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Retrospective Study

Association between depression and malnutrition in pulmonary tuberculosis patients: A cross-sectional study

Fang XE *et al*. Depression and nutritional status in PTB

Abstract

BACKGROUND

Depression has been reported to be prevalent in patients with pulmonary tuberculosis (PTB). Moreover, several clinical symptoms of PTB and depression overlap, such as loss of appetite and malnutrition. However, the association between depression and malnutrition in TB patients has not been fully elucidated.

AIM

To explore the association between depression and malnutrition in patients with PTB.

METHODS

This hospital-based cross-sectional study included patients with PTB in Shanghai Pulmonary Hospital Affiliated to Tongji University from April 2019 to July 2019. The Patient Health Questionnaire-9 (PHQ-9) scale was used to evaluate depression. The cut-off value was set at 10, and the nutritional state was determined by the body mass index (BMI). In addition, the Quality of Life Instruments for Chronic Diseases was employed to establish the quality of life (QOL). Univariable analysis and multivariable analysis (forward mode) were implemented to identify the independent factors associated with depression.

RESULTS

A total number of 328 PTB patients were screened for analysis. Eight were excluded for missing demographic data, 4 were excluded for missing nutrition status, and 16 were excluded for missing QOL data. Finally, 300 PTB patients were subjected to analysis. We found that depressive state was present in 225 PTB patients (75%). The ratio of malnutrition in the depressive PTB patients was 45.33%. Our results revealed significantly lower BMI, hemoglobin, and prealbumin in the depression group than those in the control group (all $P < 0.05$). Moreover, the social status differed significantly ($P < 0.05$) between the groups. In addition, glutamic pyruvic transaminase and glutamic

oxaloacetic transaminase in the depression group were significantly higher than those in the control group (all $P < 0.05$). Multivariable logistic regression analysis showed that BMI [odd ratio (OR) = 1.21, 95% confidence interval (CI): 1.163-1.257, $P < 0.001$] and poor social function (OR = 0.95, 95%CI: 0.926-0.974, $P = 0.038$) were independently associated with depression.

CONCLUSION
Malnutrition and poor social function were significantly associated with depressive symptoms in PTB patients. A prospective large-scale study is needed to confirm these findings.

Key Words: Depression; Pulmonary tuberculosis; Malnutrition; Quality of life; Comorbidity; China

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Core Tip: In this hospital-based cross-sectional study, the data of 300 pulmonary tuberculosis (PTB) patients were subjected to analysis. The ratio of malnutrition in tuberculosis-depression syndemic patients was 45.33%. We found that body mass index and poor social function were independently associated with depression. Our present findings suggest that the early diagnosis and management of depression in patients with PTB can decrease the burden of malnutrition and improve outcomes.

INTRODUCTION
Pulmonary tuberculosis (PTB), a chronic wasting disease, is a chronic pulmonary infection which is caused by *Mycobacterium tuberculosis*. An estimated 9.0-11.1 million PTB cases were diagnosed in 2018 worldwide, 1.0 million of which were children[1]. PTB

presents as a global public health problem, and the situation in developing countries, including China, is even worse. Despite the decreasing trend of PTB prevalence in China, PTB remains a considerable threat to public health due to the high number of PTB patients and the multidrug-resistant PTB burden[2]. Cumulative evidence revealed that depression was prevalent in people with chronic diseases[3]. In addition, the ratio of PTB patients with depression was higher than that in healthy populations[4]. In a hospital-based cross-sectional study conducted in Cameroon, Kehbila *et al*[5] found that more than 50% PTB patients were affected by depression. In Manila, the Philippines, approximately 16.8% of the PTB patients reportedly had depression[6]. However, no hospital-based study has been published on the prevalence of this state in patients with PTB in China. Previous reports have evidenced that human immune deficiency virus infection, poor social support, and perceived stigma are risk factors for the development of depression in PTB patients[7-9]. Moreover, the depression in patients with PTB is associated with insufficient health care and poor treatment compliance, which has led to drug resistance, morbidity, and mortality[10], negatively affecting the health-related quality of life (QOL) of PTB patients[11,12]. Additionally, PTB patients were susceptible to malnutrition, with a ratio of malnutrition from 38.3% to 75.0%[13]. Furthermore, malnutrition also triggered PTB relapse and increased mortality[14,15]. Appropriate and timely intervention for malnutritional and/or depressed PTB patients is a medical need. We hypothesized that depression may be prevalent in malnutritional PTB patients in China. Therefore, in this study, we aimed to evaluate the association between depression and malnutrition in PTB patients in China.

MATERIALS AND METHODS

Study design

This study is a hospital-based cross-sectional study, which was conducted from April to July 2019 in Shanghai Pulmonary Hospital Affiliated to Tongji University, China. Patients with PTB were consecutively recruited for analysis. The inclusion criteria were as follows: (1) Clear consciousness; (2) Ability to communicate; (3) Patients who have

provided informed consent and voluntarily participated in this study; and (4) Age above 18 years. The following exclusion criteria were applied: (1) A history of mental illness; (2) Complications, such as disturbance of consciousness, chronic respiratory failure, and pulmonary encephalopathy; (3) Metabolic-related diseases such as thyroid disease; (4) Requirements for continuous non-invasive or invasive ventilation; (5) Unstable hemodynamics; (6) Cardiac or renal insufficiency; and (7) Extrapulmonary tuberculosis. All subjects provided written informed consent. The study protocol was approved by the Ethics Committee (No. K19-146).

