A Systematic Review: Anxiety and Depression of Multi Drug Resistant Tubercolosis (MDR-TB) Patients in Treatment Process

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ABSTRACT

Introduction

Multi Drug Resistant Tuberculosis (MDR-TB) is one type of TB *bacilli* resistance to at least two of the first line of the most effective TB drugs, namely Isoniazid and Rifampicin. The MDR-TB case is a new challenge because it requires more complicated clinical management, difficulty in diagnosis, high rates of therapy failure and death, so that it can cause anxiety and depression in patients.

Methods

The method used was searching the Proquest and Google Scholar electronic databases by using the keywords anxiety, depression, and MDR-TB. The search results were selected using the inclusion criteria and analyzed by PRISMA (Prefered Reposting Items for Systematic Review and Meta-Analysis) flow diagrams.

Results

There were 15 quantitative research journal articles have been analyzed. It was found that the factors causing anxiety and depression in patients with MDR-TB were the initial diagnosis of MDR-TB, drug side effects, psychosocial burden experienced by patients, community stigma, health problems and socioeconomic status (poverty), presence of comorbidities, length of time the patient suffered from illness, problems with access to health facilities, and attitudes and behavior of health workers.

Conclusion

Intensive proactive communication is needed with clients, family and nurses to be able to strengthen treatment plans, make decisions easier, and helps reduce family burdens that are very important for client and family care satisfaction. Nurses also need to explain about MDR-TB and the treatment process so that patients have readiness to follow the treatment process.

Keywords

Anxiety; Depression; Multi Drug Resistant Tuberculosis; MDR-TB; Treatment

BACKGROUND

Tuberculosis (TB) is still a global problem that develops in the developing countries and the number one cause of death among infectious diseases and also the third rank of 10 killer diseases in Indonesia (SR, Nurlaela, & A, 2012). In TB cases, treatment that is interrupted or not in accordance with the standards of Directly Observed Treatment, Shortcourse Chemotherapy (DOTS) can result in the emergence of multi-immunity to anti-TB drugs cases that give rise to a stronger type of TB bacteria, as known as Multi Drug Resistant (MDR-TB). MDR-TB is one type of TB bacilli resistance to at least two first-line anti-tuberculosis

(OAT) drugs namely isoniazid and rifampicin, the two most effective OAT drugs. MDR-TB is a new challenge in TB control programs because enforcement of the diagnosis is difficult, high rates of failure of therapy and death (Mulyanto, 2014).

According to WHO in 2011, tuberculosis infected around 9,000,000 annually and killed nearly 1,400,000 people worldwide. The MDR-TB case itself for the world until 2015 is estimated to be 480,000 new cases and 100,000 additional TB resistant to rifampicin with the ongoing detection crisis of MDR-TB treatment. In 2015, from an estimated 580,000 people who gott MDR-TB treatment requirements, only 125,000 (20%) were registered. Five countries contributing more than 60% of MDR-TB cases are India, China, Russian Federation, Indonesia and Nigeria with MDR-TB treatment success rates of 52% in 2013 ((WHO), 2017). The data that was about MDR-TB patients in Indonesia at 2015 were targeted at 280 cases per 100,000 population. The case data findings according to the Center for Data and Information of the Ministry of Health of the Republic of Indonesia during 2009-2015 found 15,380 cases of suspected MDR-TB.

In MDR-TB cases, clinical management is more complicated than sensitive TB because it uses line I anti-TB (OAT) and line II drugs. In the management of sensitive TB, only use 4 drugs and takes 6 months, while in MDR-TB management, use at least 5 drugs and last for 18 to 24 months. Management of MDR-TB cases is often associated with the occurrence of side effects ranging from mild to severe side effects. The selection of drugs for MDR-TB cases is using line I drugs if they are still effective, one injection drug using flurokuinolone class drugs, using drugs for group 4 (line II oral) until 4 types of effective drugs are obtained, and group 5 drugs to strengthen the regimen or when before four types of effective drugs were obtained from the previous group. MDR-TB therapy uses several types of drugs, causing some problems in terms of tolerance to these drugs. The response of each individual is unpredictable, but treatment must not be stopped only because of fear of the reaction that happened (P, Kusnanto, Eko, Pakiding, & Nurwidiasih, 2014).

