

# The Frequency of Multidrug-Resistant Tuberculosis Patient who have History of Tuberculosis, HIV, and Diabetes Mellitus at Dr. Soetomo General Academic Hospital

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## ABSTRACT

**Introduction:** The main causes of MDR TB include interperson transmission and TB treatment failure. In addition to TB, HIV and diabetes mellitus may raise the risk of TB MDR. To determine the TB MDR risk factors, it's critical to understand the prevalence of TB MDR patients with TB, HIV, and diabetes mellitus histories.

**Methods:** This study is an observational descriptive study with a retrospective design. The sample for this study was all patients from the TB and MDR-TB polyclinic at Dr. Soetomo General Academic Hospital, Surabaya, in January 2020–December 2020 who met the inclusion criteria. The data obtained were analyzed descriptively.

**Results:** There were 72 patients who met the criteria: there were 26 patients who have a history of TB, 15 patients who only have a history of diabetes mellitus, 2 patients who only have a history of HIV, 27 patients who have a history of TB with diabetes mellitus, and 2 patients who have a history of TB with HIV.

**Conclusion:** The data could support the theory of an association between MDR-TB with TB, HIV, and diabetes mellitus and increase the awareness of primary MDR TB cases with history of HIV and diabetes mellitus.

**Keywords:** Tuberculosis, Multidrug-Resistant Tuberculosis, HIV, Diabetes mellitus, Treatment history

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## INTRODUCTION

Multidrug-resistant TB (MDR-TB) is tuberculosis (TB) that resistant to at least Isoniazid and Rifampicin (World Health Organization, 2018). In 2020, according to the Ministry of Health Indonesia, there were around 7,921 cases of MDR/RR TB in Indonesia (Ministry of Health Republic of Indonesia, 2021). Multidrug-resistant tuberculosis is caused by spontaneous mutation of *Mycobacterium tuberculosis* (Rumende, 2018). MDR TB could happen by person-to-person transmission and inappropriate previous TB treatment (World Health Organization, 2018). MDR-TB is classified into two types: primary MDR-TB and acquired MDR-TB. Primary MDR TB patients don't have previous TB treatment histories or have TB treatment histories that are < 1 month, while acquired MDR TB patient does have a history of previous TB treatment and drug resistance may develop during or following chemotherapy (Li et al., 2017).

People who have TB have a risk of developing MDR TB since MDR TB could be caused by inappropriate previous TB treatment. Besides TB, it is known that there is a possible risk of MDR TB in people with HIV and diabetes mellitus. People with HIV and diabetes mellitus have low immunity, so they have a higher risk of being infected by MDR TB.

Human immunodeficiency virus (HIV) is a virus that attacks the CD4 cell which helps the body in facing infection (World Health Organization, 2021a). TB which is an opportunistic infection happens more and worse in people with HIV (National Institutes of Health, 2019). TB and HIV coinfection could increase the risk of acquiring M/XDR-TB strains (Singh et al., 2020).

Diabetes is a chronic, metabolic disease characterized by an increase in blood sugar level, with the most common type being type 2 diabetes, which occurs when the body is resistant to insulin or doesn't make enough insulin. People with TB and diabetes mellitus have a higher risk of failure of TB treatment, mortality of TB, and recurrence of TB. Failure of TB treatment could cause MDR TB (World Health Organization, 2021b; Tegegne et al., 2018).

In this study, the researcher would like to know the prevalence of MDR TB patients, who had a history of TB, HIV, and diabetes mellitus, who were treated in Dr. Soetomo General Academic Hospital, Surabaya period January 2020 – December 2020. From this study, the researchers hope that the study could increase the understanding of the prevalence of MDR TB cases especially among population who have history of TB, HIV, and diabetes Mellitus, thus to identifying the risk factors of MDR TB patient and planning the

appropriate treatment for MDR TB patient who has history of HIV and/or diabetes mellitus.

**METHODS**

This study is an observational descriptive study with a retrospective design. The samples for this study were taken from the medical records of all MDR-TB patients who met the inclusion criteria at the TB and MDR-TB Polyclinic at Dr. Soetomo General Academic Hospital. The inclusion criteria are that the patient must be 18 years of age or older, have a history of tuberculosis, HIV, or diabetes mellitus, and have been admitted to the TB and MDR-TB Polyclinic at Dr. Soetomo General Academic Hospital in Surabaya between January 2020 and December 2020. The data were collected and descriptively analyzed.

**RESULTS**

From January 2020–December 2020, there were a total of 106 MDR-TB patients who were admitted to the TB and MDR TB Polyclinic at Dr. Soetomo General Academic Hospital, Surabaya. There were 72 patients who met the criteria out of 106. The information gathered includes a history of previous TB, HIV, and Diabetes Mellitus, as well as age and gender.

