

## Research Article

# Psychological challenges faced by multidrug-resistant tuberculosis patients: a systematic review

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### Abstract

**Purpose:** Multidrug-resistant tuberculosis (MDR-TB) patients have few adverse effects due to treatment regimens, including psychological side effects that play an important role in the successful MDR-TB management. This study was aimed to identify MDR-TB patients' challenges within the context of psychological issues and to determine suitable intervention to address psychological problems in MDR-TB patients. **Method:** We conducted a systematic review as PRISMA guidelines using databases PubMed, ProQuest, ScienceDirect, Scopus, and Portal Garuda to search for all related articles. From studies identified, 10 were included in the final analysis. **Results:** It was found that all studies have documented a range of psychological challenges faced by MDR-TB patients that were depression, anxiety, suicidal tendencies and common issues reported in the studies. **Conclusion:** There were three main strategies that can be implemented in every country to address MDR-TB adverse effect and scale-up MDR-TB treatment efficacy. These strategies require high levels of support from health workers and family member which has an important role in the treatment process.

**Keywords:** adverse effects; multidrug-resistant tuberculosis; psychological

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## INTRODUCTION

The emergence of Tuberculosis (TB) with antimicrobial resistance is considered as a new threat to world health problems. World Health Organization (WHO) in 2017 estimated that the number of Multidrug-resistant tuberculosis (MDR-TB) at 558 000 new cases, of which 240 000 deaths were due to MDR-TB. An estimated case of MDRT-TB came from 4.1% of new TB cases and 19% of previously treated TB cases [1]. MDR-TB is the condition where TB caused by *Mycobacterium Tuberculosis* infection did not respond at least to the two most effective first-line anti-tuberculosis drugs that are isoniazid and rifampicin [2]. The presence of drug resistance is attributed to poor treatment management [3]. The success rate of treatment was still far from the target which should be 75% or higher, yet only 52% MDR-TB was successfully treated [4]. Most MDR-TB patients remain incompletely treated due to the long duration of treatment where duration is often 18 - 24 months or longer [3–5]. Besides long-term treatment is needed, inadequate supply and quality of drugs, bacterial factors, and the patient's own condition also give influence. Aggravated by the cost of second-line anti-tuberculosis drugs tend to be expensive and have severe drug side effects [6].

Living with long-term treatment needs, MDR-TB patients will not get only unfavorable effects on the physical aspects. These effects are manifested bilateral deafness, tinnitus, nausea, weakness and pain in the shoulder and limbs, back spasms, sensory neuropathy, persistent loss of bladder and bowel control [6–9]. Furthermore, psychological issues often play an important role in successful MDR-TB control. The challenge is compounded by MDR-TB drugs regimen and due to prolonged treatment which can develop into psychological distress and a number of psychiatric illnesses such as anxiety, depressive disorders, even in more severe cases the risk of suicide can occur [10–12]. Comorbidities of physical and mental disorder lead to synergistically impair medication and treatment adherence. Psychological support interventions are needed for patients with MDR-TB(13). Consolidated evidence about the psychological problems among MDR-TB patients is limited. To address the evidence gap, we aimed to review psychological issues that must be faced by MDR-TB patients and to address these problems with related interventions and to minimize the likelihood of withdrawal medication.

## METHOD

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement [6,13]. A systematic search of relevant articles in PubMed, ProQuest, ScienceDirect, Scopus, and Portal Garuda was used

to identify all published articles using the following keywords: multidrug-resistant tuberculosis, tuberculosis drug resistance, mental health, mental disorders, and psychological factors.

Eligible studies were included if they met the following criteria were all cultures confirmed in adult patients with MDR-TB who either are undergoing or have undergone treatment, the articles published from January 1st, 2013 to October 1st, 2018, the English and Bahasa articles, all articles identified by each reviewer base on full text review, and the provided full search strategy. The exclusion criteria were standardized first-line therapy in the treatment protocol.

