Prevalence and Determinants of Depression among Multi Drug Resistant (MDR) TB cases registered under National Tuberculosis Elimination Program in Ahmedabad City

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Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) increases the risk of depression, lowers treatment compliance leading to poor outcomes. **Objectives:** To (1) document the prevalence of depression among MDR-TB cases registered at tuberculosis units (TUs) of Ahmedabad city and (2) assess determinants of depression. **Methodology:** Adult MDR-TB patients registered at all (23) TUs of Ahmedabad city, were studied using semi-structured questionnaire along with Gujarati translated version of the Hamilton Depression Rating Scale (HAM-D) to assess the severity of depression based on 17 items. The sample size at 95% level of significance, was 251. Probability proportional to size sampling was adopted for selecting participants from each of the 23 TUs. Proportions and odds ratio with confidence interval with probability value were calculated. **Results:** Of 251, only 185 (73.7%) cases could be contacted. Mortality proportion among selected cases was 18.7%. More than one-fifth (22%) had ≥1 comorbidity and 9.7% had another active TB case in the family. 161 (87.1) experienced ≥1 adverse event. Financial, social, or psychological stressors were reported by 22% of cases. Based on the HAM-D scale, 16.2% suffered from depression, determinants of depression by univariate analysis showed significant association with recent family issues, discrimination, financial/other troubling issues, and the presence of adverse drug event. **Conclusion:** MDR-TB cases are more vulnerable for developing depression as the prevalence was 16.2% among them. Hence, cases need to be monitored closely for depression at TU as well at community level.

Keywords: Cluster sampling, depression, determinants, Hamilton Depression Rating Scale, multidrug-resistant tuberculosis cases

Introduction

Tuberculosis (TB) a disease of public health importance, ranks among the top 10 causes of global deaths. Three countries with the largest share of its global burden are India (27%), China (14%), and the Russian Federation (8%). Globally in 2019, 3.3% of new and 17.7% of previously treated TB cases had multidrug-resistant (MDR)/RR-TB.[1] Representative state-wide survey in Gujarat reported overall proportion of MDR-TB as 5.3% (range 0%–35%).[2] Depression at any given time affects around 10% of the population and is the most common conditions recorded by general practitioners (along with hypertension). A study of British patients from Tel Aviv University found that taking one course of antibiotics can raise the risk of depression and anxiety by around a quarter and taking between two and five course raises the risk by nearly half.[3] Studies reported high prevalence of psychiatric comorbidity among MDR-TB cases[4] and that prevalence of depression significantly correlates with the severity and duration of the disease.[5,6] Drug-resistant (DR) type TB increases the risk of depressive tendencies. This coupled with side effects of the multiple drugs and prolonged therapy also increases the risk of depression.[7,8] DR-TB patients with comorbid depression have lower adherence and poor outcomes.[9] MDR-TB and depression both are public challenges in

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reaching Global Elimination level for TB. In view of this, the current study was planned with objectives of finding out the prevalence of depression and its determinants among adult MDR-TB cases registered at various TUs of Ahmedabad city.

