Indian Journal of Tuberculosis xxx (xxxx) xxx

Contents lists available at ScienceDirect

Indian Journal of Tuberculosis

journal homepage: www.journals.elsevier.com/indian-journal-of-tuberculosis/

Tuberculosis and alcohol use; findings from a subnational TB prevalence survey in India

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ARTICLE INFO

Keywords:
Pulmonary tuberculosis
Alcohol addiction
Alcoholism
Alcohol drinking habits
Alcohol consumption
Alcohol use disorder
Alcohol-related disorders

ABSTRACT

Background: Population based surveys are crucial in understanding the relation between alcohol usage and tuberculosis epidemiology.
Methods: A state-wide population-based large sample size cross-sectional Tuberculosis (TB) survey was conducted in India. Participants from 180 clusters were screened with x-ray and sputum examination.
Results: In total 130,932 participants were screened. Among the "alcohol-use" population 115(0.6 %) and among non-alcoholics 129(0.12 %) were diagnosed with microbiologically confirmed pulmonary tuberculosis (MCPTB). The adjusted prevalence ratio (aPR) of MCPTB in the alcohol-use population was 4.2(3.24–5.45). The adjusted-PR(aPR) of MCPTB disease in 'alcohol-use' population was significantly associated with increasing age, under nutrition and past history of TB. The aPR for age between 31 and 45 years was 2.85(0.9–8.6); 46–60 years was 6.24(2.3–16.8) and >60 years was 7.77(2.7–21.6). For BMI of 18.50–22.99 was 3.2(1.6–6.2), BMI of 16.50–18.49 was 9.9(4.7–21.1) and BMI of <16.50 was 14.0(6.3–31.5)). For past history of TB was 3.76 (2.2–6.5). The number needed to screen to diagnose one participant with MCPTB in the general population was 537 and in 'alcohol-use' group was 168.
Conclusion: The prevalence of MCPTB in 'alcohol-use' individuals is four times higher when compared to non-alcoholic individuals. Increases in age, undernutrition and past history of PTB were highly associated with MCPTB disease among 'alcohol-use' participants.

1. Introduction

Tuberculosis (TB) and alcohol use are major global public health problems leading to significant morbidity and mortality.[1,2] Globally more than three million deaths are happening due to alcohol use every year. This represents more than 5 % of all deaths.[2] Harmful use of alcohol is the cause of more than 200 diseases and injuries.[2] Apart from health consequences, alcohol use causes significant social and economic losses, especially in middle and low-income countries. Alcohol use affects significant damage, especially during early life (20–39 years).[2] Tuberculosis, alcohol use and smoking are the deadliest combination.[3] India is the topmost country in TB burden in absolute numbers and India contributes nearly 27 % of the total TB cases which are reported globally. Nearly one-third of the Indian population has TB infection and one tenth of the infected will develop TB disease in their lifetime.[1,4,5] The five major risk factors for TB are malnutrition, smoking, alcohol, diabetes and HIV infection.[1] In India, malnutrition is the major risk factor for TB disease followed by alcohol use.[6] Alcohol consumption decreases immunity by impairing the immune function of alveolar macrophages. Chronic alcohol use also increases oxidative stress in the alveolar space which facilitates Mtb growth.[7] About 10 % of the TB cases globally were estimated to be attributable to alcohol.[8]

A systematic review has shown that there was a 30 % (24–35) prevalence of AUD (Alcohol Use Disorder) among patients with TB. Prevalence was higher in the Asian and European populations (37 %) when compared to US and African populations 24 %.[9] A recent study from Gujarat in India has revealed that 20 % of the patients with TB had alcohol usage and the prevalence of alcohol usage among the patients

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https://doi.org/10.1016/j.ijtb.2025.03.005
Received 2 January 2025; Received in revised form 7 March 2025; Accepted 10 March 2025
Available online 12 March 2025

with TB was associated with the use of smokeless tobacco, family history, and residence closer to spurious liquid brewing.

