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An Evaluation of Reported Anti-Tuberculosis Drug Reactions at the DOTS Pharmacy Depot in Al-Ihsan Regional Hospital, West Java

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ABSTRACT:
Tuberculosis (TB) remained a major public health concern in Indonesia, which ranked second globally after India in TB burden. As TB treatment relied on long-term administration of combined Anti-Tuberculosis Drugs (OAT), patients often experienced treatment challenges, including adverse drug reactions that could reduce adherence and compromise therapeutic success. However, local data regarding the pattern of these reactions—particularly in West Java—had been limited, creating a gap in monitoring practices that were essential for improving patient outcomes. This study aimed to evaluate the types and frequencies of adverse drug reactions reported by TB patients receiving treatment at the DOTS Pharmacy Depot of Al-Ihsan Regional Hospital.
This research used a descriptive design with primary data collected from the DOTS Pharmacy Depot. Reported adverse reactions were compiled and analyzed, then presented in tables and graphs to provide a clear overview of the distribution of events. The evaluation focused on patients undergoing Category I OAT therapy during 2023, allowing the study to capture real-world reactions experienced over the course of standard TB treatment.
The findings showed that female patients experienced more adverse reactions than males, suggesting potential sex-related differences in susceptibility or reporting. Overall, gastric pain emerged as the most common adverse effect (39.09%), followed by itching (33.04%), headache (11.07%), hyperuricemia (6.64%), nausea and vomiting (5.15%), and epigastric pain (4.13%). These reactions aligned with the known pharmacological profiles of first-line OAT regimens, particularly rifampicin and pyrazinamide, which are commonly associated with gastrointestinal irritation and metabolic disturbances.
In conclusion, the study highlighted the urgent need for enhanced pharmacovigilance, early recognition of common adverse reactions, and improved patient education to support treatment adherence. Understanding local patterns of drug reactions provided valuable insights for clinicians and contributed to more effective TB management strategies in West Java.

KEYWORDS: Anti-Tuberculosis Drugs, Adverse Drug Reactions, DOTS Pharmacy, Pulmonary Tuberculosis, West Java.

INTRODUCTION:

Tuberculosis (TB) was a contagious disease caused by *Mycobacterium tuberculosis*, primarily affecting the lungs but also capable of attacking other organs, such as the meninges, skin, bones, and lymph nodes, when the bacteria spread through the bloodstream. This condition, known as extrapulmonary tuberculosis, posed significant clinical challenges due to its varied manifestations and complications (Permenkes No 67, 2016). Despite global efforts to control TB, Indonesia remained one of the countries with the highest disease burden, ranking second after India, with approximately 969,000 cases and 93,000 deaths annually—equivalent to 11 deaths per hour. TB incidence was highest among productive age groups, particularly individuals aged 45 to 54 years, emphasizing the urgent public health impact of this disease (Kemenkes, 2016).

The cornerstone of TB treatment involved a combination of anti-tuberculosis drugs (OAT) administered over a minimum of six months, including an intensive phase of two months followed by a continuation phase of four months. These regimens were carefully structured to ensure effective eradication of the bacteria, but in practice, patient adherence often fell short, increasing the risk of multi-drug resistance. In Indonesia, first-line TB therapy consisted of fixed-dose combination tablets, containing either four or two active ingredients tailored to patient body weight, with Category I and II regimens available through national DOTS programs (Kemenkes, 2016).

Despite the availability of standardized treatment, adverse drug reactions (ADRs) remained a major obstacle in TB management. ADRs such as gastrointestinal discomfort, itching, headaches, hyperuricemia, nausea, and vomiting frequently led to interruptions in therapy, undermining treatment success and contributing to persistent infection and increased morbidity and mortality (Nilamsari *et al.,* 2021). These challenges highlighted the urgent need for systematic monitoring of drug reactions to prevent treatment discontinuation and the development of drug resistance.

Patient adherence was influenced not only by the duration of therapy but also by the occurrence of adverse reactions and patients' awareness of their condition. Proper monitoring of OAT-related ADRs, combined with patient education about potential side effects—including dizziness, nausea, abdominal pain, skin reactions, and changes in urine color—was essential to ensure treatment efficacy and minimize complications (Syahrina *et al.,* 2024). However, limited studies had examined the pattern and prevalence of ADRs in local hospital settings, particularly in West Java, creating a gap in knowledge that hindered optimal patient management.

In response to this gap, this study aimed to evaluate the reported adverse drug reactions associated with anti-tuberculosis therapy at the DOTS Pharmacy Depot of Al-Ihsan Regional Hospital, West Java. By identifying the most common reactions and their distribution across patient groups, the research sought to provide insights that could improve monitoring, patient counseling, and adherence strategies, ultimately supporting more effective TB management in the region.

