, making the results less generalizable to a broader population.

Despite these limitations, this study provides clinically relevant real-world evidence on ATD-related side effects among patients receiving treatment for drug-sensitive TB at Mayjend H.A. Thalib General Hospital, a referral hospital in Sungai Penuh, Indonesia. As the study was conducted in a referral-care setting serving the local population, the findings provide important context-specific evidence on the burden and clinical patterns of ATD-related side effects in Sungai Penuh. Nevertheless, given the single-centre design, the findings should not be interpreted as population-level estimates for the entire city.

More importantly, the findings indicate that treatment toxicity should not be viewed merely as a collection of isolated symptoms. Its occurrence appears to intersect with comorbidity, treatment phase, drug formulation, and treatment completion. These relationships highlight the potential value of integrating pharmacovigilance with routine clinical follow-up and adherence support. Prospective multicentre studies incorporating standardized ADR definitions, severity grading, causality assessment, laboratory monitoring, adherence measurement, and multivariable modelling are warranted to determine independent predictors and evaluate whether early, risk-based management of ATD-related toxicity can

improve treatment completion and clinical outcomes.

CONCLUSIONS

ATD-related side effects were common among patients with drug-sensitive TB treated at Mayjend H.A. Thalib General Hospital, with more than half experiencing at least one side effect. Gastrointestinal and cutaneous manifestations predominated, particularly nausea, itching, vomiting, and decreased appetite. ATD formulation, comorbidities, treatment duration, and treatment outcomes were significantly associated with the occurrence of side effects. However, these associations should be interpreted cautiously given the retrospective design, small subgroup sizes, and absence of multivariable adjustment. These findings emphasize the importance of early detection and systematic monitoring of ATD-related toxicity, particularly among patients with comorbidities and during the early phase of treatment. Integrating pharmacovigilance, patient counselling, and timely management of side effects into routine TB care may improve treatment tolerability and support treatment completion.

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