Attaining the 2030 global target of END TB by India would be highly challenging without addressing these issues.[10,11] In this line, a survey was conducted by the ICMR National Institute for Research in Tuberculosis (ICMR - NIRT), Chennai in association with the Government of Tamil Nadu to understand the burden of TB at the state level to implement appropriate control measures. A sub-analysis was conducted to understand the association between TB and alcohol use from the main study data.[12]

2. Methods

In this state, a population-based survey was conducted with the aim to estimate the prevalence of TB in all thirty-two districts from February 2021 to July 2022 and their risk factors were captured during the survey. A detailed methodology was available in the previous paper.[12] Participants aged fifteen and above were included in this study. Cluster sampling was done where 180 clusters were covered across the state with an average of 800 participants per cluster. Informed consent to participate in the study was obtained. Participants were initially interviewed, and symptomatic participants were advised to give sputum. All the participants underwent digital X-ray Chest. Participants who had any Chest X-ray abnormality were also asked to provide sputum for testing. TB testing was done using Cartridge-based nucleic acid amplification test (CBNAAT), smear microscopy (SM) and liquid culture (LC). Participants diagnosed with TB were immediately linked with National Tuberculosis Elimination Programme (NTEP) and appropriate care was ensured.

Survey operational definition: A participant was defined as MCPTB when there was two bacteriological evidence in sputum or one bacteriological and one radiological evidence. Alcohol use was defined as self-reported consumption of alcohol at least once in their lifetime. Current alcohol use was described as participants admitting to currently consuming alcohol, while past alcohol use referred to self-reported previous alcohol consumption that is not ongoing. The number needed to screen is the number of eligible participants need to be screened to get one TB diseased participant (NNS = 1/(prevalence)). Field Investigators were given intensive training in data collection. A ten membered Central Project Monitoring Unit (CPMU) was formed to taken care the quality of data collection in the field. Quality assurance was taken care proper training and assessing the Field Workers, repeated field visits, verification of data and monitoring of participants enrolment by the team members on a daily basis through GPS monitoring system embedded in the electronic data collection tool. Data was immediately transferred to the local server at the field site and then connected to central server at ICMR NIRT.

2.1. Statistical analysis

Data for the tuberculosis (TB) prevalence survey were collected electronically through Android and web applications, which functioned offline and transmitted data to a central server upon re-establishment of internet connectivity. The data collection modules were meticulously designed to ensure completeness and minimize logical errors, integrating information from reference laboratories and teleradiology panels. Upon receipt at the institute, the data underwent a thorough verification process to check for duplication, outliers, and logical consistency. Queries were promptly addressed to maintain data accuracy prior to analysis. Statistical analysis was conducted using STATA v15.0 (Stata Corporation, College Station, TX, USA). Descriptive statistics summarized participant characteristics as frequencies and percentages. The crude prevalence estimate of microbiologically confirmed pulmonary tuberculosis (MCPTB) per 100,000 individuals, along with 95 % confidence intervals, was computed using the exact binomial formula. The association between alcohol use and various demographic factors was assessed using the chi-square test, while age differences by alcohol use status were evaluated using the Wilcoxon rank-sum test. Univariate and multivariate generalized linear models with binomial and log link functions were employed to identify factors associated with TB disease. Prevalence ratios and adjusted prevalence ratios were calculated using Stata "svy" commands to account for clustering effects. All statistical analyses were two-sided, with a significance level set at alpha = 0.05.

Ethical Considerations: The protocol was approved by the Institutional Human Ethics Committee of National Institute for Research in Tuberculosis (017/NIRT-IEC/2021).

Results About 2,23,709 individuals were enumerated and out of which 1,43,005 were eligible to participate in the survey, in this 1,30,932 were screened (91.6). Among the 19,273 participants with alcohol use history, 115 (0.6 %) were diagnosed with microbiologically confirmed pulmonary tuberculosis (MCPTB) and among the 1,11,641 non-alcoholics 129 (0.1 %) were diagnosed with microbiologically confirmed pulmonary tuberculosis (MCPTB) (Fig. 1).