The search strategy was used in this review. Titles and abstracts were excluded if they are irrelevant to this review. Data collected included reference, study location, year, method, and findings. We defined psychological distress as any adverse effect on the mental status of the MDR-TB patients resulting from either the illness itself or treatment undertaken. When available in original studies, the association between MDR-TB and our outcomes of interest were extracted, along with their 95% confidence interval (95%CI). Thematic synthesis method for extracting related pieces of evidence was systematically transformed into a descriptive review using a narrative approach.

Due to the multiple research methodologies used, we used the Critical Appraisal Skills Programme (CASP) checklist to rate the quality of each research using a narrative approach. We rated the quality of research using components of CASP designed to be used for each of the research methods. According to the needs of appraisal tools, we used tools for systematic reviews, Qualitative studies, cohort studies, and case-control studies. The CASP included 10 until 12 questions that help us to analyze those questions divided into 3 sections, they are, the validity of results, how is the result, and how these results can help locally.

## RESULTS

Of the publications, 356 identified, 346 were excluded because they did not meet eligibility inclusion criteria. Among the 10 studies selected were conducted in different countries including Mexico in 2013 [6], India in 2013 [10,14,15], Pakistan in 2016 [10,14], Nepal in 2016 [10], South Korea in 2017 [8], India in 2017 [12], Indonesia in 2017 [12,16], and Serbia in 2018 [9]. The remaining two studies have not clearly mentioned the study setting [5,17]. Of the 10 studies, five were original studies which of three were qualitative methodology, one study was conducted retrospective and consecutive review based on medical records [8,16], one study was the case report, and one study was case-control [16]. All the 10 studies were focused on psychological issues faced by MDR-TB patients.

