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## PROFILE OF PATIENTS WITH MULTIDRUG-RESISTANT PULMONARY TUBERCULOSIS AT MERAUKE REGIONAL GENERAL HOSPITAL, MERAUKE REGENCY, SOUTH PAPUA, JANUARY 2021 – DECEMBER 2024

By

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### Article History:

Received: 12-11-2025

Revised: 20-11-2025

Accepted: 15-12-2025

### Keywords:

TB MDR, OAT, Character  
Statistic

**Abstract:** Pulmonary MDR-TB is tuberculosis that is resistant to first-line drugs, especially isoniazid and rifampicin, due to genetic mutations at drug target sites, so it requires combinations of drugs from Groups A and B, and if needed, Group C. This descriptive study used medical records of MDR-TB patients treated at Merauke Regional Hospital from January 2021 to December 2024 and was analyzed univariately with SPSS version 26. Most patients were 18–59 years old (90.6%), female (53.1%), and had a history of previous TB treatment (89.3%), with a small proportion experiencing treatment interruption and treatment failure. Comorbidities included diabetes mellitus (6.3%) and HIV (18.8%), and the mortality rate was relatively high at 40.6%.

## INTRODUCTION

Pulmonary tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, an acid-fast bacillus that primarily affects the lungs and can spread to other organs. Transmission occurs through droplet nuclei expelled by patients with smear-positive pulmonary TB, making the disease highly contagious, especially in densely populated environments with poor ventilation. Globally, TB remains one of the leading causes of morbidity and mortality. The 2020 WHO report places Indonesia among the countries with a very high TB burden, with an estimated 845,000 new cases and 98,000 deaths per year, influenced by factors such as poverty, inadequate housing, malnutrition, smoking, and limited access to health services.

Indonesia is one of the 30 countries with the highest TB burden and ranks third globally. In 2018, the TB incidence was estimated at 316 per 100,000 population, with a prevalence of approximately 753 per 100,000 and a mortality rate of 35 per 100,000 population. The 25–34-year age group, which represents the productive age group, is the most affected, so TB has a significant impact on socio-economic conditions and productivity.

One of the main challenges in TB control is the emergence of drug-resistant tuberculosis. Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance at least to isoniazid and rifampicin. Drug resistance may present as monoresistance, polyresistance, MDR, XDR, or even TDR, and generally arises due to inappropriate regimens, inadequate

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Journal of Innovation Research and Knowledge

Vol.5, No.8, Januari 2026



14 duration of treatment, poor adherence, and weak treatment program monitoring. Globally, 24 in 2023 there were an estimated 400,000 new MDR/RR-TB cases, but fewer than half were diagnosed and started on treatment. The treatment success rate for MDR-TB is around 68%, indicating that gaps remain in diagnosis and case management.

35 TB treatment consists of an intensive phase and a continuation phase, with the aims of 47 curing patients, preventing death, reducing transmission, preventing relapse, and preventing the emergence of drug resistance. In the management of TB-MDR, second-line drugs are grouped into Groups A, B, and C; a combination of three Group A drugs and two Group B drugs is recommended, with the addition of Group C drugs when needed. In late 2022, WHO 29 introduced the BPaLM regimen (bedaquiline, pretomanid, linezolid, moxifloxacin), an all-oral 10 six-month regimen that is shorter and more convenient than previous regimens, although it cannot yet be applied to all patient groups and still requires drug susceptibility testing.

15 In resource-limited settings such as Merauke Regency, challenges in TB-MDR control 36 include limited diagnostic facilities, a shortage of trained personnel, and limited availability of second-line drugs, compounded by geographical barriers that increase the risk of delayed diagnosis and loss to follow-up. RSUD Merauke, as a referral hospital, plays an important role in the diagnosis and management of TB-MDR; however, local data on the clinical and 30 demographic profile of pulmonary MDR-TB patients for the 2021–2024 period are still limited. Therefore, this study was conducted to describe the profile of pulmonary MDR-TB patients at RSUD Merauke, South Papua, as well as trends in cases from January 2021 to December 2024, as a basis for planning and strengthening TB-MDR control programs in the region.

