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Prevalence of tuberculosis and mental disorders comorbidity: a systematic review and meta-analysis

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Abstract

Persons with tuberculosis (TB) also often have a mental disorder (MD). We examined TB-MD comorbidity prevalence and its impact on TB treatment outcomes as reported in studies set in the United States or in the top five countries of origin (Mexico, the Philippines, India, Vietnam, and China) for non-US–born persons with TB. We searched MEDLINE, EMBASE, OVID, PsycINFO, CINAHL, and Scopus for articles published from database inception through September 2018. Of the 9 studies analyzed, one was set in the United States. The estimated pooled prevalence of comorbid TB-MD from eight non-US studies, with 2921 participants, was 34.0% (95% confidence interval [CI] 21.1%–49.5%). Comorbid TB-MD prevalence varied by country in the studies evaluated. Additional research might elucidate the extent of TB-MD in the United States and the top five countries of origin.

Keywords

mental health; mental disorders; tuberculosis; treatment outcome

INTRODUCTION

Tuberculosis (TB) is the most common infectious disease globally. During 2018, TB disease was diagnosed among approximately 10 million persons [1]. Common mental disorders (MD), including anxiety and depression, are also leading causes of morbidity worldwide, with approximately 30% of adults having experienced a common MD during their lifetime[2]. However, the association between TB and MD is neither well-researched nor fully understood. Nevertheless, evidence from systematic reviews indicates that approximately one in two persons experiences MD after receiving a TB diagnosis [3, 4].

TB and MD are known to disproportionately affect vulnerable populations, including persons who experience poverty, displacement because of political strife, or who reside in

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a congregate setting [5-7]. Moreover, persons with MD are more likely not to complete treatment because of low compliance or nonadherence to anti-TB drug regimens [8]. Furthermore, persons with TB can acquire MD through adverse effects of anti-TB drug treatment or through their response to having the disease—which can lead to social and physical isolation, along with adversely affecting a person's livelihood [6, 8].

The interplay between TB and migration is well-described in the literature, especially its impact on increased TB incidence rates among persons emigrating from high to low TB-incidence countries [9-12]. In the United States, the TB rate for non–US-born persons is approximately 16 times greater than that for US-born persons [13]. However, published data regarding TB-MD comorbidity are limited. Our review describes the nature and extent of comorbid MD and TB in the United States and in the top five countries of origin (Mexico, the Philippines, India, Vietnam, and China) for non-US–born persons with diagnosed TB in the United States during 2014–2018 [14].

METHODS

Definition

Our review focused on selected common adult MD diagnosed by health professionals in the United States, as referred to in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. (DSM-5) [15], including anxiety disorders, depressive disorders, bipolar and related disorders, nonaffective and psychotic disorders, substance-related and addictive disorders, and trauma and stressor-related disorders.

Search strategy

We developed a search strategy with guidance from a professional librarian for locating English-language TB and MD studies published from database inception through September 2018. Electronic databases searched included MEDLINE, EMBASE, OVID, PsycINFO, CINAHL, and Scopus. The complete search strategy is available in Supplementary Table 1.

Study selection

Studies were included in our review if (1) the focus was on drug-susceptible TB-MD comorbidity among persons residing in the United States, Mexico, the Philippines, India, Vietnam, or China; (2) the study designs were prospective or retrospective cohort, case-control, or cross-sectional; and (3) the study reported outcomes regarding TB-MD prevalence, TB treatment completion or failure, and medication adherence. Non-English language studies, outbreak investigations, conference abstracts, systematic reviews, case studies and reports, and studies published before 1980 were excluded.

Data abstraction

Included studies were abstracted by two independent reviewers using a data abstraction form developed for this purpose. The following information was extracted from each included study: first author; journal title and year of publication; study location; study design; setting; participant characteristics (e.g., age, race/ethnicity, and sex); target population

(e.g., general, homeless, or hospitalized); type of MD; instrument or scale used to assess, measure, or diagnose MD (e.g., Beck Depression Inventory [16]); instrument or scale used to measure medication adherence (e.g., Morisky Medication Adherence Scale); type of outcome(s) reported (e.g., prevalence or medication adherence); sample size; number of participants with TB-MD comorbidity; and number of participants completing TB treatment. Discordance of data abstraction elements between reviewers was resolved by consensus between them.

