Anxiety and depression level of patients with multidrug-resistant tuberculosis (MDR-TB) in two hospitals in Banten province, Indonesia

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ABSTRACT

Purpose: Anxiety and depression can be found in patients diagnosed with multidrug-resistant Tuberculosis (MDR-TB). The purpose of this research is to measure the level of anxiety and depression in new patients with MDR-TB.
Methods: One hundred two new patients newly diagnosed with MDR TB in two hospitals in Banten province, Indonesia, are measured for depression and anxiety symptoms. The measurements used the Indonesian language version of the Zung Anxiety Self-Assessment Scale Questionnaire and the Indonesian version of Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis Patients that have been validated. The results include the demographic data presented descriptively as tables and charts.
Results: The mean age of the patients is 39,57 + 12,48 years. The monthly income of the patients is 54,9% low and 45,1% medium with no high income. Male is 61,8%, and 38,2% are female. The mean score of the anxiety index is 57,32 + 10,23. The mean score of the depression index is 55,02 + 12,36. The percentage of patients with no anxiety is 13,7%, minimal to moderate anxiety 46,1%, marked to severe anxiety 33,3%, and most extreme anxiety 6,9%.
Conclusions: A significant proportion of patients newly diagnosed with MDR-TB experience anxiety and depression.

List of abbreviations and acronyms

MDR-TB	Multidrug-resistant Tuberculosis
XDR-TB	Extensively drug resistant-Tuberculosis

1. Introduction

Tuberculosis is a human disease caused by Mycobacterium tuberculosis that affects the lungs, making the pulmonary disease the most common presentation [1]. It commonly affects organs such as the gastrointestinal (GI) system, the lymphoreticular system, the skin, the central nervous system, the musculoskeletal system, the reproductive system, and the liver [2]. Tuberculosis bacteria can develop resistance to drugs; hence they are called Multi-Drug Resistant Tuberculosis (MDR-TB) which refers to tuberculosis which the Mycobacterium has developed resistance to at least isoniazid and rifampicin, the two most potent Tuberculosis drugs. The extensive drug resistant-Tuberculosis (XDR-TB) is a more severe type of MDR-TB

that is resistant to isoniazid, rifampin, fluoroquinolone, and second-line drugs (such as amikacin, kanamycin, or capreomycin) [3].

According to the data gathered by WHO global tuberculosis report, in 2019, tuberculosis globally has been estimated at over 10 million cases with a prevalence of 130 per 100.000 population per year [4]. In 2020, the cases declined to 9.9 Million with a prevalence of 127 per 100.000 population per year. MDR - TB cases were reported in 2019, with over 202.000 cases. Meanwhile, in 2020 reported cases declined to an estimated 158.000 cases [5]. For Indonesia, according to the data gathered by the Indonesian ministry of health. In 2019, there were reports of 568.987 with a prevalence of 312 per 100.000 population; in 2020, it declined to 393.323 cases with a prevalence of 301 per 100.000 population. For MDR - TB in 2019, the Indonesian Ministry of Health reported over 11.000 cases. Meanwhile, in 2020 they reported cases of 7.921 [6].

Depression is a common mental disorder characterized by persistent sadness and lack of interest in activities. Anxiety is produced due to the body's reaction to stressful or unfamiliar situations [7]. Anxiety disorders can be attributed to several factors, and most people experience multiple combinations of risk factors, such as neurobiological factors, genetics,

personality traits, and environmental factors. People with depression often experience symptoms similar to anxiety disorder, such as nervousness, irritability, and problems sleeping and concentrating. However, each condition has its causes and behavioral manifestations [8].

MDR-TB needs a prolonged treatment and lasts 18 to 24 months after the sputum culture conversion [9]. Treatment for MDR-TB also has side effects, such as depression, convulsions, consciousness, psychosis, rash, anxiety, and hepatitis [10].

Several studies reported a relationship between mental health and the risk of active tuberculosis. Nevertheless, there are very few studies on the relationship between MDR-TB and the anxiety also depression levels of patients in Indonesia [11]. Henceforth, this study is conducted to measure the level of anxiety and depression detected in new patients diagnosed with MDR-TB.

Patients with Multidrug-resistant Tuberculosis (MDR-TB) are prone to experience higher anxiety and depression because of the longer treatment period and the worse side effect of MDR-TB treatments compared with usual tuberculosis treatments (non-MDR-TB). In this article, we measure the level of anxiety and depression of newly diagnosed MDR-TB patients in 2 hospitals in Banten province Indonesia authorized by the Indonesian government to diagnose and treat patients with MDR-TB. The Indonesian government provides these two hospitals with GeneXpert equipment to diagnose MDR-TB patients rapidly.

