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ORIGINAL ARTICLE

Psychiatric Co-Morbidity and its Associated Risk Factors among Tuberculosis Patients

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ABSTRACT

Aim: To assess psychiatric co-morbidity (i.e., depression and anxiety) and its associated risk factors among Multidrug/Rifampicin Resistant Tuberculosis (MDR/RR-TB) patients.
Methods: It was an analytical cross-sectional study carried out in Department of Chest Medicine, Jinnah Post Graduate Medical Centre from February to August, 2015. Eighty diagnosed and registered patients of MDR/RR-TB, able to comprehend Urdu language, between the age range of 18 to 60 years were approached by using convenient sampling technique. Psychiatric co-morbidity i.e., depression and anxiety were assessed by using the Urdu adapted version of Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder Questionnaire (GAD – 7).
Results: By applying the standard cut off score of 10 or more on PHQ-9 and GAD-7, the frequency of depression was 58 (72.5%) and for anxiety it was 53 (66.25%) out of 80 MDR/RR-TB patients. The multivariant analysis, intensive phase of TB treatment (OR = 3.02; 95% CI = 0.97-9.41) was found to be significantly associated with depression by using PHQ-9 and age group of 18 to 30 years (OR=0.156; 95% CI= 0.02-0.86), pulmonary TB (OR=6.33e+7; 95% CI=0.00-inf) and intensive phase of treatment (OR= 3.892; 95% CI=1.14-13.20) were significantly associated with anxiety by using GAD-7.
Conclusion: Frequency of psychiatric co-morbidity was higher among MDR/RR-TB patients. Age group of 18 to 30 years, pulmonary TB and intensive phase of treatment were found to be the risk factors for depression and anxiety among TB patients. Psycho-social factors are strong factors in the successful treatment of tuberculosis. Early detection and proper management of psychiatric co-morbidity during the treatment of MDR-TB needs special attention.
Keywords: Anxiety, Depression, Drug resistance, Multidrug resistance tuberculosis, psychiatric co-morbidity,

INTRODUCTION

Multidrug-/Rifampicin Resistant Tuberculosis (MDR/RR-TB) is a public health problem.[1] Recent update (2017) of World Health Organization (WHO) reports globally 600,000 new cases of MDR/RR-TB and became the cause of 240,000 deaths mostly in Asia[2]. MDR/RR-TB is a type of Drug Resistance (DR-TB) caused by bacteria that shows resistance to treatment with first-line anti-TB drugs (Isoniazid and Rifampin or specifically with Rifampin)[1].

Second-line anti-TB drugs are used as the treatment for MDR-TB and it requires up to 2 years of extensive chemotherapy treatment that is quite expensive and toxic[1]. Researches indicated that these drugs are associated with psychiatric comorbidity such as stress, anxiety, depression, psychosis and sleep problems[1,3]. That presents a great challenge for the successful MDR-TB treatment[4]. These psychiatric disorders could either be medication induced or may be associated with psychosocial factors. However, in both cases aggressive management is required[3,4].

Pakistan is the fourth highest MDR/RR-TB burdened country worldwide.[1] In June, 2010, the Programmatic Management of Drug Resistant TB (PMDT) was initiated in Pakistan. Despite this initiative, there is little data available regarding the prevalence, risk factors and management of MDR/RR-TB[5,6]. A study conducted in the region of Punjab found 42.8% (out of 1279) depression among MDR-TB patients[7]. There are also few studies conducted in different region of Pakistan are evident of psychiatric co-morbidity among MDR-TB patients[5,6,8].

Usually in DR-TB programs, the bio-medical model dominates the entire treatment approach and psycho-social factors remain overlooked[9]. This is the main cause that mental health issues are highly prevalent among MDR/RR-TB patients[5,6,8]. They usually remain undiagnosed, untreated and contribute to poor treatment adherence for treatment[7].

The objective of the study was the assessment of psychiatric co-morbidity and its associated risk factors among MDR/RR-TB patients.