Table 1. Age distribution of MDR-TB patients at Dr. Soetomo General Academic Hospital TB and MDR TB outpatient clinic

Age (year)	Frequency (N=72)	Percentage (%)
< 65	67	93.1
≥ 65	5	6.9

Table 2. Sex distribution of MDR-TB patients at Dr. Soetomo General Academic Hospital TB and MDR TB outpatient clinic

Sex	Frequency (N=72)	Percentage (%)
Male	46	63.9
Female	26	36.1

Table 3. History of TB treatment or case of MDR TB patients at Dr. Soetomo General Hospital TB and MDR TB outpatient clinic

Disease history	Frequency (N=72)	Percentage (%)
New Case*	17	23.6
Relapse	30	41.7
Drop Out	11	15.3
Treatment failure	11	15.3
Did not convert	2	2.8
Others	1	1.4

Note:

\*Primary MDR TB

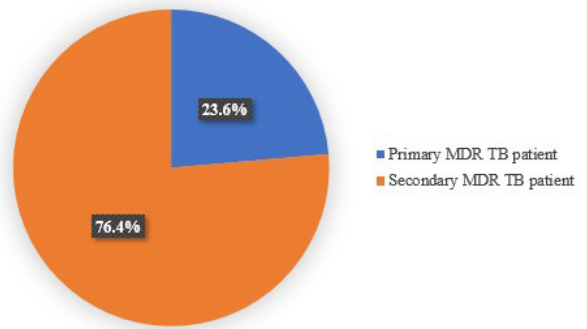


Diagram 1. Primary and secondary MDR TB patients with history of TB, HIV, and diabetes mellitus at Dr. Soetomo General Academic Hospital TB and MDR TB outpatient clinic in January 2020 - December 2020 who met the inclusion criteria.

Table 4. TB, HIV, and Diabetes Mellitus history of MDR TB patients at Dr. Soetomo General Academic Hospital TB and MDR TB outpatient clinic

Disease history	Frequency (N=72)	Percentage (%)
TB	26	36.1
HIV*	2	2.8
Diabetes Mellitus*	15	20.8
TB and Diabetes Mellitus	27	37.5
TB and HIV	2	2.8
TB	26	36.1

Note:

\*Primary MDR TB

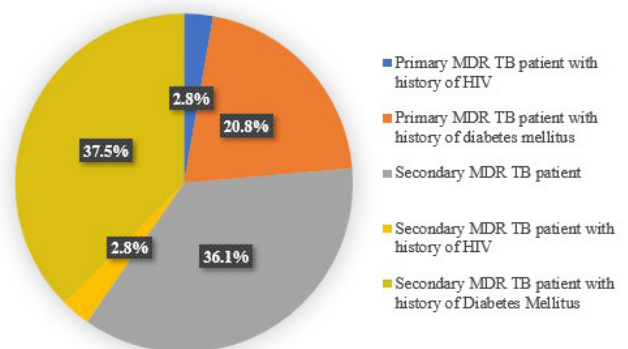


Diagram 2. MDR TB patients with history of TB, HIV, and diabetes mellitus at Dr. Soetomo General Hospital TB and MDR TB outpatient clinic in January 2020 - December 2020 who met the inclusion criteria.

Based on history of previous TB treatment and history of previous TB, HIV, and diabetes mellitus, from 72 MDR TB patients in Dr. Soetomo General Hospital TB and MDR TB outpatient clinic that met the inclusion criteria, most patients were having relapse, which

around 30 patients (41.7 %) and had history of previous TB with diabetes, which around 27 patients (37.5%).

## DISCUSSION

Based on this study, of the 106 patients who were treated at Dr. Soetomo General Academic Hospital TB and MDR TB outpatient clinic, Surabaya, from January 2020–December 2020, there were 72 patients who met the inclusion criteria of this study. From these 72 patients, there were 26 patients (36.1%) that had secondary MDR-TB without HIV or diabetes mellitus history, 2 patients (2.8%) that had secondary MDR-TB with a history of HIV, and 27 patients (37.5%) that had secondary MDR-TB with a history of diabetes mellitus.

We divided the patients into two groups based on their age: the productive age group, which included patients under the age of 65 (65 years old), and the unproductive age group, which included patients who were 65 years old or older. In this study, we found that most of the patients were in the productive age group (67 patients). According to a study conducted in Gujarat, India, the highest prevalence of MDR-TB is among the productive age population, which is around 21–40 years old and 41–60 years old (Waseem et al., 2021).