## LITERATURE REVIEW

### Pulmonary Tuberculosis

8 Drug-resistant TB is classified into monoresistant TB, polyresistant TB, MDR-TB, 2 extensively drug-resistant TB (XDR-TB), and total drug-resistant TB (TDR). MDR-TB is defined as TB with resistance to at least isoniazid and rifampicin, the two most potent first-line anti-tuberculosis drugs. Resistance arises mainly due to inadequate use of anti-tuberculosis drugs (regimens that do not follow guidelines, incorrect dose or duration), poor patient adherence, poor drug quality, and weak treatment program monitoring. These conditions create a selection pressure that allows resistant mutants to survive and multiply, leading to the development of MDR-TB.

### Risk Factors for MDR-TB

7 Risk factors for MDR-TB include patient-related factors, treatment-related factors, 3 and health system factors. A history of previous TB treatment (treatment failure, loss to 16 follow-up, or incomplete treatment) is one of the strongest risk factors for MDR-TB. 33 Comorbidities such as diabetes mellitus and HIV/AIDS also play an important role because they weaken the immune system and impair treatment response. Socioeconomic factors (low education, poverty, overcrowded housing) and barriers to accessing health services contribute to delayed diagnosis and poor adherence to treatment. From the health system perspective, limited diagnostic facilities, lack of directly observed therapy (DOT), and unstable availability of second-line drugs further increase the risk of MDR-TB.

### Principles of MDR-TB Treatment

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Drug-resistant TB is classified into monoresistant TB, polyresistant TB, MDR-TB, extensively drug-resistant TB (XDR-TB), and total drug-resistant TB (TDR). MDR-TB is defined as TB with resistance to at least isoniazid and rifampicin, the two most potent first-line anti-tuberculosis drugs. Resistance arises primarily from inadequate use of anti-tuberculosis drugs (regimens that do not follow guidelines, incorrect dose or duration), poor patient adherence, poor drug quality, and weak monitoring of treatment programs. These conditions create a selection advantage for resistant mutants, allowing them to survive and proliferate, ultimately leading to the development of MDR-TB.

### Risk Factors for MDR-TB

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Risk factors for MDR-TB include patient-related factors, treatment-related factors, and health system factors. A history of previous TB treatment (treatment failure, loss to follow-up, or incomplete treatment) is one of the strongest risk factors for the occurrence of MDR-TB. Comorbidities such as diabetes mellitus and HIV/AIDS also play an important role because they weaken the immune system and impair the response to therapy. Socioeconomic factors (low education, poverty, overcrowded housing) and barriers to accessing health services contribute to delayed diagnosis and poor adherence to treatment. From the health system side, limited diagnostic facilities, lack of directly observed therapy, and unstable availability of second-line drugs also increase the risk of MDR-TB.

### Principles of MDR-TB Treatment

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The goals of MDR-TB treatment are to cure the patient, prevent death, reduce transmission, prevent relapse, and prevent the development of further resistance to second-line drugs. National and international guidelines classify second-line drugs into Groups A, B, and C; recommended regimens generally consist of three Group A drugs and two Group B drugs, with the addition of Group C drugs when an effective combination cannot be constructed from Groups A and B alone. WHO also recommends a short all-oral regimen based on bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) for selected patient groups, with a treatment duration of approximately six months. Although this new regimen improves convenience and treatment success, its implementation requires adequate diagnostic capacity, reliable drug supply, and close monitoring of adverse effects and patient adherence.

In resource-limited settings such as South Papua, including RSUD Merauke, MDR-TB management is more challenging due to limited diagnostic facilities, transportation barriers, shortage of trained personnel, and constrained availability of drugs. Therefore, local data on patient profiles, comorbidities, and treatment outcomes are crucial for planning and evaluating MDR-TB control programs in the region.

## METHODS

### Study Design and Type

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This study is a quantitative, non-experimental research with a retrospective descriptive design. It aims to describe the profile of patients with multidrug-resistant pulmonary tuberculosis (MDR-TB) based on demographic, clinical, and treatment characteristics at RSUD Merauke during the period January 2021–December 2024.