In order to know the exact level of anxiety and depression of newly diagnosed MDR-TB patients using the Indonesian languages version of the Zung Anxiety Self-Assessment Scale Questionnaire for Pulmonary Tuberculosis Patients and the Indonesian languages version of Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis Patients that have been validated for tuberculosis patients [12,13]. With the knowledge about the exact level of anxiety and depression of newly diagnosed MDR-TB patients, we can prepare for better treatment of these patients who often present with complexity.

2. Material and methods

Patients with MDR-TB are not common, and the diagnosis and treatments in Indonesia are centralized. Treatment modalities are often available only in a few hospitals that the Indonesian government provided with the GeneXpert tools. Tangerang Selatan General Hospital and Drajat Prawiranegara General Hospital Serang are two hospitals that were given GeneXpert tools and were appointed by the Indonesian government to diagnose and give comprehensive treatments to MDR-TB patients in Banten province. In Indonesia, the first rapid decision to be given MDR-TB regiment drugs is based on this GeneXpert result.

We measure the level of anxiety and depression of all newly diagnosed MDR-TB patients diagnosed and treated in Tangerang Selatan General Hospital and Drajat Prawiranegara General Hospital Serang, Banten Province, Indonesia, that meet the inclusion and exclusion criteria. The rapid first diagnosis of MDR-TB and the decision to be given MDR-TB regiment drugs were made in that two hospitals using the GeneXpert method. The measurement of the level of anxiety and depression was done using two validated instruments, namely the Indonesian versions of the Zung Anxiety Self-Assessment Scale Questionnaire for Pulmonary Tuberculosis Patients and Indonesian versions of the Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis Patients. Indonesian languages version of the Zung Anxiety Self-Assessment Scale Questionnaire for Pulmonary Tuberculosis Patients that have been validated showed that 19 questions of all 20 have Corrected Item-Total Correlation values more than r table (>0,174) and Cronbach's Alpha 0,892. Meanwhile, the Indonesian version of the Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis Patients showed that all 20 questions had Corrected Item-Total Correlation values more than the r table (>0,195). This questionnaire is also reliable with r Alpha value (Cronbach's Alpha) 0,887 [12,13] The measurement of anxiety and depression was done before the MDR-TB regimen drugs were started to be given to the patients.

This research was approved by the Research Ethical Committee of Faculty of Public Health Universitas Indonesia, Indonesia, with letter number 599/UN2.F10/PPM.00.02/2017. All newly diagnosed MDR-TB patients in Tangerang Selatan General Hospital and Drajat Prawiranegara General Hospital Serang, Banten Province, Indonesia, were given an explanation and informed consent. The patients that agreed to participate in this research were screened using the inclusion and exclusion criteria. If they passed the screening processes, they were given the Indonesian languages version of the Zung Anxiety Self-Assessment Scale Questionnaire for Pulmonary Tuberculosis Patients and the Indonesian versions of the Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis Patients that have been validated to be fulfilled by themselves. After the questionnaires were fulfilled, they were collected for score calculation. The inclusion criteria are 1) male or female 17 – 65 years old, 2) Sputum test using GeneXpert showed Rifampicin resistant Tuberculosis, 3) Newly MDR-TB diagnosed patients. The exclusion criteria are: 1) patients clinically suffered from cognition impairments (mental retardation, dementia, patients with psychotic symptoms) diagnosed by a psychiatrist, 2) patients who cannot read and write, 3) patients who refused to participate in this research, 4) patients with a previous history of depression episodes. The research was done at Tangerang Selatan General Hospital and Drajat Prawiranegara General Hospital Serang, Banten Province, Indonesia, from January 2018 until January 2019.

Demographic data collected and analyzed are age, income, and gender. All the measurement results were collected on the same day as the day of explaining informed consent and distributing the questionnaires (the questionnaires were not taken home). The raw scores measured using the Indonesian version of the Zung Anxiety Self-Assessment Scale Questionnaire for Pulmonary Tuberculosis Patients and Indonesian languages version of Zung Self-Rating Depression Scale Questionnaire for Pulmonary Tuberculosis were converted to index score and then classified into categorical level of anxiety and depression [14,15].

All data analysed using Statistical Product and Service Solutions program (SPSS) version 28.0.1.1. Mean, median, mode, minimum, maximum and distribution of the data were calculated for age, anxiety index score, and depression index score. Gender, income, anxiety level, and depression level were presented in percentages.

