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# Depression and its associated factors among people with multidrug-resistant tuberculosis in Myanmar

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**ABSTRACT**

**Objectives:** To estimate the prevalence and risk factors of depression in persons with multidrug-resistant tuberculosis (MDR-TB) in Myanmar.

**Methods:** A cross-sectional survey among MDR-TB participants at Aung San MDR-TB treatment center in Yangon during routine clinic follow-up visits. Patients Health Questionnaire-9 (PHQ-9) in the local language was used to screen for depression and structured questionnaires conducted. Univariable and multivariable logistic regression models were performed to identify associations.

**Results:** 329 participants were enrolled between 19th December 2019 to 31st January 2020; 33% (111/329) in the intensive treatment phase. The prevalence of depressive symptoms (PHQ9 ≥10) was (34/329) 10.33%. Multivariable analysis indicated financial hardship as a result of MDR-TB symptoms/treatment (aOR=2.63, 95%CI: 1.12-6.67), suffering ≥1 respiratory symptoms (aOR=6.72, 95%CI: 2.41-18.76), high education level (aOR=4.26, 95%CI: 1.70-10.70), reported diabetes (aOR=3.05, 95%CI: 1.16–7.99) as associated with depressive symptoms, with weak evidence of an association in females (aOR=2.09, 95%CI: 0.94-4.65).

**Conclusion:** Depressive symptoms are more common in those with co-morbidities/TB-symptoms. Further research is

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/TMI.13637

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required to determine effects of interventions to support persons with depressive symptoms identified using simple, standardized validated tools like PHQ-9.

**Keywords:** Multidrug-resistant tuberculosis, Depression, Adverse effects, Myanmar

**Sustainable Development Goal**: Good health and well-being

## INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) threatens global tuberculosis (TB) care and prevention, and continues to be a major public health crisis. In 2018, WHO estimated global incidence of MDR-TB at 400,000 associated with 200,000 deaths.[1] Myanmar is one of the 30 MDR-TB high burden countries, estimated to contribute 10,000 MDR-TB cases in 2018.[1]

Depression is also a growing global health threat, reported as the single largest contributor to global disability and the major contributor to suicide deaths.[2] In 2015, WHO estimated that the total number of people living with depression exceeded 300 million, representing 4.4% of the global population.[2] In 2017 it was estimated that nearly two million people in Myanmar suffered from depression, equivalent to 3.7% of the total population.[3]

The prevalence of depression among persons with TB is reported to be between 3-6 times higher than the general population.[4] A systematic review and meta-analysis of mental health disorders that included 40 studies conducted in 20 countries (including 7 in low- and middle-income countries (LMIC), but only 1 in SE Asia and none in Myanmar), estimated a pooled prevalence of 25% (95%CI 14-39%) of depression in MDR-TB, However, the review also reported the overall study quality as low to moderate; most were retrospective, did not clearly describe the methods used to assess depression/common mental disorders or relied on self-report of symptoms.[5]

Compared to treatment for drug-susceptible TB, the treatment for MDR-TB is longer, higher-priced and more toxic with poorer treatment outcomes.[1] Persons with TB disease suffer psychological stress from both the disease and its treatment including potential manifestation of psychiatric symptoms attributable to several of the TB drugs used.[6,7] The presence of comorbid depression in persons with MDR-TB can reduce medication adherence and impair therapeutic efficacy, and may lead to high loss-to-follow-up and suicide.[7,8] Detection, monitoring, and management of

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depression are important, not only for TB treatment outcomes but also for long-term health and resilience of themselves and their households and is recognized as part of holistic patient-centered care – one of the pillars of the 2030 End TB strategy.[9]

The prevalence and determinants of depression among MDR-TB in Myanmar are largely unknown, and no previous published studies could be found. However, we had anecdotal evidence for the occurrence of depression and suicidal tendency during MDR-TB treatment. The present study aimed to estimate the prevalence and potential risk factors of depression in persons with MDR-TB in Yangon, Myanmar.

