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LETTER

Assessment of persistent depression among TB patients

Dear Editor,

Affecting over 264 million people, depression is a common mental health problem in the general population and remains one of the leading causes of ill health and disability.[1] Depresion contributes to both increased health care costs and reduced economic productivity.[2,3] Notably, depression at the time of TB diagnosis has been linked to non-adherence, TB-related morbidity[4] and increased risk for developing multidrug-resistant TB and community transmission.[5,6] Early identification and management of depression is critical for those at risk. However, the epidemiology of persistent depression symptoms (PDS) spanning anti-tuberculosis treatment (ATT) among people with TB remains unknown, and TB programs currently fail to identify and treat depression within routine TB care.[7] Understanding the epidemiology of PDS would help identify target populations at risk and inform appropriate mental health screening strategies and interventions to be integrated into TB programs.

We have therefore conducted a prospective observational cohort study to assess the prevalence and risk factors of PDS among adult (>18 years) pulmonary TB patients enrolled in the Cohort for Tuberculosis Research by the Indo-US Medical Partnership (C-TRIUMPh) study in India. This study was conducted at the National Institute for Research in Tuberculosis in Chennai and Byramjee Jeejeebhoy Government Medical College in Pune, and approved by the Institutional Review Boards. Written informed consent was obtained, and participants were followed from ATT initiation through 18 months.

Participants enrolled between 2014 and 2017 were interviewed at ATT initiation and ATT completion (Month 6). A structured form was used to collect sociodemographic and clinical data. The Alcohol Use Disorder Identification Test (AUDIT) scale was used to assess alcohol dependence (defined as AUDIT score ≥8), food insecurity was assessed using household food insecurity survey. Stigma was captured as "yes" if reported in response to question "Have you experience any problems due to TB treatment" Depression was assessed at both time points using the validated Center for Epidemiological Studies-Depression scale-10 (CES-D-10),[8,9] measuring 10 main symptoms of psychological distress over the preceding 7 days on a four-point Likert scale. Responses range from 'none of the time' to 'all of the time' with total CES-D-10 scores ranging from 0 to 30. The primary outcome was PDS, defined as depressed (CES-D-10 score >9) at both ATT initiation and completion.

The proportion of baseline depression symptoms (BDS) and PDS and the corresponding 95% exact confidence intervals (CIs) were estimated in the overall sub-cohort and by risk group; differences were compared using Fisher's exact test. Univariable multivariable logistic regression analysis was performed to assess independent risk factors associated with BDS and PDS. Variables with $P < 0.1$ in univariable analysis were included in multivariable models of PDS. Effect modification was checked, and if present, appropriate interaction terms were added to multivariable models. An analysis stratified by gender was performed to assess gender-specific risk factors that may be associated with PDS.

Of 464 adult TB patients enrolled, 40 were lost to follow-up, and 3 did not have baseline depression data. Among the remaining 421 participants, 200 (47.5%) has BDS and depression symptoms disappeared for 145 patients at the end of treatment. Of 221 (52.5%) who were not depressed at baseline, 22 developed depression symptoms by the end of treatment. Of 421 participants, 55 (13%) had PDS (Figure). Baseline characteristics show that the majority were male (64%); age <40 years (58%); married (78%); had at least primary school education (82%); lived in a rural area (46%); and had a monthly income >5000 Indian rupees (<US$100) (68%). Other characteristics included were alcohol dependence (32%); household food insecurity (35%); diabetes (28%); and TB-related stigma (13%). The overall prevalence of PDS was 13% (95% CI 10–17); the median CES-D-10 score was 15 (interquartile range [IQR] 12–19) at ATT initiation and 14 (IQR 11–16) at ATT completion. The prevalence of BDS and PDS by risk group and risk factor analysis results are presented in the Table. In univariate analysis, BDS was more likely among female (odds ratio [OR] 2.01, 95% CI 1.34–3.01), separated or widowed (OR 2.58, 95% CI 1.02–6.55), and reported TB stigma (OR 2.81, 95% CI (1.53–5.17). Women reporting TB stigma were more likely to have BDS (OR 9.49; 95% CI 2.72–33.14). PDS was more likely among participants who were female (OR 1.57, 95% CI 0.88–2.78), age >40 years (OR 5.66, 95% CI 1.68–19.09), separated or widowed (OR 14.67, 95% CI 2.86–75.22), illiterate (OR 3.23, 95% CI 1.74–6.00), residing in urban area (OR 2.13, 95% CI 1.19–3.81), alcohol-dependent (OR 1.78, 95% CI 0.99–3.17), and had comorbid diabetes (OR 2.48, 95%

