



Psychiatric Morbidity among Patients with Pulmonary and Extrapulmonary Tuberculosis on Treatment: A Cross-Sectional Study.

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Abstract

Background: Tuberculosis (TB) is a chronic infectious multisystem disease and remains a leading infectious cause of death worldwide. TB and common mental disorders share risk factors such as poverty, substance use and homelessness, and psychiatric comorbidity in TB is linked to poor treatment adherence and worse outcomes; yet screening for mental illness is not part of routine TB programme guidelines in India. **Aim and Objectives:** To study psychiatric morbidity in patients diagnosed with pulmonary and extrapulmonary tuberculosis on treatment; to describe their sociodemographic and clinical profile; and to assess the severity of anxiety and depression in the two groups. **Materials and Methods:** A cross-sectional observational study was conducted over 18 months (February 2021 to July 2022) in the Department of Respiratory Medicine of a rural medical college hospital. One hundred consenting patients aged 18–70 years, 4–8 weeks after initiation of the DOTS-Plus regimen, were recruited by simple random sampling. A semi-structured proforma, the Mini International Neuropsychiatric Interview-Plus (MINI-Plus) with ICD-10 confirmation, and the Hamilton Anxiety (HAM-A) and Hamilton Depression (HAM-D) rating scales were used. Data were analysed using SPSS 22.0 with Chi-square/Fisher exact test; $p < 0.05$ was considered significant. **Results:** Psychiatric morbidity was present in 53 (53%) of the 100 patients. Among those affected, depression was commonest (22; 41.5%), followed by anxiety disorders (16; 30.2%), substance use disorders (11; 20.8%), somatoform disorders (3; 5.7%) and psychotic disorder (1; 1.9%). The distribution of grades of depression differed significantly by type of TB ($p = 0.01$), severe depression being proportionately more frequent in extrapulmonary TB (40.0%) than in pulmonary TB (17.6%); grades of anxiety did not differ significantly ($p = 0.66$). No sociodemographic variable was significantly associated with the severity of anxiety or depression. **Conclusion:** More than half of patients on antitubercular treatment had a diagnosable psychiatric disorder, chiefly depression. Mental health screening and management should be integrated into national TB control activities.

Keywords: Tuberculosis; Pulmonary; Extrapulmonary; Psychiatric morbidity; Depression; Anxiety.



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INTRODUCTION

Tuberculosis (TB), the oldest human pandemic, remains one of the leading infectious causes of death despite the availability of a live attenuated vaccine and several effective antibiotics (1). The disease is caused by infection of the lung with *Mycobacterium tuberculosis*, identified as a pathogen by Robert Koch in 1882. TB is predominantly a pulmonary disease, with pulmonary involvement accounting for roughly 70% of cases, but the organism can disseminate to lymph nodes, bone, meninges and other organs to produce extrapulmonary disease (2). Approximately one-quarter of the global population is latently infected, providing a large reservoir for future active disease, mostly in low- and middle-income settings where poverty, poor living environments and inadequate medical care prevail (3).

India carries the largest TB burden in the world. According to the Global Tuberculosis Report, the estimated incidence of all forms of TB in India was 188 per 100,000 population in 2020, and 19,33,381 incident (new and relapse) patients were notified during 2021 (4). India adopted the World Health Organization-endorsed Directly Observed Treatment, Short-course (DOTS) strategy under the Revised National Tuberculosis Control Programme in 1997, and case notification has since risen substantially, narrowing but not closing the gap between estimated and notified incident cases (5,6). While developed countries increasingly regard tuberculosis as a disease of the past, for many low- and middle-income countries the elimination of TB as a major public health problem remains an unrealized goal.

Common mental disorders — depression, anxiety and somatoform disorders — constitute a parallel global burden that continues to grow, with major consequences for health, human rights and economies (7). Depression manifests as depressed mood, loss of interest or pleasure, reduced energy, guilt or low self-worth, disturbed sleep and appetite and poor concentration (8); it accounts for a substantial proportion of disability-adjusted life-years worldwide and is a major contributor to suicide (7,8). Anxiety, a subjective feeling of uneasiness, apprehension, tension and impending doom, is associated with reduced functioning and quality of life and commonly accompanies the onset or recurrence of respiratory illness (9). Nevertheless, most people with mental health problems in low- and middle-income countries remain undiagnosed or inadequately treated (7).

