



Health-Related Quality of Life, Depression and Anxiety in Hospitalized Patients with Tuberculosis

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Background: Much of the attention of tuberculosis (TB) programs is focused on outcomes of microbiological cure and mortality, and health related quality of life (HRQL) is undervalued. Also, TB patients have a significantly higher risk of developing depression and anxiety compared with those in the general population. We intend to evaluate the HRQL and the prevalence of symptoms of depression and anxiety in hospitalized patients with TB.

Methods: Cross-sectional study in a tertiary care hospital in Brazil. Adult patients with pulmonary TB that were hospitalized during the study period were identified and invited to participate. HRQL was measured using the Medical Outcomes Study Short Form-36 (SF-36) version 2. Hospital Anxiety and Depression Scale (HADS) was used to record symptoms of anxiety and depression.

Results: Eighty-six patients were included in the analysis. The mean age of all patients was 44.6±15.4 years, 69.8% were male, and 53.5% were white. Thirty-two patients (37.2%) were human immunodeficiency virus positive. Twenty-seven patients (31.4%) met study criteria for depression (HADS depression score ≥11) and 33 (38.4%) had anxiety (HADS anxiety score ≥11). Scores on all domains of SF-36 were significantly lower than the Brazilian norm scores ($p < 0.001$).

Conclusion: The present study shows that TB patients may have a poor HRQL. Additionally, we found a possible high prevalence of depression and anxiety in this population. Health care workers should be aware of these psychological disorders to enable a better management of these patients. The treatment of these comorbidities may be associated with better TB outcomes.

Keywords: Tuberculosis; *Mycobacterium tuberculosis*; Mental Disorders; Depression; Anxiety; Comorbidity; Quality of Life

Introduction

Tuberculosis remains a public health threat with significant annual impacts on morbidity and mortality. Brazil is ranked 16th among the 22 high-burden countries that collectively account for 80% of tuberculosis (TB) cases globally, with an incidence of 33.5 cases/100,000 inhabitants/yr in 2014. The city of Porto Alegre has the highest incidence of TB in the country (99.3 cases/100,000 inhabitants/yr in 2014)¹.

At present, much of the attention of TB programs is focused on outcomes of microbiological cure and mortality, and health related quality of life (HRQL) is undervalued. HRQL may be fundamental in influencing treatment outcome. Studies showed that as compared with the general population, TB pa-

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tients reported reductions in their physical health, psychological health, and social functioning^{2,3}. There are several aspects of TB that may lead to deficits in HRQL, like social stigma, prolonged therapy, potentially toxic drugs, lack of knowledge regarding the disease and its treatment, anxiety, and depression⁴⁻⁷.

TB patients have a significantly higher risk of developing depression compared with those in the general population⁸. Depression in individuals with TB is associated with delays in seeking health care and poor treatment compliance, that can lead to drug resistance, morbidity and mortality⁹. Rates of mental illness of up to 70% have been identified in TB patients¹⁰. In a study that evaluated hospitalized TB patients, depression was present in about 80%¹¹. Anxiety disorder is also high among patients with TB¹².

The evaluation of HRQL and the identification of psychiatric comorbidities, such as depression and anxiety, in patients with TB are important for characterizing the physical and mental health of these patients. It is possible that these factors have an influence on treatment adherence, and their knowledge can enable a better understanding of the attitudes of these patients regarding their disease. Therefore, the aim of this study is to evaluate the HRQL, the prevalence of symptoms of depression and anxiety in hospitalized patients with TB, and to compare the characteristics of patients with and without depression, and with or without anxiety.

Materials and Methods

We conducted a cross-sectional study in a general, tertiary care, university-affiliated hospital with 750 beds, located in the city of Porto Alegre, Rio Grande do Sul State, in southern Brazil. The study was approved by the Ethics Committee at Hospital de Clínicas de Porto Alegre in January 22, 2013 (number 13-0022).

Adult patients (≥ 18 years old) with pulmonary TB that were hospitalized during the study period (January 2013–June 2015) were identified and invited to participate. We included only the patients who began treatment for TB after hospitalization. Patients who were already receiving treatment at admission, who are unable to comply with study procedures and those who refused signing the consent form were excluded from this study. Pulmonary TB was diagnosed according to the Brazilian Guidelines for Tuberculosis¹³.