## METHODS AND MATERIALS

### Study Design

A single-site cross-sectional survey utilizing a structured questionnaire and extraction of data from medical records.

### Study setting

Myanmar has an estimated population of approximately 51 million.[10] The Yangon Region has 4 districts, including 45 townships (out of 330 nationally), and a total population of approximately 7.3 million, with the highest population density and the second-highest ageing index.[10] Although 14% of the national population live in the Yangon region, around 50% of MDR-TB cases are notified and enrolled annually in this region.[11] A total of eight MDR-TB treatment centers deliver services in Yangon region, including our research site: Aung San MDR-TB treatment center.

### Sample Size

Assuming a 10% non-response rate, a sample size of 317 was estimated to be required to determine the prevalence of depression among persons with MDR-TB with 95% confidence and 5% absolute precision around a probable prevalence of 25%.[5]

### Study participants

All adult (≥18 years) persons with MDR-TB from Aung San MDR-TB treatment center registered between January 2018

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and January 2020 and attending a routine follow-up visit at that clinic during the study period were potentially eligible. Exclusion criteria included persons with drug-sensitive TB or extensively drug-resistant TB (XDR-TB), younger than 18 years, a history of receiving psychiatric treatment before starting MDR-TB treatment or if critically ill or with severe communication problems. Eligible and consenting persons were consecutively enrolled 5 days a week during the study period.

**Data collection and definitions**

Three data collectors conducted face-to-face interviews using structured questionnaires in Myanmar language with direct electronic data capture on tablets using open data kit (ODK).[12] The same data collectors conducted anthropometry (height, weight and mid-upper arm circumference (MUAC)) using standard methods. Body mass index (BMI) was calculated as $kg/m^2$ and defined as per standard criteria.[13] MUAC ≤ 23cm was defined as under-nourished.[14] HIV status, new or retreatment status, culture results and some adverse effects of MDR-TB treatment were extracted from MDR-TB registers and patients' treatment cards.

The Patient Health Questionnaire-9 (PHQ-9) was chosen as the screening instrument for depression because of its validity, reliability, brevity, and ease of scoring, including a validated translated version in Myanmar.[15,16] PHQ-9 is designed as a depression screening tool in primary-care and outpatient settings, is used in epidemiological research,[17] and is reported to be diagnostically superior in the primary-care setting for persons with chronic physical diseases compared to the Hospital Anxiety and Depression Scale (HAD-S),[18] the Hopkins Symptom Checklist (HSCL-25),[19] and similar to the Hamilton Depression Rating Scale (HAM-D).[20] The PHQ-9 comprises nine-items asking participants how they have experienced the stated problems over the previous two weeks as: 0 = not at all, 1 = several days, 2 = more than half the days, 3 = nearly every day) resulting in a final score ranging from 0–27. The nine items focus exclusively on Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for depressive disorders.[21] We used PHQ-9 ≥ 10 to indicate depression.[22,23] The internal consistency reliability of the PHQ-9 in the current study was high, with Cronbach's alpha of 0.85.

The Modified Medical Research Council Dyspnea Scale (mMRC) was used to assess severity of respiratory disease.[24]

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Adherence was calculated as the number of TB medication doses taken by participants divided by the number of planned medication doses in the previous month, expressed as a percentage with <95% defined as non-adherence.[25]

**Data management and statistical analysis**

Data were downloaded, exported and labelled from ODK aggregate server to STATA software (15.1) using ODK Briefcase and checked for missing, out of range or inconsistent values. Internal consistency of PHQ-9 was checked using Cronbach's alpha. Potential risk factors for depression were investigated using univariable and multivariable logistic regression models. A final multivariable model was built using forward stepwise selection of potential risk-factor variables grouped in three blocks in the order of socio-demographic characteristics, TB symptoms/related adverse effects and finally other clinical variables. Independent variables with p-values <0.2 in univariable analysis were selected to be taken forwards in the model building process, with the variables in each block, assessed for inclusion in the model by order of decreasing statistical significance from the univariable analysis. Variables associated with the outcome with likelihood ratio test (LRT) p<0.05 were retained in each model building step. LRT p-values, crude odds ratios (OR) and adjusted odds ratios (aOR) with 95% confidence intervals are reported. Level of statistical significance was set at 5%.