3. Results

There were 153 newly diagnosed MDR-TB patients in Tangerang Selatan General Hospital and Drajat Prawiranegara General Hospital Serang, Banten Province, Indonesia, from January 2018 until January 2019. Screened using inclusion and exclusion criteria, we found 106 patients meet the inclusion and exclusion criteria. When data collected 4 patients did not fill the data completely, so that there are only data from 102 patients can be analysed.

Mean age of the patients in this population is $39,57 + 12,48$ years old. Median, mode, minimum, and maximum age of the patients are 39,6 years old, 38,2 years old, 17,8 years old, and 65 years old. Data distribution of the patient's ages is tested for normality using Kolmogorov-Smirnov test with Liliefors significance correction and showed that the data distribution is not normal with p = 0,038. The histogram can be seen in Fig. 1. Male patients in this population are 63 patients (61,8%) and the rest 38 patients (38,2%) are female patients. This is presented in Fig. 2. The income of patients that newly diagnosed with MDR-TB in this research are 46 patients (45,1%) have medium income and 56 patients (54,9%) have low income. The table can be seen in Table 1.

Raw anxiety scores from the questionnaires were converted to anxiety index score to be categorized into anxiety level. Mean, median, mode, minimum, and maximum scores of the anxiety index score are $57,32 + 10,23$, 58, 51, 34, and 84. Data distribution of this anxiety index score is tested using Kolmogorov-Smirnov test with Liliefors significance correction and showed that the data distribution is normal with p = 0,2. The histogram can be seen in Fig. 3. The categorical classification of the anxiety level showed that the percentage of patients within normal range with no anxiety
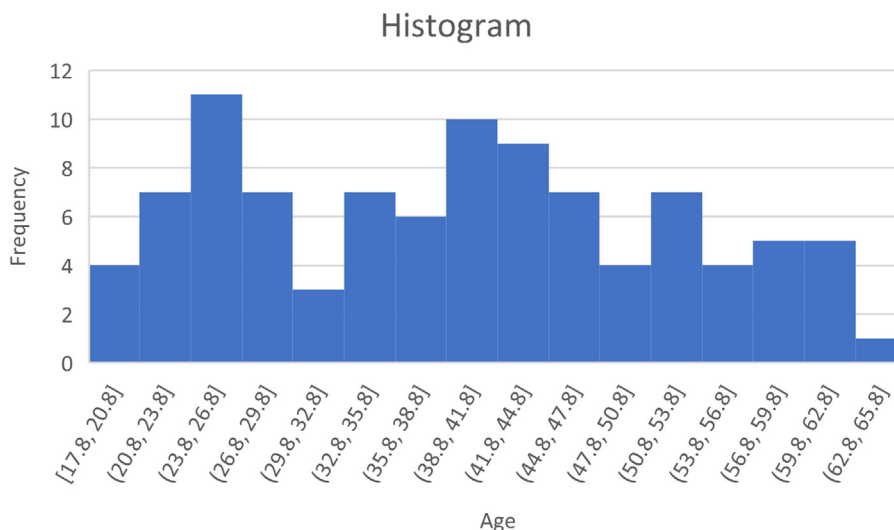
Histogram

Fig. 1. The data distribution of patients ages is not normal with p = 0,038 using Kolmogorov-Smirnov Test.
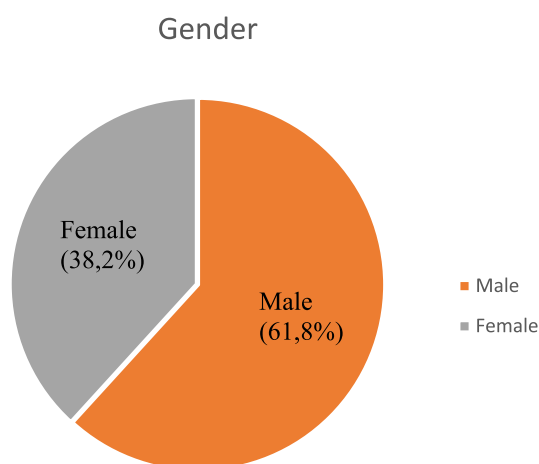
Gender

Fig. 2. The gender of the patients is dominated by male (61,8%).

is 13,7%, minimal to moderate anxiety 46,1%, marked to severe anxiety 33,3%, most extreme anxiety 6,9%. The chart can be seen in Fig. 4.

Self-rated raw depression scores from the questionnaires were converted to self-rated depression index to be categorized into depression level. Mean, median, mode, minimum, and maximum scores of self-rated depression index are 55,02 + 12,36, 55, 51, 30, and 86. Data distribution of this self-rated depression index is tested using Kolmogorov-Smirnov test with Liliefors significance correction and showed that the data distribution is normal with p = 0,2. The categorical classification of the anxiety level showed that the percentage of patients within normal range with no depression is 31,4%, mildly depressed 32,4%, moderately depressed 25,5%, severely depressed 9,8%. The chart can be seen in Fig. 5.

