



Psychological stress and health-related quality of life among tuberculosis patients: a prospective cohort study

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Shareable abstract (@ERSpublications)

Tuberculosis patients experience significant psychological stress that can negatively impact their quality of life and warrants proper screening and intervention. <https://bit.ly/3jfMEJA>

Cite this article as: Febi AR, Manu MK, Mohapatra AK, et al. Psychological stress and health-related quality of life among tuberculosis patients: a prospective cohort study. *ERJ Open Res* 2021; 7: 00251-2021 [DOI: 10.1183/23120541.00251-2021].

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This article has supplementary material available from openres.ersjournals.com

Received: 11 April 2021
Accepted: 21 June 2021

Abstract

Economic, social and psychological distress is common in individuals affected by tuberculosis (TB). However, the magnitude of distress, psychological interventions and their effect on the treatment outcomes are often under-evaluated. We examined the level of psychological stress and health-related quality of life (HRQoL) of such patients and the effect of antituberculosis therapy on them.

Our prospective cohort study included newly diagnosed adult pulmonary and extrapulmonary TB patients. Assessment of psychological stress was done using the seven-item Generalised Anxiety Disorder questionnaire for anxiety and the nine-item Patient Health Questionnaire for depression. HRQoL was assessed by using the WHOQOL-BREF questionnaire.

Of the 86 patients studied, 21 (24.4%) had anxiety symptoms at the baseline, which reduced to 5.8% and 1.2% at 2 months and treatment completion, respectively ($p < 0.001$). Among the subjects, 18 (20.9%) patients had depression, which reduced to 7% and 2.3% at 2 months and treatment completion, respectively ($p < 0.001$). All the mean domain scores of HRQoL were poor at the baseline, which showed improvement at treatment completion ($p < 0.001$).

Anxiety and depression were common among TB patients, and there was significant progressive reduction during and after treatment. TB had remarkable negative impacts on HRQoL, with the physical domain being the most affected, and all the domain scores showed significant improvement at treatment completion. Routine screening for depression and anxiety and timely referral to a psychiatrist are required in TB patients to improve the outcome of the disease and quality of life.

Introduction

Tuberculosis (TB), a chronic communicable disease caused by *Mycobacterium tuberculosis* (MTB), is a significant cause of morbidity and mortality worldwide [1]. The World Health Organization (WHO) consider TB as one of “the top 10 causes of death worldwide and the leading cause of death from a single infectious agent” [1]. Economic, social and psychological distress are seen in individuals affected by TB, affecting their quality of life [2]. However, the magnitudes of distress and psychological interventions and their effect on treatment outcomes are often undervalued and have not been adequately evaluated. This issue highlights the importance of measuring health indicators beyond traditional parameters such as morbidity and mortality rates.

The WHO Global Tuberculosis Report 2020 describes TB as “a disease of poverty, economic distress, vulnerability and marginalisation” [1]. Such patients routinely encounter social reproach and discrimination. Along with the physical symptoms of pulmonary TB (PTB) and extrapulmonary TB (EPTB), they usually face various social, psychological and economic issues, with a higher quantum of



issues seen in drug-resistant TB [3]. Psychiatric illnesses such as anxiety or depression can occur as comorbidities in TB patients and may negatively influence quality of life and therapeutic results [4, 5]. Hence, besides routine clinical, microbiological and radiological assessment, a broader evaluation of the patient's overall health profile is necessary.

Prospective Indian studies assessing psychological stress and health-related quality of life (HRQoL) in TB patients are lacking. Hence, we aimed to measure these parameters in newly diagnosed TB cases and evaluate the impact of treatment on them.

Material and methods

Study setting

The prospective cohort study was conducted at Kasturba Hospital, Manipal, a teaching centre attached to a medical school, from October 2018 to June 2020.

Study population and data collection

We included 86 newly diagnosed adult PTB and EPTB patients who were newly initiated on antituberculosis treatment (ATT) or had started ATT less than a month ago. We excluded multidrug-resistant/extensively drug-resistant cases, those aged less than 18 years, those on ATT for more than a month, those with underlying psychiatric illness and those who refused to consent. After obtaining informed consent, we collected the patient's demographic and socioeconomic characteristics. Information about education, housing, employment and cigarette and alcohol consumption were captured. We assessed the clinical presentation, comorbid illnesses, microbiological and radiological characteristics.

Psychological stress was measured using the Patient Health Questionnaire nine-item depression scale (PHQ-9) and the seven-item Generalized Anxiety Disorder scale (GAD-7). These were selected for the study since they are well-validated, frequently used screening tools, which are easy and reliable [6].