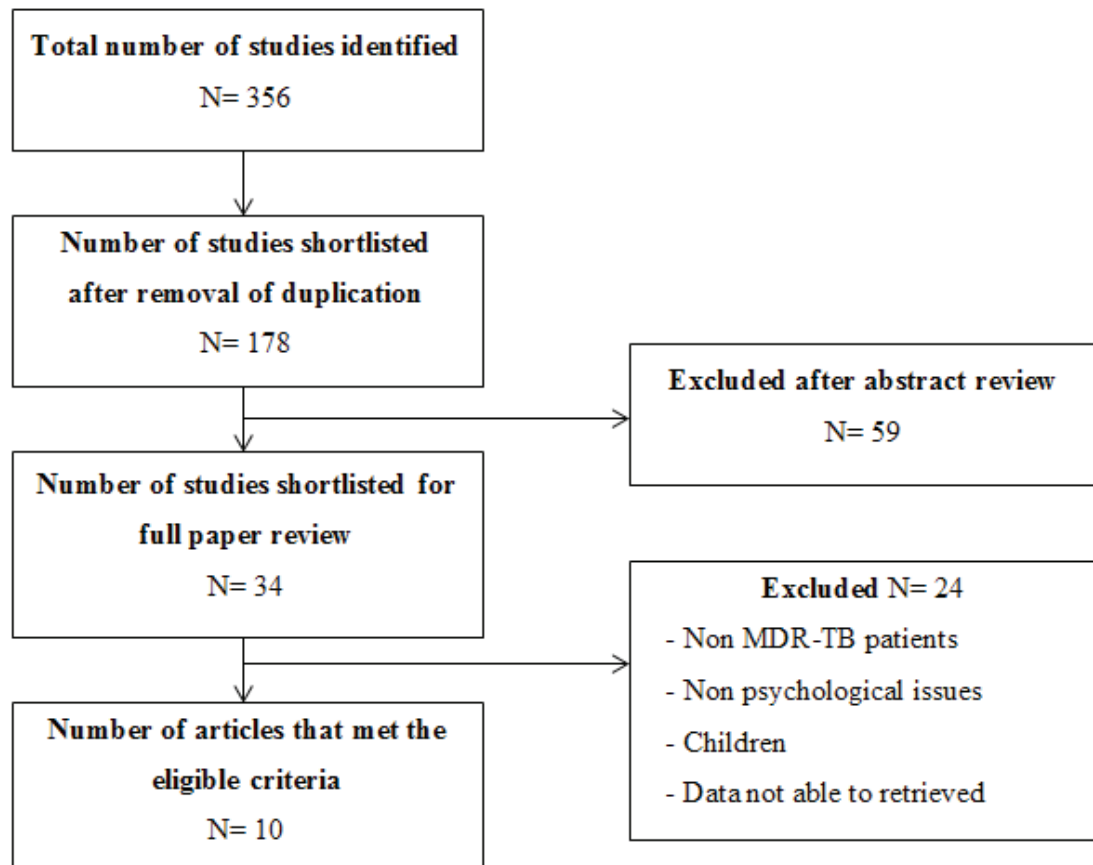


Fig 1. Flow diagram indicating the process of selecting the studies

Four studies identified the psychological issues faced by MDR-TB patients caused by the adverse effect of second-line drugs [8,12,15,17]. It was reported that cycloserine regimen induced psychiatric symptoms such as depression, anxiety, consciousness, disorientation to time and place, experiencing perceptual disturbances in the form of visual hallucinations as well-known delirium, and even worse severe suicidal tendencies [12].

One study has reported that depression as primarily side effects was associated with cycloserine. Other studies found half of the MDR-TB patients had one or more comorbid conditions, including depression that often occurs while undergoing treatment. Even in one study reported that the number of patient depression due to second-line drug effects was very high [17]. Other than that some psychiatric illnesses which if not treated properly were resulting in worse outcomes as though suicide incidents, also increase the risk of morbidity and mortality [16,17]. Despite several studies the scarce sources stated that the MDR-TB drugs lead to suicide [17]. Measly incident does not rule out the possibility of subsequent cases. MDR-TB patients with neuropsychiatric side effects have been found to have significantly worse outcomes and a higher likelihood of death [5,10].

Five studies identified the psychological issues associated with prolonged treatment [5,6,10,14,18]. Whether as consequences of drug side effects or due to prolonged

treatment, psychological distress comorbid are frequently found in MDR-TB patients [5]. Psychological distress tends to be a debilitating treatment that manifests with disordered in the areas of emotions, perceptions, thinking, and memory and have no established biological basis [17]. The magnitude of psychological distress significantly associated with the period of treatment. A positive association between patients administered within 1-2 months of treatment initiation and high psychological distress incidence rate has previously been reported by a study conducted elsewhere. Any study notified that most emotions often expressed by MDR-TB when initially diagnosed with the disease was hopelessness and fear feelings [12].

Three studies identified regarding feelings reflect the MDR-TB patient's opinion about the treatment that is final option for them [6,14,15]. These feelings reflect the MDR-TB patient's opinion about the treatment that is final option for them [10,15]. Much perceived fear of MDR-TB treatment ineffectiveness offered them cure for their illness. The level of patient reliance on the effectiveness of the treatment may influence their sense of hope and belief in being cured [10]. Compounded by witness other patients dying from MDR-TB generate difficulties to remain optimistic. The MDR-TB treatment challenges that are frequently observed as follows patients complaint regarding taking too many medicines at one time, having to undergo length daily treatment, painful

injections, and awful taste of medicine [8,17]. Which are not a few patients who experience these treatments feel very stressful and have developed anxiety immediately upon learning about their disease [6]. Most of the patients who remained sick more than one year after the diagnosis of MDR-TB had received multiple incidental of treatment and complicated pathways of care could be possible reasons for significantly lower mental health. Especially for patients who previously treated and find treatment failure was mostly horrified and lacked any faith to cure their disease [17]. The majority of MDR-TB patients generally lacked knowledge whether it's about the disease itself, treatment, or side effects, which of fuelled patient's anxieties. Inadequate information meant whether patients must to do, whether they should seek providers help, whether their conditions need to be consulted, and whether how to address their difficulties in treatment related to psychological distress.