### Population and Sample

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**Journal of Innovation Research and Knowledge**  
**Vol.5, No.8, Januari 2026**

The study population consists of all patients diagnosed with pulmonary MDR-TB at RSUD Merauke during the study period. The sample comprises medical records of pulmonary MDR-TB patients who met the predefined inclusion and exclusion criteria. A total sampling technique was used, so all eligible cases were included as samples.

### Data Collection Technique

The data used in this study are secondary data obtained from patient medical records. Data collection began with obtaining ethical and administrative approval from the Faculty of Medicine and the Merauke District Health Office. After formal approval was granted, the researcher coordinated with the medical records unit/PMDT TB team at RSUD Merauke to gain access to the medical records of pulmonary MDR-TB patients.

The researcher then identified all medical records of pulmonary MDR-TB patients documented between January 2021 and December 2024 and screened them according to the inclusion and exclusion criteria. Medical records that met the criteria were included as samples, and the required information was extracted into a data collection form, including age, sex, TB treatment history, comorbidities (diabetes mellitus/HIV), MDR-TB drug regimen used, and mortality status.

### Operational Definitions

In this study, age is defined as the patient's age in years at the time of MDR-TB diagnosis and is categorized into 5–9, 10–17, 18–59, and  $\geq 60$  years (interval scale). Sex is categorized as male or female (nominal scale). History of TB treatment refers to previous TB therapy status, categorized as treated, loss to follow-up (interrupted treatment), or treatment failure (nominal scale). Comorbidity refers to the presence of coexisting diseases, specifically DM or HIV, recorded in the medical record (nominal scale). Mortality is defined as the patient's status as dead or alive during the observation period (nominal scale). MDR-TB regimen is defined as the combination of drugs used in MDR-TB treatment, such as Bdq–Lzd–Mfx–Pa–Vit B6, Bdq–Lzd–Pa, or Bdq–Cfz–Cs–Lfx–Lzd–Vit B6 (nominal scale).

### Data Processing and Analysis

Data processing in this study was carried out through several steps: editing to check data completeness and consistency, coding to convert qualitative data into numerical codes, data entry into SPSS version 26, and tabulating to construct frequency and percentage tables. Data were then analyzed descriptively (univariate analysis) to obtain the frequency distribution and percentage of each variable, which were subsequently presented in tables and narrative form to describe the profile of pulmonary MDR-TB patients at RSUD Merauke.

## RESULTS AND DISCUSSION

### Results

#### Patient Characteristics

This study analyzed 32 patients with pulmonary MDR-TB who were hospitalized and/or received treatment at RSUD Merauke, South Papua, during the period January 2021–December 2024. The patient characteristics assessed included age, sex, treatment history, comorbidities, mortality, and trends in the use of MDR-TB treatment regimens.

#### Patient Characteristics by Age



**Table 3.1. Distribution of MDR-TB Patients by Age**

Age (years)	Number	Percentage
11-17	3	9,4%
18-59	29	90,6%
Total	32	100%

Table 3.1 shows the prevalence of pulmonary MDR-TB by age group at RSUD Merauke, South Papua, in 2021–2024. The highest number of cases was found in the 18–59-year age group, with 29 patients (90.6%), while the lowest was in the 11–17-year age group, with 3 patients (9.4%).

**Patient Characteristics by Sex**

**Table 3.2. Distribution of MDR-TB Patients by Sex**

Sex	Number	Percentage
Male	15	46,9%
Female	17	53,1%
Total	32	100%

Table 3.2 shows the prevalence of MDR-TB by sex at RSUD Merauke, South Papua, in 2021–2024. Female patients had a higher frequency of MDR-TB than male patients, with 17 females (53.1%) and 15 males (46.9%).