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Table Prevalence of baseline and PDS by risk group among pulmonary TB index cases in India*

Characteristic	Total ($n = 421$)	Baseline depression† Prevalence ($n = 200$, 47.5%) % (95% CI)	Baseline depression† Univariate analysis OR (95% CI)	Baseline depression† Univariate analysis *P* value	Persistent depression symptoms‡ Prevalence ($n = 55$, 13%) % (95% CI)	Persistent depression symptoms‡ Univariate analysis OR (95% CI)	Persistent depression symptoms‡ Univariate analysis *P* value	Persistent depression symptoms‡ Multivariate analysis§ aOR (95% CI)	Persistent depression symptoms‡ Multivariate analysis§ *P* value
Sex				0.001					
Male	269 (64)	41 (35–47)	1		11 (8–16)	1	0.12		
Female	152 (36)	59 (50–66)	2.01 (1.34–3.01)		16 (11–23)	1.57 (0.88–2.78)			
Age, years									
<25	80 (19)	43 (32–54)	1	0.57	4 (1–11)	1	0.04	1	0.26
25–40	164 (39)	46 (39–54)	1.17 (0.68–2.00)	0.22	12 (8–18)	3.56 (1.03–12.37)	0.005	2.40 (0.52–11.24)	0.19
>40	177 (42)	51 (43–58)	1.40 (0.82–2.38)		18 (13–25)	5.66 (1.68–19.09)		3.18 (0.56–18.01)	
Marital status									
Not married	68 (16)	38 (27–51)	1	0.11	3 (1–11)	1	0.02	1	0.85
Married	321 (78)	49 (43–55)	1.54 (0.90–2.64)	0.04	14 (10–18)	5.24 (1.23–22.17)	0.001	0.84 (0.14–5.17)	0.64
Separated/widowed	26 (6)	62 (41–80)	2.58 (1.02–6.55)		31 (14–52)	14.67 (2.86–75.22)		1.62 (0.21–12.62)	
Education									
≥Primary school	346 (82)	46 (40–51)	1	0.11	10 (7–14)	1	<0.001	1	0.22
Illiterate	75 (18)	56 (44–67)	1.51 (0.92–2.50)		27 (17–38)	3.23 (1.74–6.00)		1.69 (0.72–3.97)	
Income, INR (1INR = 0.014USD)									
>5000	149 (68)	40 (32–48)	1	0.18	10 (6–16)	1	0.22		
≤5000	69 (32)	49 (37–62)	1.48 (0.83–2.63)		16 (8–27)	1.69 (0.73–3.91)			
Residence									
Urban	229 (54)	46 (39–53)	1	0.46	9 (6–14)	1	0.01	1	0.88
Rural	192 (46)	49 (42–57)	1.16 (0.79–1.70)		18 (13–24)	2.13 (1.19–3.81)		1.06 (0.47–2.39)	
AUDIT score¶									
<8	286 (68)	48 (42–53)	1	>0.95	11 (7–15)	1	0.05	1	0.07
≥8	135 (32)	47 (39–56)	0.99 (0.66–1.50)		18 (12–25)	1.78 (0.99–3.17)		2.98 (0.92–9.67)	
DM									
No DM	198 (47)	46 (39–54)	1	0.31	10 (6–15)	1	0.6	1	0.7
Pre-DM	104 (25)	40 (31–50)	0.78 (0.48–1.26)	0.12	12 (6–19)	1.23 (0.57–2.64)	0.006	1.20 (0.47–3.03)	0.73
DM	115 (28)	56 (46–65)	1.45 (0.91–2.29)		21 (14–29)	2.48 (1.29–4.77)		1.18 (0.47–2.93)	
Food insecurity									
Secure	178 (65)	46 (38–53)	1	0.09	13 (9–19)	1	0.05	1	0.12
Not secure	96 (35)	56 (46–66)	1.54 (0.93–2.53)		23 (15–33)	1.90 (1.00–3.62)		1.80 (0.86–3.78)	
TB stigma							0.04		
No	366 (87)	44 (39–49)	1	0.001	12 (9–15)	1			
Yes	55 (13)	69 (55–81)	2.81 (1.53–5.17)		22 (12–35)	2.10 (1.03–4.28)			
Stigma + gender									
No stigma and males	235 (56)	39 (32–45)	1	0.03	11 (7–16)	1	0.9	1	0.66
Stigma and males	34 (8)	59 (41–75)	2.26 (1.09–4.70)	0.004	12 (3–27)	1.07 (0.35–3.29)	0.58	0.73 (0.18–2.91)	0.07
No stigma and females	131 (31)	54 (45–70)	1.87 (1.22–2.89)	<0.001	13 (8–20)	1.20 (0.62–2.30)	0.001	3.15 (0.92–10.77)	0.005
Stigma and females	21 (5)	86 (64–97)	9.49 (2.72–33.14)		38 (18–62)	4.95 (1.87–13.05)		9.87 (1.98–49.17)	
Loss of family support									
No	409 (97)	47 (42–52)	1	0.07	13 (9–16)	1	0.23		
Yes	12 (3)	75 (43–95)	3.42 (0.91–12.83)		25 (5–57)	2.29 (0.60–8.72)			