METHODOLOGY

An observational cross-sectional study was conducted at Ahmedabad, the largest city of Gujarat (population 57 lakhs),[10] with the highest burden of drug-sensitive and -resistant TB cases in the state. There are 23 tuberculosis units (TUs) under Amdavad Municipal Corporation. The sample size was calculated based on the prevalence of depression among MDR-TB cases. Considering the wide variation (32%–74%)[2,4,11] and taking mean prevalence of depression in MDR-TB cases as 60% with relative allowable error of 10%, estimated sample size at 95% confidence interval (CI), accounting for finite population correction, was 228. To account for 10% nonresponse, the sample size was 251. TU was taken as a cluster and the number of cases from each cluster (TU) was as per probability proportional to size (PPS). Stratified sampling was adopted for selecting participants from each of the 23 TUs of Ahmedabad city. After enumerating TU wise cases, as per PPS, appropriate number of cases were randomly selected from each TU using Microsoft excel generated random numbers. Details of sampled cases were shared with senior treatment supervisor and interviews were scheduled to coincide with their follow-up visit to the TU. Cases who could not be contacted at TU were interviewed at home/ workplace through video call (during COVID-19 lockdown) after taking consent. All infection prevention and control guidelines issued during COVID-19 pandemic were strictly adhered to while doing these interviews. The study tool was a semi-structured predesigned pretested questionnaire to collect sociodemographic details as well as various determinants of depression. Gujarati translated version of the Hamilton Depression Rating Scale (HAM-D)[12] was used to assess the severity of depression in patients. The study population comprised adult (>18 years) MDR-TB (microbiologically confirmed TB case resistant to both rifampicin and isoniazid with/without resistance to other first-line drugs) cases registered at all (23) TUs of Ahmedabad city between July 1, 2018, and June 30, 2019, and willing to participate by giving written informed consent. Known cases of any psychiatric illness before DR-TB registration or unwilling to participate were excluded from the study. To address ethical issues, the study protocol was approved through the Institutional Ethical Committee. Those who scored higher on the HAM-D scale were referred for possible depression. The MOs TU/counselors were intimated of the referral to the Psychiatry Department of Medical College/nearby government hospital.

After taking the telephonic appointment, 185 (73.7) participants were interviewed through structured questionnaire when they visited TU to collect their drugs as per their scheduled visit. Others who could not be approached at TUs or completed treatment or defaulters, were interviewed at home/workplace (including roadside where 1 case was selling slippers) [Figure 1].

RESULTS

Of 185 participants, 100 (54.1%) were males and rest were females. The average age of patients was 34.1 (13.3) years. The majority (85.4%) were locals. Total 124 (67.0%) were currently married followed by 48 (25.9%) unmarried and 13 (7.1%) either separated or widow (er) or divorced. With average household size 5, 56.2% belonged to nuclear families and almost 80% belonged to middle class (social class 2, 3, and 4).[13] Comorbidity/ies were seen in 41 (22.2%) cases; the most common being diabetes followed by chronic obstructive pulmonary disease and hypertension. More than half (53%) had past history of TB; mostly (84%) pulmonary TB. All of them took treatment for the same, mostly at government facilities (62%). Of 185 cases, 99 (53.5%) had family history of one or other chronic illnesses including 34 (18.4%) with family history of TB, 18 (9.7%) cases had another active case of TB within the family. It was found that 57 (30.8%) of the cases had one or other addictions (45 had single and 12 had multiple addictions). Tobacco chewing (22.2%) was most common followed by smoking (9.2%) and alcohol (8.6%).

Information about the adverse events (AEs) was gathered and graded into mild, moderate, severe, and potentially life threatening. Grade 1 and 2 (mild and moderate), manageable through domiciliary treatment alone while rest Grade 3 and 4) may require hospitalization.[14] Severe and potentially life-threatening AE (55/161) were reported by 42 participants [Table 1]. It was found that 161 (87.1%) experienced one or more AE. Depression
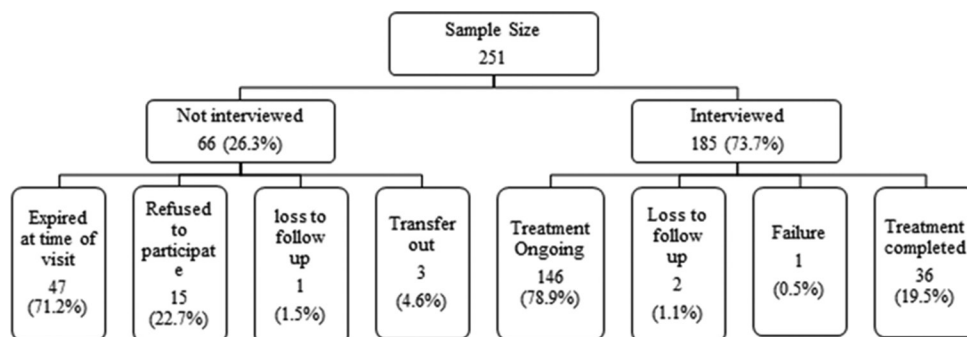

Figure 1: Pathway of sampled participants (*n* = 251)

as an "AE" was reported by 9.2% of the participants and was severe (Grade III–IV) in 30% of them.