Table 1
Income of the patients.

Income		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Medium income	46	45.1	45.1	45.1
	Low Income	56	54.9	54.9	100.0
	Total	102	100.0	100.0	

4. Discussion

To our knowledge, this is the first study to describe depression and anxiety among MDR-TB in Banten province, Indonesia. Our previous study on non-multidrug-resistant TB in the same province, albeit in different healthcare facilities, showed that the prevalence of depression is 70.5%, with 28.5% among those with moderate to severe depression [16]. In line with that result, we found a high proportion of depression (68.6%) and anxiety (86.3%) in the current study. This figure is arguably much higher than the prevalence of depression and anxiety in the general Indonesian population, estimated at 9.8% of the total population [17].

The prevalence of depression among persons with MDR-TB in our population is higher than in other countries, ranging from 10.33% to 69.55% [18–23]. Our finding of depression prevalence is also higher than other studies among the MDR-TB population in Indonesia by Supriyanto et al. [24] in Yogyakarta (12.5%), Ariyanto, Sofro, and Dwidayani [25] (27.7%), and Azam et al. [26] (26.4%). The latter two were conducted in Semarang, a major city in Central Java province. This wide variation, globally and locally, is not surprising concerning the use of different instruments, and cut-off points for defining depression, disease stages, treatment stages, and other differences in study settings. Regarding anxiety, previous global studies show different prevalences ranging from 12%–54% [27–30]. In Indonesia, Fitrianur, Soeharto, and Supriati [31] found a 62% prevalence of anxiety in a hospital-setting population in East Java. Supriyanto et al. reported 10.94% anxiety prevalence, recorded as "adjustment disorder with anxiety", based on secondary data analysis [24].

This high prevalence of mental illness comorbidity among patients with MDR-TB is consistent with other studies. Various factors might contribute to depression and anxiety among MDR-TB patients, such as the course of the chronic illness and the treatment's side effects [18,32]. For example, a second-line TB drug, cycloserine, which used to be known as potentially inducing psychosis, could also cause depression [33,34]. This might be explained by the effect of cycloserine on the N-methyl-D-aspartate (NMDA) receptor and gamma-aminobutyric acid (GABA) neurotransmitter [24,35]. However, recent studies [36,37] show no association between cycloserine and depression; therefore, further studies need to confirm this association and explore the effect of other drugs used in MDR-TB. In this research, however, the measurement of anxiety and depression was done in recently diagnosed patients where the MDR-TB regimen drugs had not been given to the patients. Suppose patients were detected to have suffered from depression and anxiety before the drugs were given; in that case, there is a probability that the condition could worsen after the pharmacotherapy of second-line drugs for TB.
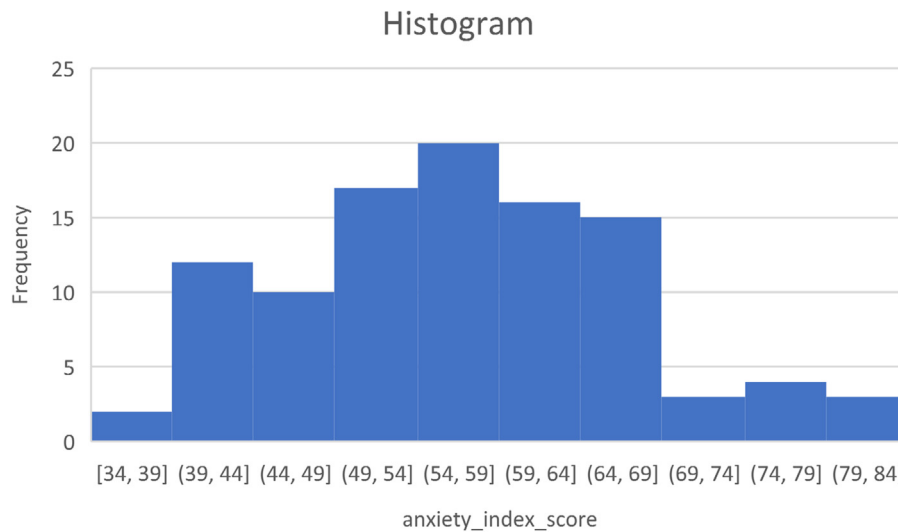
Histogram

Fig. 3. The data distribution of patient's anxiety index score is normal with p = 0,2 using Kolmogorov-Smirnov Test.