**Patient Characteristics by Treatment History**

**Table 3. Distribution of MDR-TB Patients by Treatment History**

Treatment history	Number	Percentage
Treated	25	78,1%
Lost to follow-up	5	15,6%
Treatment failure	2	6,3%
Total	32	100%

Table 3 shows the distribution of MDR-TB cases by treatment history at RSUD Merauke, South Papua, for the period 2021–2024. Patients who had received complete TB treatment accounted for the largest proportion, namely 25 patients (89.3%), while those with a history of treatment interruption numbered 2 patients (7.1%) and those with treatment failure 2 patients (6.3%). This study also found that most MDR-TB patients received long-course treatment (18 patients; 64.3%), while 10 patients (35.7%) received short-course treatment. The MDR-TB drugs used at RSUD Merauke included bedaquiline 100 mg, pretomanid 200 mg, linezolid 250 mg, moxifloxacin 400 mg (BPALM), as well as clofazimine 100 mg and cycloserine 250 mg. The MDR-TB regimens employed were BPALM and the combination 6 Bdq–Lfx–Lzd–Cfz–Cs–Vit B6 followed by 14 Lfx–Cfz–Cs–Vit B6.

**Table 4. Distribution of MDR-TB Patients by Comorbidity**

Comorbidity	Number	Percentage
DM	2	6,3%
ODHIV	14	40,6%
None	16	51,1%
Total	32	100%

**Patient Characteristics by Mortality**



**Table 5. Distribution of MDR-TB Patients by Mortality**

Mortality	Number	Percentage
Yes	13	40.6%
No	19	59.4%
Total	32	100%

Table 5 shows the prevalence of mortality among MDR-TB patients at RSUD Merauke, South Papua, in 2021–2024. A total of 13 patients (40.6%) died, while 19 patients (59.4%) survived.

**Trend of Pulmonary MDR-TB**

**Table 6. Distribution of MDR-TB Patients by MDR-TB Trend**

Year	Most frequently used drug combination	Drug group	Number of patients	Percentage
2021	6 Bdq-Lfx-Lzd-Cfz-Cs-VitB6 / 14 Lfx-Cfz-Cs-VitB6	A dan B	4	100%
2022	6 Bdq-Lfx-Lzd-Cfz-Cs-VitB6 / 14 Lfx-Cfz-Cs-VitB6	A dan B	10	100%
2023	6 Bdq-Lfx-Lzd-Cfz-Cs-VitB6 / 14 Lfx-Cfz-Cs-VitB6	A dan B	1	100%
2024	Bedaquiline Pretomanid Linezolid Moxifloxacin (BPALM)	A dan B	9	56,3%

Table 6 shows the trend of MDR-TB cases at RSUD Merauke, South Papua, from 2021 to 2024. Throughout 2021 to 2023, the most commonly used MDR-TB regimen at RSUD Merauke predominantly consisted of a combination including bedaquiline, levofloxacin, linezolid, clofazimine, cycloserine, and vitamin B6, namely 6 Bdq-Lfx-Lzd-Cfz-Cs-Vit B6 / 14 Lfx-Cfz-Cs-Vit B6, which falls under WHO drug Groups A and B. This regimen was used for all patients who initiated MDR-TB treatment in 2021 (4 patients), 2022 (10 patients), and 2023 (1 patient).

However, in 2024 there was a shift toward the BPALM regimen (bedaquiline, pretomanid, linezolid, and moxifloxacin), which also belongs to Groups A and B. BPALM was administered to 9 patients, accounting for 56.3% of the total MDR-TB cases that year. This change reflects the adoption of a shorter all-oral regimen in line with the latest WHO recommendations, which emphasize the benefits and safety of using bedaquiline and pretomanid in the treatment of MDR-TB.

**Discussion**

**Age**

Most pulmonary MDR-TB patients at RSUD Merauke were in the 18–59-year age group (90.6%), indicating that the disease predominantly affects individuals in the productive age range. This finding is consistent with several studies reporting that MDR-TB cases are dominated by young to middle-aged adults with high mobility and frequent social interaction, which increases the risk of exposure and transmission.

**Sex**



Slightly more patients were female (53.1%) than male (46.9%). Previous studies have shown varying results: some report higher MDR-TB cases among women, while others find a predominance among men. These differences are influenced by biological, social, and economic factors, as well as lifestyle-related risks such as smoking and alcohol consumption. This suggests that the role of sex in MDR-TB occurrence is context-dependent and may vary by setting and population.