Tuberculosis and common mental disorders are linked in several ways. They share risk factors including poverty, substance misuse, malnutrition and homelessness; chronic lung disease is itself strongly associated with psychiatric disorder; and the stigma, isolation, prolonged treatment and adverse drug effects of TB generate considerable psychological distress (10,11). Anxiety, depression and emotional distress in TB have been related to the number and severity of reported symptoms, greater use of health services, poor treatment compliance, longer treatment courses, poorer disease control and death (11). A systematic review and meta-analysis estimated pooled depression prevalence among TB patients at roughly 45% (12), while Indian studies have reported figures ranging from about 24% to over 40% (13-15), and international estimates range even more widely depending on the screening instrument used (16,17).

Despite this evidence, psychiatric illness in TB is often neglected in India, and current programme guidelines contain no recommendation for screening for psychiatric comorbidity at the initiation of therapy or during treatment. Furthermore, most published work has examined pulmonary TB, and comparatively little is known about whether psychiatric morbidity differs between pulmonary and extrapulmonary disease. The present study was therefore undertaken to determine the pattern of psychiatric morbidity, and the severity of anxiety and depression, in patients with pulmonary and extrapulmonary tuberculosis receiving treatment in a rural tertiary care setting.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted over a period of 18 months (February 2021 to July 2022) in the Department of Respiratory Medicine of a medical college and research hospital at Hoskote, a rural area of Bengaluru Rural district, in collaboration with the Department of Psychiatry. The study was commenced after obtaining approval from the Institutional Ethics Committee.

Patients diagnosed with tuberculosis by the chest physician and attending the Department of Respiratory Medicine formed the study population. Patients aged 18–70 years with either pulmonary or extrapulmonary tuberculosis, who were 4–8 weeks after initiation of the DOTS-Plus regimen and who gave written informed consent, were included. Patients already diagnosed with a psychiatric illness and receiving treatment for it, and patients with HIV co-infection, were excluded so that pre-existing psychiatric disorder and HIV-related neuropsychiatric morbidity would not confound the findings.

The sample size was calculated using the standard formula for estimating a proportion in a cross-sectional study, taking a confidence level of 95% ($Z = 1.96$) and an absolute precision of 0.08, which yielded a minimum of 94 subjects (18); this was rounded to 100. Participants were selected by simple random sampling from the register of eligible patients. After obtaining informed consent, sociodemographic data (age, gender, education, socioeconomic status and marital status) and clinical data (type of tuberculosis, duration of illness and comorbid medical conditions) were collected using a semi-structured proforma designed for the study.

All participants were interviewed by the investigator using the Mini International Neuropsychiatric Interview-Plus (MINI-Plus), a short structured diagnostic interview developed for DSM-IV and ICD-10 psychiatric disorders that takes approximately 15 minutes to administer (19); diagnoses were subsequently confirmed against ICD-10 clinical descriptions and diagnostic guidelines (20). The severity of anxiety and depression was graded with two clinician-rated instruments. The Hamilton Anxiety Rating Scale (HAM-A), developed by Hamilton in 1959, consists of 14 items each rated 0–4, giving a total score of 0–56, with higher scores denoting greater severity (21). The Hamilton Depression Rating Scale (HAM-D), a multiple-item clinician-rated questionnaire, was used to rate the severity of depression; in the 17-item version a score of 0–7 is regarded as normal and a score of 20 or more indicates at least moderate depression (22). Both scales were administered by the same trained clinician to minimize inter-rater variation.

Data were entered into a Microsoft Excel spreadsheet and analysed using SPSS version 22.0. Descriptive statistics were expressed as mean, standard deviation and standard error of the mean for quantitative variables and as frequencies and proportions for qualitative variables. Associations between two qualitative variables were tested using the Chi-square test or Fisher exact test as appropriate, and means of two groups were compared using the unpaired t test. A p value of less than 0.05 was considered statistically significant and a p value of less than 0.001 was considered highly significant.