* PDS analysis was reported among 421 pulmonary TB patients. Prevalence of PDS among those depressed at baseline was 27.5% (55/200).
† Defined as CES-D-10 score >9 out of 30 at ATT initiation.
‡ Defined as CES-D-10 score >9 out of 30 at ATT initiation and ATT completion.
§ Adjusted for age, marital status, education, urban/rural residence, AUDIT score, food insecurity and - (stigma+gender). Multivariate analysis was not done for baseline depression symptoms.
¶ Defined as AUDIT score ≥8.
PDS = persistent depression symptoms; TB = tuberculosis; OR = odds ratio; CI = confidence interval; aOR = adjusted OR; INR = Indian rupee; AUDIT = Alcohol Use Disorder Identification Test; DM = diabetes mellitus; ATT = anti-tuberculosis treatment; CES-D-10 = Center for Epidemiological Studies-Depression scale-10.

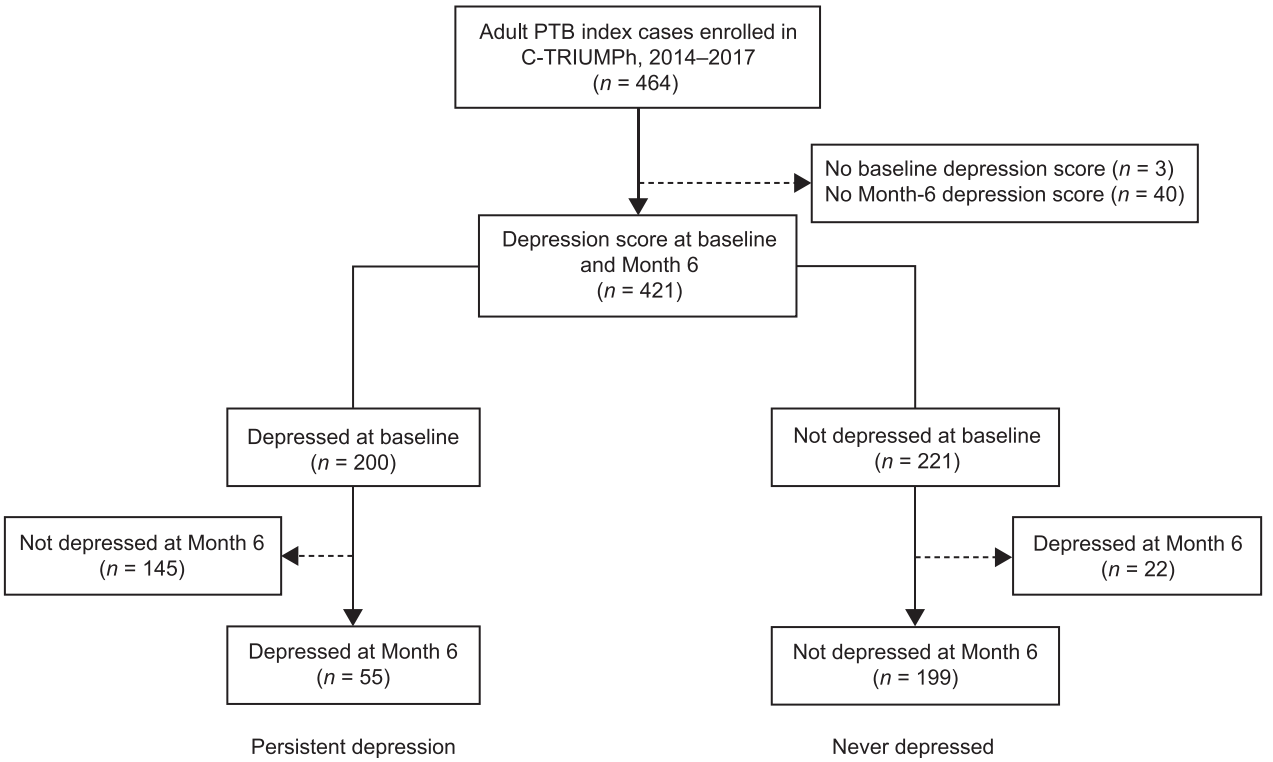

Figure Flow chart for the diagnosis of PDS in study participants. PTB = pulmonary tuberculosis; PDS = persistent depression symptoms.

CI 1.29–4.77) and reported TB stigma (OR 2.10, 95% CI 1.03–4.28). After adjusting for significant covariates (age, education, marital status urban/rural residence, AUDIT score, diabetes, food insecurity, TB stigma and gender) in multivariate models, alcohol dependence (adjusted OR [aOR] 2.98, 95% CI 0.92–9.67) marginally remained independently associated with PDS. Women reporting TB stigma were more likely to have PDS (aOR 9.87, 95% CI 1.98–49.17) than men after adjusting for interactions.