The following data were collected from patient records using a standardized data extraction tool: demographic data (sex, age, race, and years of schooling), behavioral data (smoking status, alcohol abuse, and injection drug use), and medical history (clinical form of TB, symptoms at admission, methods of diagnostic, presence of comorbidities, prior TB treatment, drug regimen, interval from hospital admission until diagnosis, length of hospital stay, intensive care unit [ICU] admission,

length of mechanical ventilation, and hospitalization outcome [death or discharge]). A current smoker was defined as reporting smoking at least 100 cigarettes in their lifetime, and at the time of the survey were smoking at least one day a week. A former smoker was defined as reporting smoking at least 100 cigarettes in their lifetime but who, at the time of the survey, did not smoke at all. Never smoked reported having smoked <100 cigarettes in their lifetime. Alcohol abuse was defined as daily consumption of at least 30 g (equivalent to a pint and a half of 4% beer) for men and 24 g (equivalent to a 175 mL glass of wine) for women. An independent physician analyzed the chest X-rays and classified them as typical or compatible with active TB, according to previously described guidelines¹⁴.

HRQL was measured using the Medical Outcomes Study Short Form-36 (SF-36) version 2, which is a reliable, validated questionnaire^{15,16}. This questionnaire contains eight domains assessing diverse aspects of health including physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health, and two summary measures, physical and mental components. For all the SF-36 domains, higher scores indicate better health. Brazilian normative data for the SF-36 version 2 were used for comparative purposes¹⁷. Scores of Brazilian men and women ranged according to age and gender were included as a Supplementary Tables 1 and 2.

Human immunodeficiency virus (HIV) positive patients also completed the World Health Organization Quality of Life instrument for HIV clients (WHOQOL-HIV). Several specific instruments for individuals with HIV are found in the international literature, but only the WHOQOL-HIV was validated for use in Brazil^{18,19}. This questionnaire will be administered by the possibility of change in HRQL be related to HIV (and not tuberculosis, or even due to the two diseases). This instrument contains 31 items and for each item there is a fivepoint Likert scale where 1 indicates low or negative perceptions and 5 high or positive perceptions. These items contain six domains: physical health (4 items), psychological well being (5 items), social relationship (4 items), environmental health (8 items), level of independence (4 items), and spiritual health (4 items). There were two general questions about general QOL and perceived general health. The physical domain contained information regarding presence of pain, energy, and sleep. The psychological domain consisted of negative and positive feelings, self esteem, and thinking. The social domain covered social support, personal relationships and sexual activity. Mobility, work capacity, and activities were included in the level of dependence. Financial issues; home and physical environment; availability of transport; physical safety and security, and participation in leisure activities were included under the environmental domain. The spirituality domain did contain questions about death and dying; forgiveness and blame and concern about the future.

The Hospital Anxiety and Depression Scale (HADS)²⁰, pre-

viously validated in Brazil²¹, was used to record symptoms of anxiety and depression. This questionnaire was developed to identify caseness (possible and probable) of anxiety disorders and depression among patients in nonpsychiatric hospital clinics, not with the diagnostic purpose, but as screening. It avoids recording details of the biological symptoms of depression that might arise as a result of the physical complaints. It is divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D) both containing seven questions. The overall score for each subscale goes from 0 to 21. Scores of 11 or above on the anxiety or depression subscale are taken as indicative of probable for either disorder.

Also, self-esteem was evaluated by Rosenberg's Self-Esteem Scale, validated in Brazil²². This is a one-dimensional measure, and consists of 10 statements related to a set of feeling of self-esteem and of self-acceptance that assesses global self-esteem. The items are answered in a Likert scale of four points: strongly agree, agree, disagree, and strongly disagree. The overall score goes from 10 to 40. Scores ≤ 15 indicate low self-esteem.

Data analysis was performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Data were presented as number of cases, mean \pm standard deviation, or median with interquartile range. Categorical comparisons were performed by chi-square test using Yates's correction if indicated or by Fisher exact test. Continuous variables were compared using the t test or Wilcoxon test. SF-36 results were compared with Brazilian normative data using a paired t test. A two-sided p-value < 0.05 was considered significant for all analyses.