The crude prevalence and adjusted prevalence of TB in alcohol use participants given in detail in Table 1. Participants characteristics by alcohol status is given in Table-2.

The adjusted PR (aPR) of MCPTB disease in alcohol use population was significantly associated with increasing age, undernutrition and past history of TB. However significant association in the alcohol use population was not established in other risk factors for TB like geographical location, below poverty line, diabetes and smoking (Table 3).

The number needed to screen to diagnose one participant with PTB in the general population was 537 (473–611), however, in alcohol use group was only 168 (140–203). Among participants with a history of alcohol use NNS in specific categories given in Table 4.

3. Discussion

There are five notable findings in our study. The first one was that the prevalence of MCPTB among participants using alcohol was 600/1,00,000 and was 4.2 times higher than the non-alcoholics. However in the general population this was only 186/1,00,000 (163–210) in Tamil Nadu.[12] As per National TB Prevalence Survey of India, prevalence of TB among general population was only 316/1,00,000 (290–342).[4] A meta-analysis by Simou E et al., showed that alcohol use increases the relative odds of acquiring TB disease (OR1.9(1.63–2.23)) and further subgroup analysis documented that there was a three folds increase in the risk of acquiring TB with alcohol consumption (HR 2.81 (2.12–3.74)).[13] Similarly, another meta-analysis by Lonnroth K et al., showed that alcohol use increases the relative risk of acquiring TB by 2.94 times (Pooled RR 2.94 (1.89–4.59).[14]

We have done further subgroup analysis among alcohol users to understand the associated risk factors for TB. Increase in age, undernutrition and participants with past history of TB were more likely to have TB among the population using alcohol.

The second notable finding was the prevalence of PTB among the population using alcohol increases with increased age, which is 2.85 times higher in the age group of 31–45 years, 6.24 higher in the age group of 46–60 years and 7.8 higher in the age group more than sixty years when compared to the baseline reference of age less than thirty. The prevalence of PTB also increased with age general population.[4] However, the rate of increase in alcohol users is high when compared to the general population.[4] The national prevalence study done in India showed that the rate of increase was only 26 % in the age group between 35 and 54 years (PR 1.26) and 2.7 times in the age group >54 years (PR 2.71).[4]

The third finding was that PTB prevalence was increasing with undernutrition among the population using alcohol. Participants with BMI <16.50 kg/m^2 had a 14 times higher prevalence, those with BMI 16.50–18.49 kg/m^2 had 10 times higher prevalence of PTB and those with BMI 18.50–22.99 kg/m^2 had 3.18 times higher prevalence of TB