## DISCUSSIONS

The research on psychological issues in MDR-TB patients is still rare, however robust research regarding these issues is extremely important for the successful MDR-TB management. This review focuses on the various psychological distress due to the disease itself as well as the treatment side effects. Some studies reported psychological distress were the second most common reason leading to treatment withdrawal [8]. The psychological distress also significantly inhibit adherence of MDR-TB treatment where the problem of medication adherence is the most challenging factor which affected discontinued treatment [16,19]. The fact that treatment interruption can be dangerous for the patients also compromises treatment efficacy which of them may remain infectious, dealing with mortality related TB and increased possibilities of XDR-TB [18].

Treatment experience faced by MDR-TB patients reflected complex interplay adverse effects, not only physical side effects, but also psychological challenges. Once initiated on treatment, the patient needed to adjust to all medication difficulties which there were no other treatments and no way out [14]. The following were possible adverse effects of MDR-TB drugs that are nausea, vomiting, bilateral deafness, tinnitus, weakness and pain in the shoulder and limbs, also psychological distress such as anxiety, depression, psychosis and suicidal tendencies [8,10,14,16]. The MDR-TB drug side-effects were perceived as bad as or worse than the illness itself [15]. The second line drug regimens used in the MDR-TB treatment are more severe than the first-line drugs including neuropsychiatric effects. Compared to other second-line drugs, cycloserine has a higher number of neurologic side effects than others, however the effects of cycloserine particularly dose-related [11].

One of the causes of high rates of non-adherence and loss to follow-up in MDR-TB treatment may be due to undiagnosed and comorbid psychological distress that is untreated [5]. Psychological distress symptoms are often abandoned and not considered as a big deal by MDR-TB patients, even when they noticed these symptoms they prefer to be reticent to disclose which causes this issue is frequently overlooked by clinicians and policymakers [5]. Furthermore, another challenge encountered was the support tool to diagnose the psychological distress of MDR-TB patients and provide suitable interventions [20]. The WHO guidelines for the programmatic management of drug-resistant tuberculosis illustrated the assessment for patient's psychological conditions with routinely questions whether the patients of MDR-TB ever thought of committing suicide and other psychological distress which might exist related to their illness and treatment of the disease [5,21].

Strategies for managing the possibility of ineffective treatment in terms of psychological distress require special attention. The first thing to do begins with the knowledge that every stakeholder needs to have regarding MDR-TB disease, treatment, also presence of drugs side effects [5]. The intended stakeholders including MDR-TB patients, clinicians, and program providers that involved in MDR-TB treatment should be educated to identify the relevant symptoms associated with adverse effect due to treatment which can increase awareness of psychological distress among MDR-TB patients [21,22]. Specifically to address MDR-TB outpatient treatment issues, clear information suggested the provision of drugs for patients also their family members to take at home were provided by health workers [22]. Target information including patient's family members would assist to address drug non-adherence also stigma issues that have sprung up in the community.

As a caretaker, the family members are the key to supporting patients at this time which has been acknowledged for their important role in the treatment process [23]. Especially for parents and wives or husband were fully involved in the day of the patient's care belonging accompanying patients, facilitating discussions, and providing psychological support [10].

The second strategies according to the WHO guidelines suggested that mandatory programs that need to be followed by MDR-TB patients with psychological distress symptoms are individual counseling and group therapies [5,24]. Patients in denial terms and unable to absorb information will be more suitable for discussion and sharing their experiences [10,22]. The counseling and group therapy were aimed to minimize asymmetric information where communication limited to one-way and not patient-centered, with a little consideration of information patients' needs [22]. With discussion, especially during group therapy consists of fellow MDR-

