

Prevalence and Factors Associated with Depression in Patients with Diabetes Mellitus and Pulmonary Tuberculosis (DM-PTB): A Hospital-Based Cross-Sectional Study

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Background and Objectives: A high incidence of depression has been reported in patients with pulmonary tuberculosis and diabetes mellitus (DM-PTB). However, the association between depression and DM-PTB is poorly understood and requires further investigation. This study aimed to evaluate the prevalence of depression and the associated factors in patients with DM-PTB.

Methods: A cross-sectional study was conducted among DM-PTB patients at the Tuberculosis Department of Shanghai Pulmonary Hospital Affiliated to Tongji University, China, enrolled between June 2021 and October 2021. The depression status, nutritional status, and the quality of life of the patients were evaluated using Patient Health Questionnaire-9 (PHQ-9), Nutritional Risk Screening 2002 (NRS2002), and Quality of Life Instruments for Chronic Diseases-Pulmonary Tuberculosis (QLICD-PT), respectively.

Results: A total number of 280 DM-PTB patients were screened, of whom 22 were excluded for missing data. Among the 258 DM-PTB patients subjected to analysis, 199 patients (77.13%) had PHQ-9 scores above 10. The patients with depression are more likely to have a lower monthly income, body mass index (BMI), and QLICD-PT than those without depression. The NRS2002 score and glutamic pyruvic transaminase (GPT) and glutamic oxaloacetic transaminase (GOT) levels in the depression group were more likely to be higher than those in the control group. Multivariate logistic regression analysis showed that physical function [OR = 0.798, 95% confidence interval (CI), 0.716–0.889, $P < 0.001$] was a protective factor against depression, whereas NRS2002 ≥ 3 (OR = 2.299, 95% CI, 1.095–4.825, $P = 0.028$), GPT (OR = 1.048, 95% CI, 1.018–1.079, $P = 0.002$), and social function (OR = 1.103, 95% CI, 1.033–1.179, $P = 0.004$) were risk factors of depression.

Conclusion: Depression in DM-PTB patients may be associated with monthly income, BMI, QLICD-PT scores, NRS2002 scores, GPT, and GOT levels.

Keywords: depression, pulmonary tuberculosis, diabetes mellitus, cross-sectional study

Background

Pulmonary tuberculosis (PTB) is a chronic contagious disease caused by *Mycobacterium tuberculosis* infection that primarily affects the lungs.¹ Diabetes mellitus (DM), on the other hand, is a metabolic disease marked by abnormally high blood glucose levels, either induced by reduced insulin production or insulin resistance.² Both PTB and DM are major health issues that affect millions of people worldwide, and the PTB and DM comorbidity (DM-PTB) has become an emerging public health challenge, since PTB and DM may collectively lead to severe sequelae and complications, poor treatment outcomes, and increased mortality.³ It has been showed that DM patients were more susceptible to PTB

due to weakened immune systems.⁴ In addition, PTB may promote existing insulin resistance and aggravate DM management.⁵ As reported by the World Health Organization (WHO), DM ranked the fifth risk factor for PTB incidence and was responsible for approximately 0.4 million of the new PTB cases in 2021.⁶ Accordingly, there is an urgent need for resolving their clinical complications and the associated risk factors of DM-PTB.

Besides the direct physiological and pathological impacts of chronic diseases (such as PTB and DM), accumulating evidence suggests a higher risk of depression in patients with chronic diseases.⁷ A previous study revealed that the prevalence of depression in PTB patients was higher than that of healthy populations.⁸ Human immunodeficiency virus (HIV) infection, poor social support, and perceived stigma being were found to be major risk factors for this condition.^{9–11} Moreover, depression in PTB patients is often associated with insufficient health care and poor treatment compliance, leading to increased drug resistance, morbidity, and mortality,⁴ thus negatively affecting their health-related quality of life (QOL).^{5,6} Consequently, understanding the essential relationships between depression and DM-PTB is urgently needed. Although the association between depression and PTB has been extensively investigated,^{7–9} little is known about the prevalence and risk factors of depression in DM-PTB patients. Therefore, this hospital-based cross-sectional study aimed to evaluate the prevalence of depression and the associated factors in DM-PTB patients.

Methods

Study Design and Subjects

This hospital-based cross-sectional study was conducted from June 1st to October 30th 2021 in Shanghai Pudong Hospital. Young adult participants with DM-PTB were recruited through convenience sampling. The following inclusion criteria were applied: (1) patients with DM-PTB;¹⁰ (2) age of ≥ 18 and ≤ 44 years; (3) signed an informed consent form. The exclusion criteria were as follows: (1) incomplete medical history; (2) diagnosed with extrapulmonary TB. This study was approved by the Ethics Committee of Shanghai Pulmonary Hospital Affiliated to Tongji University (No. K19-146).