Sample size calculation was based on a previous study²³. Considering an expected proportion of 0.70 (prevalence of symptoms of depression and anxiety, 70%), an amplitude of the confidence interval of 0.20 and a 95% confidence level, we estimated a sample size of 81 patients.

Results

One hundred nineteen patients met the inclusion criteria. Seventeen patients refused to participate and 16 were unable to comply with study procedures (all were ICU patients), then 86 patients were included in the analysis. The characteristics of participants are summarized in Table 1. The mean age of all patients was 44.6 \pm 15.4 years, 69.8% were male, and 53.5% were white. Thirty-two patients (37.2%) were HIV positive.

Twenty-seven patients (31.4%) met study criteria for depression (HADS depression score ≥ 11) and 33 (38.4%) had anxiety (HADS anxiety score ≥ 11). Scores on all domains of SF-36 were significantly lower than the Brazilian norm scores ($p < 0.001$) (Table 2). Patients with probable depression were more frequently current smokers (44.4%) than patients with no probable depression (15.3%) ($p = 0.008$) (Table 3). Low self-esteem was more common in patients with probable de-

Table 1. Characteristics of study patients (n=86)

Characteristic	Value
Demographic characteristic	
Age, yr	44.6 \pm 15.4
Male sex	60 (69.8)
White race	46 (53.5)
<8 years of schooling*	57 (66.3)
Current smokers	21 (24.4)
Alcoholism	30 (34.9)
Drug use	29 (33.7)
Symptoms	
Cough	72 (83.7)
Night sweats	56 (65.1)
Fever	59 (68.6)
Weight loss	72 (83.7)
Previous TB	17 (19.8)
Previous default from TB treatment	13 (15.1)
Comorbidities	
HIV positive	32 (37.2)
Diabetes mellitus	3 (3.5)
Radiographic patterns	
Typical of TB	56 (65.1)
Compatible with TB	30 (34.9)
HADS depression score ≥ 11	27 (31.4)
HADS anxiety score ≥ 11	33 (38.4)
Rosenberg's Self-Esteem Scale score ≤ 15	20 (23.3)
SF-36v2 health domain scores	
Physical functioning	45.0 (13.8–86.3)
Role-physical	0 (0–25.0)
Bodily pain	52.0 (20.0–84.0)
General health	45.0 (30.0–60.0)
Vitality	50.0 (32.5–75.0)
Social functioning	50.0 (12.5–100)
Role-emotion	0 (0–66.6)
Mental health	56.0 (28.0–80.0)
Physical component score	38.9 (33.6–44.2)
Mental component score	40.7 (37.7–44.9)
WHOQOL-HIV domain scores [†]	
Physical	11.4 \pm 2.8
Psychological	11.9 \pm 2.6
Social	13.0 \pm 3.8
Environmental	12.2 \pm 2.6
Level of independence	13.3 \pm 2.6
Spiritual	10.9 \pm 3.8

Values are presented as n (%), mean \pm standard deviation, or median (interquartile range).

*In Brazil, the primary (or elementary) school cycle is 8 years long.

[†]The scores range between 4 and 20, where higher scores denote higher quality of life.

TB: tuberculosis; HIV: human immunodeficiency virus; HADS: Hospital Anxiety and Depression Scale; SF-36v2: Medical Outcomes Study Short Form-36 version 2; WHOQOL-HIV: World Health Organization Quality of Life instrument for HIV clients.

Table 2. Comparison between SF-36 scores and Brazilian norm scores

Scores	Study group score	Brazilian norm score	p-value
Physical functioning	48.4±36.5	80.5±10.4	<0.001
Role-physical	15.99±29.7	81.4±7.9	<0.001
Bodily pain	52.0±35.3	80.5±6.8	<0.001
General health	46.2±19.7	73.2±7.0	<0.001
Vitality	51.6±27.8	74.6±4.6	<0.001
Social functioning	52.3±38.8	86.7±5.1	<0.001
Role-emotion	29.8±42.5	84.7±5.7	<0.001
Mental health	53.7±31.3	76.6±3.7	<0.001
Physical component score	38.9±7.9	51.1±3.9	<0.001
Mental component score	40.7±4.5	52.3±2.6	<0.001

Values are presented as mean±standard deviation.
SF-36: Medical Outcomes Study Short Form-36.

pression (55.6% vs. 8.5%, $p<0.001$). Probable depression was significantly associated with six of the SF-36 domain scores (physical functioning, general health, vitality, social functioning, role emotional, and mental health). In addition, HIV patients with probable depression had a lower quality of life in all but one domain (physical) of WHOQOL-HIV as compared with HIV patients with no probable depression.