Quality assessment

Study quality was independently assessed by the same two reviewers using a tool adapted from the Newcastle-Ottawa Quality Assessment Scale [17]. Out of 9 maximum points, studies that received a score of ≥7 points were classified as good quality, 4–6 points as fair quality, and <4 points as poor quality.

Data synthesis

Medians and interquartile intervals (IQI) are reported to describe characteristics of included studies. Meta-analyses were conducted to assess the prevalence of comorbid TB-MD and TB treatment completion and medication adherence if two or more studies reported on the outcome of interest. Pooled estimates and 95% confidence intervals (CIs) were calculated by using a random effects model because of heterogeneity among study participants across designs and location. For studies reporting multiple disorders as an outcome, the average of the individual effect estimates was calculated and reported. Statistical heterogeneity across studies was assessed with Higgins' I^2 statistics [18]. I^2 values range from 0% to 100%, and for this review, values ≥50% were considered to be indicative of substantial heterogeneity.

Group analyses were also conducted by study design, setting, location, target population, study quality, and publication date (i.e., before 2010 versus after 2010) to explore possible sources of heterogeneity. Publication bias was assessed by using the trim-and-fill method and visual inspection of funnel plots [19, 20]. All statistical analyses were conducted with the "metafor" and "meta" packages in R, version 3.6.3 [20-22]. Analyses were completed in June 2020.

RESULTS

Search yield and quality assessment

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram displaying the selection of articles from the literature search is provided in Figure 1 [23]. The search strategy identified a total of 8087 articles published from database inception through September 2018. After removing 2151 duplicate articles, 5936 titles and abstracts were screened for relevance; of those screened, 172 articles underwent full-text review. In total, 9 studies met the inclusion criteria and were included in the qualitative analysis and 8 studies were included in the meta-analysis [24-32]. The summary evidence table for included studies is provided in Supplementary Table 2. The body of evidence in this review was of mixed quality. Of the 9 included studies, three were determined to be of good quality [24, 30, 31]; four were of fair quality [25, 27-29]; and two were of poor quality [26, 32].

Study and population characteristics

Table 1 displays the study characteristics of the included studies. This body of evidence was published during 1985–2018, with the majority of studies published after 2010 [25, 26, 28, 30-32]. Of the 9 included studies, four had been conducted in India [26, 27, 29, 30], one in the United States [25], two in China [31, 32], one in Vietnam [24], and one in the Philippines [28]. No studies from Mexico were identified. The majority of included studies were of a cross-sectional design [24-28, 31, 32]; other study designs included a prospective and case-control design [29, 30]. Six studies had been conducted in a hospital setting [24-27, 29, 30], and three had been conducted in a community setting [28, 31, 32]. Four included studies targeted hospitalized populations [24, 25, 29, 30], of which one US-study focused on pregnant women [25]. The remaining studies targeted the general population of the community [26-28, 31, 32].

The study populations comprised working-age adults (median age = 41.9 years; IQI = 41–47.7), and the majority of participants were men (69.2%). A median of 55.9% (IQI = 44.2%–68.3%) of participants from four studies reporting education levels had not graduated from high school [24, 27, 28, 32]. Studies conducted outside the United States did not report race/ethnicity; however, one US study reported race/ethnicity for a diverse population [25].

TB-MD comorbidity prevalence

The eight non-US studies with 2921 participants reported prevalence of TB-MD comorbidity [24, 26-32]. As displayed in Figure 2, the pooled estimated random effects prevalence of comorbid TB-MD in China, India, the Philippines, and Vietnam was 33.9% (95% CI 21.1%–49.5%). One US study reported comorbid TB-MD with 4053 participants [25]. The Fernandez et al. study, which targeted hospitalized pregnant women with HIV and TB coinfection reported an estimated TB-MD prevalence of 2.6% (95% CI 2.1%–3.1%) [25]. Significant heterogeneity was identified for the pooled non-US studies that reported prevalence as an outcome, with I^2 >50% and *P* values <.05. An I^2 >50% persisted even when the prevalence of comorbid TB-MD was assessed on the basis of moderator variables (e.g., setting, study design, location, publication period, and study quality).