MATERIALS AND METHODS:

Study Design

This study used a descriptive research design based on primary data collected from patients undergoing anti-tuberculosis therapy. All information gathered during the study was organized, summarized, and displayed in tables and graphs to illustrate patterns of reported adverse drug reactions. This design allowed the researchers to observe the frequency and characteristics of side effects associated with first-line anti-tuberculosis drugs in a real clinical setting.

Study Setting and Period

The research was conducted at the DOTS Pharmacy Depot of Al-Ihsan Regional Hospital, West Java, where standardized OAT regimens were dispensed and monitored. Data collection took place in January 2024. The study population consisted of all pulmonary tuberculosis patients treated at the hospital

throughout 2023, while the sample included those who were diagnosed as pulmonary TB patients and recorded in the DOTS program during the same year.

Population, Sample, and Study Variables

The main study variable was the occurrence of adverse drug reactions related to first-line anti-tuberculosis therapy. Operationally, an adverse reaction was defined as any undesirable effect experienced by a patient while consuming OAT, measured using MESO data archived in the DOTS Pharmacy Depot. The results were later visualized through tables and graphs. The inclusion criteria required that participants be pulmonary TB patients receiving Category I (OAT I) therapy. The exclusion criteria eliminated patients who were color-blind, or those who had died or dropped out before completing therapy, as their incomplete data could compromise the reliability of the study.

Research Instruments and Measurement Tools

The primary research instrument consisted of MESO records documented at the DOTS Pharmacy Depot in 2023, which detailed drug-related reactions experienced by TB patients. These MESO files also functioned as the measurement tool, providing structured evidence of each adverse event. After data retrieval, the information was processed using tables and diagrams to help compare the frequency and distribution of different adverse reactions.

Data Processing and Analysis

Data analysis focused on identifying the types and frequency of adverse effects experienced by pulmonary TB patients during 2023. Each reported reaction was summarized and plotted into annual graphs, and the data were grouped to determine which reactions occurred more or less frequently. The analysis also involved linking each reaction to the RHZE regimen to understand the pharmacological basis for the adverse events, as well as considering relevant non-pharmacological factors. Finally, the dataset was grouped by sex to determine whether male or female patients experienced more adverse reactions, followed by a brief interpretation of the possible reasons behind these differences.

RESULT:

Based on the collected MESO data, a total of 2,328 adverse drug reaction events were recorded during 2023, with gastric pain appearing as the most frequent reaction as shown in Table 1. Itching ranked second in frequency, followed by headaches, hyperuricemia, nausea and vomiting, and epigastric pain, all of which are detailed in Table 1. The data also showed that female patients reported more reactions than male patients, indicating a possible difference in susceptibility.

Table 1. Reported Adverse Drug Reactions and Patient Distribution at the DOTS Pharmacy Depot, Al-Ihsan Regional Hospital, 2023

Adverse Reaction & Medication Used	Total Patients	Male	Female
Gastric Pain – Omeprazole 20 mg	918	397	521
Itching – Cetirizine 10 mg	776	392	384
Headache – Paracetamol 500 mg	260	108	152
Hyperuricemia – Allopurinol 300 mg	156	67	89
Nausea and Vomiting – Ondansetron 4 mg	121	44	77
Epigastric Pain – Clixid 5 mg	97	32	65
TOTAL	**2,328**	**1,010**	**1,286**

When expressed proportionally, gastric pain accounted for 40% of all reported reactions, making it the dominant adverse effect experienced by patients, as illustrated in Table 2. Itching accounted for another significant share at 33%, while headaches contributed 11%. Hyperuricemia, epigastric pain, and nausea and vomiting made up smaller portions of reaction categories, each shown in the percentage breakdown in Table 2.

Table 2. Percentage Distribution of Adverse Drug Reactions Among TB Patients in 2023

Adverse Reaction	Percentage (%)
Hyperuricemia	7
Headache	11
Epigastric Pain	4
Gastric Pain	40
Itching	33
Nausea and Vomiting	5

Overall, the results emphasized that gastrointestinal symptoms were the most prominent concerns among TB patients during therapy, with the highest frequencies consistently appearing in Table 1 and the largest percentage share captured in Table 2. These findings suggested a clinical need for strengthened monitoring strategies and patient education efforts to manage the most common symptoms throughout OAT therapy.