Although other research indicated that women have a higher chance of developing MDR-TB, the majority of the MDR-TB patients in this study at the Dr. Soetomo General Academic Hospital, Surabaya's TB and MDR-TB Polyclinic between January 2020 and December 2020 were men. A study conducted in Sudan showed there was no significant risk difference between males and females (Elduma et al., 2019). A study in Argentina showed that males have a higher risk of TB since more males are smoking and drinking alcohol than females (Echazarreta et al., 2018).

In this study, it was found that 17 patients had primary MDR-TB. Of these 17 patients, 15 had a history of diabetes mellitus, and 2 had a history of HIV. A study that was conducted in Shandong, China, from January 2004–December 2018, found that of the 11,467 new MDR-TB cases, around 2,173 (18.95%) were primary MDR-TB (Song et al., 2019). Another study conducted in China found that of 3,037 new TB cases, 1,867 were first-line drug-resistant TB (Lv et al., 2017).

The high prevalence of secondary MDR-TB is consistent with an explanation from the WHO, that inappropriate TB treatment could cause TB drug resistance (World Health Organization, 2018). Around 11 patients had a history of failure in previous TB treatment, and another 11 patients had a history of dropping out of TB treatment. Relapse of tuberculosis (TB) could be a sign of failure in previous TB treatment (McIvor et al., 2017); in this study, approximately 30 patients had a history of TB relapse.

Some MDR-TB patients who were treated at Dr. Soetomo General Academic Hospital, also had a history of HIV and diabetes mellitus. Around 2 primary MDR-TB patients (2.8%) had a history of HIV, 15 primary MDR-TB patients (20.8%) had a history of diabetes mellitus, 2 secondary MDR-TB patients (2.8%) had a history of HIV, and 27 secondary MDR-TB patients (37.5%) had a history of diabetes mellitus. There are a lot of differences among studies about the association between HIV and MDR-TB in various countries. According to a study conducted in Mali, it was found that HIV is not a risk factor for MDR-TB (Baya et al., 2019). However, a study conducted by Pradipta et al. showed that HIV is a risk factor for MDR-TB. Drug interactions, overlapping drug toxicities, high pill burden, drug malabsorption, and immune reconstitution inflammatory syndrome (IRIS) have potential to cause the development of drug-resistance and failure of treatment in

patients with TB-HIV co-infection (Pradipta et al., 2018).

At the 4th World Health Organization/International Union Against Tuberculosis and Lung Disease global drug-surveillance report meeting, only 11 countries reported a strong association between MDR-TB events and HIV, with the majority of those countries being from Eastern Europe and Central Asia. Despite having a high incidence of HIV and MDR-TB, Sub-Saharan and Asia-Pacific nations were reporting low rates of co-infection with HIV and MDR-TB; however, this could be due to late diagnosis, a rise in disease progressivity, and a lack of adequate infrastructure and facilities (National Institutes of Health, 2019). According to a study conducted by Sultana et al., the South-East Asia region has a high risk of MDR-TB among HIV patients (Sultana et al., 2021). Based on this study, only 4 MDR-TB patients had history of HIV.

The prevalence of TB patients who had diabetes mellitus in Indonesia was relatively low (13.2%), but significantly associated with TB. The prevalence of MDR-TB patients who had a history of diabetes mellitus is still unknown, but a study that was conducted in several hospitals in Indonesia showed that around 18.8%–23.3% of MDR-TB patients who were treated in those hospitals had a history of diabetes mellitus (Saktiawati and Subronto, 2018). People with diabetes and TB have a higher risk of failure of TB treatment, mortality from TB, and relapse from TB, failure of TB treatment could lead to MDR TB (World Health Organization, 2021b).

## CONCLUSION

From 106 MDR TB patients who were treated at Dr. Soetomo General Academic Hospital, Surabaya, 72 patients met the criteria. Secondary MDR TB affected 26 patients, 15 of whom had only a history of diabetes mellitus, 2 of whom had a history of HIV, 27 of whom had a history of TB with diabetes mellitus, and 2 of whom had a history of TB with HIV. The data could support the theory of an association between MDR TB with TB, HIV, and diabetes mellitus and increase awareness of primary MDR TB cases with histories of HIV and diabetes mellitus. Further research regarding the association between MDR TB with HIV and diabetes mellitus, identifying the risk factors of MDR TB, and screening of MDR TB especially in high-risk populations, should be conducted.

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## CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

## ETHICS CONSIDERATION

This research was ethically cleared and approved by Ethical Committee for Health research of Dr Soetomo General Academic Hospital certificate.

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This research was self funded.

## AUTHOR CONTRIBUTION

All author have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.



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