Data collection

Data including age, educational level, occupation, marital status, body mass index (BMI), income, comorbidity, treatment duration, hemoglobin (Hb), albumin, liver function [alanine transaminase (ALT), aspartic acid aminotransferase (AST)], and medical cost origin were collected by nurses (Fang XE, Chen DP, and Tang LL) who received uniform training by face-to-face interviews. On post-admission day, the patient's height and weight were measured. The height was measured using a calibrated ruler ($\pm$ 0.5 cm); the actual body weight was measured using a corrected scale ($\pm$ 0.2 kg). BMI was calculated as [weight (kg)/height (m)^2]. Next, BMI was used to assess the nutritional status[16] (Supplementary Table 1), and BMI less than 18.5 kg/m^2 was considered to represent malnutrition[17].

Patient Health Questionnaire-9

Depression was evaluated by Patient Health Questionnaire-9 (PHQ-9)[18], which consists of nine questions and has been validated in China with a Cronbach's alpha value higher than 0.8. Each item was scored as 0 (not at all), 1 (several days), 2 (more than half of the days), or 3 (nearly every day); the total score ranged from 0 to 27. A PHQ-9 value higher than 10 showed a higher susceptibility to depression[19]. Hence, the included PTB patients were divided into two groups: Depression and control, based on a PHQ-9 threshold of 10.

QOL assessment

The level of QOL was assessed by QLICD-PT[20], which has been validated in China with a Cronbach's alpha value higher than 0.7. QLICD-PT includes three domains and a specific model: Physiological function (basic physiological function, independence, energy, and discomfort), psychological function (cognition, emotion, will, and personality), social function (interpersonal interaction, social support, and social role), and specific module (respiratory symptoms, systemic symptoms, drug side effects, and special psychology).

Sample size: The sample size for this study was calculated using the formula: $n = (z)^2 p(1-p)/e^2$, z is 1.96 [the value at 95% confidence interval (CI)], e is the standard error (estimated at 1/8), and p is the ratio of depression. We estimated that 50% of the PTB patients would develop depression. Considering a potential 20% loss, we established that at least 300 PTB patients for inclusion were required.

Statistical analysis

SPSS software (version 20.0 Chicago, IL, United States) was used to analyze the data. Continuous data are presented as mean ± SD. Normality distribution was determined by Shapiro-Wilk test. Student's independent *t*-test or Mann-Whitney test was used depending on the normality. Categorical data are expressed as a number (percentage) and analyzed using c^2 test. Univariable analysis was applied to identify the independent factors which are associated with depression. To identify potential confounders, factors with $P < 0.1$ in the univariable analysis were entered into the multivariable logistic regression model and were assessed using the forward mode. $P < 0.05$ was considered to indicate statistically significant differences.

RESULTS

Demographic data

A total number of 328 PTB patients were recruited. Of them, we excluded 8 for missing data, 4 for missing nutrition indicators of blood, and 16 for missing QLICD-PT scale data. Finally, 300 PTB patients (91.46%) were subjected to analysis (Figure 1). The mean age of the respondents was 35.96 years (± 13.17; range 21-40, median 30). A number of 189 (63%) were men, 180 (60%) were married, 93 (31%) had undergraduate education, and 170 (56.67%) were unemployed (Table 1).

Factors associated with depression in PTB patients
Based on the PHQ-9 score at 10, the PTB patients were divided to depression (n = 225, 75%) and control (n = 75, 25%) groups. The ratio of malnutrition among depressive status with PTB patients was 45.33% (Table 2). No statistically significant differences were detected between the groups in age, gender, marital status, education level, occupation, monthly income, TB treatment duration, comorbidity, and origin of medical costs (all $P > 0.05$). The values of BMI ($P < 0.001$), Hb ($P < 0.05$), prealbumin ($P < 0.05$), and social function of QLICD-PT ($P < 0.05$) in the depression group were significantly lower than those in the control group. In addition, AST and ALT in the depression group were significantly higher than those in the control group (Table 2). Finally, logistic regression analysis was used to evaluate the possible factors that influence depression. As can be seen in Table 3, BMI [Odd ratio (OR) = 1.21, 95%CI: 1.163-1.257, P < 0.001] and poor social function (OR = 0.95, 95%CI: 0.926-0.974, P = 0.038) were independently associated with depression.

DISCUSSION
The assessment of the depressive state in patients with PTB using the PHQ-9 scale showed that 75% of the study subjects developed depression. In addition, the results of the present study also suggest that nutritional status and social function were independent risk factors for depression. In clinical practice, nutrition management and psychological counseling for PTB patients are highly necessary.