HRQoL was measured using a widely used tool, the WHOQOL BREF questionnaire, which has proven to be reliable for TB patient research [7, 8].

At the end of 2 months of treatment and at the time of treatment completion, we reassessed the GAD-7 and PHQ-9 scores. If the scores were ≥ 11 at any stage of assessment, we referred them for psychiatric evaluation. We measured HRQoL again at the end of the treatment.

For the calculation of sample size, we assumed a 40% prevalence of depression at baseline and expected a reduction in its prevalence by at least 20% at the end of 6 months. To detect a 20% difference in the prevalence of depression with 0.1 intra-class correlation, 5% level of significance and 80% power, the sample size needed was 77. With an anticipated 10% attrition rate, the modified sample size needed was 86.

Data analysis

Frequency and percentage were used to depict categorical data. Mean and standard deviation were used in order to sum up the continuous data. Data were analysed using SPSS Statistics for Windows, version 16.0 (SPSS Inc., Chicago, Ill., USA). Improvements in median scores of GAD-7 and PHQ-9 were analysed using the non-parametric Friedman test. The Cochran Q test was used to test the differences in the frequency of anxiety and depression. Correlation between psychological stress and parameters such as age was done by using the Mann-Whitney test and this test was also used to analyse changes in the GAD-7 and PHQ-9 scores of treated and non-treated groups. Correlations with addictions such as alcoholism and smoking were assessed using Fischer's exact test. The paired t-test was the parametric test used in the study, which was used to compare the mean WHOQOL-BREF scores from the first and last visits. Patients who were lost to follow-up or had missing data were excluded from analysis.

Ethical considerations

The study was approved by our institutional review board approval (IEC: 548/2018; Clinical Trial Registry of India: CTRI/2018/10/016230) and informed consent was obtained from every participant.

Results

Baseline characteristics

We screened 119 cases and excluded four, which resulted in 115 patients who met the inclusion criteria. We lost 29 participants at the first (end of 2 months of intensive phase of chemotherapy) and end of treatment follow-up visits (21 and eight, respectively). The study group eventually comprised 86 patients (Figure S1). The median age of the population was 40 years, ranging from 18 to 76 years. There were 27

females (31.4%) and 59 males (68.6%). Other details such as education, employment, housing and details of substance use were collected (table 1).

Clinical presentation and comorbidities

Among the study subjects (n=86), 61 (70.9%) had PTB and 25 (29.1%) had EPTB. Pleural TB accounted for 14 (56%) of the EPTB subjects. There were six cases (24%) of cervical lymphadenopathy, three skeletal TB (12%), one axillary lymphadenopathy (4%) and one abdominal TB (4%).

Among the study population (n=86), 28 (32.6%) had diabetes mellitus. Among them, 15 (17.4%) had the disease for more than 5 years, nine (10.5%) had it for less than 5 years, while three (3.5%) were newly diagnosed. Other premorbid illnesses such as hypertension, ischaemic heart disease and alcohol liver disease were present in 17 (29.7%) patients. One patient was HIV positive.

Diagnosis

Among the 86 patients, 61 (70.9%) cases had PTB and 25 (29.1%) had EPTB. In 45 out of 61 PTB patients (73.7%), sputum acid fast bacilli (AFB) smears were positive of which 37 (82.2%) were positive for sputum GeneXpert and 34 (75.5%) for MTB culture. Among the 16 sputum AFB smear negative cases, three were positive for sputum GeneXpert and MTB culture. 11 of the sputum smear negative cases underwent bronchoscopy. Among them, bronchial washing AFB smear, GeneXpert and MTB culture were positive in five patients, one was positive for GeneXpert and MTB culture, four patients were positive for bronchoalveolar lavage GeneXpert alone. One patient, who was negative for all the three investigations, was diagnosed based on endobronchial biopsy. Two sputum smear-negative PTB cases were detected by histopathology of transthoracic needle biopsy samples.

Of the pleural TB (n=14) cases, 13 were diagnosed based on pleural fluid lymphocytosis and high adenosine deaminase level and one was started on ATT empirically. All six cases of cervical lymphadenopathy were histopathology proven, four GeneXpert and one MTB culture positive. The three skeletal TB cases were biopsy proven, of which GeneXpert and MTB culture positivity was seen in one each. The sole axillary lymphadenopathy was diagnosed based on histopathology and GeneXpert. The abdominal TB case was biopsy proven. No GeneXpert-positive cases (PTB and EPTB) showed resistance to rifampicin. There were no cases of disseminated TB.

