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Association between alcohol consumption and risk of developing tuberculosis in patients with diabetes: a nationwide retrospective cohort study

Chiwook Chung[1], Kyu Na Lee[2], Kyungdo Han[2], Junhee Park[3], Dong Wook Shin[4,5*†] and Sei Won Lee[6*†]

Abstract

Background Diabetes mellitus (DM) and alcohol consumption are risk factors for tuberculosis (TB). We investigated the association between alcohol consumption and TB development in individuals with type 2 DM (T2DM).

Methods Individuals who underwent the national health examination during 2009–2012 were screened using the Korean National Health Information Database. In total, 2,437,443 eligible individuals with T2DM were followed up until December 2018. We identified 21,275 individuals with newly developed TB. Alcohol consumption was evaluated based on the health examination questionnaire, and individuals were categorized into none (0 g/day), mild-to-moderate (1–29.9 g/day), and heavy (≥ 30 g/day) drinkers. Multivariate Cox proportional hazard models were used to estimate the adjusted hazard ratio (aHR) of risk factors for TB.

Results Mild-to-moderate alcohol drinkers had a lower risk of developing TB (aHR 0.92, 95% confidence interval [CI] 0.89–0.96), and heavy alcohol drinkers had a higher risk of developing TB (aHR 1.21, 95% CI 1.16–1.27) than nonalcohol drinkers. When categorized by an alcohol intake of 5 g/day, alcohol drinkers of < 5 g/day had the lowest risk (aHR 0.85, 95% CI 0.81–0.90). The risk increased with alcohol intake, resulting in ≥ 20 g/day as the threshold (20–25 g/day, aHR 1.09, 95% CI 1.02–1.16). Stratified analysis revealed that current smokers had an increased risk of developing TB even among mild-to-moderate drinkers.

Conclusions Heavy alcohol consumption has been linked to an increased risk of developing TB in patients with T2DM. In contrast, mild-to-moderate alcohol consumption was associated with a reduced risk of TB, except in current smokers, where it led to a higher risk of TB. The risk of TB substantially increased with alcohol intake of 20 g/day or more, following a J-shaped curve.

Keywords Alcohol consumption, Type 2 diabetes mellitus, Tuberculosis

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Introduction

Tuberculosis (TB) remains a leading cause of mortality from infectious diseases and important public health problems worldwide [1]. In 2022, South Korea reported a total of 20,383 cases of TB (39.8 per 100,000 population), with 16,264 being new cases (31.7 per 100,000 population). Notably, older adults aged 65 years and above accounted for more than half of the new cases (55.8%, 9,069 cases, 100.6 per 100,000 population), a proportion that continues to rise annually [2]. Diabetes mellitus (DM) is also a global public health problem, which is attributed to aging, urbanization, diet, sedentary lifestyles, and obesity [3]. The global trend of increasing DM incidence has been considered an emerging threat of TB control [4], because DM is associated with a two- to fourfold increased risk of developing active TB [5]. It is estimated that by 2050, approximately one-third of TB incidence and half of TB mortality would be attributed to DM in Asia–Pacific countries [6].

Heavy alcohol consumption, defined as an alcohol intake of >30–40 g/day, or a clinical diagnosis of alcohol use disorder, is a well-established risk factor for latent TB infection and active TB [7–11]. Nonetheless, it remains uncertain whether mild-to-moderate drinking elevates TB risk [7–11]. A recent linear dose–response meta-analysis reported that a low alcohol intake (≤24 g/day) was not associated with TB risk; however, it included only five studies, of which three were case–control studies [8]. Furthermore, a prospective cohort study conducted in Singapore (including 63,257 participants) reported that a low alcohol intake (monthly-to-weekly alcohol drinking) was associated with a decreased risk of developing TB [12]. Therefore, it is necessary to elucidate the association between alcohol consumption and TB risk.

In South Korea, high-risk alcohol consumption, defined as more than seven drinks per session for men and more than five for women, at least twice per week, was observed in 22.8% of adults (31.1% of men and 4.2% of women) with DM in 2020 [13]. Another study that explored the relationship between lifestyle changes in alcohol consumption and TB development in patients with type 2 DM (T2DM) described that consistently heavy drinkers and heavy drinking quitters had higher risks of developing TB than new heavy drinkers and nondrinkers [14]. However, that study focused on only lifestyle changes in alcohol consumption and requires further investigation on the aspects of valid alcohol definition and quantitative analysis of alcohol intake [14]. Therefore, we investigated the association between alcohol consumption and TB development in individuals with DM using a national health examination questionnaire.