Group analyses were also conducted on the basis of the MD type. Six non-US studies reported depression among persons with TB, with a pooled prevalence of 41.4% (95% CI 39.3%–43.5%) [26-30, 32]. Two non-US studies also reported outcomes for anxiety, with a pooled prevalence of 45.0% (95% CI 31.3%–59.5%) [26, 30]. Moreover, two non-US studies reported aggregate outcomes for MD, including schizophrenia, psychotic disorders, and other psychological conditions [24, 31]. Xu and colleagues used the Kessler Psychological Scale [33] to assess psychological distress among TB patients and reported a TB-MD prevalence of 65.2% (223/342). By contrast, Van Duc et al. evaluated the prevalence of TB among persons hospitalized in a psychiatric hospital with various psychological disorders and reported an estimated TB-MD prevalence of 8.0% (24/300). No US studies reported anxiety as an outcome.

When evaluated by study quality, the three non-US studies assessed as good quality reported an estimated pooled prevalence of 32.7% (95% CI 7.6%–74.2%) for comorbid TB-MD

[24, 30, 31], and the three non-US studies assessed as fair quality reported an estimated pooled prevalence of 25.7% (95% CI 9.9%–52.3%) [27-29]. Two non-US studies assessed as poor quality reported an estimated pooled prevalence of 48.1% (95% CI 45.5%–50.7%) for TB-MD.

TB medication adherence

The study from China also reported on TB medication adherence [32]. Using the Center for Epidemiologic Studies Depression Scale to assess the severity of depression [34], Yan et al. reported that persons with TB who experienced mild or severe depression had higher odds of low medication adherence (odds ratio [OR] = 1.92; 95% CI 1.34–2.75; OR = 3.67; 95% CI 2.04–6.61, respectively) as defined by a score of <6 on the 8-item Morisky Medication Adherence Scale [35], compared with that of TB patients without depressive symptoms.

Publication bias

Visual inspection of the funnel plots for studies reporting outcomes related to TB-MD appeared symmetrical and did not indicate potential publication bias. Additionally, a trim-and-fill analysis was not statistically significant (−0.33; 95% CI −1.17 to 0.51).

DISCUSSION

In this review, we explored the extent of the comorbidities of TB and MD in the United States and in the top five countries of origin for non-US–born persons with diagnosed TB in the United States—China, India, Mexico, the Philippines, and Vietnam. Our review identified a highly variable co-prevalence of MD among persons with drug-susceptible TB —namely, depression and anxiety—in four of these five countries; no identified studies were set in Mexico.

To our knowledge, this is the first review to examine the extent of comorbid TB-MD from the five aforementioned countries. Our findings are consistent with other reviews that examined this topic from a broader perspective [3, 36, 37]. In a recent review of 25 studies from low- and middle-income countries, Duko et al. reported the estimated prevalence of depression among persons with TB as 45.1% (95% CI 38.0%–52.6%), which is slightly higher than the pooled prevalence estimated in this review, but falls within our 95% CI [3]. Doherty et al. identified depression rates ≤68% among hospitalized persons with TB; high rates of anxiety and psychosis were also reported during TB treatment [37]. Similarly, the Bender et al. review also reported high rates of depression and anxiety among migrant populations with TB [36]. In another review focused on MD among persons with multidrug-resistant (MDR) TB, one in four persons with MDR TB experienced depression and anxiety during treatment [38]; this finding is slightly lower than the prevalence estimated in our review for persons with drug-susceptible TB disease. Although one might expect a higher prevalence for comorbid MDR TB-MD than drug-susceptible TB-MD, our review revealed the contrary. The discordance in review findings might be explained by the Alene et al. review having more high-quality, better-designed studies with longer follow-up than those included in our review (i.e., more cohort than cross-sectional studies).