**Ethical considerations**

Ethical approval was obtained from the Ethics Committees, School of Tropical Medicine and Global Health, Nagasaki University, Japan and the Institutional Review Board of the Department of Medical Research, Ministry of Health and Sports, Myanmar. Written informed consent was obtained from all participants conducted in the Myanmar language.

**RESULTS**

**Characteristics of the study participants**

A total of 329 study participants were enrolled between 19th December 2019 to 31st January 2020. Complete data were obtained for all variables. Socio-demographic characteristics of the study participants are summarized in Table 1. The majority of participants were 18-35 years of age and 65.4% were male. Two thirds had experienced job loss after

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being affected by MDR-TB. Just over half of participants (51.7%) reported facing financial hardship including using savings, borrowing from others, selling assets, and stopping essential spending. Although 37.1% and 42.0% of participants were former smokers or drinkers, very few (1.2%) continued to smoke or drink alcohol while receiving MDR-TB treatment.

Clinical characteristics of study participants are shown in Table 2**.** Half were new MDR-TB cases and one third were receiving the shorter MDR-TB treatment regimen. Even though two thirds were in the continuation phase, nearly half (47.1%) were still suffering ≥1 respiratory symptoms, particularly cough, dyspnea and chest pain. Almost two-thirds reported ever experiencing ≥4 adverse effects including mainly: gastrointestinal symptoms such as nausea, vomiting, abdominal pain and diarrhea (n=278, 84.5%), dizziness (n=247, 75.1%), joint pain (n=234, 71.1%) and ototoxicity (tinnitus and hearing impairment) (n=114, 34.65%). The prevalence of co-morbid conditions was 33.7% for moderate/severe malnutrition (BMI<17.0 kg/m$^2$), 12.2% for HIV, and 16.1% for reported diabetes.

Almost all participants reported being satisfied with their TB treatment and with the services provided, and only 3 participants (0.91%) were defined as non-adherent (Supplementary Table 1).

**Depression and its associated factors**

The prevalence of moderate or severe depressive symptoms (PHQ-9 ≥10) was 10.3% (95%CI: 7.46-14.14). There was no evidence of a difference in the prevalence or severity of depressive symptoms between the MDR-TB shorter or longer treatment regimens (Table 3). Thirty-five participants (10.6%) reported ever in the previous two weeks having had suicidal thoughts or of hurting themselves, and 67 participants (20.4%) reported feeling bad about themselves and/or regarding themselves as a failure. Proportions for each score of each PHQ-9 item in those with moderate to severe depressive symptoms, *vs.* those with none or mild depressive symptoms are shown in Supplementary Figure 1.

Univariable analysis results are shown in Tables 4 and 5**.** Being female, having a higher education level (University/graduate) compared to lower levels of education, reported financial hardship, undernutrition as assessed by MUAC (≤23 cm), number of current respiratory symptoms and mMRC dysnpea score ≥2 were all significantly associated with increased odds of moderate/severe depressive symptoms. There was no evidence of as association for treatment regimen, treatment phase or new compared to previously treated MDR-TB cases.

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Table 6 shows two alternative multivariable models. In model 1 undernutrition (MUAC <23 cm) is included and in model 2, undernutrition is replaced by the number of current respiratory symptoms, which was found to be highly associated with MUAC defined undernutrition and confounded this association. In both models moderate/severe depressive symptoms were independently and significantly associated with facing financial hardship, a university-level education, reported co-morbid diabetes and non-significantly with female sex. In model 1 undernutrition defined by MUAC was independently, but weakly (p=0.039) associated with moderate/severe depressive symptoms. In model 2, increasing number of current respiratory symptoms compared to none was highly associated with moderate/severe depressive symptoms (p<0.001). During the development of the multivariable models, mMRC dysnpea grade ≥2 and TB treatment-related adverse effects were dropped as highly correlated with the number of respiratory symptoms and explained less variation.

