Prevalence of Depressive Symptoms and Related Risk Factors among Patients with Tuberculosis in China: A Multistage Cross-Sectional Study

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Abstract. Poor mental health among tuberculosis (TB) patients affects not only their compliance with treatments but also their daily lives. Few studies in China have evaluated depressive symptoms among TB patients. The present study aimed to determine the prevalence of depressive symptoms and its associated risk factors among Chinese TB patients. A total of 1,342 TB patients were recruited using a multistage sampling method and interviewed using a structured questionnaire. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale. Multinomial logistic regression analysis was performed to identify risk factors of depressive symptoms. Of the 1,342 participants included in this study, 48.0% had depressive symptoms. Of these, 34.8% and 13.2% had mild and moderate-to-severe depressive symptoms, respectively. Factors associated with depressive symptoms included family dysfunction, TB-related stigma, poor doctor–patient communication, and lack of knowledge about TB. Depressive symptoms are common among TB patients in China. Efforts of government and stakeholders in the development of relevant policy documents to prevent stigma and create social support for TB patients are necessary. This would not only promote their mental health but also improve their compliance with treatments.

INTRODUCTION

Tuberculosis (TB) has existed for millennia and remains a major global health problem. According to the Global TB Report 2016, there were an estimated 10.4 million new TB cases with 1.4 million TB deaths, globally, in 2015.[1] China ranks the third highest among 22 high TB disease–burdened countries in the world. The incidence of TB in China remained at 67 cases per 100,000 populations in 2015.[1] High prevalence of depression among TB patients has also been reported in various studies from different countries, with great variations between studies. Such high prevalence was reported in Nigeria (27.7%),[2] India (39.5%),[3] Ethiopia (43.4%),[4] Pakistan (46.3%),[5] and Cameroon (61.1%).[6]

Findings of research indicate that patients with TB often experience depression because of the chronic nature of the TB infection or its related psychosocioeconomic stressors.[7–9] Moreover, isoniazid, a monoamine oxidase inhibitor and a core anti-TB drug, may have significant interactions with other psychotropic medicines.[10] Previous studies showed that the prevalence of depression among TB patients was relatively high.[2–6] Depression is a condition that adversely affects patients' ability to cope with stress, the side effects of treatment, and everyday life. Many studies also found that depression had negative effect on treatment adherence, a very important aspect in TB control.[11] Furthermore, poor treatment adherence is not only a concern in terms of individual patient outcome but it also poses a threat to the health of the public with the potential of developing multidrug resistant form of TB. Therefore, it is necessary to study the prevalence and the related risk factors of depression among patients suffering from TB.

Currently, few studies have determined the prevalence of depression among TB patients in China. No study has also explored the effect of key factors such as family function, stigma, and doctor–patient communication on depressive symptoms among TB patients. Therefore, the aim of the present study was to determine the prevalence of depressive symptoms and related risk factors among TB patients.

METHODS

Ethics statement. The study protocol and the questionnaire were reviewed and approved by the Ethics Committee of Huazhong University of Science and Technology, Wuhan, China. Participation was voluntary and all participants gave written informed consent before being involved in the study. All identity details of study participants were kept confidential.

Participants and sampling. This cross-sectional study was conducted from October 1, 2013 to March 31, 2014, in Hubei Province in central China. The participants were selected using a multistage sampling design. In the first stage, counties across Hubei Province were divided into three categories using their economic development status (upper, middle, and lower levels); then, a county was randomly selected from each category. In the second stage, all TB patients who visited the county TB dispensaries at the study sites during the study period were screened. The participants were individuals meeting the following criteria: 1) active TB patient diagnosed according to the national TB program guidelines, 2) absence of psychosis, and 3) willingness to participate in the study. During the study period, 1,430 participants were enrolled and completed a structured self-administered anonymous questionnaire. Of the collected 1,430 questionnaires, 88 were discarded because of missing data. Finally, data on 1,342 TB patients were included in the analysis.

Measurement. In this study, the outcome (depressive symptoms) was measured using the Center for Epidemiologic

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Studies Depression Scale (CES-D).[12] Center for Epidemiologic Studies Depression Scale is a 20-item rating scale that assesses depressive symptoms across these four domains: "depressed affect," "positive affect," "somatic complaints/activity inhibition," and "interpersonal difficulties." A value of "0," "1," "2," or "3" is assigned to responses on symptoms of depression experienced by participants over the past week based on the 20-item scale. Possible range of scores is from 0 to 60, with the higher scores indicating the presence of more symptoms. The CES-D score, based on the severity of depressive symptoms, was categorized as "no depressive symptoms" = 0–15, "mild depressive symptoms" = 16–25, and "moderate-to-severe depressive symptoms" = 26–60. The CES-D has been used extensively in China and in the present study, the reliability was strong (Cronbach's α = 0.86).