Outcomes

All 86 patients completed the treatment successfully and were declared cured. We assessed ATT-related complications. 59 (68.6%) patients had no complications with the medications. Gastritis occurred in 18 (20.9%), hepatitis in seven patients (8.1%) and skin rash in two patients (2.3%). These complications were not associated with significant increases in anxiety and depression ($p=0.84$).

Psychological parameters

GAD-7 and PHQ-9 questionnaires were used during three visits to conduct psychological screening to find patients with anxiety or depression. The median and interquartile range of GAD-7 and PHQ-9 scores from these three visits were estimated (table 2)

At the time of diagnosis, 21 patients (24.4%) had anxiety, among which eight (9.3%) had severe anxiety with a score more than 15. Baseline depression was present in 18 patients (20.9%), among which six (7%) had severe depression with a score higher than 16. 10 (11.6%) patients had coexistence of anxiety and depression and 56 (65.1%) had none.

The correlation of various parameters with the prevalence of psychological stress was studied (table 3). The mean age of the population with anxiety was 49.9 ± 1.3 and that without anxiety was 38.8 ± 1.5

TABLE 1 Socio-demographic characteristics

Gender n (%)	Education n (%)	Employment n (%)	Housing n (%)	Nicotine use n (%)	Alcohol use n (%)
Males: 27 (31.4)	Illiterate: 21 (24.4)	Unemployed: 22 (25.6)	Thatched house: 19 (22.1)	41 (47.7)	34 (39.5)
Females: 59 (68.6)	Primary: 28 (32.6)	Employed: 55 (64)	Tiled house: 33 (38.4)		
	Pre-university: 8 (9.3)	Student: 9 (10.5)	Concrete house: 30 (34.9)		
	Graduate: 29 (33.7)		Two-storey house: 4 (4.7)		

TABLE 2 Prevalence of anxiety and depression at baseline and the changes during the follow-up visits

	No anxiety n (%)	Anxiety n (%)	No depression n (%)	Depression n (%)	GAD-7 median (IQR)	PHQ-9 median (IQR)
First visit	65 (75.6)	21 (24.4)	68 (79.1)	18 (20.9)	6 (7.3)	7.5 (7)
Second visit	81 (94.2)	5 (5.8)	80 (93)	6 (7)	3 (4.3)	3 (6)
Third visit	85 (98.8)	1 (1.2)	84 (97.7)	2 (2.3)	1 (2)	1 (2.3)
Cochran Q	23.1		32.0			
p-value	<0.001 [#]		<0.001 [#]		<0.001 [¶]	<0.001 [¶]

[#]Cochran Q test. [¶]Friedman test; anxiety: GAD-7 score>11; depression: PHQ-9 score >11. GAD-7: seven-item Generalized Anxiety Disorder scale; PHQ-9: Patient Health Questionnaire nine-item depression scale; IQR: interquartile range.

(p=0.005). The mean age of the population with depression was 46±1.5 and that without depression was 40.3±1.5 (p=0.18).

Psychiatry referral

If the GAD-7 or PHQ-9 scores were found to be more than 11 at any stage of assessment, the patients were referred to the department of psychiatry for evaluation. Psychiatry evaluation was indicated in 25 patients (29.1%) of which 12 patients (14%) refused it. Six patients (7%) were given appropriate counselling and seven patients (8.1%) received medication. Changes in the mean values of the GAD-7 and PHQ-9 scores from the first and last visits were significantly higher in the group that had psychiatry referrals and received counselling or medication when compared to the other group (p<0.001). Patients who were started on medication following a psychiatric evaluation showed a significant decrease in mean GAD-7 score compared to patients who were counselled following the referral (12.71±2.62 and 9.33±5.71, respectively, p<0.001). However, the decrease in PHQ-9 score in the above subset was not statistically significant (8.85±5.45 and 8.83±5.07, p=0.053).

Quality of life

HRQoL was assessed twice during the study using the WHOQOL-BREF questionnaire. Domain scores were estimated using the equations given in the WHOQOL-BREF scoring guidelines and subsequently analysed (table 4).