RESULTS

One hundred patients diagnosed with pulmonary or extrapulmonary tuberculosis and receiving treatment were studied.

Table 1: Sociodemographic profile of the study participants (n = 100)

Variable	Category	n	%
Age (years)	<20	3	3.0
	21–30	14	14.0
	31–40	27	27.0
	41–50	29	29.0
	51–60	17	17.0
	>60	10	10.0
Gender	Male	49	49.0
	Female	51	51.0
Education	Illiterate	8	8.0
	Primary	35	35.0
	Secondary/higher secondary	40	40.0
	Graduate	17	17.0
Socioeconomic status	Lower	84	84.0
	Middle	5	5.0
	Upper	11	11.0
Marital status	Married	82	82.0
	Unmarried	18	18.0

The largest proportion of patients belonged to the 41–50 year age group (29%), followed by the 31–40 year group (27%); only 3% were younger than 20 years and 10% were older than 60 years. Males and females were almost equally represented (49% and 51% respectively). Educationally, 40% had studied up to secondary or higher secondary level and 35% up to primary level, while 17% were graduates and 8% were illiterate. An overwhelming majority (84%) belonged to the lower socioeconomic stratum, and 82% were married (Table 1).

Table 2: Clinical profile of the study participants (n = 100)

Variable	Category	n	%
Comorbid condition*	Hypertension	36	36.0
	Hyperthyroidism	24	24.0
	COPD	23	23.0
	Diabetes mellitus	19	19.0
	Hypothyroidism	19	19.0
	Asthma	16	16.0
Duration of illness (months)	<12	94	94.0
	>12	6	6.0

*Multiple response variable; percentages therefore do not total 100.

Comorbid medical conditions were frequent. Hypertension was the commonest (36%), followed by hyperthyroidism (24%), chronic obstructive pulmonary disease (23%), diabetes mellitus and hypothyroidism (19% each) and asthma (16%). The duration of tubercular illness was less than 12 months in the great majority of patients (94%) and exceeded 12 months in only 6% (Table 2).

Table 3: Distribution of psychiatric disorders among patients with psychiatric morbidity (n = 53)

Psychiatric disorder	n	%
Depression	22	41.5
Anxiety disorder	16	30.2
Substance use disorder	11	20.8
Somatoform disorder	3	5.7
Psychotic disorder	1	1.9
Total	53	100.0

Of the 100 patients studied, 53 (53%) had a diagnosable psychiatric disorder while 47 (47%) had none. Among those with psychiatric morbidity, depression was the most frequent diagnosis (22; 41.5%), followed by anxiety disorders (16; 30.2%) and substance use disorders (11; 20.8%). Somatoform disorder was present in 3 patients (5.7%) and psychotic disorder in 1 patient (1.9%) (Table 3).

Table 4: Severity of anxiety according to type of tuberculosis (n = 16)

Grade of anxiety	Pulmonary TB n (%)	Extrapulmonary TB n (%)	Total n	p value
Mild	7 (53.8)	1 (33.3)	8	0.66
Moderate	4 (30.8)	1 (33.3)	5	
Severe	2 (15.4)	1 (33.3)	3	
Total	13 (100.0)	3 (100.0)	16	

Among the 16 patients with anxiety, 13 had pulmonary and 3 had extrapulmonary tuberculosis. Mild anxiety accounted for 53.8% of the pulmonary group and 33.3% of the extrapulmonary group, moderate anxiety for 30.8% and 33.3%, and severe anxiety for 15.4% and 33.3% respectively. The difference in the distribution of grades of anxiety by type of tuberculosis was not statistically significant ($p = 0.66$) (Table 4).

Table 5: Severity of depression according to type of tuberculosis (n = 22)

Grade of depression	Pulmonary TB n (%)	Extrapulmonary TB n (%)	Total n	p value
Mild	10 (58.8)	2 (40.0)	12	0.01
Moderate	4 (23.5)	1 (20.0)	5	
Severe	3 (17.6)	2 (40.0)	5	
Total	17 (100.0)	5 (100.0)	22	

Among the 22 patients with depression, 17 had pulmonary and 5 had extrapulmonary tuberculosis. Mild depression was proportionately more common in pulmonary tuberculosis (58.8% versus 40.0%), whereas severe depression was proportionately more common in extrapulmonary tuberculosis (40.0% versus 17.6%). This difference in the distribution of grades of depression by type of tuberculosis was statistically significant ($p = 0.01$) (Table 5).