MDR-TB treatment takes a long time and is complicated due to several things, one of which is the side effects of drugs that make patients experience psychocial problems such as anxiety and depression, so special efforts are needed to support the continuation of MDR-TB treatment until complete and cured. In addition to the motivation of patients seeking treatment and recovery, psychosocial support, health workers tracking patients who are lost to follow-up, bringing treatment services closer to patients' homes, and referring MDR-TB patients whenever necessary are ways and efforts to ensure the continuity of patient treatment. So it is expected that patients with MDR-TB can recover again (Health, 2013). Inadequate treatment is usually the result of one or more conditions, namely (1) Regimen, dosage, and improper use; (2) Irregularity and disobedience of patients to take medicine; (3) Disconnection of OAT availability and (4) low drug quality (Nawas, 2010).

Seeing these conditions, many of the patients with MDR-TB experience anxiety and even lead to depression. Apart from the patient's condition, the process of treatment that takes a long time is also a factor in the emergence of anxiety and depression in patients with MDR-TB. It also when patients have a diagnosis of other diseases such as HIV-AIDS which will

affect the level of anxiety of these patients. So that, in this case appropriate psychological support is needed for patients with MDR-TB. The purpose of this systematic review is to see the trigger factors for anxiety and depression in MDR-TB patients undergoing treatment.

METHODS

The method of this study used data searching on electronic databases and obtaining analysis results from several journals that met the inclusion criteria. The author got results from several journals namely Journal BMC Psychiatry, Journal of Academia and Industrial Research (JAIR), Journal of Epidemiology and Public Health, Original Article Acta Medica International, Journal of Depression and Anxiety, BMJ Journal, Global Health Action, J Anal Res Clinic Med (JARCM), Journal of Tuberculosis Research, Recent Researches in Modern Medicine, BMC Medicine, Article Mental Health in Family Medicine, Original Article : Pak J Chest Med (PJCM) Journal, Public Health Journal and Indonesian Nursing Journal. Journal publications sought by researchers started from April-May 2018. The main concept sought by researchers was about Anxiety and Depression in patients with Multidrug Resistant Tuberculosis (MDR-TB). Subjects related to several research areas were mental health, psychiatric, nursing, especially mental health nursing. After searching through the database, the author makes a selection process based on the title and abstract of the selected article. The article was assessed if it has a complete text using PRISMA (Prefered Reposting Items for Systematic Review and Meta-Analysis) flow diagrams so as to obtain as many as 15 articles worthy of research, that were 15 quantitative studies. The PRISMA search flow diagram can be seen in Figure 1.
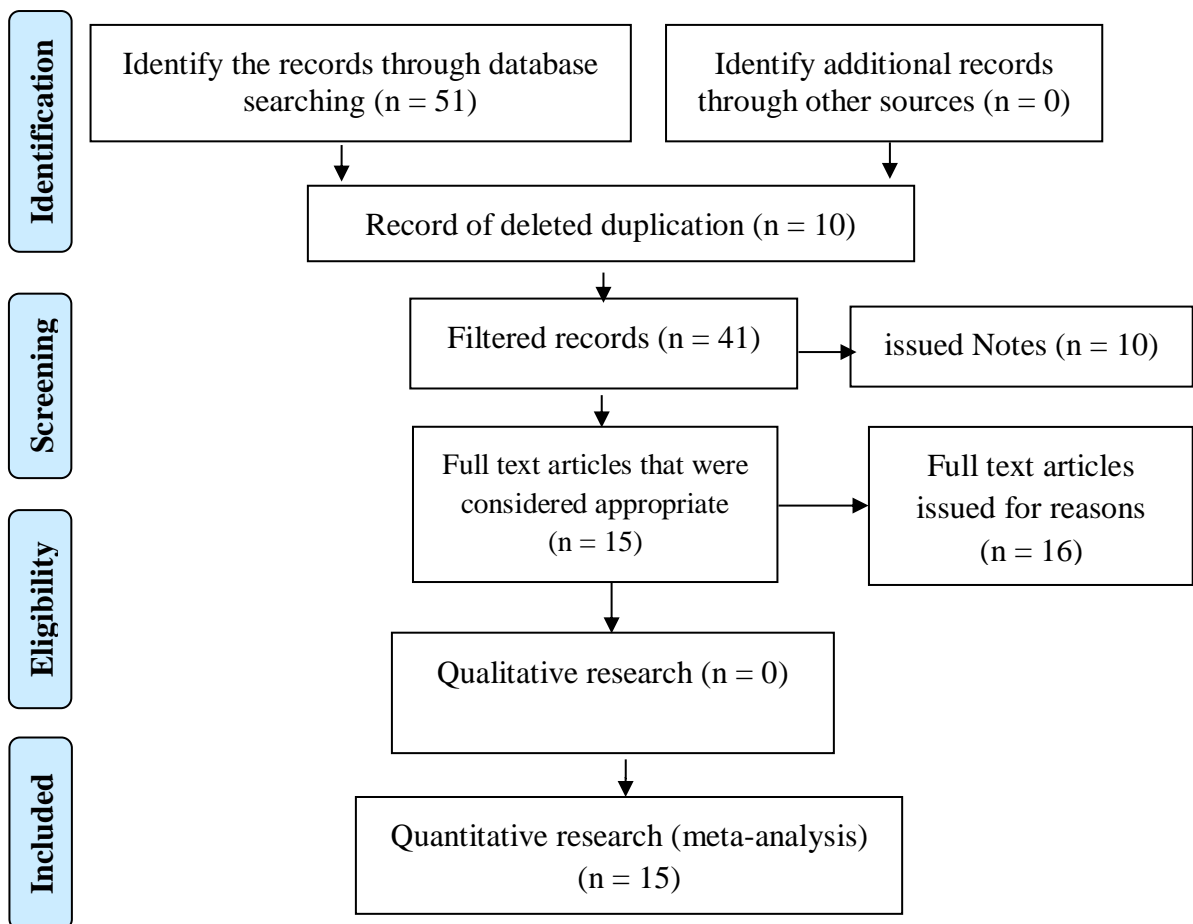
Figure 1. The flow diagram of PRISMA