TABLE 3 Association of psychological stress with other parameters

		No anxiety n (%)	Anxiety n (%)	Chi-square	p-value	No depression n (%)	Depression n (%)	Chi-square	p-value																																																																																															
Gender	Male	43 (66.2)	16 (76.2)	0.74	0.38	45 (66.2)	14 (77.8)	0.88	0.34																																																																																															
	Female	22 (33.8)	5 (23.8)			23 (33.8)	4 (22.2)			Education [#]	Illiterate	13 (20)	8 (38.1)	–	0.06	16 (23.5)	5 (27.8)	–	0.47	Primary schooling	19 (29.2)	9 (42.9)	21 (30.9)	7 (38.9)	Pre-university	8 (12.3)	0 (0)	8 (11.8)	0 (0)	Graduate	25 (38.5)	4 (19)	23 (33.8)	6 (33.3)	Employment [#]	Unemployed	16 (24.6)	6 (28.6)	–	0.60	17 (25.0)	5 (27.8)	–	0.74	Employed	41 (63.1)	14 (66.7)	43 (63.0)	12 (66.7)	Student	8 (12.3)	1 (4.8)	8 (11.8)	1 (5.6)	Smoking	No	37 (56.9)	8 (38.1)	2.25	0.13	38 (55.9)	7 (38.9)	1.64	0.19	Yes	28 (43.1)	13 (61.9)	30 (44.1)	11 (61.1)	Alcohol use	No	43 (66.2)	9 (42.9)	3.60	0.05	45 (66.2)	7 (38.9)	4.43	0.03	Yes	22 (33.8)	12 (57.1)	23 (33.8)	11 (61.1)	Complications	Nil	45 (69.2)	14 (66.7)	–	0.84	46 (67.6)	13 (72.2)	–	0.40	Gastritis	14 (21.5)	4 (19)	14 (20.6)	4 (22.2)	Hepatitis	5 (7.7)	2 (9.5)	7 (10.3)	0 (0)
Education [#]	Illiterate	13 (20)	8 (38.1)	–	0.06	16 (23.5)	5 (27.8)	–	0.47																																																																																															
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	Hepatitis	5 (7.7)	2 (9.5)			7 (10.3)	0 (0)																																																																																																	
	Skin Rash	1 (1.5)	1 (4.8)			1 (1.5)	1 (5.6)																																																																																																	

[#]Fischer's exact test was done, as assumption of Chi-square was not met. *p<0.05 (two-tailed).

TABLE 4 Mean WHOQOL-BREF scores at first and last visit

Domains	First visit (mean±sd)	Last visit (mean±sd)	t-value [#]	p-value
Physical health	12.16±3.32	14.98±3.29	-9.95	<0.001
Psychological health	12.54±2.82	14.23±2.62	-5.54	<0.001
Social relationship	12.79±4.61	14.86±3.87	-4.93	<0.001
Environment health	12.25±3.80	15.31±3.63	-8.06	<0.001
Question 1	3.30±1.15	3.89±0.93	-5.00	<0.001
Question 2	3.15±1.12	3.72±1.03	-4.40	<0.001

[#]Paired t-test.

Other than the four major domains of the WHOQOL-BREF questionnaire, the two general questions regarding overall quality of life and general health were also analysed. Among the participants, 18 (20.93%) perceived poor or very poor general HRQoL and 22 (25.58%) had a dissatisfied perception of general health at the baseline, which improved to nine (10.46%) and 15 (17.4%), respectively, at the end of treatment ($p<0.001$).

Quality of life and psychological stress

There was a significant negative correlation between low WHOQOL-BREF domain scores and high PHQ-9 and GAD-7 scores. A high PHQ-9 score at the first visit was associated with a low score in all domains of the WHOQOL-BREF. There was significant correlation between PHQ-9 score and the physical, psychological and environmental domains of WHOQOL-BREF ($p=0.009$, 0.002 and 0.001 , respectively). A high GAD-7 score from the first visit was associated with low scores in all HRQoL domains, which correlated significantly with the psychological and environmental domains ($p=0.002$, $p=0.001$, respectively). All these scores showed improvement at the end of treatment.

Discussion

To the best of our knowledge, there are no prospective Indian studies available that assess both psychological stress and HRQoL in TB patients. Our study demonstrated that anxiety and depression were common among TB patients and there was negative impact on the quality of life.