HAM-D[12] was administered to all percipients to assess depression. Thirty participants (including 26 at the time of survey) scored >7 on the scale resulting a period prevalence of 16.2% [Table 2]. In an extreme case on home visit, one case was found to have committed suicide. The most common symptoms (of depression) observed are depressed mood (88.5%) and difficulty/loss of interest in work and activities (84.6%) [Table 3]. Determinants by univariate analysis showed significant association of depression with recent family issues, discrimination, financial/other troubling issues, and the presence of adverse drug event. However, ethionamide TB cases showed a protective effect [Table 4 & Figure 2].

Discussion

Of sampled 251, only 73.5% were interviewed as 18.7% died-proportion of mortality was higher than 15.4% observed in another study from the same area among cured Cat 1 TB cases.[15] It may be due to higher mortality among MDR-TB than TB itself. It was also higher from, 15.3% where outcome in 657 cured cohort was either as dead or relapse.[16] TB can affect anyone anywhere, but mostly seen in adults, same was seen in the current study where the mean age was 34 years. Male dominance seen may be due to more outdoor exposure and gender-specific treatment-seeking behavior. Most of them were local living in nuclear family and belonged to middle social class, characteristically seen in an urban area. Upper class patients take treatment from private providers and lower class is ignorant about their illness. Four health-related risk factors namely, diabetes, HIV infection, smoking, and alcohol use are associated with TB incidence. India due to its epidemiological transition experiences dual burden, accordingly 22.2% of them had comorbidity (the most common being diabetes). Continuous follow-up is the key for better outcome as earlier study[15] reported 1 year after FU of cured Cat 1 cases, 16.2% developed symptoms suggestive of TB, of this, half of them (51.6%) developed within 1 year and 48.3% later. It is in agreement with the current study where more than half had past history of TB. Efforts are required to reduce the pool of TB/RR/DR cases by acting at comorbidities such as depression leading to neglected self-care, nonadherence to medication hindering compliance, and ultimately increasing the mortality.[11] Though drug-resistant TB has microbial, clinical, and programmatic causes but is a man-made phenomenon due to poor treatment adherence. Assurance and immediate help are necessary to minimize this phenomenon. Adverse drug events or AEs are an important predictor of compliance and adherence to chemotherapy. Close monitoring of AE is desirable to prevent default and loss to follow-up. Total 87.1% of the participants experienced one or more AE. Depression as AE reported by participants was severe type in 30% of them. Severe and potentially life-threatening AE were also reported by 42% of the participants.

Table 1: Adverse events profile among multi drug resistant tuberculosis cases (*n*=185)

AEs	Mild to moderate (Grade 1 and 2)	Severe to very severe (Grade 3 and 4)	Total, *n* (%)
Nausea/vomiting/GI upset	72	8	80 (43.2)
Darkening of skin	62	2	64 (34.6)
Weakness/fatigue	52	5	57 (30.8)
Dizziness/vertigo	33	1	34 (18.4)
Dyspnea	25	9	34 (18.4)
Headache	27	4	31 (16.8)
Anorexia	28	1	29 (15.7)
Hearing problem/tinnitus	18	8	26 (14.1)
Arthralgia	23	1	24 (13.0)
Weight loss	18	0	18 (9.7)
Depression	12	5	17 (9.2)
Pruritus	15	0	15 (8.1)
Sleep disturbance	13	2	15 (8.1)
Rash/allergy	14	0	14 (7.6)
Paresthesia	11	2	13 (7.0)
Fever	11	0	12 (6.5)
Visual disturbance	7	5	12 (6.5)
Others*			43 (23.2)

*Mouth ulcers, chest pain, numbness, leg pain, back pain, anger, suicidal thoughts, anxiety, swellings, seizure, diarrhea, palpitations, Jaundice. AEs: Adverse events, GI: Gastro intestinal upset