RESULTS

Table 1. Journal Review Anxiety and Depression of Multidrug Resistant Tuberculosis (MDR-TB) Patients in Treatment Proces

Title and Year	Place	Method	Population	Objective	Result
Depressive Syndrome, Anxiety and Illness Perception in Tuberculosis Patients. (Adina et al., 2010)	Rumania	Cross Sectional Study	60 patients treated for tuberculosis	To evaluate the incidence of depressive syndrome and anxiety in tuberculosis patients hospitalized	Depression and anxiety are very high in patients with tuberculosis, in our study (6,78 % for severe depression, 32,20% moderate depression and 32,20 for severe, 40,68% for moderate anxiety). For patients at first admission in hospital (new case) the anxiety score is high than for chronic patients or with multiple admission.
Prevalence of Depression in Tuberculosis Patients in Comparison with Non-Tuberculosis Family Contacts Visiting the DOTS Clinic in a Nogerian Tertiary Care Hospital and its Correlation with Disease Pattern. (Ige & Lasebikan, 2011)	Ibadan, Nigeria	Prospective Study	88 patient and 81 control	This study aimed at determining the prevalence of depression in tuberculosis patients in comparison with non-tuberculosis controls, and its correlation with disease pattern.	The prevalence of depression was 45.5% among patients and 13.4% among family members. The prevalence of depressive episode among those with and without tuberculosis was 23.7% and 6.8%, respectively ($P < 0.001$).

Prevalence of psychological distress and associated factors in tuberculosis patients in public primary care clinics in South Africa. (Peltzer et al., 2012)	South Africa	Cross-Sectional Survey	4900 Tuberculosis Public Primary Care Patients	Assessed the prevalence and predictors of psychological distress as a proxy for common mental disorders among tuberculosis (TB) patients in South Africa, where over 60 % of the TB patients are co-infected with HIV.	32.9 % and 81 % of tuberculosis patients had symptoms of distress, respectively. In the final model mental illness co-morbidity (hazardous or harmful alcohol use) and non-adherence to anti-TB medication and/or antiretroviral therapy were not associated with psychological distress.
Risk Factor of Multi Drug Resistant Tuberculosis (MDR-TB). (SR et al., 2012)	Purwokerto, Indonesia	Observational study, case control	32 case, 32 control	The purpose of research was to determine MDR-TB risk factors.	The results showed that the risk factors of MDR-TB were low patient motivation OR=4.2 (CI=1.478 to 11.94) and treatment irregularity OR=2.3 (CI=1.38 to 10,28). Required a variety support, especially from family and environment in order to motivate patients with pulmonary tuberculosis that their disease can be cured and do the treatment regularly.
HIV, Multidrug-Resistant TB and Depressive Symptoms : When Three	Mumbai, India	Retrospective review, HIV-/MDR-TB	45 HIV/MDR-TB	To address limited evidence on the baseline psychiatric conditions of HIV-infected MDR-TB patients.	A total of 45 HIV/MDR-TB patients underwent baseline assessment using the PHQ-9 tool,