Data Collection

Structured questionnaires were used to collect the enrolled participants' information before the start of anti-TB drug treatment. All patients were interviewed by nurses who had received systematic and standardized training. The interviews lasted approximately 15–20 min for each patient. Demographic data, including age, educational level, occupation, marital status, body mass index (BMI), and income were collected. The height and weight of the patients were measured under the same conditions on the first post-admission day. BMI was used to assess the patients' nutritional status.¹¹ Patients with BMI below 18.5 kg/m^2 were considered underweight or with malnutrition.¹² Basic medical data, including comorbidities, treatment duration, hemoglobin (Hb), albumin (ALB), liver function (indicated by glutamic-pyruvic transaminase, GPT, and glutamic oxaloacetic transaminase, GOT), and medical cost origin were also collected from medical records.

The Nutritional Risk Screening 2002 (NRS2002) guidelines were used for evaluating the nutritional status of the recruited patients.¹³ The NRS2002 score was defined as the sum of the nutritional score, the severity of disease score, and the age adjustment score. The total NRS2002 score ranged within 0–7. Patients with total scores < 3 were considered with no nutritional risk, whereas those with scores ≥ 3 were considered to have nutritional risks.

The depression status of the patients was assessed by the Patient Health Questionnaire-9 (PHQ-9),¹⁴ consisting of nine items. 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 of the PHQ-9 ranged between 0 and 27. Since patients with PHQ-9 scores over 10 are considered more prone to depression,¹⁵ we divided the PTB patients into a depression group (score ≥ 10) and a control group (score < 10).

The patients' quality of life (QoL) was assessed by the Quality of Life Instruments for Chronic Diseases-Pulmonary Tuberculosis (QLICD-PT),¹⁶ which included three domains as well as one specific model: Physiological function (essential physiological function, independence, energy, and discomfort), psychological function (cognition, emotion, will, and personality), social function (interpersonal interaction, social support, and social role), plus a specific module (respiratory symptoms, systemic symptoms, drug side effects, and particular psychology).

Statistical Analysis

Data analysis was conducted using the SPSS software version 21.0 (IBM, USA). The patients' demographic and disease characteristics were analyzed with independent *t*-tests and Pearson's correlation coefficient tests where appropriate. $P < 0.1$ in univariate analysis were entered into the multivariate logistic regression and analyzed using the forward mode. $P < 0.05$ was considered to indicate statistically significant differences.

Results

Demographic Characteristics

A total number of 280 PTB patients were initially recruited, of whom 15 were excluded due to missing data and medical history of PTB, 5 were excluded due to missing blood nutritional indicators of PTB, and 2 were excluded due to missing QLICD-PT data. Finally, the data of a total number of 258 DM-PTB patients (92.14%) were subjected to analysis (Figure 1). The mean age of the patients was 31.00 ± 7.67 years (range 18–44 years, median 27 years). Of these included patients, 156 (60.47%) were men, 134 (51.94%) were married, 204 (79.07%) received senior primary, secondary, or above education, 147 (56.98%) were unemployed, and 116 (44.96%) had a monthly income above 5000 yuan (Table 1).

Risk Factors Associated with Depression in DM-PTB Patients

With the threshold of PHQ score set to 10, the DM-PTB patients were divided into depression ($n = 199$, 77.13%) and control ($n = 59$, 22.87%) groups. There was no significant difference in age, gender, marital status, education level, occupation, TB treatment duration, sputum bacterial test results, comorbidities, and origin of medical costs between the two groups. A tendency for a lower monthly income was observed in the patients in the depression group. The BMI, overall QLICD-PT scores, and QLICD-PT scores of the physical, psychological, social, and specific functions of the depression group were significantly lower than those of the control group. Besides, a larger percentage of patients in the depression group had $NRS2002 \geq 3$ than in the control group. Additionally, the GPT and GOT levels in the depression group were significantly higher than those in the control group, indicating potentially impaired liver functions (Table 2). [Supplementary Table 1](#) displays the detailed comparison of the data the nutritional status of the DM-PTB patients,

