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Literature Review: Factors Influencing the Incidence of Multi-Drug Resistant in Tuberculosis Patients

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ABSTRACT
Multi-Drug Resistant (MDR) tuberculosis was tuberculosis resistance to at least two first-line drugs: isoniazid and rifampicin. This resistance meant that rifampicin and isoniazid were ineffective in eradicating the Mycobacterium bacteria. The primary factor contributing to MDR TB was treatment adherence. Non-adherence led to high rates of treatment failure and was directly linked to an increase in MDR TB cases. Therefore, it is crucial to understand the contributing factors of MDR TB to prevent and reduce new occurrences. To analyze the risk factors causing MDR TB incidence in Indonesia through a literature review. The study employed a literature review method, with data obtained from Google Scholar, Research Gate, Connected Papers, and Google Books. The study found several factors that contributed to MDR TB incidence, including patient adherence, motivation, alcohol consumption, smoking, nutritional status, diabetes mellitus, history of previous treatment, the role of healthcare workers, and contact with other TB patients. The conclusion of the 13 articles reviewed shows that adherence to treatment, motivation, alcohol consumption, smoking, nutritional status, diabetes mellitus, history of treatment, role of health workers, and contact with patients were factors influencing the occurrence of MDR-TB.

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis (Umar, 2023). Tuberculosis ranks second as a cause of death in Indonesia (WHO, 2020). Ninety-five percent of TB cases and 98 percent of TB deaths worldwide occur in developing countries. According to data from the Indonesian Ministry of Health's dashboard, the number of TB cases increases annually. In 2023, there were 821,200 cases, and in 2024, there were 856,420 cases. The latest data, as of May 5, 2025, showed 254,081 TB cases (Ministry of Health, 2025). The increase in TB cases in Indonesia is due to drug resistance. Tuberculosis resistance occurs when TB bacteria become immune to anti-tuberculosis drugs (OAT) (Wibowo, 2021). There are 6 types of resistance to OAT, including monoresistance, polyresistance, Multidrug Resistance (MDR), Pre-Extensively Drug Resistance (XDR), Extensively Drug Resistance (XDR), and Rifampicin-Resistant TB (RR) (P2P, 2020).

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Tuberculosis treatment requires patients to take medication regularly and continuously for six consecutive months. Patient discipline in treatment requires direct supervision by a close family member, as a reminder to take the medication regularly. Patients who discontinue treatment and do not comply with the standards will experience relapse and the development of resistance. Discontinuing treatment and not adhering to the Directly Observed Treatment, Short-course (DOTS) standard can lead to the emergence of multiple resistance to anti-tuberculosis drugs, which creates a stronger strain of TB bacteria, known as Multi-Drug Resistant (MDR-TB).

*Multi Drug Resistant (*MDR-TBis the biggest obstacle in eradicating tuberculosis. According to the Indonesian Ministry of Health, the number of MDR TB cases in 2024 reached 9,573. The latest data as of May 5, 2025, the number of MDR TB cases discovered reached 3,742. Multidrug Resistance (MDR) is a stage or condition in which Mycobacterium tuberculosis becomes minimally resistant to rifampicin and INH (insonicotinylhydrazine) with or without anti-tuberculosis drugs (OAT) (Soleha, 2018). Both drugs are no longer effective in eradicating Mycobacterium tuberculosis bacteria, so different treatment standards and regimens are required for OAT (Pratama et al, 2020). Rifampicin and INH are first-line tuberculosis drugs. In the treatment of tuberculosis, Rifampicin works by inhibiting the elongation of messenger RNA. Meanwhile, INH is a prodrug activated by the enzyme catalase. MDR TB which is resistant to rifampicin and INH is caused by mutations in the codon (Rahmawati & Lestari, 2024)

The occurrence of MDR TB is caused by various factors, one of which is medication adherence. Medication adherence in tuberculosis patients is crucial for successful therapy (Putri et al., 2025). Irregular treatment can lead to resistance in Mycobacterium tuberculosis. Non-adherence to treatment results in a high failure rate for TB patients, and patient non-adherence is closely related to the cause of MDR TB (Kusmandari et al., 2023). Management of MDR TB is very complex and requires approximately 18-24 months. MDR treatment generally uses at least five types of drugs. The large number of drugs used in MDR TB often causes problems with drug tolerance. In addition to the large number of drugs, the treatment of MDR TB is uncertain (Mashidyanti, 2020).

The existence of MDR TB incidents is necessary to determine the factors causing MDR TB. With,Knowing the factors causing resistance can prevent and reduce new cases related to MDR-TB incidents.Therefore, researchers are interested in conducting a review article to determine the factors that influence the occurrence of Multidrug Resistance in TB patients.

METHOD

The method used in this study was to collect articles obtained from Google Scholar, Research Gate, Connected Paper, and Google Books. The keywords used in the search process were "Causes of MDR in tuberculosis patients," "Factors causing multidrug tuberculosis," and "Description of the causes of MDR in TB patients." Journals used in writing the literature review spanned the last 10 years.