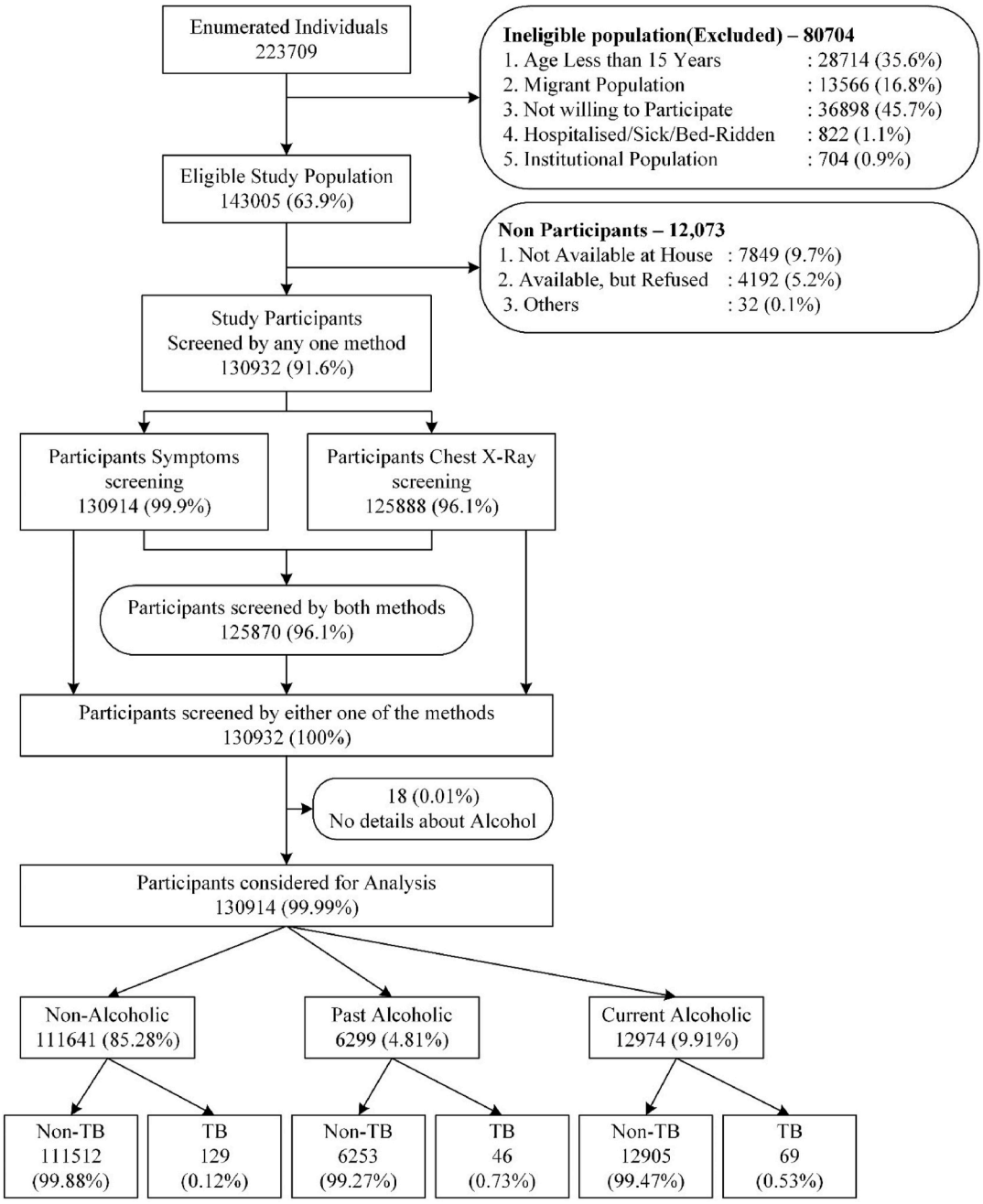

Fig. 1. Consort diagram.

Table 1
Prevalence estimates of Tuberculosis in alcohol use population.

	Non-Alcoholic	Past/Current Alcoholic	Past Alcoholic	Current Alcoholic
Screened	111641 (85.3)	19273 (14.7)	6299 (4.8)	12974 (9.9)
TB disease	129 (52.9)	115 (47.1)	46 (18.9)	69 (28.3)
Crude prevalence per 1000 (95 % CI)	1.16 (0.96, 1.37)	5.97 (4.93, 7.16)	7.30 (5.35, 9.73)	5.32 (4.14, 6.73)
Adjusted prevalence per 1000 (95 % CI)	1.47 (1.21, 1.73)	6.00 (4.98, 7.01)	7.15 (5.51, 8.80)	5.45 (4.10, 6.80)
Prevalence ratio (95 % CI)	Reference	4.20 (3.24, 5.45); p < 0.0001	5.18 (3.74, 7.18); p < 0.0001	3.73 (2.74, 5.08); p < 0.0001

than those with the BMI (≥23.00). Malnutrition is the single most risk factor for TB in India and its association with alcohol use has increased the prevalence of TB in a larger magnitude.[6] Similarly like age, TB in general population with BMI <18.5 kg/m^2 was only is only 6 times higher (cRR 6.02), however among population using alcohol was as high as 14 times.[12]