Both TB and MD have a negative impact on immigrant and minority health [36]. This impact will likely be exacerbated because a diagnosis with TB can worsen MD. Persons with TB might experience anxiety and depression related to disease. Additionally, TB requires a lengthy and often complicated treatment period, and persons may also experience stigma related to the diagnosis, which may contribute to MD [39-41]. Immigrants to the US might also experience anxiety and depression related to their relocation [42]. For example, immigrants often experience social and economic issues related to overcrowding, challenging labor conditions, and literacy, along with problems accessing health care. These factors can have a detrimental effect on TB disease diagnosis and treatment, as well as on mental health. Combined efforts to diagnose and treat both TB and MD are key to addressing the impact of these health issues among immigrants and refugees.

Given the prevalence of comorbid TB-MD from the evidence evaluated in this review, US TB control programs should consider a patient-centered approach to screen persons under TB treatment for MD. Persons with comorbid TB-MD are more likely to miss treatment doses and be lost to follow-up, thus leading to higher rates of treatment failure and drug resistance [6, 8]. Drug resistance could potentially prolong infectiousness, possibly leading to community transmission of drug-resistant *Mycobacterium tuberculosis* [43-45] and large outbreaks that strain public health resources at the state and local levels. Using the collaborative care model [46], TB programs could partner with a primary care provider to ensure that adequate mental health services are provided to persons experiencing MD during TB treatment. Components of the collaborative care model for persons experiencing MD might include patient education, patient follow-up to track MD outcomes and adherence to treatment, and adjustment of treatment plans for patients who do not experience clinical improvement [46].

Limitations

The findings in this review are subject to at least three limitations. First, the vast majority of included studies used a cross-sectional design; thus, directionality or causation between TB and MD cannot be assessed. Additionally, substantial heterogeneity was reported when outcomes were assessed by study location, target population, and setting; therefore, the findings from this review should be interpreted with caution, especially given the relatively small sample sizes in the included evidence. Second, although a sizable proportion of TB cases in the United States are among persons born in Mexico, our review did not identify any studies set in Mexico. In fact, our review only included one study from North America (i.e., United States or Mexico), which indicates (1) a lack of systematic data collection and reporting of MD among persons with TB in the United States and Mexico; (2) a research gap for evidence that examines the association between TB and MD among persons from the United States and Mexico; or (3) potential exclusion of relevant Spanish-language articles because of the search strategy and inclusion criteria used in this review. Third, although the literature search was limited to the top five countries of origin for non-US–born persons with diagnosed TB in the United States, the generalizability of our findings to residents of the United States born in these countries is unknown.