To control for the effect of confounding factors which may be associated with depressive symptoms, information on demographic characteristics (gender, age, education, marital status, race, and religious beliefs), history of prior anti-TB treatment, family function, TB-related stigma, knowledge about TB, and doctor–patient communication was collected.

Family function was measured using the "Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR)" index.[13] The Family APGAR index assessed the degree to which respondents were satisfied with social support received from their family members. A Family APGAR index score of 0–3 suggests "serious family dysfunction," 4–6 suggests "certain family dysfunction," whereas 7–10 suggests "good family functioning." In our study, the Family APGAR index demonstrated high internal consistency (Cronbach's α = 0.86).

Tuberculosis-related stigma was measured using the TB-related stigma scale, which was developed by us, with a good reliability (Cronbach's α = 0.88). The scale consists of nine items. Each item is scored on a 4-point Likert scale, ranging from "strongly disagree" to "strongly agree" coded with values from 0 to 3. The total score is computed as the sum of all items to provide the stigma score, ranging from 0 to 27, with higher scores indicating higher levels of TB-related stigma.

Patients' knowledge about TB was measured with six multiple-choice questions: 1) etiology of TB, 2) route of transmission of TB, 3) whether TB is curable or not, 4) duration of the standardized treatment regimen for TB, 5) common clinical symptoms of TB, and 6) unhealthy behaviors that make TB spread easily. Of the six questions, the first four have a single correct answer and the patient receives 1 point for each correct answer; the remaining two questions have four correct answers and the patient receives 0.5 point for each correct choice. A question is scored with 0 points if the answer is incorrect or "I do not know." Thus, in total, the score of TB knowledge ranges between a minimum of 0 and a maximum of 8. The higher the TB knowledge score, the more the TB knowledge a patient has. The questions used to assess patients' knowledge about TB came mostly from the questionnaire used in the National Tuberculosis Epidemiological Survey of China.[14]

Doctor–patient communication was measured with four questions: 1) satisfaction with the doctors' service attitude, 2) extent to which the doctor introduces the illness, 3) extent to which the doctor explains the details of taking anti-TB agents, and 4) extent to which the doctor explains adverse drug reactions to anti-TB agents. Patients were asked to rate their answers on a satisfaction or detail scale ranging from 1 to 3 for the aforementioned four questions. The total score ranged from 4 to 12, with higher scores meaning better doctor–patient communication.

Statistical analysis. Statistical analysis was conducted using the statistical analysis system (SAS) 9.4 for Windows (SAS Institute, Inc., Cary, NC). We carried out descriptive analyses on baseline characteristics (gender, age, education, marital status, race, and religious beliefs) of participants and reported numerical variables with mean and standard deviation (SD), whereas categorical data were reported as frequency and percentages. The participants were divided into three groups for all remaining analyses based on depressive symptoms (no, mild, and moderate-to-severe depressive symptoms). Rank-sum tests were conducted to compare prevalence of depressive symptoms across groups defined by demographic data, prior anti-TB treatment, and Family APGAR index. One-way analysis of variance (ANOVA) and Student–Newman–Keuls multiple range test were conducted to compare the mean knowledge score of TB, the mean TB-related stigma score, and the mean doctor–patient communication score between groups with different depressive symptoms (no, mild, and moderate to severe). Finally, multinomial logistic regression analysis was performed to determine the potential risk factors of depressive symptoms. All comparisons were two-tailed. The significance threshold was set at P value ≤ 0.05.

RESULTS

Table 1 shows the participants' characteristics and the prevalence of depressive symptoms (mild and moderate-to-severe depressive symptoms). The mean age of respondents was 47.7 (SD = 17.1) years, whereas majority were males (67.4%), had primary or less education (42.8%), were married (78.7%), were of Han race, and had no religious beliefs (88.9%). The mean standard score of CES-D was 15.9 (SD = 8.2). The overall prevalence of depressive symptoms among 644 participants of the total 1,342 participants was 48.0%, with the prevalence of mild and moderate-to-severe depressive symptoms reported at 34.8% and 13.2%, respectively. Associations between demographic characteristics and depressive symptoms were assessed using the rank-sum tests (Table 1). All demographic characteristics except religious beliefs and prior anti-TB treatment and family function were associated with depressive symptoms ($P <$ 0.05). Findings of ANOVA indicated that there were significant differences in knowledge about TB, doctor–patient communication, and stigma among respondents within the different depressive symptom categories (Table 2).