The fourth finding was the prevalence of PTB among alcohol population was 3.76 times higher among those with the past history of PTB. However increase in prevalence the general population with past history of TB was 12 times (cRR-12.36). A meta-analysis by Weiangkham D et al., showed that the probability of relapse (OR = 3.64; 95 % CI: 2.26–5.88, $p < 0.001$) and mortality (OR = 1.72; 95 % CI: 1.40–2.12, $p < 0.001$) also increased in the TB patients who consume alcohol.[15] Geographical location, below poverty line, diabetes and smoking were not independently associated with TB among the alcohol use population however these are independent risk factors for TB in the General

Table 2
The participants characteristics by Alcohol status.

Characteristic	Overall N = 130914	Non-Alcoholic N = 111641 (85.3 %)	Alcoholic N = 19273 (14.7 %)	p-value
Age in years				**<0.001**[a]
Median (IQR)	43.0 (30.0, 56.0)	43.0 (30.0, 56.0)	46.0 (35.0, 57.0)	
Age Classification, n (%)				**<0.001**[b]
Age: 15-30	33,158 (25.3 %)	30,026 (26.9 %)	3132 (16.3 %)	
Age: 30-45	38,701 (29.6 %)	32,262 (28.9 %)	6439 (33.4 %)	
Age: 45-60	37,362 (28.5 %)	30,978 (27.7 %)	6384 (33.1 %)	
Age: 60+	21,693 (16.6 %)	18,375 (16.5 %)	3318 (17.2 %)	
Gender, n/N (%)				**<0.001**[b]
Female	77,619 (59.3 %)	77,338 (69.3 %)	281 (1.5 %)	
Male	53,295 (40.7 %)	34,303 (30.7 %)	18,992 (98.5 %)	
Residential Area, n (%)				**<0.001**[b]
Rural	68,758 (52.5 %)	57,693 (51.7 %)	11,065 (57.4 %)	
Urban	62,156 (47.5 %)	53,948 (48.3 %)	8208 (42.6 %)	
Occupation, n (%)				**<0.001**[b]
Unemployed/ N–W	12,840 (9.8 %)	11,300 (10.1 %)	1540 (8.0 %)	
H–W/ST	56,926 (43.5 %)	55,964 (50.1 %)	962 (5.0 %)	
Employed	61,148 (46.7 %)	44,377 (39.7 %)	16,771 (87.0 %)	
Below poverty line, n (%)				**<0.001**[b]
Non-BPL	74,576 (57.0 %)	62,739 (56.2 %)	11,837 (61.4 %)	
BPL	56,338 (43.0 %)	48,902 (43.8 %)	7436 (38.6 %)	
Self-reported smoking status, n (%)				**<0.001**[b]
Non-Smoker	117,091 (89.4 %)	109,233 (97.8 %)	7858 (40.8 %)	
Smoker	13,823 (10.6 %)	2408 (2.2 %)	11,415 (59.2 %)	
Hypertension, n/N (%)				**0.009**[b]
Non-Hypertension	117,909 (90.1 %)	100,451 (90.0 %)	17,458 (90.6 %)	
Hypertension	13,005 (9.9 %)	11,190 (10.0 %)	1815 (9.4 %)	
Self-reported diabetes status, n/N (%)				**<0.001**[b]
Non-diabetes	118,253 (90.3 %)	100,979 (90.4 %)	17,274 (89.6 %)	
Diabetes	12,661 (9.7 %)	10,662 (9.6 %)	1999 (10.4 %)	
HIV status, n/N (%)				**<0.001**[b]
Negative	14,309 (10.9 %)	11,672 (10.5 %)	2637 (13.7 %)	
Positive/ Unknown	116,605 (89.1 %)	99,969 (89.5 %)	16,636 (86.3 %)	
BMI Classification, n/N (%)				**<0.001**[b]
BMI≥23.0	72,464 (55.4 %)	62,525 (56.0 %)	9939 (51.6 %)	
BMI 18.50 to 22.99	41,552 (31.7 %)	34,609 (31.0 %)	6943 (36.0 %)	
BMI 16.50 to 18.49	10,923 (8.3 %)	9260 (8.3 %)	1663 (8.6 %)	
BMI<16.5	5975 (4.6 %)	5247 (4.7 %)	728 (3.8 %)	
History of TB treatment, n/N (%)				**<0.001**[b]
No Past-TB	129,164 (98.7 %)	110,466 (98.9 %)	18,698 (97.0 %)	
With Past-TB	1750 (1.3 %)	1175 (1.1 %)	575 (3.0 %)	
On TB treatment, n/N (%)				**<0.001**[b]
Not on ATT	130,787 (99.9 %)	111,554 (99.9 %)	19,233 (99.8 %)	
On ATT	127 (0.1 %)	87 (0.1 %)	40 (0.2 %)	
CBNAAT, n/N (%)				**<0.001**[b]
Xpert Negative	130,688 (99.8 %)	111,526 (99.9 %)	19,162 (99.4 %)	
Xpert Positive	226 (0.2 %)	115 (0.1 %)	111 (0.6 %)	
AFB smear, n/N (%)				**<0.001**[b]
Smear Negative	130,791 (99.9 %)	111,576 (99.9 %)	19,215 (99.7 %)	
Smear Positive	123 (0.1 %)	65 (0.1 %)	58 (0.3 %)	
MGIT, n/N (%)				**<0.001**[b]
MGIT Negative	130,790 (99.9 %)	111,577 (99.9 %)	19,213 (99.7 %)	
MGIT Positive	124 (0.1 %)	64 (0.1 %)	60 (0.3 %)	
TB Diagnosis, n/N (%)				**<0.001**[b]
Non-TB	130,670 (99.8 %)	111,512 (99.9 %)	19,158 (99.4 %)	
TB	244 (0.2 %)	129 (0.1 %)	115 (0.6 %)	