The prevalence of depression in the PTB patients included in the present study was estimated to be higher than that determined in other studies; for example, it was 41.1% in Nigeria[21], 61.1% in Cameron[5], 56% in Pakistan[22], 54% in Ethiopia[23], and 69.6% in Liaoning Province of China[3]. In other investigations, the comorbidity of mental disorders in hospitalized patients ranged from 19%[24] to 80%[25]. In research performed in the Philippines, the depressive state among PTB patients was 16.8%[6]. These findings suggest that the depressive state in PTB patients varies and is country-specific. In the present study, the depression ratio was 75%, which was higher than those in most of the published reports. This discrepancy may be due to differences in the sample size, race, country-specific features, patient populations (hospitalized or not), and the specific depression assessment tool implemented.

Here, we found that the ratio of malnutrition among depressive PTB patients was 45.33%. Patients with non-depression status had higher levels of BMI, Hb, and prealbumin than patients with depression. Furthermore, the ratio of anemia among depressive PTB patients was 86.32%, which may due to the effect of TB on red blood cell production, such as decreased erythrocyte lifespan, poor erythrocyte iron incorporation, and decreased sensitivity to erythropoietin[16]. Masumoto *et al*[6] also recommended that additional attention should be exerted to malnourished PTB patients and those with poor social support to identify depression. Therefore, nutritional support for PTB patients may be necessary.

Nutrition problems may be caused by mental health issues, and thus the symptoms of malnutrition and psychological distress may overlap[26]. In this study, we found an association between malnutrition and depression, in which. The following factors might be involved or causative: (1) Depression may lead to loss of appetite and digestive dysfunction; (2) Continuous mental stimulation leads to serious vegetative nerve dysfunction and endocrine imbalance, which affects the body's absorption of nutrients; and (3) The disease itself can increase catabolism, promoting protein decomposition and reducing protein synthesis. In addition, a negative association between depression and poor social function may exist. There may be a vicious circle, including malnutrition,

QOL, and depression. Malnutrition may aggravate depression and seriously affect the QOL, while the loss of appetite in depressed patients can lead to malnutrition.

This study is not without limitations. As it was hospital-based cross-sectional, the risk factors for depression in different treatment periods in patients with PTB could not be identified. Additionally, no additional validation of the depression and QOL scales was performed. Moreover, the nutritional status was evaluated by BMI, while many other indicators could also reflect the nutritional status. The energy intake was not assessed, which could have introduced bias. Furthermore, data of the severity of PTB were not collected. Socio-economic status was reported to be a confounding factor between nutritional status and depression[27]. However, we did not explore that association.

CONCLUSION

In conclusion, the findings of the present study suggest that depression is common in hospitalized PTB patients, and psychological counseling or management and nourishment adjustments may be needed. To confirm the findings of the present study, a well-designed prospective large-scale study is needed.

ARTICLE HIGHLIGHTS

Research background

It has been reported that depression is prevalent in patients with pulmonary tuberculosis (PTB). Moreover, several clinical symptoms of PTB and depression overlap, such as loss of appetite and malnutrition. However, the association between depression and malnutrition in TB patients has not been fully understood.

Research motivation

The present study aimed to explore the association between depression and malnutrition in patients with PTB.

Research objectives

The present study aimed to explore the association between depression and malnutrition in patients with PTB.

Research methods

This hospital-based cross-sectional study included patients with PTB in Shanghai Pulmonary Hospital Affiliated to Tongji University from April 2019 to July 2019. The Patient Health Questionnaire-9 (PHQ-9) scale was used to evaluate depression and the cut-off value was set at 10, and the nutritional state was determined by the body mass index (BMI). In addition, the Quality of Life Instruments for Chronic Diseases was employed to quantify the quality of life (QOL). Univariable analysis and multivariable analysis (forward mode) were used to identify the independent factors associated with depression.

Research results

A total number of 328 PTB patients were screened for analysis. 8 were excluded for missing demographic data, 4 were excluded for missing nutrition status and 16 were excluded for missing QOL data. Finally, 300 PTB patients were subjected to analysis. It was found that depressive state was presented in 225 PTB patients (75%). The ratio of malnutrition in the depressive PTB patients was 45.33%. It was found that BMI, hemoglobin, and prealbumin in the depression group were significantly lower than those in the control group (all $P < 0.05$). Moreover, the social status ($P < 0.05$) was significantly differed between the groups. In addition, glutamic pyruvic transaminase and glutamic oxaloacetic transaminase in the depression group were significantly higher than those in the control group (all $P < 0.05$). Multivariable logistic regression analysis showed that BMI [Odd ratio (OR) =1.21, 95% confidence interval (CI): 1.163-1.257, $P < 0.001$] and poor social function (OR = 0.95, 95%CI: 0.926-0.974, $P = 0.038$) were independently associated with depression.

Research conclusions

Malnutrition and poor social function were significantly associated with depressive symptoms in PTB patients. A prospective large-scale study is needed to confirm these findings.

Research perspectives

Malnutrition and poor social function were significantly associated with depressive symptoms in PTB patients. A prospective large-scale study is needed to confirm these findings.

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