**DISCUSSION**

The prevalence of moderate/severe depressive symptoms among persons with MDR-TB in Aung San MDR-TB treatment center was higher than estimated for the general population in Myanmar (10.33 % vs 3.7%)[3] but low when compared to other studies in persons with MDR-TB, ranging from 11.35% to 69.55%.[5,26–29] Such wide variations may result from the use of different tools and cut-off points for defining depression, different stage of treatment at assessment and different study designs in dissimilar settings. However, a recent meta-analysis estimated depression incidence in MDR-TB of 11%.[30] Despite steady progress in implementation of free-of-charge diagnostic, treatment and follow-up services for all people in need, half of our participants still reported suffering financial hardship as a result of MDR-TB which was independently and strongly associated with depression. More appropriate levels or better implementation of financial and social protection may have important impacts on patients' mental health and wellbeing which could potentially be assessed using simple tools like the PHQ-9 used here.

The present study finding on sex concurs with evidence from other studies that depression is higher in women than in men, including in persons with MDR-TB.[27,28] Gender equity, related to social and cultural context as well as underlying biological factors are likely to be underlie these observations.[31]

Some studies have reported undernutrition to be associated with depression in persons with pulmonary TB.[32,33]

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The present study also identified undernutrition as measured by MUAC, but not BMI to be associated with depression. However, despite the high prevalence of moderate and severe undernutrition by BMI, undernutrition by BMI was not associated and by MUAC weakly in multivariable analysis with evidence of confounding by indicators of disease severity. It is known that undernutrition is both a risk factor and potential consequence of TB disease [REF]. The physiological effects will be moderated by the socio-economic and psycho-social background affecting ability to meet increased nutrient needs and to manage loss of appetite and nausea that may occur from the TB disease and/or drug side effects. Arguably, the integration of nutritional supplement provision, into routine MDR-TB management programs should be considered as part of a holistic, patient-centered care, regardless of possible associations with depression; and its effectiveness to prevent or resolve acute undernutrition and impact on TB treatment outcomes assessed, for which there is surprisingly little good evidence.[9]

Similar to other studies, in our participants co-morbid diabetes and TB treatment adverse effects were independently associated with depression.[26,28] This may indicate that those with multiple conditions or side-effects may not be getting the additional support they need, perhaps in terms of adequate management of drug side effects, drug-drug interactions and increased impact on quality-of-life.

Contrary to other studies,[8,29] in our population higher (college or university) level of education was positively associated with depression. This could relate to limited opportunities and job security in relation to the skills and expectations acquired during education. However, it is also possible that the validity of the questionnaire and translation differs by education level resulting from differences in the understanding and experience of depression in those with higher education.

As concluded in a recent meta-analysis, depression is associated with poor medication adherence in a range of chronic diseases.[34] However in our study just three participants reported low treatment adherence (<95%) and none of these had depressive symptoms. It is possible that adherence may have been over-estimated due to self-reporting in face-to-face interviews. However, perhaps more importantly, as a facility-based study with more than half of participants in the continuation phase of treatment, the study participants may represent a biased sample of all those who were diagnosed and those who initiated treatment, which could result in underestimation of both adherence and depression.

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As a cross-sectional, single facility-based study, the most important limitations relate to the inability to make inferences on causality and that the results may not be generalizable to other areas of Myanmar or the region. Other limitations include: that we were not able to confirm diagnoses of depression subsequent to PHQ-9, which is designed as a screening tool, and that other psychological problems were not simultaneously assessed. To our knowledge, the PHQ-9 tool and determination of optimum cut-offs and performance of individual items have not been fully investigated in persons with tuberculosis or similar conditions in low-middle income country settings. Finally, as face-to-face interviews were conducted in the same premises as participants treatment center, this may have inhibited participants to accurately report their adherence or express their dissatisfaction with services. However, interviews were conducted by trained interviewers not involved in TB care in the research site. Furthermore, the potential sample bias, resulting from interviewing only participants who had remained in care may have under- but is unlikely to have over-estimated depression.