[a] Wilcoxon rank sum test.
[b] Pearson's Chi-squared test.

population, for example smokers were having prevalence of TB 5 times and diabetes were 2.7 times higher in the Tamil Nadu general population.[12]

The fifth finding which is highly helpful for Health Programmes was the number needed to screen (NNS) to diagnose one case of PTB disease among persons using alcohol which was only 168 when compared to 537 in the general population. The NNS was much less among the sub-groups of participants using alcohol which was least among the participants with past history of TB (NNS = 25), followed by undernutrition (NNS = 42) and older age group (NNS = 79). This finding will help in deciding the targeted screening of higher-risk groups while planning active screening in the community or opportunistic screening in the health facility.

Apart from the prevalence and incidence of TB disease, Alcohol use affects the outcome of the treatment for TB. Alcohol use increases the odds of poor outcomes in DSTB (OR1.99(1.57–2.51)) and MDR-TB treatment outcomes 2.0(1.73–2.32).[16] A cohort from India has shown that alcohol dependence has increased the poor outcome in TB treatment by 72 % (recurrence, failure and death).[17] The TB patients will be consuming hepatotoxic drugs for a long term, in addition to this alcohol consumption will augment the problem of hepatotoxicity, gastritis and poor drug adherence.[18] TB programme should be strengthened in the management of Alcohol Use Disorders. A study from Karnataka has shown that there was a gap between TB programme and tobacco cessation as well as alcohol treatment services.[19] An intervention study from India has shown that individual counselling sessions during treatment has shown improvement in treatment outcome and adherence to medications.[20] Four states in India have banned Alcohol sales, however, this ban has created other issues like illegal brewing of alcohol, methanol poisoning and other substance abuse.[21] Effective intervention should be planned to address the alcohol use associated with TB. A limitation in this study was that the other relevant histories related to alcohol use were not collected. The amount of alcohol and severity of the disease were not studied. This is a large sample sized prevalence study and could not able to collect more information on alcohol, however systematic reviews revealed there is a dose-dependent association between alcohol use and TB Disease.[22] An exposure-response analysis of a systematic review revealed an increase in 12 % of TB risk, for every 10–20 g of daily alcohol intake.[23] Another limitation was there was no time cutoff was kept for past alcohol. When the participant agrees that he consumed alcohol in the past but not continuing was taken as "past alcohol use".