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METHODS

It was a cross sectional analytical study carried out in Department of Chest Medicine, JPMC, Karachi from February, 2015 to June 2015. The approval to conduct this study was taken by Institutional Review Board of JPMC under the reference no. F.2.81/2015-GENL/11126/JPMC. In this study, all the new and follow-up patients of pulmonary and extra-pulmonary tuberculosis were approached. During this period, 97 MDR/RR-TB patients were registered among which 10 were transferred to other PMDT sites, 06 were died and 01 patient was lost to follow-ups. That's why, data was collected from 80 MDR/RR-TB patients who consented to take part in this study. Only the registered and diagnosed MDR/RR-TB patients by DR-TB physician were selected. The set standard for selecting MDR-TB was resistance with Isoniazid and Rifampin and for RR-TB resistance with Rifampin. The age range of study participants was 18 to 60 years and those who were able to comprehend Urdu language. The exclusion criteria were comprised of patients who already completed their treatment or suspected MDR-TB or not gave consent to take part in study.

Participants were interviewed to fill their demographic information form and their files were thoroughly studied to get the details of their illness. The Urdu adapted version of *Patient Health Questionnaire- PHQ-9*[10] was administered to measure the level of patients' depression. It's a brief 9 items based self-administered scale to assess depression and its severity. In this scale participant is required to rate the symptoms of depression by using four-point rating scale i.e., "not at all", "several days", "more than half of the days" and "nearly every day". The range of total obtained score is from 0 to 27. The cut point for the assessment of severity of depression i.e., "Minimal/none", "mild", "moderate", "moderately severe" and "severe" is represented by the score range of 0-4, 5-9, 10-14, 15-19 and 20-27, respectively. However, most of the studies have identified the score of 10 or more as the optimal cutoff point to detect depression[11].

For the assessment of anxiety, the Urdu adapted version of *Generalized Anxiety Disorder-GAD-7*[12] was administered on patients. It is also 7 items based, self-rating scale, in which participant is required to rate the symptoms of anxiety by using four-point rating scale i.e., "not at all", "several days", "more than half of the days" and "nearly every day". The range of total obtained scores on GAD-7 is from 0 to 21. The cut point for the

assessment of severity of anxiety i.e., "minimal", "mild", "moderate" and "severe" is represented by the score range of 0-4, 5-9, 10-14 and 15-21 respectively. However, the GAD-7 can also work as dichotomous scale by optimal cut-off point to detect anxiety on score of 10 or more[12].

SPSS (V-19.0) was used for the analysis of data. Descriptive statistics (frequency, percentage and standard deviation) was used to get the estimation of the demographic characteristics of participants such as gender, age, marital status and overall frequencies of depression and anxiety among tuberculosis patients. Binomial regression analysis was applied for further analysis. Bivariate and multivariate models were constructed to find the predictor variables in association with psychiatric co-morbidity. Crude/unadjusted odd ratio (OR) (reported from bivariate analysis) and adjusted OR (reported from multivariate analysis) in association with depression and anxiety are stated with the 95% of confidence interval (CI). Bivariate model was constructed for individual predictors (i.e., gender, age group, site of TB, resistance type and treatment phase) and multivariant model was constructed on the basis of significant outcome variables ($p<0.05$) of bivariate model. For both dependent variables, R^2 describes the proportion of variance from multivariant model.

RESULTS

Out of 80 participants of the study, 28(35%) were male and 52(65%) were females with the mean age of 32.26 years (St. Deviation=14.47). Majority of the participants were young between the age range of 18-30 years 36(45%), 29(36.25%) participants were from the age group of 31 to 44 years and 15(18.75%) participants were from 45 years and above age group. Regarding their marital status, 26(32.5%) were single, 49(61.25%) were married and only 5(6.25%) were widowed/ separated/ divorced.