**CONCLUSION**

The current study reports a prevalence of depression in persons with MDR-TB in Yangon, Myanmar, higher than that previously estimated for the general population, and which is likely an under-estimate of the true prevalence in all persons starting TB treatment, at least in similar urban settings to our study site. Persons with additional chronic comorbidities such as diabetes, those experiencing more adverse effects of treatment and financial hardship are more at risk. The Global End TB Strategy[9] includes the provision of patient centred comprehensive care and support for both physical and mental wellbeing. Hence, further prospective and nationally/regionally representative research is required to understand the determinants of depression and to support the design and evaluation of interventions to support persons with depressive symptoms identified using simple, standardized validated tools like PHQ-9.

**ACKNOWLEDGEMENTS**

The authors would like to appreciate the support and cooperation of the study participants and staff from Myanmar National Tuberculosis Programme and acknowledge Benjamin Faguer (School of Tropical Medicine and Global Health, Nagasaki University) and LSHTM Open Research Kits (odk.lshtm.ac.uk) for the provision of electronic data solutions for

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data collection, management and curation. This study was conducted in partial fulfilment of Master degree of the principal investigator, and was funded by The School of Tropical Medicine and Global Health, Nagasaki University and a Human Resource Development Scholarship by Japanese Grant Aid (JDS).

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**Table 1.** Socio-demographic characteristics of the study participants (N=329)

| **Variables** | **Level** | **n (%)/ mean ± SD** |
|---|---|---|
| Mean age, years ±SD | | 38.98 ± 14.15 |
| Age groups | 18-35 years | 148 (44.98) |
| | 36-50 years | 109 (33.13) |
| | 51-65 years | 57 (17.33) |
| | ≥ 65 years | 15 (4.56) |
| Sex | Male | 215 (65.35) |
| | Female | 114 (34.65) |
| Living situation | Living alone | 20 (6.08) |
| | Living with family | 309 (93.92) |
| Marital status | Single | 112 (34.04) |
| | Married | 167 (50.76) |
| | Separated/ divorced | 22 (6.69) |
| | Widowed | 28 (8.51) |
| Education level | Illiterate | 16 (4.86) |
| | Read and write | 22 (6.69) |
| | Primary | 43 (13.07) |
| | Middle | 98 (29.79) |
| | High | 86 (26.14) |
| | College/University | 64 (19.45) |
| Occupation | Dependent | 51 (15.5) |
| | Professional/ managerial | 31 (9.42) |
| | Sales and services | 55 (16.72) |
| | Skilled manual | 126 (38.3) |
| | Others | 66 (20.06) |
| Ability to work affected as a result of TB? | Yes | 77 (76.60) |
| | No | 252 (23.40) |
| Financial hardship as a result of TB? | Yes | 170 (51.67) |
| | No | 159 (48.33) |
| Impacts of financial hardship (N=170) | Using savings | 51 |
| | Borrowing money | 67 |
| | Selling assets | 50 |
| | Reduced essential spending (e.g. School fees) | 2 |
| Smoking | Never smoker | 203 (61.7) |

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| | | |
|---|---|---|
| | Former smoker | 122 (37.08) |
| | Current smoker | 4 (1.22) |
| Alcohol drinking | Never drinker | 187 (56.84) |
| | Former drinker | 138 (41.95) |
| | Current drinker | 4 (1.22) |