Table 3
Factors associated with TB disease in individuals with past/current alcoholic habits in the survey.

Factors	Screened [N = 19273]	TB disease [N = 115]	PR; p-Value (95 % CI)	aPR; p-Value (95 % CI)
	n (%[1])	n (%[2]) (95 % CI)		
Age Classification				
≤30	3132 (16.3)	4 (0.13) (0.03, 0.33)	Reference	Reference
31–45	6439 (33.4)	17 (0.26) (0.15, 0.42)	2.07; p = 0.196 [0.69, 6.21]	2.85; p = 0.064 [0.94, 8.64]
46–60	6384 (33.1)	52 (0.81) (0.61, 1.07)	6.38; p < 0.001 [2.37, 17.14]	6.24; p < 0.001 [2.31, 16.84]
>60	3318 (17.2)	42 (1.27) (0.91, 1.71)	9.91; p < 0.001 [3.58, 27.45]	7.77; p < 0.001 [2.79, 21.64]
Gender				
Female	281 (1.5)	2 (0.71) (0.09, 2.55)	Reference	
Male	18992 (98.5)	113 (0.59) (0.49, 0.71)	0.84; p = 0.571 [0.45, 1.55]	
Geographical location				
Rural	11065 (57.4)	75 (0.68) (0.53, 0.85)	1.39; p = 0.088 [0.95, 2.03]	1.27; p = 0.207 [0.88, 1.83]
Urban	8208 (42.6)	40 (0.49) (0.35, 0.66)	Reference	Reference
Below poverty line				
Non-BPL	11837 (61.4)	72 (0.61) (0.48, 0.77)	Reference	Reference
BPL	7436 (38.6)	43 (0.58) (0.42, 0.78)	0.95; p = 0.791 [0.65, 1.38]	0.74; p = 0.12 [0.50, 1.08]
Body Mass Index Classification [BMI] Kg/m2				
≥23.00	9939 (51.6)	17 (0.17) (0.10, 0.27)	Reference	Reference
18.50 to 22.99	6943 (36.0)	41 (0.59) (0.42, 0.80)	3.45; p < 0.001 [1.83, 6.52]	3.18; p = 0.001 [1.63, 6.22]
16.50 to 18.49	1663 (8.6)	34 (2.04) (1.42, 2.85)	11.95; p < 0.001 [6.06, 23.56]	9.95; p < 0.001 [4.71, 21.06]
<16.50	728 (3.8)	23 (3.16) (2.01, 4.70)	18.47; p < 0.001 [9.43, 36.17]	14.03; p < 0.001 [6.26, 31.45]
Self-reported diabetes status				
Non-diabetes	17274 (89.6)	98 (0.57) (0.46, 0.69)	Reference	Reference
Diabetes	1999 (10.4)	17 (0.85) (0.50, 1.36)	1.50; p = 0.108 [0.92, 2.46]	1.60; p = 0.076 [0.95, 2.68]
Self-reported smoking status				
Non-Smoker	7858 (40.8)	30 (0.38) (0.26, 0.54)	Reference	Reference
Smoker	11415 (59.2)	85 (0.74) (0.60, 0.92)	1.95; p = 0.006 [1.21, 3.14]	1.42; p = 0.155 [0.87, 2.30]
Past history of TB				
No	18698 (97.0)	92 (0.49) (0.40, 0.60)	Reference	Reference
Yes	575 (3.0)	23 (4.00) (2.55, 5.94)	8.13; p < 0.001 [5.04, 13.10]	3.76; p < 0.001 [2.18, 6.47]

1column percentage, 2 row percentage with CI

PR – Prevalence ratio; aPR – Adjusted prevalence ratio; CI – Confidence interval.