Table 3 shows the result of the multinomial logistic regression analyses. Knowledge about TB and doctor–patient communication was negatively associated with mild or moderate-to-severe depressive symptoms (compared with no depressive symptoms). Stigma was positively associated with mild or moderate-to-severe depressive symptoms (compared with no depressive symptoms). The ethnic minorities and those with "serious" and "certain" family dysfunctions showed a higher likelihood of mild and moderate-to-severe depressive symptoms compared with good family function. Participants with high school or higher education showed a lower likelihood of moderate-to-severe depressive

TABLE 1
Participants' characteristics and associations with depressive symptoms of the TB patients

Variables	Total (N = 1,342)		Mild (N = 467)		Moderate to severe (N = 177)		P
	n	%	n	%	n	%	
Age (years)	47.7 ± 17.1		48.4 ± 16.5		51.1 ± 16.8		< 0.01*
Gender							< 0.01
Males	905	67.4	306	33.8	98	10.8	–
Females	437	32.6	161	36.8	79	18.1	–
Education	–	–	–	–	–	–	< 0.01
Primary or less	574	42.8	214	37.3	106	18.5	–
Secondary	540	40.2	188	34.8	59	10.9	–
High school or higher (above)	228	17.0	65	28.5	12	5.3	–
Marital status (missing = 33)							< 0.01
Married	1,030	78.7	367	35.6	138	13.4	–
Single	224	17.1	69	30.8	24	10.7	–
Separated/divorced/widowed	55	4.2	24	43.6	15	27.3	–
Race (missing = 11)							< 0.01
Han	945	71.0	305	32.3	99	10.5	–
Ethnic minorities	386	29.0	161	41.7	76	19.7	–
Religious beliefs (missing = 46)							0.34
No	1,152	88.9	399	34.6	157	13.6	–
Yes	144	11.1	56	38.9	11	7.6	–
Prior anti-TB treatment							0.01
No	1,174	87.5	401	34.2	148	12.6	–
Yes	168	12.5	66	39.3	29	17.3	–
Family APGAR index							< 0.01
Serious family dysfunction	57	4.3	29	50.9	19	33.3	–
Certain family dysfunction	435	32.4	186	42.8	96	22.1	–
Good family function	850	63.3	252	29.7	62	7.3	–

APGAR = adaptability, partnership, growth, affection, and resolve; TB = tuberculosis.
* This P value is associated with analysis of variance; all other P values are associated with rank-sum tests.

symptoms ($P < 0.05$). Females and separated/divorced/widowed participants showed a higher likelihood of moderate-to-severe depressive symptoms ($P < 0.05$). Only age, religious beliefs, and prior anti-TB treatment showed no significant association with depressive symptoms ($P > 0.05$).

DISCUSSION

Our study assessed the prevalence of depressive symptoms among TB patients in central China and explored the related risk factors. The mean standard CES-D score among our study participants (15.9 ± 8.2) was greater than the national norm score (13.2 ± 10.3) for the Chinese general population.[15] The previous study that applied CES-D to assess the prevalence of depressive symptoms among Chinese general population showed that the prevalence varied from 18.3% to 23.4%.[16–18] Tuberculosis patients in our study are twice (48.0%) more likely than the Chinese general population to have depressive symptoms, which suggests that depressive symptoms are common among TB patients. The prevalence of depressive symptoms in our study was similar with the findings of studies conducted in Ethiopia (43.4%),[4] Pakistan

(46.3%),[5] and Angola (49.4%).[19] The presence of depression in TB patients leads to poor compliance with anti-TB treatment and hence, poor prognosis, thus increasing the morbidity and mortality due to TB.[8] In view of the high prevalence and the potential negative effects of depressive symptoms, it is, therefore, important to explore effective intervention strategies to reduce depressive symptoms among TB patients.

Previous studies have shown that people with perceived stigma may have a low self-image and be socially isolated, which may predispose them to depression.[20,21] Our study indicates that patients with higher stigma score were more likely to have depressive symptoms. The government and other stakeholders including clinicians should, therefore, pay greater attention to TB patients' concerns about stigma. It is thought that this may be beneficial to their mental health.