SD = standard deviation

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**Table 2.** Clinical characteristics of the study participants (N=329)

| **Variables** | **Level** | **n (%) / mean ± SD** |
|---|---|---|
| MDR treatment category | New | 167 (50.76) |
| | Previously treated | 162 (49.24) |
| TB MDR-regimen | Shorter | 101 (30.70) |
| | Longer | 228 (69.30) |
| TB treatment phase | Intensive | 111 (33.74) |
| | Continuation | 218 (66.26) |
| Family history of TB (previous 2 years) | No | 286 (87.2) |
| | Yes | 38 (11.59) |
| | Unknown | 5 (1.52) |
| HIV reactive?* | Yes | 40 (12.16) |
| | No | 289 (87.84) |
| Reported comorbid diabetes? | Yes | 53 (16.11) |
| | No | 276 (83.89) |
| BMI, kg/m$^2$ | <16 (severe undernutrition) | 66 (20.06) |
| | 16-<17 (mod undernutrition) | 45 (13.68) |
| | 17-<18.5 (mild undernutrition) | 57 (17.33) |
| | 18.5 – <23 (normal) | 123 (37.39) |
| | ≥ 23 (overweight) | 38 (11.55) |
| Mean BMI, kg/m$^2$ | | 18.89 ± 4.24 |
| MUAC ≤ 23 cm | Yes | 187 (56.84) |
| | No | 142 (43.16) |
| Mean MUAC. cm, | | 23.05 ± 3.49 |
| Current Respiratory symptoms | No symptoms | 174 (52.89) |
| | 1-3 symptoms | 140 (42.55) |
| | ≥ 4 symptoms | 15 (4.56) |
| Dyspnea (mMRC dyspnea score ≥ 2) | Yes | 39 (11.85) |
| | No | 290 (88.15) |
| Current AEs | No AEs | 53 (16.11) |
| | 1-3 AEs | 238 (72.34) |
| | ≥ 4 AEs | 38 (11.55) |
| Previous AEs | No AEs | 21 (6.38) |
| | 1-3 AEs | 205 (62.31) |
| | ≥ 4 AEs | 103 (31.31) |
| Overall AEs | No AEs | 11 (3.34) |

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| | | |
|---|---|---|
| | 1-3 AEs | 97 (29.48) |
| | ≥ 4 AEs | 221 (67.17) |

*SD = Standard Deviation; HIV = Human Immunodeficiency Virus; *= Existing diagnosis or HIV reactive on point-of-care screening test in NTP; BMI = Body Mass Index; MUAC = mid-upper arm circumference; mMRC = Modified Medical Research Council Dyspnea Scale; AEs = Adverse Effects*

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**Table 3.** Severity of depressive symptoms (PHQ-9 score) by MDR-TB treatment regimen

| **Severity of depressive state** | | **PHQ-9 score** | **Shorter Regimen n=101 n (%)** | **Longer Regimen n=228 n (%)** | **All n=329 n (%)** |
|---|---|---|---|---|---|
| Non depressive state | No/minimal depression | 0-4 | 84 (83.17) | 177 (77.63) | 261 (79.33) |
| | Mild depression | 5-9 | 8 (7.92) | 26 (11.4) | 34 (10.33) |
| Depressive state | Moderate depression | 10-14 | 6 (5.94) | 16 (7.02) | 22 (6.69) |
| | Mod/severe depression | 15-19 | 2 (1.98) | 6 (2.63) | 8 (2.43) |
| | Severe depression | 20-27 | 1 (0.99) | 3 (1.32) | 4 (1.22) |
| ***Total depressive state*** | | | 9 (8.91)* | 25 (10.97)* | 34 (10.33) |

*PHQ-9 = Patient Health Questionnaire; * p-value=0.57 for difference between treatment regimens.*