Patients' files were also evaluated regarding the details of their diagnosis and treatment, 76(95%) patients were identified with pulmonary TB and 4(05%) with Extra Pulmonary TB. In addition, 44 (55%) patients were identified with MDR-TB and 36(45%) patients with MTB Rif Resistance. With regard to their treatment phase, 60(75%) patients were in intensive treatment phase and 20(25%) in continuation treatment phase.

Overall, in this study the frequency of depression was 58(72.5%- PHQ9 >10) and for anxiety it was 53(66.25% - GAD7 >10) out of 80 patients. The frequency for the severity of depression i.e., minimal symptoms, mild, moderate, moderately severe and severe was found to be 14(17.5%), 8(10%), 9(11.25%), 16(20%) and 33(41.25%) patients, respectively. Similarly, frequency for the severity of anxiety i.e., minimal, mild, moderate and severe was 17(21.5%), 10(12.5%), 12(15%) and 41(51.25%), respectively.

Bivariate analysis of variables indicated pulmonary tuberculosis, MDR-TB and intensive treatment phase are statistically significantly related to the diagnosis of depression (PHQ-9 ≥10) among DR-TB patients. In multivariant analysis, intensive treatment phase (OR=3.02; 95% CI=0.97-9.41) is related to the diagnosis of depression (PHQ-9 ≥10). Moreover, the bivariate and multivariate analysis of variables revealed that the age group of 18 to 30 years (OR= 0.156; 95% CI=0.02-0.86), pulmonary TB (OR=6.33e+7; 95% CI=0.00-inf) and intensive treatment phase (OR=3.892; 95% CI= 1.14-13.20) are significantly associated with anxiety (GAD-7 9≥10) among DR-TB patients (Table 1).

Table 1 Predictors of psychiatric co-morbidity (depression and anxiety) among MDR/RR-TB patients

Variables	PHQ-9 (10 or more)		GAD-7 (10 or more)	
	Crude OR (95% CI)	Adjusted OR[a]	Crude OR (95% CI)	Adjusted OR[b]
Gender				
Male	0.704 (0.25-1.93)	-	0.54 (0.20-1.41)	-
Female				
Age Group				
18-30 years	0.500 (0.11-2.12)	-	0.172 (0.03-0.87) *	0.156 (0.02-0.86) *
31-44 year	0.786 (0.17-3.61)	-	0.404 (0.07-2.20)	-
45 years and above				
Site of TB				
Pulmonary	9.00 (0.88-91.76) *	4.30 (0.38-48.51)	3.61 (0.00-inf) *	6.33e+7 (0.00-inf) *
Extra pulmonary				
Resistance type				
MDR	0.296 (0.09-0.90) *	0.40 (0.12-1.30)	0.255 (0.08-0.73)	-
MTB Rif				
Treatment phase				
Intensive	4.00 (1.357-11.79) **	3.02 (0.97-9.41) *	4.50 (1.54-13.10) *	3.892 (1.14-13.20) *
Continuation				

**P<0.05; **P<0.001*

[a] *Hosmer and Lemeshow Chi-square 1.981, df 2, 0.371; Cox and Snell R^2 0.104; Nagelkerke R^2 0.150.*

[b] *Hosmer and Lemeshow Chi-square 2.784, df 5, 0.733; Cox and Snell R^2 0.237; Nagelkerke R^2 0329.*

DISCUSSION

Overall, this study finds elevated frequency of depression and anxiety (72.5% and 66.25% according to PHQ-9 score 10 or above and GAD-7 score10 or above, respectively) among tuberculosis patients visiting PMDT site, Department of Chest Medicine, JPMC, Karachi. Multivariant analysis identified intensive treatment phase as significantly linked variable with depression and age group of 18 to 30 years, pulmonary site of TB and intensive treatment phase as significantly linked with anxiety.

