



Patients with Multiple Drug-Resistant Pulmonary Tuberculosis at Dr. Mohammad Hoesin General Hospital, Palembang: Association of Body Mass Index on Drug Side Effects

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ARTICLE INFO

Keywords:

Body mass index
MDR-TB
Tuberculosis
Underweight

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All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/JRP.v4i2.49>

ABSTRACT

Patients with Multiple Drug-Resistant Pulmonary Tuberculosis at Dr. Mohammad Hoesin Palembang: Association of Body Mass Index on Drug Side Effects. Tuberculosis (TB) is an infectious disease transmitted by acid-resistant bacteria, namely, *Mycobacterium tuberculosis* (MTb). TB enters the respiratory tract and infects the lungs, and it can spread to other organs both hematogenously and lymphogenously. Pulmonary TB is the most common occurrence. Based on resistance, there are 2 types of pulmonary TB infection: drug-sensitive and drug-resistant. Multiple drug-resistant pulmonary TB (MDR-TB) is a type of pulmonary TB bacteria that is resistant or immune to rifampicin and/or isoniazid treatment. In the treatment of pulmonary TB, MDR uses a multi-drug combination therapy regimen in which each drug has both major and minor side effects. One of the risk factors for side effects is body mass index (BMI). In this study, conducted using a retrospective descriptive method during the 2019–2021 period at Dr. Mohammad Hoesin General Hospital Palembang, 52 subjects met the inclusion and exclusion criteria. 33 subjects (63.5%) were under weight, and 19 subjects (36.5%) were normoweight. Of the 52 subjects, 27 experienced minor ESO and 25 experienced major ESO. The most common major ESO is hearing loss, with 12 events, and in the underweight group, with 10 events. The most common minor ESO was nausea, which occurred 14 times in the overweight group and 9 times in the underweight group. The chi square test showed that there was a significant relationship between underweight BMI and the incidence of major ESO with a p value of 0.029 and an odds ratio (OR) of 3.67x. We concluded that a low body mass index had a 3.67x effect compared to a normal BMI on the increased incidence of major side effects of anti-tuberculosis drugs in MDR-TB patients at Dr. Mohammad Hoesin General Hospital Palembang.

1. Introduction

Tuberculosis (TB) is a contagious infectious disease caused by the acid-fast bacterium *Mycobacterium tuberculosis* (MTb) which often attacks the lungs. Pulmonary tuberculosis is the fourth leading cause of death after ischemic heart disease, cerebrovascular disease and diabetes mellitus (DM) in Indonesia.¹

Global tuberculosis report World Health Organization (WHO) 2018 reports that there are 6.7

million cases of pulmonary TB worldwide and as many as 160,684 of them suffer from multidrug-resistant tuberculosis (Multidrug-resistant tuberculosis: MDR TB). Multiple drug-resistant tuberculosis is a tuberculosis infection that is at least resistant to the two main first-line treatments isoniazid and rifampicin. The prevalence of MDR TB in the world is found to be 3.5% of new cases of pulmonary TB and 18% of cases of pulmonary TB with therapy. Indonesia and China are listed as

countries with the highest burden of MDR pulmonary TB. In Indonesia there are as many as 23,000 cases of MDR pulmonary TB with an incidence of 8.8 per 100,000 population and a prevalence of 2.4% of new cases of pulmonary TB and 13% of cases of pulmonary TB with therapy.²

The occurrence of tuberculosis can be influenced by a damaged immune system, and this can be caused by nutritional imbalances, such as being underweight. Nutritional imbalances which can be seen from the Body Mass Index (BMI) are also expected to affect the treatment of TB patients.³ Santy et al.'s research also confirms that patients with normal BMI or more, can have a higher potential for healing compared to patients with less BMI.⁴ MDR cure Pulmonary TB is not only predicted from nutritional status, because the cure for MDR pulmonary TB also depends on how severe the side effects of treatment are experienced by the patient.⁵ However, in South Sumatra, no studies have been found that discuss how the tendency of BMI to side effects suffered by patients Pulmonary TB MDR. So the researchers wanted to know whether there was an effect of BMI on the incidence of drug side effects in MDR pulmonary TB patients at Dr. Mohammad Hoesin General Hospital Palembang.

2. Methods

This research is a retrospective descriptive study. This research was conducted at the Medical Record Installation of Dr. Mohammad Hoesin General Hospital Palembang with an estimated time from October - November 2022. The population of this study was all patient medical record data in the TB Information System (SI-TB) at the Medical Record Installation of Dr. Mohammad Hoesin General Hospital Palembang. The sample of this study was medical record data for all patients diagnosed with MDR pulmonary TB at the Medical Record Installation of Dr. Mohammad Hoesin General

Hospital Palembang 2019-2021 who meets the inclusion and exclusion criteria. With the total sampling method, which is a sampling technique in which researchers take all data that fits the inclusion criteria to find research subjects.