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RESULTS AND DISCUSSION

Research result

In this study, 13 journals were obtained which showed the factors causing Multi Drug Resistance in tuberculosis patients.

Table 1. Results of Article Review Analysis

No	Author and Year	Research Design	Research result
1	Mashidayanti A., Nurlely, Kartinah N., 2020	*Cross-sectional.*	Regularity of taking medication
2	Aristiana CD, Wartono M., 2018	*Cross-sectional*	Patient motivation, medication compliance, alcohol consumption, smoking habits, and nutritional status
3	Imam FRS, Umboh JML, Tuda JSB, 2023	*Case control*	Diabetes mellitus and history of TB treatment
4	Buryanti S., Fibriana AI, 2021	*Case control*	Contact history, treatment history
5	Muhammad M., Fadli., 2019.	Analytical observation	Motivation, regularity of taking medication, role of officers
6	Aisyah W, O, N., Azim LOL, Sabilu Y., 2024	Observational analytical study	Compliance with taking medication
7	Chasanah KF, Trinawati I., Istiono W., 2022	*Case control*	History of TB treatment, contact with TB patients
8	Simorangkir L., Ginting F., Rupang ER, Sinaga SP, 2022	Descriptive	Medication compliance, smoking history
9	Fahlafi MR, Usman S., Ismail N., 2023	*Case control*	Smoking, diabetes mellitus
10	Burhan SL, Wahiduddin., Maria IL, Bustan MN, Saleh LM, Balqis., 2024	*Case control*	Previous medical history
11	Janna TAS, Arsin AA, Arsyad DS, Arsyad M., 2025	*Case control*	Nutritional status, medication history
12	Cahyani R., Keswara UR, Winarno R., 2025	*Purposive sampling*	History of comorbidities, nutritional status, and previous treatment history
13	Aswar S., Istyanto F., 2023	*Case control*	Nutritional status, role of PMO (Drug Swallowing Supervisor), compliance with taking medication

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Discussion

Regularity of Treatment

Regularity of medication intake is the most influential factor in the incidence of MDR-TB. Regularity of medication intake is determined by punctuality and adherence to medication regimens. TB patients who fail to take their medications regularly can lead to therapy failure and antibiotic resistance. This is in line with research by Mashidayanti et al. (2020), Aristiana & Wartono (2018), Muhammad & Fadli (2019), Aisyah et al. (2024), Simorangkir et al. (2022), and Aswar & Isyanto (2023), which states a relationship between the incidence of MDR-TB and regularity of medication intake, with a significance value <0.005.

TB patients who are not compliant or regular with their treatment have a 10.73 times greater risk of developing MDR-1 (Multi Drug Reliability) than patients who are compliant or regular in taking their medication (Aristiana & Wartono, 2018). Irregularity in taking medication is caused by boredom with the daily requirement to take the medication at a set time. This makes patients reluctant to undergo treatment. Furthermore, the long treatment duration is burdensome for patients, leading to neglect of medication (Mashidayanti et al, 2020).

Treatment adherence below 90% can impact the healing process. Patients must take their medications regularly according to the prescribed schedule to prevent therapy failure. Intensive TB treatment requires special attention and must be carried out according to procedure. Failure to comply with treatment procedures can potentially lead to the development of multidrug-resistant tuberculosis (MDR-TB) (Muhammad M. & Fadli, 2019).

Patients who are non-compliant with TB medication are at greater risk of developing MDR-TB than those who are compliant. Non-compliance can render treatment ineffective and allow TB bacteria to persist and develop resistance to standard drugs. Furthermore, inadequate dosing due to non-compliance reduces the effectiveness of treatment in completely eradicating the bacteria (Aisyah et al, 2024).

Treatment adherence in TB patients is crucial for preventing multidrug-resistant TB (MDR-TB) and treatment failure. Compliance is crucial for TB patients undergoing long-term treatment, as non-adherence contributes to the development of resistance (Simorangkir et al., 2022).

The development of resistance due to non-adherence to anti-TB treatment can lead to TB bacteria becoming resistant to the drugs used. This can potentially lead to multidrug-resistant TB (MDR-TB), which occurs when the bacteria become resistant to the two main drugs used in standard TB treatment (Aswar & Istyanto, 2023).

Sufferer Motivation

The results of research by Aristiana & Wartono (2018) showed a significant relationship between patient motivation and MDR TB with a p-value of <0.05. Furthermore, research conducted by Muhammad & Fadli (2019) revealed a relationship between family support and the behavior of MDR TB patients with a p-value of <0.05.

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TB patients who have low motivation have a risk factor of getting MDR TB 47.5 times greaterCompared to highly motivated TB patients, low motivation is caused by a lack of knowledge and methods for treating the disease (Aristiana & Wartono, 2018).