#### Characteristics of MDR-TB Treatment History

Most patients received the Bdq-Cfz-Cs-Lfx-Lzd-Vit B6 regimen, followed by Bdq-Lzd-Mfx-Pa-Vit B6 and Bdq-Lzd-Pa. Nearly half of the patients (46.9%) experienced adverse drug reactions, mainly gastrointestinal complaints, peripheral neuropathy, visual disturbances, skin discoloration, and elevated liver enzymes, which were associated with drugs such as linezolid, clofazimine, ethambutol, and bedaquiline. The literature indicates that the complexity of regimens, the large number of drugs used, and severe side effects often lead to treatment interruption, therapeutic failure, and broader patterns of drug resistance. Low levels of knowledge, a history of prior TB, and treatment default also contribute to the increasing incidence of MDR-TB.

#### Comorbidities in MDR-TB Patients

The main comorbidities identified in this study were diabetes mellitus and HIV, with a relatively high proportion of people living with HIV (PLHIV). This aligns with studies showing that DM and HIV are important risk factors for MDR-TB, as they are associated with impaired immunity, more severe disease progression, and poorer treatment outcomes. These conditions highlight the importance of integrating TB-HIV services and managing comorbidities comprehensively to improve patient outcomes.

#### Mortality

The mortality rate among MDR-TB patients at RSUD Merauke was relatively high (40.6%). The increasing number of cases per year and the high mortality rate are likely influenced by both patient-related and system-related factors. On the patient side, these include non-adherence to treatment, limited knowledge, financial constraints, barriers to accessing care, and lack of family support. On the health system side, contributing factors include regimens that are not fully aligned with standards, treatment that is not based on drug susceptibility testing, weak monitoring and follow-up, and limited availability of drugs and laboratory facilities.

#### Trends in MDR-TB Regimens

From 2021 to 2023, treatment was dominated by the regimen 6 Bdq-Lfx-Lzd-Cfz-Cs-Vit B6 / 14 Lfx-Cfz-Cs-Vit B6 (Group A and B drugs). In 2024, a shift began toward the BPALM regimen (bedaquiline, pretomanid, linezolid, moxifloxacin), an all-oral, shorter regimen in accordance with the latest WHO recommendations. Meta-analysis studies have shown that well-structured combination regimens with shorter duration can significantly improve culture conversion rates and reduce the risk of death. These findings indicate that RSUD Merauke has started to align with global developments in MDR-TB therapy. However, long-term outcome monitoring is still needed to evaluate the effectiveness and safety of the BPALM regimen in the local context.

#### CONCLUSION

This study shows that pulmonary MDR-TB at RSUD Merauke during the period January 2021–December 2024 occurred predominantly in the productive age group of 18–59 years (90.6%) and was slightly more common in females (53.1%), with the majority of patients having a history of prior TB treatment (89.3%). The most frequently used regimen was the combination Bdq–Cfz–Cs–Lfx–Lzd–Vit B6, followed by Bdq–Lzd–Mfx–Pa–Vit B6 and Bdq–Lzd–Pa. The main comorbidities identified were diabetes mellitus and HIV, and the mortality rate was relatively high (40.6%). Case trends and treatment patterns indicated an increase in the number of MDR-TB patients over the years, accompanied by a shift toward the BPALM regimen in 2024, in line with WHO recommendations on short-course all-oral regimens.

Theoretically, these findings reinforce that MDR-TB is closely associated with productive age, suboptimal prior TB treatment, and the presence of comorbidities. Practically, there is a need to strengthen patient education and treatment adherence, enhance monitoring of adverse drug reactions, integrate TB–DM–HIV services, and conduct continuous evaluation of BPALM implementation to improve treatment success rates and reduce mortality.

### Acknowledgements

The authors would like to express their gratitude to the Faculty of Medicine, Universitas Kristen Indonesia (FK UKI), the Merauke District Health Office, as well as the Director and all staff of RSUD Merauke, particularly the medical records unit and the TB/MDR team, for their permission, assistance, and support during the research process. The authors also extend their sincere thanks to their academic supervisors, colleagues, and family members for their prayers, encouragement, and motivation, which greatly contributed to the completion of this research and the writing of this article.

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HALAMAN INI SENGAJA DIKOSONGKAN