Patients with probable anxiety had more frequently a history of default from TB treatment (69.2%) than patients with no probable anxiety (30.8%) ($p=0.016$) (Table 4). HIV diagnosis was significantly more common in patients with probable anxiety (57.6% vs. 24.5%, $p=0.004$). Six of the SF-36 domain scores (bodily pain, general health, vitality, social functioning, role emotional, and mental health) were significantly reduced in patients with probable anxiety as compared with patients with no probable anxiety. Significantly lower median social, environmental, and level of independence domains were reported by patients with probable anxiety.

Discussion

The present study was an attempt to evaluate the HRQL and the prevalence of symptoms of depression and anxiety in hospitalized patients with TB. We found that the scores on all domains of SF-36 were significantly lower than the Brazilian norm scores. In addition, more than one third of patients had a diagnosis of depression (31.4%) or anxiety (38.4%), according to HADS.

According to the World Health Organization (WHO), health is defined as a state of complete physical, mental, and social well-being and not a mere absence of disease²⁴. Therefore, we have to consider that any disease will impact not only on physical health but also on all other aspects of an individual's health. Thus, TB has a substantial and encompassing impact

on patients' quality of life. Median domain scores of SF-36 reported by participants in this study were significantly lower than the Brazilian norm scores. Several studies have showed that TB patients reported deficits in their physical and mental well-being in comparison with the general population^{2,3}. Also, one study³ demonstrated that even after treatment completion and microbiological cure, TB patients may still have significantly lower HRQL when compared to U.S. norms.

HRQL was even lower among patients who met depression or anxiety criteria in our study. This is an important finding once we also demonstrated that more than one third of patients met the study criteria for depression or anxiety. Studies have shown that the prevalence of depression and other psychiatric disorders, like generalized anxiety disorder, adjustment disorder and organic brain disorders, is high among patients with TB^{12,25}. Although rates of major depression are expected to be higher in those individuals with medical illness than in the general population, they may be still higher in TB patients²⁶. In a previous investigation¹¹, depression was present in about 80% of the TB patients, using Beck's Depression Inventory. In this study, it was more common in males, and young and elderly patients. In addition, they found that the main factors associated with depression were altered social relationships, among male TB patients, and TB stigma among females. One study also conducted with hospitalized TB patients, the authors demonstrated that 68% of patients met the criteria for depression²⁷. These different prevalence rates might possibly be due to the differences in the sensitivity of the depression screening instruments used.

Depressive disorder in TB patients has been recognized as a cause of poor treatment compliance and poor disease outcomes, like treatment default or death²⁸. A retrospective cohort analysis of 440 TB patients has revealed a high rate of relapse due to poor medication compliance, and psychiatric disorders have been implicated²⁹. Several factors were signifi-

Table 3. Factors associated with a HADS depression score ≥ 11 (probable depression)