Table 1 Studies on psychological issues of MDR-TB patients

Reference	Year	Place	Objective	Method	Pop	Findings
Meghan D. Morris et al	2013	Mexico	psychological impacts of MDR-TB treatment	Qualitative	12	Patients notified their feeling distressed and depressed to have to change their living behavior
Petros Isaakidis et al	2013	India	Psychological challenges experienced by MDR-TB patients	Qualitative	12	Patients voiced concern about adverse effects of the treatment which being worse than the disease itself
Nafees Ahmad et al	2016	Pakistan	Effects MDR-TB treatment seen through patient's quality of life	Prospective follow-up	81	Patients with MDR-TB have been reported had lower scores on psychological health, and indication of more mental distress and role limitation which affects as a predictor of unsuccessful treatment
Beena Elizabeth Thomas et al	2016		Psychological challenges of MDR-TB patients also psychological intervention models of MDR-TB care	Systematic review		Neurologic side effects included depression, anxiety, convulsions, consciousness, psychosis, and suicide issues of MDR-TB patients also the importance of psychological intervention their offer
Debaleena Das	2017	India	Adverse effect of cycloserine	Case report	1	Cycloserine in psychotic, manic or depressive patients suffering from MDR-TB may impose a risk of either manic switch or exacerbation of depression
Sudeepa Khanal et al	2017	Nepal	Psychological support Intervention for MDR-TB with developing patient-centered care	Qualitative	15	Patient reported anxiety and depression. Developing intervention through improving communication skill of health worker, involvement of family members, and assessing psychosocial issues as part intervention evaluation
Tae Won Yang, MD et al	2017	South Korea	Psychological adverse effects of MDR-TB drugs	Retrospective of medical records	256	Among adverse effects of MDR-TB treatment, psychological disorders symptoms such as depression, anxiety, nightmares, and psychotic have positive association with second line anti tuberculosis drug
LinaAlfiyani et al	2017	Indonesia	Factors treatment adherence due to biopsychosocial issues faced by MDR-TB patients	Case-control	304	Drug taking adherence significantly affected by depression, support of family members intervention to address depression and treatment adherence
I.F Walker et al	2017	China, Pakistan, Bangladesh, Nepal	Comorbid mental disorder among MDR-TB patients	Perspective review		Psychosocial impact experience of people with MDR-TB often lead to depression and anxiety, social stigma, and psychiatric illness due to regimen MDR-TB treatment
StosicMaja et al	2018	Serbia	Risk factors among MDR-TB patients	Case-control	124	Mental health, defaulting of treatment, sadness, and using sedatives significantly associated with MDR-TB patients experienced

TB sufferers, patients openly and freely express their feelings regarding their illness and especially on drugs adverse effect [6]. As well as improve of properly design communication to supporting MDR-TB management.

Attributed to the high number of psychological distress during MDR-TB treatment, the last strategy has been directly handled by specialist physicians. Continuing the prescribed treatment regimen with additional medication is most appropriate for patients who are experiencing mild adverse effects [21]. The psychiatric adverse effect that has been reported primarily associated with MDRT-TB medication which initially used with an antidepressant, antipsychotic, or anticonvulsant therapy

[24]. Giving pyridoxine also known as vitamin B6 to patients who consume cycloserine or terizidone would prevent psychiatric adverse effects. In the worst case where additional medication not going well to manage psychiatric side effects, the intended drugs need to be replaced or suspended. Still, replacement drugs may not be available in MDR-TB patients likewise suspending the medication will reduce treatment regimen effectiveness. Suggested strategies for emergency psychiatric cases are stopping the suspected drug for a short period of time around 1- 4 weeks until the patient is stable. Another method is reducing treatment regimen without compromise [8,23,25]. To eliminate or lessen the

psychiatric adverse effect of cycloserine and ethionamide, commonly reducing to 500 mg daily. It is recommended to improve medication adherence also avoid drug withdrawal in MDR-TB patients [21].

## LIMITATIONS

This review has some limitations. Firstly, there are still a small number of study which focuses on the psychology of patients with MDR-TB. Secondly, the study method which is identified did not focus one type because of the limitation of appropriate articles with inclusion criteria.

## CONCLUSION

The emergence of psychological distress in MDR-TB patients due to the disease itself as well as the side effects of treatment needs special attention. Undiagnosed and untreated psychological distresses in MDR-TB patients' cases are highly prevalent whereas it can be dangerous for both the patients and the treatment efficacy. The various psychological adverse effects of MDR-TB treatment directly leads to medication non-adherence which may then be withdrawn. The assessing psychological side effects were aimed to increase awareness and offer the best intervention option for MDR-TB patients. The appropriate intervention to address drug' side effects is the key for the success of MDR-TB management.

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