Research conducted by Iskandar et al. (2021) suggests that family and friend support plays a crucial role in increasing motivation for treatment. TB patients desperately need family support to adapt to physical, psychological, and social stressors. Furthermore, family support can improve patients' hope and quality of life (Fadli & Muhammad, 2019).

Alcohol Consumption

Alcohol consumption shows significant results with MDR TB, which means that TB patients who consume alcohol have a greater risk factor for suffering from MDR TB.Alcohol consumption in sufferers causes TB germs to survive longer in macrophages due to the weakened effectiveness of the phagocytosis process (Aristiana & Wartono, 2018).

Smoke

Smoking can increase the risk of developing MDR-TB by seven times. This is in line with research by Aristiana & Wartono (2018), which showed a significant association between smoking and MDR-TB, with a p-value of <0.005. This finding is supported by research by Fahlafi et al. (2023), which found that smoking increases the risk of MDR-TB, with a p-value of <0.005.

Smoking makes a person susceptible to TB. The damage*mucociliary clearance*Caused by smoking. Cigarette smoke can increase airway obstruction and impair macrophage function in destroying invading bacteria, resulting in treatment failure (Aristiana & Wartono, 2018; Fahlafi et al., 2023; Simorangkir et al., 2022). Therefore, patients undergoing TB treatment while smoking are at risk of developing MDR-TB (Simorangkir et al., 2022).

Nutritional status

Poor nutritional status can increase the risk of developing MDR-TB more than normal nutritional status. This is consistent with several studies, including Aristiana & Wartono (2018), Janna et al. (2025), and Aswar & Istyanto (2023), which revealed a significant relationship or influence with a p-value <0.005.

According to research by Janna et al. (2025), nutritional status is a key factor in maintaining the body's resistance to bacterial transmission. This is reinforced by research by Aristiana & Wartono (2018), who found that TB patients with malnutrition are at risk of relapse after treatment. Poor nutrition accelerates the growth of bacteria and weakens the immune system, making healing difficult. Furthermore, research by Cahyani et al. (2025) suggests that malnutrition in TB patients can increase the risk of developing MDR-TB. To avoid the risk of MDR-TB, underweight nutritional status needs to be addressed with balanced and nutritious nutrition and intake. Protein, minerals, and vitamins can strengthen the body's immunity and maintain optimal health (Aswar & Istyanto, 2023).

Diabetes mellitus

Diabetes Mellitus (DM) has a significant relationship with MDR-TB, meaning that a history of DM in TB patients increases the risk of developing MDR-TB. According to research by Imam et al. (2023), TB patients with a history of DM have a higher bacterial count.

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More frequent at the beginning of treatment, potentially leading to resistance and mutation. This is supported by research by Fahlafi (2023), who found that DM affects the final outcome of TB treatment, leading to treatment failure and reduced immunity.

Previous Medical History

Patients with a history of treatment significantly increase the risk of developing MDR-TB (Chasanah et al., 2021). This is supported by research by Janna et al. (2025) that found that treatment history significantly influenced the incidence of MDR-TB with a p-value <0.005. Research by Buryanti & Fibriyani (2021) found that those with a history of TB treatment had a 3.54-fold greater risk than those without a history. Long duration of TB treatment is a reason why patients discontinue treatment. Discontinuation of TB treatment generally occurs because patients feel cured and decide not to take the medication (Cahyani et al., 2025). Janna et al. (2025) stated that TB patients with a history of previous treatment with relapses, treatment failures, and treatment interruptions have the potential to develop drug resistance. This is caused by inappropriate treatment regimens, patient non-compliance with treatment, and lack of supervision during therapy.

Role of Officers

The results of a study by Muhammad & Fadli (2019) found a significant relationship between the activeness of officers and the incidence of MDR-TB, with a p-value <0.005. Consistent with the results of a study by Aswar & Isyanto (2023), the lack of officers observing patients taking medication has the potential to cause MDR-TB. To address this issue, patient education is needed regarding the importance of proper supervision in taking TB medication.

Contact with Patients

The results of a study by Buryanti & Fitriyana (2021) suggest a relationship between a history of contact with MDR-TB patients and the incidence of MDR-TB. This study obtained a p-value <0.005 with an OR of 2.40, meaning that patients with a history of contact with MDR-TB patients have a 2.4-fold greater risk compared to those without contact with MDR-TB patients. This is in line with the research of Chasanah et al. (2022), which found that a history of contact with MDR-TB patients is a risk factor strongly associated with the incidence of MDR-TB. The relationship between a history of contact with MDR-TB patients and MDR-TB strains is caused by patients developing primary resistance to drugs. This means that patients are directly infected with drug-resistant bacteria.

CONCLUSION

Based on the review of articles that have been conducted, the factors causing Multi Drug Resistance include, patient regularity, motivation, alcohol consumption, smoking, nutritional status, diabetes mellitus, previous treatment history, the role of officers, and contact with patients.

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