Variable	HADS depression score ≥ 11 (n=27)	HADS depression score < 11 (n=59)	p-value
Age, yr	43.6 \pm 13.4	45.1 \pm 16.3	0.686
Male sex	17 (63.0)	43 (72.9)	0.499
White race	13 (48.1)	33 (55.9)	0.661
< 8 years of schooling	19 (70.4)	38 (64.4)	0.766
Current smokers	12 (44.4)	9 (15.3)	0.008
Cough	24 (88.9)	48 (81.4)	0.534
Weight loss	22 (81.5)	50 (84.7)	0.947
Previous TB	4 (14.8)	13 (22.0)	0.625
Previous default from TB treatment	4 (30.8)	9 (69.2)	0.617
HIV	14 (51.9)	18 (30.5)	0.097
Smear positive	17 (63.0)	41 (69.5)	0.549
Cavity	10 (37.0)	17 (28.8)	0.446
Low self-esteem	15 (55.6)	5 (8.5)	<0.001
Probable anxiety	19 (57.6)	14 (42.4)	<0.001
SF-36v2 domain			
Physical functioning	25.0 (5.0–45.0)	65.0 (20.0–95.0)	0.002
Role-physical	0 (0–0)	0 (0–25.0)	0.091
Bodily pain	41.0 (10.0–64.0)	52.0 (20.0–100)	0.157
General health	35.0 (25.0–40.0)	50.0 (40.0–67.0)	<0.001
Vitality	25.0 (5.0–45.0)	65.0 (50.0–80.0)	<0.001
Social functioning	25.0 (12.5–62.5)	62.5 (25.0–100)	0.028
Role-emotion	0 (0–0)	0 (0–100)	0.049
Mental health	24.0 (4.0–40.0)	76.0 (44.0–88.0)	<0.001
Physical component score	38.9 (32.2–44.2)	38.9 (33.6–44.2)	0.837
Mental component score	40.8 (35.6–44.9)	41.3 (37.7–44.9)	0.670
WHOQOL-HIV domain*			
Physical	10.9 \pm 2.8	11.8 \pm 2.8	0.402
Psychological	10.7 \pm 2.3	12.7 \pm 2.6	0.033
Social	10.4 \pm 3.4	15.1 \pm 2.7	<0.001
Environmental	10.7 \pm 2.1	13.3 \pm 2.4	0.003
Level of independence	12.1 \pm 2.3	14.2 \pm 2.5	0.023
Spiritual	9.4 \pm 3.9	12.1 \pm 3.3	0.038

Values are presented as mean \pm standard deviation, number (%), or median (percentile 25–percentile 75).

*n=32.

HADS: Hospital Anxiety and Depression Scale; TB: tuberculosis; HIV: human immunodeficiency virus; SF-36v2: Medical Outcomes Study Short Form-36 version 2; WHOQOL-HIV: World Health Organization Quality of Life instrument for HIV clients.

cantly associated with depression in persons with a TB diagnosis, like personal, socio-demographic (age and financial status), environmental, and clinical (persistent cough)²⁸. In our study, low self-esteem and current smoking were significantly associated depression.

We found that patients with probable depression were significantly more likely to have low self-esteem. Also, approximately 20% of our sample had criteria for low self-esteem according to Rosenberg scale. Another study with hospitalized patients with TB showed that self-esteem scores dropped in

Table 4. Factors associated with a HADS anxiety score ≥ 11 (probable anxiety)

Variable	HADS anxiety score ≥ 11 (n=33)	HADS anxiety score < 11 (n=53)	p-value
Age, yr	42.1 \pm 10.4	46.2 \pm 17.7	0.184
Male sex	20 (60.6)	40 (75.5)	0.223
White race	13 (39.4)	33 (62.3)	0.065
<8 years of schooling	24 (72.7)	33 (62.3)	0.445
Current smokers	11 (33.3)	10 (18.9)	0.208
Cough	31 (93.9)	41 (77.4)	0.085
Weight loss	27 (81.8)	45 (84.9)	0.706
Previous TB	10 (30.3)	7 (13.2)	0.097
Previous default from TB treatment	9 (69.2)	4 (30.8)	0.016
HIV	19 (57.6)	13 (24.5)	0.004
Smear positive	18 (54.5)	40 (75.5)	0.050
Cavity	12 (36.4)	15 (28.3)	0.433
Probable depression	19 (57.6)	8 (15.1)	<0.001
Low self-esteem	15 (45.5)	5 (9.4)	<0.001
SF-36v2 domain			
Physical functioning	35.0 (20.0–85.0)	50.0 (7.5–90.0)	0.765
Role-physical	0 (0–12.5)	0 (0–37.5)	0.324
Bodily pain	31.0 (10.0–63.0)	62.0 (31.0–100)	0.004
General health	40.0 (25.0–54.5)	47.0 (36.0–63.5)	0.049
Vitality	40.0 (15.0–52.5)	65.0 (45.0–80.0)	<0.001
Social functioning	25.0 (12.5–62.5)	75.0 (25.0–100)	0.001
Role-emotion	0 (0–0)	0 (0–100)	0.001
Mental health	28.0 (12.0–40.0)	76.0 (56.0–88.0)	<0.001
Physical component score	38.9 (35.9–44.2)	38.9 (33.6–44.3)	0.971
Mental component score	40.8 (37.7–44.9)	41.3 (37.7–44.9)	0.724
WHOQOL-HIV domain (n=32)			
Physical	11.1 \pm 3.1	11.9 \pm 2.4	0.470
Psychological	11.3 \pm 2.7	12.7 \pm 2.3	0.144
Social	11.9 \pm 3.9	14.7 \pm 3.1	<0.001
Environmental	10.9 \pm 2.2	14.1 \pm 1.9	<0.001
Level of independence	12.0 \pm 2.3	15.1 \pm 2.0	<0.001
Spiritual	10.6 \pm 4.0	11.4 \pm 3.5	0.561