The contribution of social factors to the pathogenesis of depression and anxiety in MDR-TB patients, and the barrier in the healthcare system to address them, also require attention from the clinician, policymakers, and

Fig. 4. The anxiety level of MDR-TB patients.

Fig. 5. The depression level of MDR-TB patients.

other stakeholders. The factors included in this categories are stigma, poverty, and difficult access to mental health care, which contribute to increased risk of mental disorder among MDR-TB patients [38,39]. MDR-TB patients may face financial and practical difficulties as a result of their illness and combined with stigma as well as discrimination, this will increase the level of their emotional distress [40]. Access to mental health care could also be challenging, as the mental health system itself, in our context, is considerably underdeveloped, stigmatized, and not very easy to access, centralized in specialized care instead of community [41]. Considering the complex needs of MDR-TB, policymakers might need to focus on developing integrated care and provide it in a place where it is accessible to most people; the community and primary care services [42,43]. To mitigate the effect of stigma, it is also important to increase the effort to educate the public continuously, to increase public understanding and support for patients.

Given the high prevalence of these conditions that could influence clinical outcomes, a proactive-early detection and prompt intervention, ideally in a collaborative setting with mental health professionals such as psychiatrists and clinical psychologists, is warranted. The benefit of psychosocial intervention for depression and anxiety among patients with MDR-TB is multi-fold. First, treating depression and anxiety might improve the patient's adherence to MDR-TB treatment, as these two are suggested to contribute to the high rates of loss to follow-up [44,45]. Second, psychiatric symptoms, such as depression, will significantly influence the patient and family's quality of life [46]. Thirdly, it has been widely known that depression has a central role in other non-communicable disease pathogenesis, such as diabetes and hypertension, if remains unaddressed [47,48].

There are several limitations of our study. First, the result of our study might not be generalizable to other areas of Indonesia and different care settings. We are also not confirming depression diagnosis with a structured clinical interview by mental health professionals. And third, we exclude patients who cannot read and write because the patients themselves should fill out the Zung questionnaires. It is more likely for our study to underestimate prevalence since those with depression, and anxiety might have less adherence to treatment and are more likely to not come to the facility.

5. Conclusions

The prevalence of anxiety and depression in patients newly diagnosed with MDR-TB in Indonesia is high. The prevalence is much higher than the prevalence in the general Indonesian population. The prevalence of depression among MDR-TB patients in Indonesia is also considerably higher than the prevalence reported in other countries. These mental illness
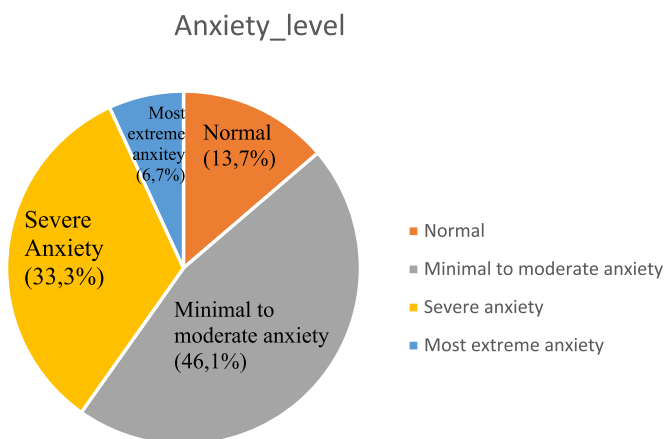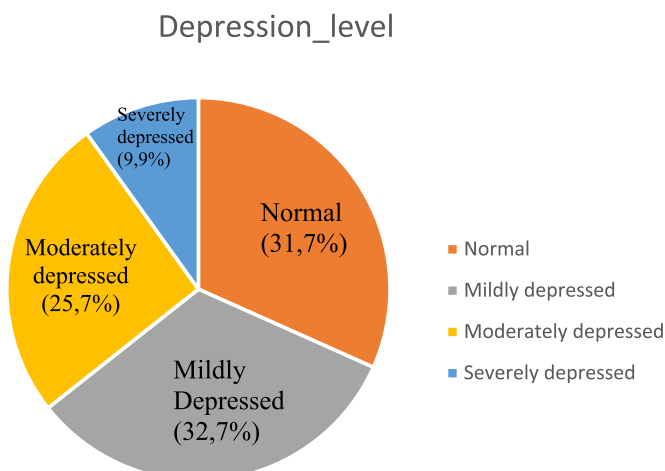
comorbidities can influence clinical outcomes, so it is important to aim for early detection and prompt intervention.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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