DISCUSSION:

The findings of this study showed that gastric pain and itching were the most frequently reported adverse drug reactions among TB patients receiving OAT therapy. Gastric pain occurred largely due to the acidic nature of rifampicin, which has been known to cause gastric irritation and potentially lead to gastric or peptic ulceration. Acidic drugs may trigger local irritation that allows gastric acid to diffuse back into the mucosa, resulting in tissue damage (Ningsih *et al.,* 2022). In this hospital, omeprazole was used to manage these symptoms. As a proton pump inhibitor, omeprazole reduced acid secretion by selectively blocking the H^+/K^+-ATPase enzyme in parietal cells, producing a prolonged inhibitory effect (Nuryati, 2017). Non-pharmacological measures—such as drinking warm water, avoiding lying down after meals, limiting caffeine and alcohol, consuming ginger, and elevating the head during sleep—were also recommended to ease gastric discomfort (Syokumawena *et al.,* 2021).

Itching also appeared frequently and was associated with hypersensitivity reactions triggered by various OAT components. In mild cases, therapy was continued with close monitoring and antihistamine support such as cetirizine. This medication has a wide therapeutic index, acts selectively, and does not cause sedation due to its low lipophilicity, which prevents it from crossing the blood–brain barrier (Gilboa *et al.,* 2014). If itching worsened or skin redness appeared, OAT was temporarily halted until symptoms resolved (Ningsih, 2022)Non-pharmacological care, including maintaining skin hygiene and applying talc powder, supported symptom relief (Syokumawena *et al.,* 2021). Hyperuricemia was another common reaction, primarily linked to pyrazinamide. This medication facilitated ion exchange in the renal tubules, causing excessive uric acid reabsorption and leading to elevated serum uric acid levels (Kondo *et al.,* 2016). Allopurinol, a uricostatic agent, was administered to reduce uric acid synthesis by inhibiting xanthine oxidation (Muthiah et al., 2020), and patients were also advised to follow a low-purine diet, maintain moderate physical activity, and apply warm ginger–lemongrass compresses (Toto, 2023).

Other reactions, such as nausea and vomiting, were associated with the emetogenic effects of OAT metabolites, which stimulated vagal release of 5-HT3 (Ningsih *et al.,* 2022). These symptoms were managed with ondansetron, a selective serotonin blocker that inhibited 5-HT3 activity in the gastrointestinal tract (Griddine, 2023). Non-pharmacological recommendations included warm water intake, avoiding lying down immediately after meals, and limiting alcohol and caffeine consumption.

Epigastric pain was also reported and linked to increased gastric acid production caused by rifampicin and isoniazid (WHO, 2015). Patients were treated with Clixid—containing chlordiazepoxide and clidinium bromide—which reduced anxiety, muscle spasms, and gastrointestinal cramping (Adelia, 2019). Complementary therapies such as massage, relaxation techniques, and Su Jok self-therapy were often encouraged to reduce discomfort (Utami, 2018; Yagil, 2019).

Headache was another reaction observed in patients receiving rifampicin and was classified as a probable adverse effect because it matched the timing of daily drug use and could not be explained by other conditions (Kementerian Kesehatan RI, 2020). Patients were usually managed with paracetamol, an analgesic believed to reduce prostaglandin production in the central nervous system (Roberts *et al.,* 2016). Non-pharmacological measures like lavender aromatherapy were helpful in promoting relaxation and reducing distress, as lavender has anxiolytic and anti-depressant effects that modulate sympathetic activity and cortisol release (Nategh *et al.,* 2015). When reactions were analyzed by sex, female patients experienced more adverse effects than males. This finding aligned with previous research showing that women generally have lower body weight, smaller organ size, different gastric motility, higher body fat percentage, and lower glomerular filtration rates—factors that influence both pharmacokinetics and pharmacodynamics (Gumanti *et al.,* 2020). Hormonal and physiological differences may also contribute to the higher incidence of adverse reactions among women.

CONCLUSION:

This study demonstrated that adverse drug reactions remained a significant challenge for patients undergoing anti-tuberculosis therapy at the DOTS Pharmacy Depot of Al-Ihsan Regional Hospital. The research addressed an important gap in local data availability, as detailed information about the types and frequency of anti-TB drug reactions in this setting had previously been limited. By analyzing patient records from 2023, the study showed that gastric pain was the most frequently reported reaction (39.09%), followed by itching (33.04%), headache (11.07%), hyperuricemia (6.64%), nausea and vomiting (5.15%), and epigastric pain (4.13%). These findings underscored the urgency of improving monitoring and early management of side effects, as they can influence treatment adherence and ultimately affect therapeutic success.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

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Nil

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ADDITIONAL INFORMATION

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