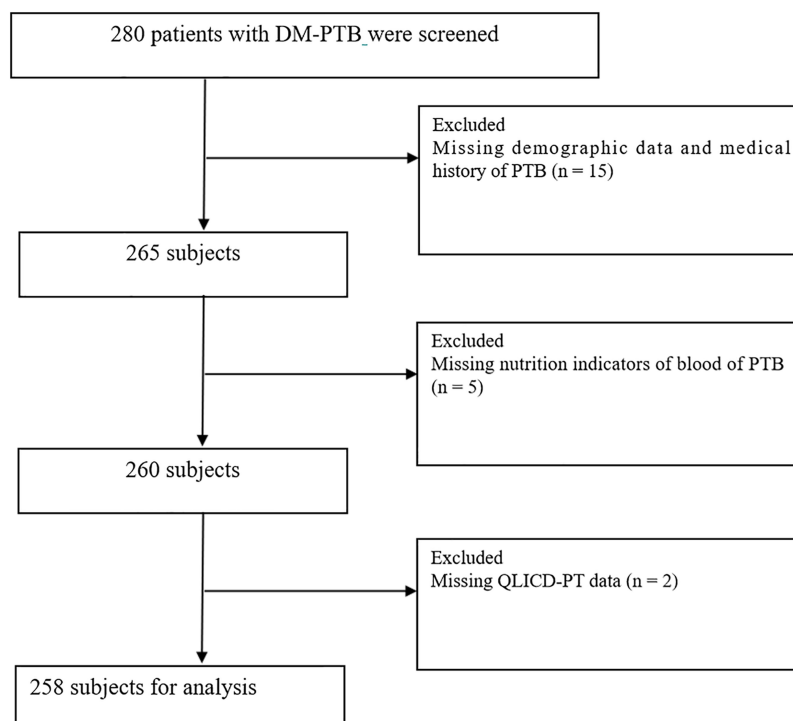


Figure 1 Flow chart.

Table I Demographic Characteristics

Variable	Mean (SD) or n (%)
Age, years	31.00 (7.67)
Gender	
Male	156 (60.47%)
Female	102 (39.53%)
Marital status	
Married	134 (51.94%)
Unmarried	124 (48.06%)
Education	
Junior primary	54 (20.93%)
Senior primary secondary and above	204 (79.07%)
Occupation	
Unemployed	147 (56.98%)
Employed	111 (43.02%)
Monthly income, yuan (1 yuan ≈ 0.155 USD)	
<5000	142 (55.04%)
≥5000	116 (44.96%)
TB treatment duration	
<6 months	126 (48.84%)
≥6 months	132 (51.16%)
Sputum bacteria	
Positive	107 (41.47%)
Negative	151 (58.53%)
Comorbidities	
Diabetes mellitus	13 (5.04%)
Hemoptysis	29 (11.24%)
Origin of medical costs	
Medical insurance	201 (77.91%)
Self-supporting	57 (22.09%)
Nutrition status	
NRS2003 ≥ 3	161 (62.40%)
BMI (kg/m ²)	20.10 (2.72)
Hb (g/L)	129.10 (18.03)
ALB (g/L)	40.45 (10.96)
Prealbumin (g/L)	192.88 (68.64)
PHQ-9 ≥ 10	199 (77.13%)
Liver function	
GPT (IU/L)	25.13 (30.21)
GOT (IU/L)	24.77 (25.23)
QLICD-PT	
Physical function	22.54 (3.97)
Psychological function	29.49 (7.28)
Social function	23.39 (5.87)
Specific function	39.64 (7.54)

Abbreviations: BMI, body mass index; Hb, hemoglobin; ALB, albumin; GPT, glutamic-pyruvic transaminase; GOT, glutamic oxaloacetic transaminase.

reflected by their BMI values. Overall, 29.46% of the DM-PTB patients were found to be underweight (BMI < 18.5). In the depression group, 130 (65.33%) of the patients had a BMI within the normal range, whereas 42 (71.19%) of the patients from the control group had normal nutritional status. Notably, the ratios of patients with mild (20.10%), moderate (8.54%), and severe thinness (3.52%) in the depression groups were higher than those in the control group (11.86%, 5.08%, and 3.39%, respectively).