Table 6: Association of severity of anxiety with sociodemographic variables (n = 16)

Variable	Category	Mild n (%)	Moderate n (%)	Severe n (%)	p value
Age (years)	21–30	1 (12.5)	0 (0.0)	0 (0.0)	0.78
	31–40	1 (12.5)	2 (40.0)	0 (0.0)	
	41–50	1 (12.5)	1 (20.0)	1 (33.3)	
	51–60	3 (37.5)	1 (20.0)	1 (33.3)	
	>60	2 (25.0)	1 (20.0)	1 (33.3)	
Gender	Male	5 (62.5)	3 (60.0)	2 (66.7)	0.58
	Female	3 (37.5)	2 (40.0)	1 (33.3)	
Education	Illiterate	3 (37.5)	2 (40.0)	1 (33.3)	0.99
	Primary	3 (37.5)	1 (20.0)	1 (33.3)	
	Secondary/higher	2 (25.0)	1 (20.0)	1 (33.3)	
	Graduate	0 (0.0)	1 (20.0)	0 (0.0)	
Socioeconomic status	Lower	4 (50.0)	2 (40.0)	1 (33.3)	0.88
	Middle	3 (37.5)	1 (20.0)	1 (33.3)	
	Upper	1 (12.5)	2 (40.0)	1 (33.3)	
Marital status	Married	5 (62.5)	3 (60.0)	2 (66.7)	0.53
	Unmarried	3 (37.5)	2 (40.0)	1 (33.3)	
Total		8 (100.0)	5 (100.0)	3 (100.0)	

Of the 8 patients with mild anxiety, the largest group was aged 51–60 years (37.5%), followed by those older than 60 years (25%). Males predominated across all grades of anxiety (62.5%, 60.0% and 66.7% of mild, moderate and severe cases respectively), and married patients likewise formed the majority in each grade. Illiterate and primary-educated patients

together accounted for three-quarters of mild cases, and patients of lower socioeconomic status formed half of the mild cases. None of these associations reached statistical significance (all $p > 0.05$) (Table 6).

Table 7: Association of severity of depression with sociodemographic variables (n = 22)

Variable	Category	Mild n (%)	Moderate n (%)	Severe n (%)	p value
Age (years)	21–30	2 (16.7)	0 (0.0)	1 (20.0)	0.85
	31–40	1 (8.3)	2 (40.0)	1 (20.0)	
	41–50	2 (16.7)	1 (20.0)	1 (20.0)	
	51–60	3 (25.0)	1 (20.0)	1 (20.0)	
	>60	4 (33.3)	1 (20.0)	1 (20.0)	
Gender	Male	7 (58.3)	3 (60.0)	3 (60.0)	0.80
	Female	5 (41.7)	2 (40.0)	2 (40.0)	
Education	Illiterate	5 (41.7)	2 (40.0)	2 (40.0)	0.99
	Primary	4 (33.3)	1 (20.0)	2 (40.0)	
	Secondary/higher	3 (25.0)	1 (20.0)	1 (20.0)	
	Graduate	0 (0.0)	1 (20.0)	0 (0.0)	
Socioeconomic status	Lower	6 (50.0)	2 (40.0)	2 (40.0)	0.82
	Middle	4 (33.3)	1 (20.0)	2 (40.0)	
	Upper	2 (16.7)	2 (40.0)	1 (20.0)	
Marital status	Married	7 (58.3)	3 (60.0)	4 (80.0)	0.73
	Unmarried	5 (41.7)	2 (40.0)	1 (20.0)	
Total		12 (100.0)	5 (100.0)	5 (100.0)	

Among the 12 patients with mild depression, the largest group was older than 60 years (33.3%) followed by the 51–60 year group (25.0%). Males accounted for approximately 60% of cases in every grade, and married patients formed the majority in each grade, rising to 80% of severe cases. Illiterate patients constituted the single largest educational category in mild, moderate and severe depression alike (41.7%, 40.0% and 40.0% respectively), and patients of lower socioeconomic status formed the largest group in each grade. None of these associations was statistically significant (all $p > 0.05$) (Table 7).