Psychiatric co-morbidity is a great challenge in the treatment adherence of DR-TB[7]. Present study findings are consistent with another local study that was conducted in Peshawar and found 69.55% depression out of 201 MDR-TB patients.[6] Similarly, another local study in the rural region of Pakistan found 72% (47 out of 65 patients) depression and anxiety among tuberculosis patients.[13]The elevated frequencies of MDR/RR-TB patients could be attributed to the longer duration of MDR-TB treatment with wide-ranging adverse effects in comparison with first line anti-tuberculosis drugs[7]. Moreover, 95% of the patients in this study were diagnosed with pulmonary TB and 75% of the patients were in intensive treatment phase. Researches have indicated that both of these factors are highly associated with psychiatric comorbidity[13,14,15].

This study identifies the age group of 18 to 30 years as the most susceptible group toward anxiety. Like Kibrisli and his colleagues[16] also found high level of social avoidance, fear of social exclusion and perceived severity of illness among young pulmonary TB patients. Moreover, the disease tuberculosis is considered as a stigmatized disease[17] and the people suffering from tuberculosis are isolated, least socially accepted because they have tendency to spread the infection to others. This stigma is highly associated with geographic region, socio-economic class, disease perception, disruptive behavior and gender. Thereby, the precautions taken by the patients or by the society often may progress anxiety and depression among them[16,18].

This study also identifies intensive treatment phase as the statistically significant predictor of depression and anxiety among DR-TB patients. In bivariate model however not in multivariate model, pulmonary TB was associated with depression. A study

carried out in the region of Taiwan also found the incidence of depression 1.16-fold greater among pulmonary TB patients[19]. With reference to intensive phase of treatment the findings of present study are similar to another study which concluded that psychological distress and symptoms are more frequent in the initial treatment phase[16].

In addition, the diagnosis of MDR-TB and lower socio-economic status are itself the significant predictor of psychological distress[15]. A part from demographic and psychosocial factors, a possible explanation for increased psychological distress could be the side effects of drugs that mostly appear in the initial months of the treatment[14]. According to WHO guideline in the initial phase of treatment when the body is very weak, nausea and vomiting are too frequent with severe anxiety symptoms due to anti tuberculosis drugs namely Cycloserine or terizidone and the aggressive management of these complication is required for the successful treatment.[20] Lack of knowledge about disease or inadequate information about disease, lack of trust on treatment to cure the disease and management of side effects are proven as anxiety provoking factors among TB patients[21].

Participants of this study were already taking psychological counseling session on monthly basis; however, regularized counseling was planned for all identified moderate and severe category of depression and anxiety. There are number of limitations identified in this study. One of the most basic limitations identified in this study was very small sample size and inclusion of TB patients from a single hospital Jinnah Postgraduate Medical Center (JPMC), of Karachi. The JPMC is a largest public sector tertiary hospital of Karachi and majority of the patients coming to JPMC are of low socio-economic strata. Thus, the findings of this study can't be generalized on all TB patients, because this study just represents anxiety and depression frequencies of patients of only a single public hospital of Karachi. Moreover, the level of anxiety and depression of patients were assessed only through standard questionnaires rather than structured clinical diagnostic interview. In addition, patients were not assessed at baseline level. So, it cannot be differentiated that whether this depression and/or anxiety is due psycho-social factors or is the direct adverse reaction of DR-TB drugs. Certain demographic factors such as marital status, occupation, family size etc. and disease related factors like presence of co-morbid conditions, treatment complications and psychosocial support from family and other society members were not considered.

CONCLUSION

In conclusion, frequency of psychiatric co-morbidity was higher among MDR/RR-TB patients. Age group of 18 to 30 years, pulmonary TB and intensive phase of treatment were found to be the associated risk factors for psychiatric co-morbidity among TB patients. Psychiatric side effects and psycho-social factors are the strong factors in the successful treatment of TB. Early detection and proper management of psychiatric co-morbidity throughout MDR-TB treatment needs special attention. Apart from clinical advancement, regularized monitoring of mental health issue should be done by the trained clinical psychologist by using standardized cost-effective measures.

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