Table 2 Univariate Analysis

Variable	Depression Status		OR (95% CI)	P-value
	PHQ \geq 10 (n = 199)	PHQ < 10 (n = 59)		
Age, years	31.27 \pm 7.64	30.10 \pm 7.77	1.137 (-3.410–1.070)	0.305
Gender			0.940 (0.520–1.700)	0.838
Male	121	35		
Female	78	24		
Marital status			0.792 (0.443–1.418)	0.434
Married	106	28		
Divorced/unmarried	93	31		
Educational level			0.954 (0.465–1.960)	0.899
Junior primary	42	12		
Senior primary secondary and above	157	47		
Occupation			1.241 (0.686–2.246)	0.475
Unemployed	111	36		
Employed	88	23		
Monthly Income, Yuan			0.515 (0.286–0.928)	0.026
<5000	117	25		
\geq 5000	82	34		
TB treatment duration			1.212 (0.677–2.169)	0.517
<6 months	95	31		
\geq 6 months	104	28		
Sputum bacteria				
Positive	77	30	0.610 (0.340–1.095)	0.096
Comorbidities				
Hypertension	10	3	0.988 (0.263–3.713)	0.985
Hemoptysis	24	5	1.481 (0.539–4.069)	0.444
Source of medical costs			1.144 (0.560–2.341)	0.712
Medical insurance	154	47		
Self-supporting	45	12		
Nutrition screening			2.306 (1.269–4.191)	0.005
NRS2002 \geq 3	143	31		
NRS2002 < 3	56	28		
Nutrition status				
BMI (kg/m ²)	19.8 3 (2.52)	21.01 (3.16)	0.396 (0.402–1.963)	0.003
Hb (g/L)	128.06 (18.25)	132.61 (16.96)	2.663 (-0.694–9.794)	0.089
ALB (g/L)	40.72 (12.86)	39.29 (4.20)	1.625 (-4.706–1.696)	0.355
Prealbumin (g/L)	189.95 (71.37)	202.78 (57.97)	10.164 (-7.185–32.845)	0.208
QLICD-PT				
Overall	114.60 (12.51)	116.63 (12.75)	1.863 (-1.645–5.693)	0.278
Physical function	21.68 (3.75)	25.45 (3.26)	0.540 (0.271–4.842)	<0.001
Psychological function	30.27 (6.79)	26.86 (8.26)	1.059 (-5.488–1.316)	0.001
Social function	24.28 (5.62)	20.41 (5.75)	0.838 (-5.520–2.219)	<0.001
Specific function	38.38 (7.48)	43.90 (6.09)	1.066 (1.760–7.615)	<0.001
Liver function				
GPT (IU/L)	27.5 0 (33.56)	17.14 (10.64)	4.439 (1.625–19.109)	0.020
GOT (IU/L)	26.95 (28.04)	17.42 (8.15)	3.700 (5.089–13.963)	0.011

Multivariate logistic regression analysis was performed to identify risk factors that independently associated with depression. As can be seen in Table 3, physical function [OR = 0.798, 95% confidence interval (CI), 0.716–0.889, $P < 0.001$] is a protective factor against depression, whereas NRS2002 \geq 3 (OR = 2.299, 95% CI, 1.095–4.825, $P = 0.028$),

Table 3 Multivariate Logistic Regression Analysis

Variable	OR (95% CI)	P-value
NRS2002	2.299 (1.095–4.825)	0.028
GPT (IU/L)	1.048 (1.018–1.079)	0.002
Physical function	0.798 (0.716–0.889)	<0.001
Social function	1.103 (1.033–1.179)	0.004

GPT (OR = 1.048, 95% CI, 1.018–1.079, $P = 0.002$), and social function (OR = 1.103, 95% CI, 1.033–1.179, $P = 0.004$) are risk factors positively associated with depression.

Discussion

In this cross-sectional study, we found that depression in DM-PTB patients was associated with a lower monthly income, BMI, and QLICD-PT scores, as well as higher NRS2002 scores, GPT, and GOT levels. Physical function was a protective factor against depression, whereas NRS2002 ≥ 3 , GPT and social function were risk factors positively associated with depression in DM-PTB patients. Understanding the occurrence and risk factors of depression in DM-PTB patients could help identify high-risk individuals, enabling early intervention and treatment to improve their QoL and prognosis.

Depression research encompasses multiple medical disciplines and requires long-term follow-up, adding complexity to the study. Despite these challenges, we prioritize addressing depression due to its potential impact on treatment outcomes, QoL, and its relatively high prevalence in DM-PTB patients. Focusing on depression allows for a comprehensive consideration of patients' mental health, promoting overall treatment effectiveness. Most of the patients in this study were males aged between 18–44 years with relatively low incomes. The prevalence of depression in PTB patients was 41.1% in Nigeria,¹⁷ 61.1% in Cameroon,¹⁸ 56% in Pakistan,¹⁹ 54% in Ethiopia,²⁰ 16.8% in Philippines,¹³ and 69.6% in Liaoning Province of China.²¹ The percentage of depressed DM-PTB patients in this study was 77.13%, which is higher than those reported for PTB patients in the above studies. Such a difference may be attributed to the fact that we studied DM-PTB patients exclusively, who might have had a higher risk of developing depression than PTB patients due to more complications, treatment difficulties, and poor general health conditions induced by PTB and DM. The sample size, race, countries, patient populations, and depression assessment criteria might have also contributed to such differences. In addition, DM-PTB patients with a monthly income below 5000 yuan were more susceptible to depression, presumably due to the increased mental stress caused by heavy economic burdens and loss of working abilities.