Table 4
Number needed to screen to diagnose one case of TB in Alcoholic and its subgroup population.

Group	Screened Population	TB	Crude Prev. (95 % CI)	Number needed to screen (NNS)
All	**130932**	**244**	**186 (164–211)**	**537 (473–611)**
Alcoholic	**19273**	**115**	**597 (493–716)**	**168 (140–203)**
Alcoholic with BMI≥18.50	16882	58	344 (261–444)	291 (225–383)
Alcoholic with BMI<18.50	2391	57	2384 (1810 - 3078)	**42 (32–55)**
Alcoholic and non-elderly (Age≤60)	15955	73	458 (359–575)	219 (174–279)
Alcoholic and elderly (Age>60)	3318	42	1266 (914 - 1707)	**79 (59–109)**
Alcoholic and Male	18992	113	595 (491–715)	168 (140–204)
Alcoholic and Female	281	2	712 (86 - 2547)	141 (39 - 1159)
Alcoholic and rural	11065	75	678 (534–849)	148 (118–187)
Alcoholic and urban	8208	40	487 (348–663)	205 (151–287)
Alcoholic and non-diabetes	17274	98	567 (461–691)	176 (145–217)
Alcoholic and diabetes	1999	17	850 (496 - 1358)	**118 (74–202)**
Alcoholic and non-Smoker	7858	30	382 (258–545)	262 (184–388)
Alcoholic and smoker	11415	85	745 (595–920)	**134 (109–168)**
Alcoholic without past history of TB	18698	92	492 (397–603)	203 (166–252)
Alcoholic with past history of TB	575	23	4000 (2552 - 5942)	**25 (17–39)**

NNS = 1/(prevalence); NA - Not applicable.

4. Conclusion

The prevalence of MCPTB in alcohol use individuals is four times higher when compared to non-alcoholic individuals. Increase in age, under nutrition and past history of PTB were highly associated with MCPTB disease among alcohol use participants.

CRediT authorship contribution statement

Giridharan Prathiksha: Methodology, Data acquisition, interpretation, review and editing the draft. **Ariarathinam Newtonraj:** Interpretation, Writing – original draft, preparation and editing the draft. **Kannan Thiruvengadam:** Formal analysis, interpretation, draft preparation, review and editing the draft. **Asha Frederick:** Interpretation and editing the draft. **Sriram Selvaraju:** Interpretation, Writing – original draft, preparation and editing the draft.

Data availability and sharing

Anonymised subset of data of the participants is available with the principal investigator, which will be shared on request with the data access agreement and administrative approval.

Source of funding

National Health Mission of Tamil Nadu, Government of India.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We acknowledge Havenesh Murugesan, J.Chitra, V.Rani, P.Munivaradhan, D.Nithyakumar, V.Rameshbabu, P.K.Venkatramana, N.Premkumar, S.V.Joseph Rajkumar, T.Thangaraj, A.Devanathan, P.Balaji, T. K.Bharath, J.Udayakumar, Wilkingson Mathew, John Arockia Doss, A. Vasudevan, K.Anbarasan, M. Mahesh Kumar, P.Kumaravel, P.Chandrasekar, K.Vasudevan, G.Eswaran, R.Krishna Bahadur, J.Jeeva, .E. Duraivel, R.Karunanidhi, S.Kathiravan, Dr. Ashok NR. All participants of the survey and local community leaders for social mobilization officials of the health and family welfare department, Tamil Nadu, ICMR – NIRT, Chennai, WHO-NTEP consultants TB prevalence survey staff and NTEP staff who helped in the implementation of the survey. We also acknowledge the support given by various general health care staff, volunteers, and the communities which supported the survey

implementation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijtb.2025.03.005.

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