Condition Collide. (Das et al., 2014)		cohort registered			and seven (16%) were found to have depressive symptoms. Of these, four patients had moderate to severe depressive symptoms. Among these 44 patients, three with baseline depressive symptoms still had depressive symptoms.
Anxiety and Depression in Tuberculosis Can Create Impact on Quality of Life of Patient. (Rubeen et al., 2014)	Karachi, Pakistan	Cross Sectional Study	140 Individual	To assess the prevalence of depression and anxiety in tuberculosis and its influence on individual perception of well being in patients attending outpatient clinic in Karachi, Pakistan	About 37.1% patients diagnosed with TB were labeled as having anxiety and depression according to HAD scale.
Assessment of Mental Status of MDR Patients in Wardha District Using Global Mental Health Assessment Tool-Primary Care Version. (G.M. Bhaware, 2014)	India	Cross-Sectional Study	267 patients	1. To estimate the prevalence of mental health disorders in tuberculosis patients using GMHAT/PC. 2. To find out and compare the prevalence of various mental health disorders among TB patients across various socio-demographic variables, type of disease and regimen of treatment	It was observed that, the frequency of psychiatric morbidity in tuberculosis patients was 69.28%, among them, 51.89% patients were with depressive disorders, 37.29% with anxiety disorders, 8.10% had alcohol abuse, 1.08% had stress, 1.08% had hypochondriasis and 0.5% had obsessive compulsive disorder.
Depression Among Patients with Tuberculosis	Ethiopia	Prospective Cohort Design	703 newly diagnosed cases	To examine the relationship between depression and TB among people newly	Depression in patients is due to chronic infection, socioeconomic

: Determinants, Course and Impact on Pathways to care and Treatment Outcomes in a Primary Care Seting in Southern Ethiopia- a Study Protocol (Ambaw, Mayston, Hanlon, & Alem, 2015)			of TB (469 without depression and 234 with depression)	diagnosed and accessing care for TB in a rural Ethiopian setting	status and side effects of TB treatment. Anticipated impact: Findings will contribute to a sparse evidence base on comorbidity of depression and TB. We hope the dissemination of findings will raise awareness of comorbidity among clinicians and service providers, and contribute to ongoing debates regarding the delivery of mental healthcare in primary care in Ethiopia.
Frequency of Depression in Multidrug-Resistant Tuberculosis Patients : An Experience From A Tertiary Care Hospital. (Mehreen et al., 2015)	Pakistan	Longitudinal study	213 patients	To find out the frequency of depression at baseline (at the time of registration) in currently diagnosed MDR-TB patients and the emergence of depression during MDR-TB treatment in registered MDR-TB patients in PMDT.	Out of 213 registered patients, 139 (65.5%) had depression at baseline. At the end of 1st quarter, only 47 (33.81%) out of 139 still had depression and at the end of 2nd quarter this number further decreased to 35 (15.10%). While the emergence of depression was 36% at the end of both 1st and 2nd quarter.
The Relationship between Anxiety Levels and Approval to undergo Treatment in Patients	Jember, Indonesia	Correlation design with cross sectional design	40 patients with MDR-TB	This study aims to determine the level of anxiety in MDR-TB patients undergoing treatment	The results using Spearman Rank shows most respondents experienced anxiety are as many as 16 respondents (53.3%) and