Nutritional status is a significant risk factor for the development of depression in DM-PTB patients. The mean BMI in the depression group was significantly lower than that in the control group. Furthermore, higher percentages of DM-PTB patients in the depression group suffered from mild, moderate, or severe thinness than in the control group. The results of the present study indicate that undernutrition enhances the impact of Tuberculosis-Depression Syndemic and even exacerbates it. We found that the ratio of patients at nutritional risk (NRS2002 ≥ 3) DM-PTB within the depression group was 71.86% and that NRS2002 ≥ 3 was a risk factor for depression. While the symptoms of undernutrition and psychological distress may overlap,²² depression and undernutrition may be closely associated due to the following reasons: (1) depression and other adverse emotions may lead to loss of appetite and digestive dysfunction, resulting in decreased protein and energy intake; (2) continuous mental stimulation may lead to severe vegetative nerve dysfunction and endocrine imbalance, inhibiting the absorption of nutrients; and (3) depression itself may increase catabolism to promote protein decomposition and reduce protein synthesis, further worsening the nutritional status. These synergistic effects between depression and undernutrition may be intensified in DM-PTB patients, who are already in urgent need for nutrients for the provision of normal immune response. Hence, even worse clinical outcomes and treatment difficulties can occur. In addition, we identified that physical function is a protective factor and social function is a risk factor for depression, highlighting the need for proper physical exercise and mental health care for DM-PTB patients for depression prevention. This study also established that DM-PTB patients with high levels of GPT and GOT were more likely to develop depression. The presence of high GPT and GOT levels of in the blood may indicate liver damage, which is potentially caused by hepatotoxic anti-tuberculous agents such as rifampicin and isoniazid. This liver damage may slow down the clearance of other metabolites from the blood, increasing the risk of depression development. Meanwhile, liver damage may also induce chest pain

and other discomforts that increase the patients' mental stress and thus enhance the risk of depression.²³ While further studies are required to validate the potential aforementioned associations, it is clear that DM-PTB patients can easily fall into a vicious circle, in which their quality of life, economic status, mental stress, and health condition may adversely affect each other.

Certain limitations of this study are to be acknowledged. First, we included only a limited number of DM-PTB patients admitted to one hospital in a period of five months within the same year. The relatively small sample size, single-centered study design, and short data collection period might have introduced biases in our results. The effects of treatment during this period might have also been neglected. Second, a more comprehensive prospective study is thus required to validate the risk factors of depression in DM-PTB patients. Third, the monthly income and socio-economic status may be confounding factors between nutritional status and depression. In addition, limited by the nature of cross-sectional design, though we indicated that most DM-PTB patients underwent depression, the causal relationship between diabetes and depression in TB patients could not be determined. Since we only included DM-PTB patients, the comparison of patients with similarly poor nutrition with diabetes and TB combined and those with just TB could not be achieved. Moreover, we could not determine if the diabetes worsens nutrition and this is the mechanism for the worsening depression. In the future, a prospective case-control study with large sample size is needed to validate the findings in the present study.

In conclusion, depression frequently occurs in DM-PTB patients. For depression prevention, a comprehensive care plan (such as nutrition management, mental counselling, and social support) is necessary in DM-PTB patients. However, further studies are needed to validate the findings of the present study.

Abbreviations

DM-PTB, Diabetes mellitus and pulmonary tuberculosis; PHQ-9, Patient Health Questionnaire-9; NRS2002, Nutritional Risk Screening 2002; QLICD-PT, Quality of Life Instruments for Chronic Diseases-Pulmonary Tuberculosis; BMI, Body mass index; GPTL, Glutamic pyruvic transaminase; GOT, Glutamic oxaloacetic transaminase; CI, Confidence interval; PTB, Pulmonary tuberculosis; DM, Diabetes mellitus; HIV, Human immunodeficiency virus; QOL, Quality of life; Hb, Hemoglobin; ALB, Albumin.

Data Sharing Statement

The data generated in this study are available within the article and its [Supplementary File](#).

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Shanghai Pulmonary Hospital Affiliated to Tongji University (No. K19-146). Informed consent was obtained from all patients (or subjects). This study complies with the Declaration of Helsinki.

Consent for Publication

Written informed consent to publish this information was obtained from the participant.

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Xiucui Li and Xuee Fang are co-first authors for this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas: took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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