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**Table 4.** Univariable analysis socio-demographic factors associated with moderate/severe depressive symptoms

| Variables | | Total n=329 | Depressed n (%) | OR (95%CI |
|---|---|---|---|---|
| Age groups | 18-35 years | 148 | 15 (10.14) | 1 |
| | 36-50 years | 109 | 11 (10.09) | 0.99 (0.44 |
| | 51-65 years | 57 | 7 (12.28) | 1.24 (0.48 |
| | ≥ 65 years | 15 | 1 (6.67) | 0.63 (0.78 |
| Sex | Male | 215 | 16 (7.44) | 1 |
| | Female | 114 | 18 (15.79) | 2.33 (1.14 |
| Living condition | With family | 309 | 31 (10.03) | 1 |
| | Alone | 20 | 3 (15.00) | 1.58 (0.44 |
| Marital status | Single | 112 | 11 (9.82) | 1 |
| | Married | 167 | 17 (10.18) | 1.04 (0.47 |
| | Widowed | 28 | 4 (14.29) | 1.53 (0.45 |
| | Separated/ divorced | 22 | 2 (9.09) | 0.92 (0.19 |
| Education level | Basic Education* | 227 | 15 (6.61) | 1 |
| | No formal education** | 38 | 6 (15.79) | 2.65 (0.95 |
| | University/ Graduate | 64 | 13 (20.31) | 3.60 (1.61 |
| Occupation status | Professional/managerial | 31 | 2 (6.45) | 1 |
| | Dependent | 51 | 8 (15.69) | 2.69 (0.53 |
| | Sales and services | 55 | 8 (14.55) | 2.47 (0.49 |
| | Skilled manual | 126 | 11 (8.73) | 1.39 (0.29 |
| | Others | 66 | 5 (7.58) | 1.19 (0.22 |
| Ability to work after affected by MDR-TB | Yes | 77 | 5 (6.49) | 1 |
| | No | 252 | 29 (11.51) | 1.87 (0.70 |
| Facing financial hardship as a result of TB | No | 159 | 11 (6.92) | 1 |
| | Yes | 170 | 23 (13.53) | 2.11 (0.99 |
| Smoking | Never smoker | 203 | 24 (11.82) | 1 |
| | Former smoker | 122 | 9 (7.38) | 0.59 (0.27 |
| | Current smoker | 4 | 1 (25.00) | 2.49 (0.25 |
| Alcohol drinking | Never drinker | 187 | 19 (10.16) | 1 |
| | Former drinker | 138 | 15 (10.87) | 1.08 (0.53 |
| | Current drinker | 4 | - | - |

*OR = Odds Ratio; 95%CI = 95% Confidence Interval; ^ = LRT global p value; *Primary, Middle and high-level education are recategorized into "basic education"; **Illiterate and read and write level education were recategorized into "no formal education".*

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**Table 5.** Univariable analysis of clinical factors associated with moderate/severe depressive symptoms