Table 2: Categories of depression based on Hamilton-depression score (*n*=185)

HAM-D score	Categories of depression	*n* (%)
0-7	Normal (no depression)	155 (83.8)
8-13	Mild depression	18 (9.7)
14-18	Moderate depression	4 (2.1)
19-22	Severe depression	3 (1.6)
>23	Very severe depression	1 (0.5)
-	Recovered from depression	4 (2.2)

HAM-D: Hamilton-depression

## Table 3: Hamilton-depression scale symptom profile of depressed patients* (*n*=26)

HAM-D Scale symptoms	*n* (%)
Depressed mood	23 (88.5)
Work and activities affected	22 (84.6)
Anxiety: Psychological	19 (73.1)
Somatic symptoms: General	18 (69.2)
Insomnia	17 (65.4)
Guilt feelings	16 (61.5)
Anxiety: Somatic	16 (61.5)
Somatic symptoms: Gastrointestinal	16 (61.5)
Suicidal thoughts	11 (42.3)
Hypochondriasis	11 (42.3)
Sexual dysfunction/menstrual disturbance	10 (38.5)

*Multiple responses. HAM-D: Hamilton-depression

Table 4: Factors associated with depression among multi drug resistant tuberculosis patients

Factor	Depression (*n*=30), *n* (%)	No depression (*n*=155), *n* (%)	*P*	OR (95% CI)
Recent family issue	15 (50)	24 (15.5)	0.005	5.4 (2.3-12.7)
Ethionamide	9 (30)	85 (54.8)	<0.001	0.4 (0.2-0.8)
Prejudice/discrimination	8 (26.7)	11 (7.1)	0.027	4.7 (1.6-13.2)
Financial stress	15 (50)	26 (16.8)	<0.001	4.9 (2.1-11.5)
Any troublesome issue	27 (90)	100 (64.5)	0.005	4.9 (1.6-21.2)
Presence of AE	30 (100)	131 (84.5)	<0.001	NA
Anorexia	10 (33.3)	19 (12.3)	<0.005	3.6 (1.4-8.8)
Weakness/fatigue	15 (50)	42 (27.1)	<0.001	2.67 (1.2-6.0)
Pruritus	6 (20)	9 (5.8)	<0.001	4.01 (1.2-12.5)
Fever	7 (23.3)	5 (3.3)	0.004	8.0 (2.6-33.3)
Arthralgia	8 (2.7)	16 (10.3)	0.023	3.1 (1.2-8.2)
Dizziness/vertigo	10 (33.3)	24 (15.5)	<0.001	2.7 (1.1-6.5)
Sleep disturbances	10 (33.3)	5 (3.2)	<0.001	14.6 (4.6-51.7)
Jaundice	3 (10)	0	0.004	NA
Depression	11 (36.7)	6 (3.9)	0.023	14.0 (4.7-45.4)
Dyspnea	13 (43.3)	21 (13.5)	<0.001	4.8 (2.0-11.5)