CONCLUSION

On the basis of the limited number of included studies in this review, the prevalence of comorbid TB-MD varied among the top five countries of origin for non-US–born persons with diagnosed TB the United States. Our review identified only one study set in the United States and none in Mexico, thus highlighting the need for additional data concerning TB-MD comorbidity. Integration of mental health care services with TB control programs can offer an opportunity for screening persons with TB for MD and for providing patient-centered care for both conditions. The World Health Organization's End TB Strategy calls for integrating TB and mental health services worldwide [47]; guidance for integrating mental health services with TB treatment within the United States might also be warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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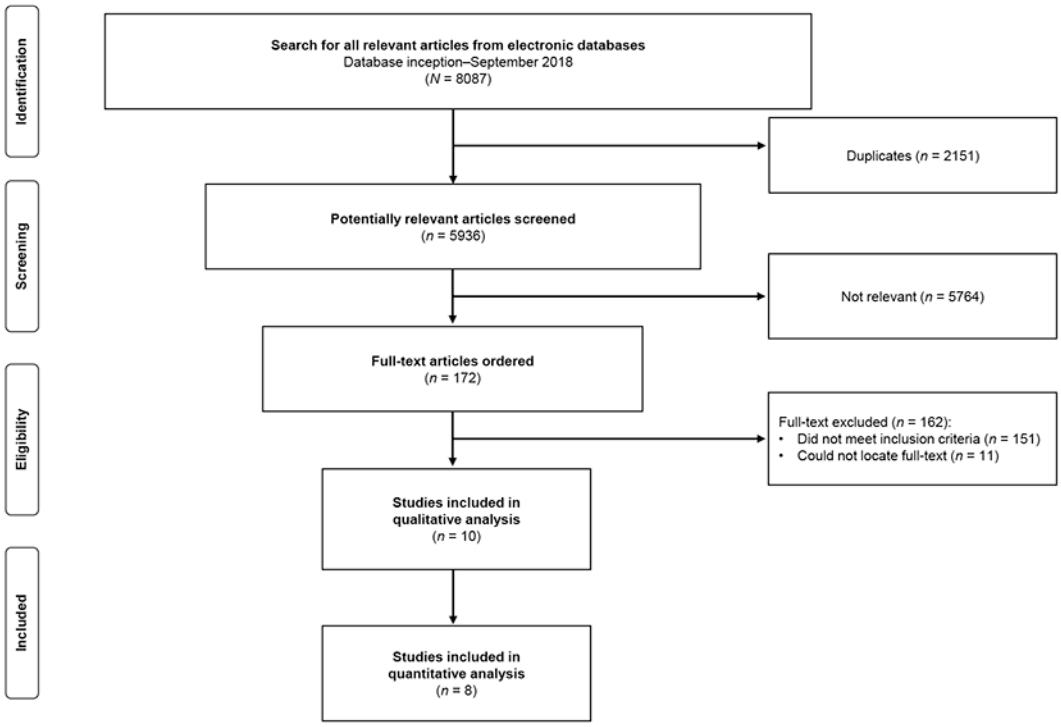

Figure 1.
PRISMA flow diagram indicating the study selection process.

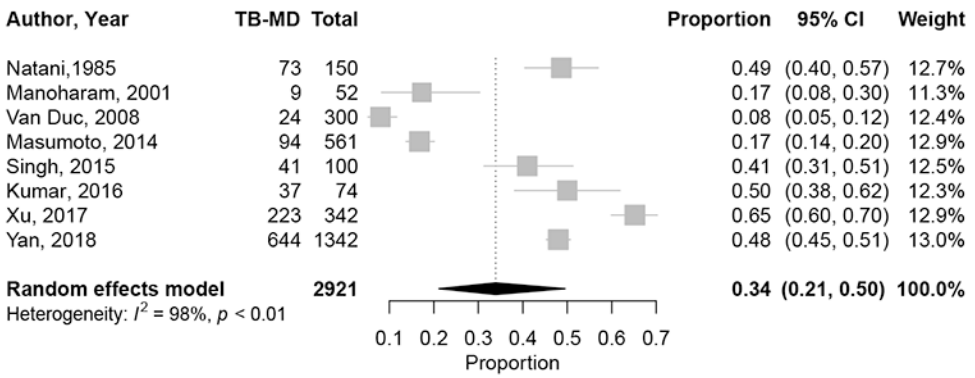

Figure 2.

Pooled prevalence of persons with comorbid TB and mental disorders in China, India, the Philippines, and Vietnam.

Abbreviations: CI, confidence interval; MD, mental disorder; TB, tuberculosis

Table 1

Characteristics of included studies (n =9).

Characteristic		No. of studies reporting (%)
Study location	United States	1 (11.1%)
	China	2 (22.2%)
	India	4 (44.4%)
	Vietnam	1 (11.1%)
	The Philippines	1 (11.1%)
Publication period	Before 2010	3 (33.3%)
	After 2010	6 (66.7%)
Target population	General	5 (55.6%)
	Hospitalized	4 (44.4%)
Setting	Health care facility	6 (66.7%)
	Community	3 (33.3%)
Study design	Cross-sectional	7 (77.8%)
	Prospective	1 (11.1%)
	Case-control	1 (11.1%)