| **Variables** | | **Total n = 329** | **Depressed n (%)** | **OR (95%CI)** |
|---|---|---|---|---|
| Type of MDR-TB | New | 167 | 18 (10.78) | 1 |
| | Previously Treated | 162 | 16 (9.9) | 0.91 (0.45 – 1.8 |
| Type of MDR-TB regimen | Shorter Regimen | 101 | 9 (8.91) | 1 |
| | Longer Regimen | 228 | 25 (10.96) | 1.26 (0.57 – 2.8 |
| Treatment Phase | Continuation Phase | 218 | 20 (9.17) | 1 |
| | Intensive Phase | 111 | 14 (12.61) | 1.43 (0.69 -2.9 |
| Family history of TB | No | 286 | 28 (9.79) | 1 |
| | Yes | 38 | 6 (15.79) | 1.73 (0.66 – 4.4 |
| | Unknown | 5 | 0 | - |
| BMI, kg/m$^2$ | 18.5 – 23 | 123 | 13 (10.57) | 1 |
| | <16 | 66 | 7 (10.61) | 1.00 (0.38 – 2.6 |
| | 16-<17 | 45 | 8 (17.78) | 1.83 (0.70 – 4.7 |
| | 17-<18.5 | 57 | 3 (5.26) | 0.47 (0.13 – 1.7 |
| | >23 | 38 | 3 (7.89) | 0.73 (0.19 – 2.6 |
| MUAC | >23 cm | 142 | 9 (6.34) | 1 |
| | ≤23 cm | 187 | 25 (13.37) | 2.28 (1.03 – 5.0 |
| Co-morbid HIV Status | Non-reactive | 289 | 30 (10.38) | 1 |
| | Reactive | 40 | 4 (10.00) | 0.96 (0.32 – 2.8 |
| Co-morbid Diabetes | No | 276 | 25 (9.06) | 1 |
| | Yes | 53 | 9 (16.98) | 2.05 (0.89 – 4.6 |
| Current Respiratory Symptoms | No symptom | 174 | 5 (2.87) | 1 |
| | 1-3 symptoms | 140 | 23 (16.43) | 6.64 (2.46 – 17 |
| | ≥4 symptoms | 15 | 6 (40.00) | 22.53 (5.77 – 8 |
| mMRC dyspnea grading | mMRC score <2 | 290 | 22 (7.59) | 1 |
| | mMRC score ≥2 | 39 | 12 (30.77) | 5.41 (2.42 – 12 |
| Current AEs | No AE | 53 | 1 (1.89) | 1 |
| | 1-3 AEs | 238 | 23 (9.66 | 5.56 (0.73 – 42 |
| | ≥ 4 AEs | 38 | 10 (26.32) | 18.57(2.26 –15 |
| Previous AEs | No AE | 21 | 1 (4.76) | 1 |
| | 1-3 AEs | 205 | 18 (8.78) | 1.93 (0.24 – 15 |
| | ≥ 4 AEs | 103 | 15 (14.56) | 3.41 (0.43 – 27 |
| Overall AEs | No AE | 11 | 1 (9.09) | 1 |
| | 1-3 AEs | 97 | 3 (3.09) | 0.32 (0.03 – 3.3 |
| | ≥ 4 AEs | 221 | 30 (13.57) | 1.57 (0.19 – 12 |

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*OR = Odds Ratio; 95%CI = 95% Confidence Interval; ^ = LRT global p value; BMI = Body Mass Index; MUAC = mid-upper arm circumference; HIV = Human Immunodeficiency Virus; mMRC = Modified Medical Research Council Dyspnea Scale; AEs = Adverse Effects*

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**Table 6.** Multivariable analysis of factors associated with moderate/severe depressive symptoms

| **Variables** | | **aOR (95%CI) Model 1** | **p value^** | **aOR (95%CI) Model 2** | **p** |
|---|---|---|---|---|---|
| Sex | Male | 1 | 0.075 | 1 | 0. |
| | Female | 2.01 (0.92 – 4.33) | | 2.09 (0.94 – 4.65) | |
| Education level | Basic Education | 1 | 0.002 | 1 | 0. |
| | No formal education | 1.73 (0.59 – 5.11) | | 1.76 (0.56 – 5.55) | |
| | University/ Graduate | 4.85 (2.04 – 11.51) | | 4.26 (1.70 – 10.70) | |
| Financial hardship | No | 1 | 0.009 | 1 | 0. |
| | Yes | 2.90 (1.27 – 6.61) | | 2.63 (1.12 – 6.17) | |
| Co-morbid Diabetes | No | 1 | 0.014 | 1 | 0. |
| | Yes | 3.39 (1.33 – 8.62) | | 3.05 (1.16 – 7.99) | |
| Undernutrition | MUAC ≥23 cm | 1 | 0.039 | - | |
| | MUAC <23 cm | 2.39 (1.00 – 5.68) | | - | |
| Current Respiratory Symptoms | No symptom | - | - | 1 | <0 |
| | 1-3 symptoms | - | | 6.72 (2.41 – 18.76) | |
| | ≥4 symptoms | - | | 15.94 (3.75– 67.81) | |

*OR = Crude Odds Ratio; ^ = LRT global p value; aOR = Adjusted Odds Ratio; 95%CI = 95% Confidence Interval*

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