A number of studies have proven that social support is significantly associated with depression.[4,22] Family and health-care workers are important sources of social support for TB patients.[23] This study indicated that family dysfunction and poor doctor–patient communication were significantly associated with depressive symptoms. Among the participants, TB patients with dysfunctional families

TABLE 2
Knowledge, doctor–patient communication, and stigma among TB patients' with different depressive symptoms

Depressive symptoms	Knowledge about TB		Doctor–patient communication		Stigma	
	Mean ± SD	SNK group	Mean ± SD	SNK group	Mean ± SD	SNK group
No	5.4 ± 1.7	A	11.6 ± 1.1	A	8.4 ± 4.4	A
Mild	4.6 ± 2.1	B	11.1 ± 1.4	B	9.7 ± 3.9	B
Moderate to severe	3.6 ± 2.2	C	11.0 ± 1.4	B	11.9 ± 3.5	C

SD = standard deviation; TB = tuberculosis. Student–Newman–Keuls (SNK) multiple range tests were conducted to compare the mean knowledge score about TB, the mean TB-related stigma score, and the mean doctor–patient communication score between groups with different depressive symptoms. Different letters for SNK group (A, B, or C) denote significant differences ($P < 0.05$) between mean values; the same letter denotes no significant difference.

TABLE 3
Multinomial logistic regression of factors associated with depressive symptoms in TB patients

Variable	Depressive symptoms	
	Mild	Moderate to severe
Age	1.0 (1.0–1.0)	1.0 (1.0–1.0)
Gender (ref = males)	1.3 (1.0–1.7)	1.7 (1.1–2.6)*
Education (ref = primary or less)		
Secondary	0.9 (0.6–1.2)	0.7 (0.4–1.1)
High school or higher (above)	0.7 (0.4–1.1)	0.3 (0.1–0.7)**
Marital status (ref = married)		
Single	0.8 (0.5–1.2)	1.0 (0.5–1.9)
Separated/divorced/widowed	1.7 (0.8–3.5)	2.4 (1.0–5.8)*
Race (ref = Han)	1.7 (1.3–2.3)***	2.4 (1.6–3.7)***
Religious beliefs (ref = no)	1.0 (0.7–1.6)	0.5 (0.2–1.1)
Prior anti-TB treatment (ref = no)	1.3 (0.9–1.9)	1.5 (0.8–2.6)
Family APGAR index (ref = good)		
Certain family dysfunction	2.3 (1.7–3.0)***	3.8 (2.5–5.8)***
Serious family dysfunction	4.5 (2.0–10.1)***	8.2 (3.1–21.7)***
Knowledge about TB	0.9 (0.8–0.9)***	0.7 (0.7–0.8)***
Doctor–patient communication	0.8 (0.7–0.9)***	0.8 (0.7–1.0)*
Stigma	1.1 (1.0–1.1)***	1.2 (1.2–1.3)***

APGAR = adaptability, partnership, growth, affection, and resolve; TB = tuberculosis. *$P < 0.05$, **$P < 0.01$, ***$P < 0.0001$.

accounted for approximately 40%. Therefore, it is important to pay more attention to individuals with dysfunctional families to enable appropriate support.[9] Furthermore, doctor–patient communication is also needed to strengthen efforts at combating depressive symptoms among TB patients.

Knowledge about TB was an important determinant of depressive symptoms in our study. This was consistent with previous research suggesting that knowledge about TB had significant effect on depression. However, the present study showed no significant statistical correlation with age, religious beliefs, and prior anti-TB treatment. This is similar to that reported in another previous study.[21]

This study has a few limitations including being a cross-sectional study, which cannot be used to establish causality and temporality between independent and dependent variables. However, our findings are consistent with other research findings on depressive symptoms among TB patients. Furthermore, although this is the first study focusing on depressive symptoms among TB patients in China, our sample was confined to TB patients in a central province. Hence, the findings of our study cannot be generalized to the entire China population. It is, therefore, necessary to conduct more representative studies to know the status of depressive symptoms among TB patients in China.

In conclusion, depressive symptoms are common among TB patients in China. Tuberculosis-related stigma, family dysfunction, poor doctor–patient communication, and insufficient knowledge about TB have negative effects on depressive symptoms. This indicates that interventions aimed at reducing depressive symptoms among TB patients should focus on improving patients' family functions, doctor–patient communication, and patients' knowledge about TB as well as alleviating TB patients' stigma.

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