OR: Odds ratio, CI: Confidence interval, AE: Adverse event, NA: Not applicable
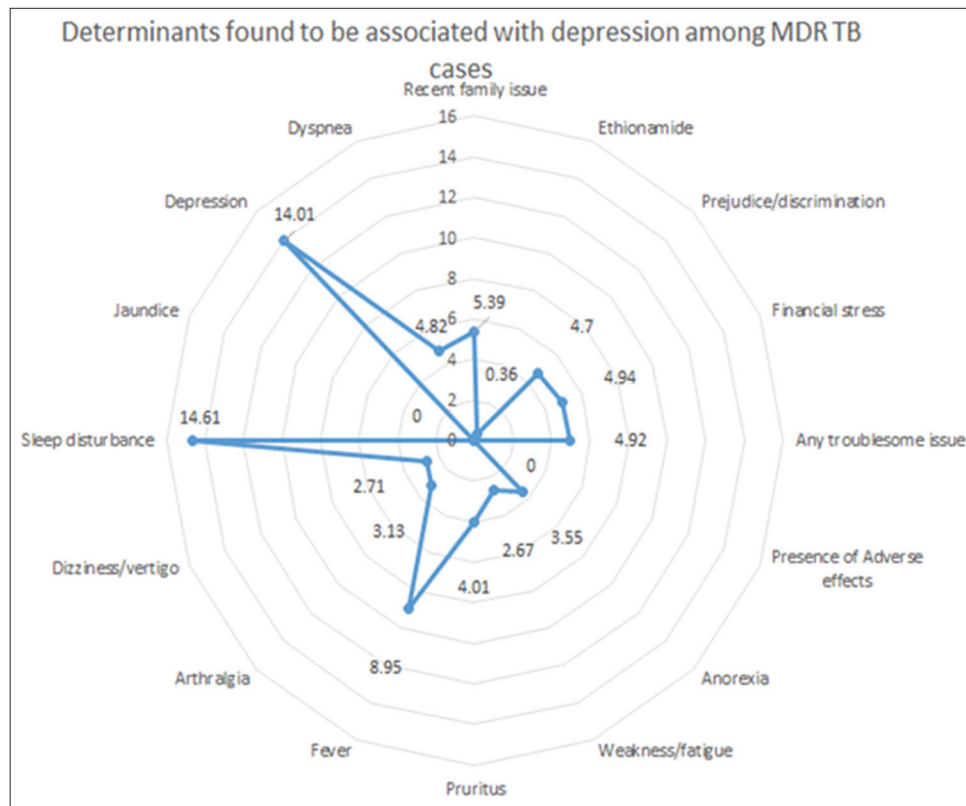
Figure 2: Web of multi factorial causation for depression

The prevalence of depression in the current study was (16.2%) lower than hospital-based studies where the prevalence of depression was as high as 31.5% among cases visiting pulmonary clinic; more among females, >45 years and unmarried/divorced patients,[11] 33.8% (95% CI: 26.7, 41.7)[17] and 45.5% from another study conducted in Nigeria.[18] Probable reason for this in the current study was that participants represent stable MDR-TB cases in community collecting drugs from the TU than severe and complicated cases visiting hospital. This holds true as a community-based study from Bangladesh had it only 4.1%.[19] Pathways between TB and depression are complex and bidirectional. TB cases may experience depression as a result of chronic infection or associated psychosocial economic stressors or stigma (of disease) or treatment effects and the development of depression can influence treatment compliance adversely. The need for routine screening and treatment for depression

throughout the treatment of MDR-TB patients with integration in routine TB care is clear from our study as well as studies in Bangladesh and other LMIC settings.[20-22] Other studies[23] have mentioned that impact of this is seen on both patient well-being and adherence to MDR-TB treatments. The current study showed recent family issues, discrimination, financial, or any troublesome issues, presence of AE (common being sleep disturbances, depression, fever, etc.) had significant association with depression while ethionamide showed a protective effect. For any chronic illness, the family is the backbone and therefore counseling must extend to the family members. As per PMDT guidelines, ethionamide has been associated with psychosis. In addition, there are other alternative pathways that state that patients may have TB due to decreased body immunity and self-care associated with depression.[24] Cycloserine may cause severe psychosis and depression leading to suicidal tendencies but in the current study, no such association was observed.

Limitations

During sample size estimation, nonresponse rate of 10% was assumed. However, despite our best efforts, we could contact only 185 cases, giving a nonresponse rate of 26%. This was primarily due to a high proportion of deceased cases.

Conclusion and Recommendations

The prevalence of depression is definitely high among MDR-TB cases. Those suffering from AEs or having stressors such as family issues and financial stress were found to be at a higher risk. While there is provision for mental health assessment under the program guidelines, it is usually ignored. A high prevalence of mental illnesses among TB patients underscores the need for the inclusion of a structured and systematic process for screening and evaluation of mental health as well as a strong referral mechanism with the nearest support system.

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Conflicts of interest

One of the investigators (TS) is involved in the implementation of NTEP in the study area.

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