Methods

Data source

The Korean National Health Information Database is a public database provided by the Korean National Health Insurance Service (NHIS) and contains data on national health examination, medical treatment and insurance claims information, health care use, sociodemographic information, and mortality of the entire South Korean population since 2001 [15, 16]. The NHIS is a sole insurer and a mandatory universal public health insurance system that covers 97% of the Korean population. A medical aid is a public assistance that covers the remaining 3% of the population in the lowest income bracket; however, the NHIS also takes care of all the administrative processes for medical aid beneficiaries.

The NHIS has provided a national health examination program for the prevention and early detection of diseases since 1995 [17]. Until 2018, all adult employees or adults aged ≥40 years with national health insurance received a national health examination every other year (every year for manual workers), including simple chest radiographs, laboratory tests, and self-report questionnaires concerning lifestyle behaviors and medical history [16, 18].

Study population

A total of 23,452,862 individuals who received a national health examination between 2009 and 2012 (the index year) were initially screened. Among them, we identified 2,746,079 individuals with T2DM according to the following operating definition: (1) insurance claim with International Classification of Diseases 10th Revision (ICD-10) codes for T2DM (E11–E14) with at least one prescription of oral hypoglycemic agents (OHAs) or insulin within a year before the health examination or (2) fasting blood glucose (FBG) concentration ≥126 mg/dL in the health examination data [14, 19, 20].

Thereafter, we excluded 441 individuals aged <20 years, 121,265 individuals with any insurance claim with ICD-10 codes for TB (A15–19) before their health examination (TB wash-out), 162,666 individuals with insufficient medical records, and 24,264 individuals identified with TB according to the rare intractable disease (RID) registry (codes V206, V246, and V000) within 1 year after the index date (1-year lag period). The 1-year lag period was applied to exclude the overdetection of TB after the health examination. Finally, the remaining 2,437,443 eligible individuals with T2DM were included and started follow-up 1 year after the index date (time zero).

Study outcome: TB diagnosis

The outcome of this study was new TB development, which was identified using the RID registration codes for TB (V206, V246, and V000). Since 2005, the NHIS

has provided a special copayment reduction (90–100%) for all patients with TB along with the national TB control policy. Attending physicians are obliged to report all newly diagnosed TB cases to nearby public health centers and register them in the RID program. Thereafter, TB cases are reviewed by the NHIS to provide copayment reduction. Under the current national TB reporting system, the RID registration codes for TB are valid measures to identify individuals with TB in the Korean population [14, 20, 21].

The study cohort were followed up until December 31, 2018, and the follow-up ended at TB development (outcome), death, or censor (e.g., out-migration). The mean follow-up duration was 6.87 ± 1.60 years, and 21,275 individuals were newly identified with TB according to the RID registry data (Fig. 1).

Main exposure: alcohol consumption

Alcohol consumption information was collected from self-reported questionnaires during the national health examination within 2 years before the index date. The parameters obtained were the average frequency of alcohol beverage intake per week and the average number of drinks per occasion. A drink of beer, soju (Korean traditional alcohol beverage), wine, or whiskey corresponded to 8 g of pure alcohol [22]. The total alcohol amount consumed per week was calculated as 8 g of pure alcohol × number of drinks per occasion × frequency per week. By dividing 7 days, a daily alcohol intake was calculated. Based on this information, the participants were classified into three groups, viz., (1) nonalcohol drinkers: 0 g of alcohol per day; (2) mild-to-moderate alcohol drinkers: 1–29.9 g of alcohol per day; and (3) heavy alcohol drinkers: ≥30 g of alcohol per day.

Covariates

Information on anthropometric measurements (body weight, height, and blood pressure) and lifestyle behaviors (cigarette smoking and physical activity) from self-reported questionnaires was collected during the