Diagnosed with Multi Drug Resistant Tuberculosis (MDR-TB) in Jember Pulmonary Hospital (Anas, 2015)					almost all respondents agreed to undergo treatment that is 24 respondents (80.0%) the remaining 14 respondents (46.7%) experienced mild anxiety and refused treatment are 6 respondents (20.0%) in obtained results there is no correlation between anxiety level with approval for undergoing treatment in patients diagnosed with MDR-TB in the Rs paru Jember and obtained p value 0.861 where p value> 0, 05 with the value of r correlation that is -0033.
Frequency of Depression and Anxiety Among Tuberculosis Patients. (Amreen & Rizvi, 2016)	Pakistan	Descriptive study	100 patients tuberculosis (50 males and 50 females)	The aim of present study was to determine the frequency of depression and anxiety among tuberculosis patients	Findings indicated that 56% tuberculosis (TB) patients had moderate to severe level of depression, whereas 65% TB patients had moderate to severe level of anxiety.
Depression and its Associated Factors with Multidrug Resistant Tuberculosis at Baseline. (Javaid et al., 2017)	Pakistan	Cross Sectional Study	289 MDR-TB Patients	To assess frequency of depression and to identify factors associated with depression at baseline among MDR-TB patients in our centre.	Among total, 201(69.55%) of the study participants were classified depressed, 127 patients (63.18%) had mild depression, 61 patients (30.35%) had moderate

					depression, 13 patients (6.46%) were diagnosed with severe depression. Depression was found in 127 (43.9%) MDR-TB patients at the time of registration associated with different factors.
Biopsychosocial Determinants of Multidrug Resistant Tuberculosis in Surakarta. (Alfiyani, Rahardjo, & Murti, 2017)	Surakarta, Indonesia	Analytic observational study with case control design	76 patients MDR-TB and 228 non MDR-TB	This study aimed to analyzed the bio-psychosocial determinants of MDR-TB in Surakarta	MDR-TB is directly affected by lack of drug-taking adherence and comorbidity. MDR-TB is indirectly affected by drug-taking supervisor, depression, and drug side effect.
Psychiatric Disorder in Patients With Multidrug Resistant Tuberculosis (MDR-TB) in Sardjito Hospital, Yogyakarta, Indonesia. (Supriyanto, Liung, Suprihatini, & Ismanto, 2017)	Yogyakarta, Indonesia	Descriptive Analytic Study	64 patients with MDR-TB	Examined the prevalence and characteristics of psychiatric disorders among MDR-TB patients in Sardjito Hospital, Yogyakarta, Indonesia.	We found that 32.8% of the patients had psychiatric disorders, some of which had multiple psychiatric diagnoses (14.1%). The diagnoses were medication induced delirium, substance/medication induced psychotic disorder, substance/medication use depressive disorder, depressive type schizoaffective disorder, bipolar I disorder current episode severe manic with psychotic features, mild depression,

					moderate depression, major depression without psychotic features, major depression with psychotic features, adjustment disorders with mixed anxiety and depressed mood, adjustment disorder with anxiety, acute stress disorder, and insomnia.
Depression Comorbid with Tuberculosis and its Impact on Health Status : Cross-Sectional Analysis of Community-Based Data from 48 low-and Middle-Income Countries. (Koyanagi et al., 2017)	Spain	Cross-Sectional	Health Survey on 242,952 individuals aged ≥ 18 years	Assessed the association between depression and tuberculosis, and the decrements in health status associated with this comorbidity in 48 low- and middle-income countries.	The prevalence of depressive episode among those with and without tuberculosis was 23.7% and 6.8%, respectively (P < 0.001). Tuberculosis was associated with a 1.98 (95% CI 1.47–2.67), 1.75 (95% CI 1.26–2.42), and 3.68 (95% CI 3.01–4.50) times higher odds for subsyndromal depression, brief depressive episode, and depressive episode, respectively.

DISCUSSION

Multidrug Resistant Tuberculosis (MDR-TB) is one type of TB bacilli resistance to at least two first-line anti-tuberculosis (OAT) drugs namely isoniazid and rifampicin, the two most effective OAT drugs. MDR-TB is a new challenge in TB control programs because enforcement of the diagnosis is difficult, high rates of failure of therapy and death (Mulyanto, 2014). The problem of drug resistance in TB treatment, especially in the cases of MDR and XDR, is a very important health problem and must be addressed. Seeing these conditions, many patients diagnosed with MDR-TB have a susceptibility to anxiety and even depression and suicide. Given that treatment for MDR-TB takes a long time and costs more. In addition, there are several other factors that trigger the anxiety and depression of MDR-TB patients, namely the initial diagnosis of MDR-TB, drug side effects, psychosocial burden experienced by patients, health problems and social status, problems with access to health facilities, and attitudes and behavior of health workers.