The demographic results of the study were consistent with other studies. In the study, the majority of patients were male, which was in accordance with the WHO report that 56% of people who developed TB in 2019 were male [1]. The majority were dwelling in thatched and tiled houses with no education or only primary education and one fourth were unemployed. This was in accordance with previous studies that showed that low socio-economic status and poor living conditions such as poor quality of life, inadequate ventilation, poor sanitation and water facilities are strong risk factors for TB [9, 10]

Among the subjects, 20.9% had PHQ-9 score ≥ 11 , suggestive of probable depression, and underwent psychiatry evaluation. Among them, 7% had severe depression as per the scoring. Previous literature determined a higher prevalence of depression among patients with TB, ranging from 43.4% to more than 50% [11, 12]. The high PHQ-9 scores observed in our study from the initial visit reduced significantly to less than 10% at 2 months and at treatment completion ($p<0.001$). The high occurrence of depression among TB patients may be due to the social stigma of the disease, a lack of family support and the complex treatment regimen along with its side effects. The high prevalence of psychological stress at baseline is clinically important for TB care as it may have a negative impact on adherence to TB medications. However, all patients who completed the study adhered to the treatment. During follow-up visits, psychological stress showed a decreasing trend even without psychiatric intervention. However, the changes in GAD-7 and PHQ-9 scores in those received an intervention were significantly higher when compared to the other group. Screening and treatment of psychological stress is important in TB patients as it is associated with poor treatment outcomes such as loss of follow up and death [13].

According to GAD-7 screening, 24.4% were found to have anxiety symptoms requiring psychiatric evaluation. This value was lower when compared to a cross-sectional study that showed more than 40% prevalence of anxiety [11]. Kumar *et al.* also found that more than 50% of TB patients suffer from anxiety [14]. However, a recent cross-sectional study found lower values of prevalence of anxiety and depression [15]. The lower prevalence of psychological stress in our patients may be due to the small sample size and the hospital setting, which makes generalisation of the findings difficult. In our study,

after psychiatric assistance, anxiety symptoms significantly reduced to less than 10% at 2 months and treatment completion. Improvement in psychological stress scores in those who were started on medications were statistically significant compared to others who were given counselling alone ($p < 0.001$).

Various other factors were found to affect psychological stress in TB patients. Increased anxiety and depression found in older individuals may be due to decreased social interactions, activities and social support. Alcoholics had significantly high psychological stress. Illiterates, those with only primary education and smokers had an increased incidence of psychological stress, but this was not statistically significant.

Quality of life scores are multi-dimensional and measured as a broad range, with the primary focus on the physical, mental and functional performance of individuals. Our study found that all the domains, namely physical, physiological, environmental health and social relationships of HRQoL, were poor at the baseline. This was in concordance with other studies and the physical domain was the most affected [16, 17]. The domain scores in our study were found to improve significantly at treatment completion. Other follow-up studies also showed consistent improvements in quality of life during standard antitubercular therapy, but many patients continued to show residual impairment [18]. This implies that HRQoL should be taken into account in various TB programmes along with microbiological cure and reduction of mortality.

There were certain limitations in our study. We had a small sample size and it was conducted in a hospital setting. Hence, the findings cannot be generalised. As the participants were recruited from a single tertiary care teaching hospital, the study population may not be reflective of patients in rural settings and could have led to bias. 29 patients were lost to follow-up and hence excluded from the final analysis. Nine of them (31%) had a baseline anxiety score higher than 11 and four (13%) had a baseline depression score higher than 11 at the time of diagnosis (Supplementary Table 1). The patients who were lost to follow up had higher, but not significant, GAD-7 and PHQ-9 scores at first visit compared to those who completed the study (Supplementary Table 2). WHOQOL-BREF scores were significantly lower in the lost to follow-up group when compared to the other. Lower quality of life might have contributed to skipping the follow-up visits. This could be a reason for selection bias. A few patients with high GAD-7 and PHQ-9 scores refused psychiatry evaluation, which might have affected the proper evaluation and management of such patients. In addition, the findings of this study cannot be applied to multidrug-resistant TB. A large community-based cohort study is needed to identify the impact of psychiatric illness on TB treatment outcome.

In conclusion, TB patients had psychological stress ranging from trivial anxiety to clinical depression and there was significant progressive reduction in the above parameters following treatment. TB had remarkable negative influence on HRQoL, among which the physical domain was the most affected and all the domain scores significantly improved at treatment completion. Hence, routine screening for depression and anxiety and timely referral to a psychiatrist is essential in TB patients and can improve the outcome as well as quality of life.

Provenance: Submitted article, peer reviewed

Conflict of interest: A.R. Febi received a RNTCP PG thesis grant of 30000 INR from the Government of Karnataka for operational research in 2018. She has no other conflict of interest to declare. M.K. Manu has nothing to disclose. A.K. Mohapatra has nothing to disclose. S.K. Praharaj has nothing to disclose. V. Guddattu has nothing to disclose.

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