To date, studies have predominantly assessed depression at the time of TB diagnosis. This prospective cohort study is among the first to report a high prevalence of depression spanning TB treatment and identifies higher risk groups, particularly women and patients experiencing TB stigma. In the context of other studies that have linked baseline depression to non-adherence,[4,10] our findings have implications for routine TB care. This underscores the need to integrate mental health screening and interventions into TB programs, as PDS could have an influence on adherence.

Overall, our analysis associates BDS as well PDS with disadvantaged and vulnerable groups. This is consistent with previous studies, which have associated BDS with a monthly income of <5000 Indian rupees, alcohol dependence and older age.[4,11,12] Furthermore, our analysis provides corroborative evidence confirming that TB-related stigma is an important correlate of depression among TB patients,[13] particularly among women who reported facing TB stigma.

Our findings emphasize the need to integrate screening for depression and TB stigma into TB care. Because the lack of mental health specialists remains a barrier to accessing treatment for symptoms of depression, particularly in resource-limited settings,[14] TB programs should hire and train counselors to provide basic mental health services and deliver interventions designed to reduce TB-related stigma.

In summary, our study identified a high prevalence of PDS among adult TB patients and particularly among women reporting TB stigma. Integrating screening for depression and TB stigma into routine TB care along with counseling support would facilitate early identification and timely intervention. This has the potential to enhance treatment adherence and overall TB care.

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