From the 15 journal articles, the results showed that almost all MDR-TB patients experience anxiety even depression. This is due to the factors that cause anxiety and depression in patients with MDR-TB are the initial diagnosis of MDR-TB, drug side effects, psychosocial burden experienced by the patient, stigma from the community, health problems and socioeconomic status (poverty), the presence of comorbidities , the length of time a patient has a disease, the problem of access to health facilities, and the attitudes and behavior of health workers. Patients who experience this disease have a higher rate of depression. The reason is that patients already feel despair, are not valuable, there is social stigma from the community and loss of income.

When we saw the process of drug-resistant TB treatment (MDR-TB) which is very complicated and takes a long time, so that it can cause feelings of boredom, anxiety, depression, isolation, rejection and feelings of uselessness, it requires good relations and communication between health workers and patients and psychological support from health workers, family and community / environment so that the treatment process can be successful until the patient is declared cured. The duration of drug resistant TB treatment (MDR-TB) is 18-24 months. Treatment will be even longer if the patient has comorbidities, for example the patient has diabetes mellitus or other disorders that inhibit TB drug absorption (OAT). During the treatment process, patients will swallow medication every day in front of health care workers, this is very uncomfortable for patients especially if there are side effects of drugs.

The likelihood of recovery in patients who stop drug-resistant TB treatment will be smaller compared to patients who stop category 1 treatment and 2. Termination of drug-resistant TB treatment prematurely will increase the likelihood of resistance to second-line drugs and will cause TB Extensive Drug Resistance (XDR) which will be more difficult to treat and increase the risk of death, so that psychosocial support from various parties is needed for drug resistant TB patients (MDR-TB) during the treatment process to complete and recover.

From these conditions, the role of health workers is very important to prevent the occurrence of anxiety and depression in patients who will undergo the treatment process. Health workers must be able to monitor the condition of MDR-TB patients regularly and regularly to help overcome obstacles that may arise during the treatment process. Health workers need to establish effective communication with patients and their families so that patients and families are motivated to complete the regimen / treatment. There were so many reasons for patients to be absent from treatment so this is the duty of health workers to be able to find out and analyze the reasons for patients being lost to follow-up and together with patients seeking the best solution. Without the efforts and hard work of all parties, MDR-TB patients, families and health workers will find it difficult to guarantee treatment success.

In general, MDR-TB patients were absent from the treatment process due to anxiety about drug side effects, psychosocial burden, socio-economic burden, transportation to health services, lack of support from family and the surrounding environment, not understanding about the illness and attitudes and behavior of officers health itself. So it is necessary to have periodic visits to be able to directly interact with patients to provide support and motivation and be able to identify potential problems that can become obstacles in the treatment process (Kesehatan, 2013).

In addition, anxiety and depression in MDR-TB patients could also occur because of social isolation in the community. The patient tries to hide his illness which will eventually complicate the treatment process. So that social support for patients is needed so that patients are able to be motivated to complete the treatment process until healed and can return to the environment without fear of being ostracized and the patient is free from anxiety and depression.

CONCLUSIONS

Multidrug Resistant Tuberculosis (MDR-TB) is a chronic disease that threatens a person's life so that intensive proactive communication with clients, families and caregivers, in this case health workers can strengthen treatment plans, help inform in terms of making decisions, can help reduce family burden and is very important for client and family care satisfaction. MDR-TB patients in undergoing the regimen / treatment process really need health workers especially a nurse to be able to be present therapeutically in terms of describing the healing experience, full of respect, alertness and compassion because when present in a relationship with the patient in a state of respect, empathy and positive things.

It is very important for nurses to be able to know patient complaints and respond patiently to patients In MDR-TB cases. Nurses need to listen without interrupting or defending themselves so that patients and families freely release feelings that make the patient feel compelled to undergo the regimen process properly. In addition, there needs to be an explanation of how the MDR-TB treatment process and what medicines will be obtained during the treatment process so that patients have readiness to follow the treatment proces (Stuart, 2016).

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