Inclusion criteria in this study were MDR pulmonary TB patients who were confirmed based on bacteriological examination, TCM or Xpert MTB/RIF. Patient data is in the range of 18-65 years and complete. BMI classification is divided into: <18.5 Underweight, 18.5-24.9 Normal, 25-29.9 Overweight, >30 Obese. The classification of drug side effects is divided into two: minor ESO that can be overcome without stopping treatment. For example: sleep disturbances, headaches, nausea, vomiting, to mild depression. Major ESO that has complaints with or without minor symptoms that must stop OAT treatment. For example: heart rhythm disturbances, hearing loss, optic neuritis, psychotic disorders, major depression, hallucinations. Data collection was carried out by researchers through secondary data from medical records that met the inclusion criteria. Then the data is analyzed according to the variables studied. Data processing and analysis using the SPSS 25 for Windows program. The data is presented in the form of tables and graphs. The data is tested whether the distribution is normal or not, if the distribution is normal then parametric and non-parametric tests are used if the data distribution is not normal.

3. Results

During the 2019 – 2021 period, 52 subjects were found who met the inclusion criteria for this study. Of the 52 subjects, 33 subjects (63.5%) were under weight and 19 subjects (36.5%) were normoweight. Of the 52 subjects, 27 subjects experienced minor ESO, and 25 subjects experienced major ESO, as shown in Table 1.

Table 1. Distribution of BMI categories and ESO events

BMI category	ESO Major		ESO Minors		Total	
	N	%	N	%	N	%
Underweight	23	69,7	10	30,3	33	63.5
Normoweight	8	42,2	11	57,8	19	36.5
Total	25	48	27	52	52	100

From Table 1. It appears that the most frequent major ESO 69.7% vs. 30.3% minor ESO. ESO was in the underweight group of 63.5% with

Table 2. Distribution of ESO Event Types

BMI category	ESO Major				ESO Minors			
	Hearing disorders	Hematological Disorders	Impaired Kidney Function	Icteric	Peripheral Neuropathy	Skin Disorders	Electrolyte Disorders	Nauseous
Underweight	10	3	2	1	5	1	2	9
Normoweight	2	3	3	1	1	2	2	5
Total	12	6	5	2	6	3	4	14

From Table 2. It was found that the most major ESO was hearing loss with 12 events, and in the underweight group with 10 events. The most common minor ESO was nausea with 14 incidents, and in the underweight group with 9 incidents.

Table 3. Relationship between BMI and ESO events

	p value	Odd Ratio	Confidence Intervals 95%
BMI (underweight/ normoweight) - ESO events (major/minor)	0.029*	3.67	1.12 – 12.05

*Chi-Square

4. Discussion

In this study the majority of MDR pulmonary TB patients were in the underweight group. This is because TB patients experience anorexia to experience underweight. In addition, low nutritional status also affects the patient's recovery which can eventually cause the patient to stop treatment.⁶

Drug-resistant TB treatment is more at risk of causing side effects than drug-sensitive TB

treatment, so routine monitoring of MDR TB patients is necessary. OAT side effects often occur in the intensive phase of treatment, namely the first 2 to 6 months. The most ESO is nausea. These results are similar to the study by Munir et al which stated that the most common ESO was digestive disorders at 20.8%.⁷ Mandhav in his research also obtained similar results where the most common ESO was intestinal disorders in the form of nausea, vomiting

and anorexia.⁸ This happened because OAT stimulated a stimulus emetic with various mechanisms ranging from stimulating the abdominal vagal nerves, disrupting the vestibular system and the central nervous system, but the specific mechanisms are still not clearly understood. The side effect of nausea is usually due to pyrazinamide, ethambutol and ethionamide. These side effects usually don't stop the medication, only reduce the dose and give medication to treat the symptoms.⁹

Hearing loss is closely related to aminoglycoside injection, because it affects the cochlea in the ear, with continuous exposure, can cause progressive damage. This ototoxicity can cause permanent damage, therefore temporary discontinuation or changing of regimens is one of the major side effects. The mechanism of ototoxicity is due to disruption of protein synthesis in mitochondria and accumulation of free radicals followed by destruction of hair cells in the cochlea.¹⁰

Park et al stated that TB patients who are underweight tend to be more at risk of experiencing severe side effects and increasing morbidity and mortality.¹¹ This is because in underweight patients there is a decrease in fat mass and protein energy malnutrition, this will increase the amount of binding protein (protein binding) decreases and causes more free drug levels and increases pharmacological activity and causes an increased risk of side effects.¹² In addition, underweight can also affect the immune system, and make the patient's immunity decrease so that he is more susceptible to other infections. This will increase the risk of death 2x greater than the normoweight BMI group.¹³⁻¹⁴

5. Conclusion

Low body mass index or underweight has an effect of 3.67x compared to normal body mass index on the increased incidence of major side effects of anti-tuberculosis drugs in MDR pulmonary TB patients at Dr. Mohammad Hoesin General Hospital Palembang.

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