Values are presented as mean \pm standard deviation, number (%), or median (interquartile range).

HADS: Hospital Anxiety and Depression Scale; TB: tuberculosis; HIV: human immunodeficiency virus; SF-36v2: Medical Outcomes Study Short Form-36 version 2; WHOQOL-HIV: World Health Organization Quality of Life instrument for HIV clients.

accordance with category of depression, revealing that low self-esteem is a characteristic of depression²⁵. Stigmatization, negative emotions, social rejection, and isolation were reported by TB patients and could contribute to low self-esteem and impairment of psychosocial well-being^{2,3}.

In our study, individuals with TB who screened positive for

depression were more likely to be current smokers. The high prevalence of cigarette smoking among people with chronic mental illness is well known³⁰. Smoking was associated with a nearly two-fold increased risk of depression relative to both never smokers and former smokers³¹. This finding is especially important since previous investigations have emphasized the

impact of smoking on many aspects of TB, such as TB infection, TB disease, and mortality^{32,33}. Indeed, mortality from TB is four times greater among smokers than among nonsmokers³².

We also found a significant association between HIV infection and anxiety. Mental health problems such as anxiety and depression in patients infected with HIV is well documented³⁴. In a study³⁵ that evaluated 649 adult patients with HIV, TB or both, the frequency of any anxiety disorder was 30.8%, and the rates of generalized anxiety disorder were highest for the HIV group. Previous default from TB treatment was also statistically associated with symptoms of anxiety in our study. It is possible that these patients were afraid of the consequences of having abandoned treatment, and this thought is reflected in a higher prevalence of anxiety.

The study has certain limitations. One of the limitations of the study is that it is cross-sectional in design thus causal relationships cannot be inferred. In addition, we evaluated only TB patients and did not compare HRQL scores with a control group. We used the SF-36, and then we compared results to the Brazilian population norms, which could neutralize this limitation. However, the Brazilian norm scores (SF-36) were obtained from a dataset of general population, which can be biased because hospitalization itself and not TB can make patients' HRQL scores lower, and depression and anxiety scores higher. Comparisons between hospitalized TB patients and patients hospitalized with other diseases, and comparisons between hospitalized TB patients and TB patients treated only in outpatient clinics are needed to get reliable conclusions. In spite of these restrictions, knowing patients' HRQL is important to understand the well being of TB patients and to plan actions to improve their health outcomes. Also, the identification and prompt treatment of depression and anxiety in patients with TB may be helpful increasing treatment compliance and reducing relapse.

In conclusion, the present study shows that TB patients may have a poor HRQL. Additionally, we found a possible high prevalence of depression and anxiety in this population. Health care workers should be aware of these psychological disorders to enable a better management of these patients. The treatment of these comorbidities may be associated with better TB outcomes.

Supplementary Material

Supplementary material can be found in the journal homepage (<http://www.e-trd.org>).

Supplementary Table S1. Descriptive measures of the standardized scores for the eight domains of the 36-item Short Form and for the two summary measures (physical and mental component) of the Brazilian male population by age groups.

Supplementary Table S2. Descriptive measures of the standardized scores for the eight domains of the 36-item Short Form and for the two summary measures (physical and mental component) of the Brazilian female population by age groups.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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