DISCUSSION

Psychiatric morbidity was present in 53% of patients receiving antitubercular treatment in the present study, confirming that mental illness is a major and frequently unrecognized accompaniment of tuberculosis. This is broadly in line with the pooled global prevalence of depression of about 45% among TB patients reported in a systematic review and meta-analysis (12), and with Indian reports of depression in about 41% of TB patients by Shyamala et al. (13) and of anxiety in 28% and depression in 39% by Tiwari et al. (14). Lower figures have also been reported, such as a depression prevalence of 23.6% at a rural DOTS centre in Delhi (15) and 17% mild depression among patients with pulmonary TB in an Indian armed forces population (23). Such variation largely reflects differences in screening instruments, cut-off scores and settings; the substantial overlap between somatic symptoms of tuberculosis and of depression — changes in appetite, sleep and energy — makes prevalence estimates based on self-report screens particularly susceptible to inflation (17).

Depression was the leading diagnosis (41.5% of those affected), followed by anxiety (30.2%) and substance use disorders (20.8%). The prominence of depression accords with almost all published series (12–15,24) and is readily understood in terms of persistent symptoms, fear of non-recovery, adverse effects of prolonged multidrug therapy, loss of earnings and the pervasive stigma that attaches to tuberculosis. The substantial proportion of substance use disorders is consistent with the shared risk profile of TB and common mental disorders, in which alcohol and tobacco use, poverty and homelessness cluster together (10,13).

A distinctive finding of this study was the significant difference in the distribution of grades of depression between pulmonary and extrapulmonary tuberculosis ($p = 0.01$), with severe depression proportionately more frequent in extrapulmonary disease (40.0% versus 17.6%), whereas grades of anxiety did not differ significantly ($p = 0.66$). Possible explanations include the diagnostic delay and longer, more complex regimens that often characterize extrapulmonary disease, and greater functional impairment when sites such as bone, spine or meninges are involved. The small number of extrapulmonary cases ($n = 5$ with depression) means, however, that this result must be regarded as hypothesis-generating rather than definitive.

No sociodemographic variable was significantly associated with the severity of anxiety or depression, although depression and anxiety were numerically concentrated among illiterate patients, those of lower socioeconomic status and those who

were married. Salodia et al. similarly found no association of depression with gender, religion, marital status or education, concluding that male and female patients with TB suffer alike and that being married or educated confers no protection (15). Others have reported that older age, never-married or separated status and lower education predict higher depression scores (16), and that severity increases with age and comorbidity (24). The absence of significant associations here is most plausibly explained by limited statistical power, since only 16 and 22 patients respectively had anxiety and depression, and by the homogeneity of the sample, 84% of whom belonged to the lower socioeconomic stratum. Other limitations include the single-centre rural setting, the cross-sectional design that precludes inference about the direction of the association, and the absence of an urban comparison group. Nevertheless, the findings reinforce the argument that routine psychiatric screening at the initiation of and during antitubercular treatment is warranted, since untreated depression and anxiety are known to reduce compliance and worsen TB outcomes (11,25).

CONCLUSION

More than half (53%) of the patients receiving treatment for pulmonary or extrapulmonary tuberculosis in this rural tertiary care setting had a diagnosable psychiatric disorder. Depression was the commonest diagnosis, followed by anxiety and substance use disorders. The severity of depression differed significantly according to the type of tuberculosis, severe depression being proportionately more frequent in extrapulmonary disease, whereas the severity of anxiety did not. No sociodemographic variable was significantly associated with the severity of anxiety or depression. These findings indicate a close association between psychiatric problems and tuberculosis that may worsen prognosis and complicate disease control. Mental health screening and treatment should be integrated into national TB control programmes, and awareness of the high prevalence of psychiatric illness among TB patients — and of its consequences for treatment success — should be actively promoted. Larger, multicentre and longitudinal studies including urban populations and untreated comparison groups are recommended.

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