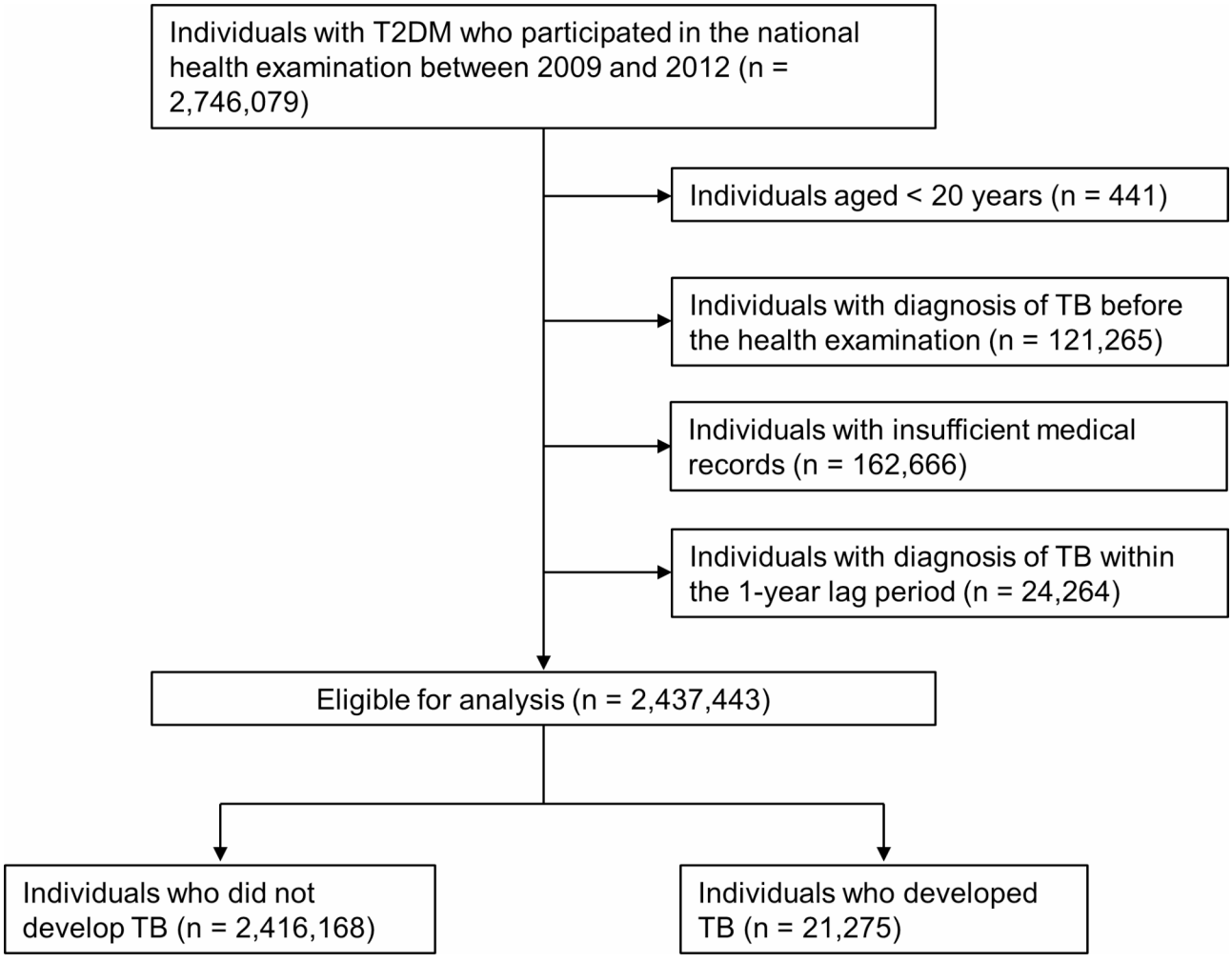

Fig. 1 Study flowchart

national health examination within 2 years before the index date [23, 24]. Body mass index (BMI) was calculated by dividing body weight by height squared (kg/m^2) [25]. Cigarette smoking was categorized into never, former, and current [14, 26]. Regular exercise was defined as >30 min of moderate physical activity at least five times per week or >20 min of vigorous physical activity at least three times per week [14, 21, 27]. The household income level was categorized into quartiles (Q1=the lowest and Q4=the highest) based on subscribers' annual national health insurance premium. Medical aid beneficiaries were included into Q1 category [28].

Comorbidities were identified based on the NHIS and national health examination data within 1 year before the index date according to the following definitions: (1) hypertension, either an insurance claim for ICD-10 codes I10–13 and I15 with a prescription of antihypertensive medications or high blood pressure (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) measured during a health examination; (2) dyslipidemia, either an insurance claim for ICD-10 code E78 with a prescription of lipid-lowering medications or serum total cholesterol ≥ 240 mg/dL measured during a health examination; and (3) chronic kidney disease (CKD), either an insurance claim for ICD-10 codes N18–19 or an estimated glomerular filtration rate < 60 mL/min/1.73 m^2 calculated using the modification of diet in renal disease equation during a health examination [29].

Statistical analysis

Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as numbers (percentage). Student's t-test and χ^2 test were used to compare continuous and categorical variables, respectively. The TB incidence rate was calculated as the ratio between the number of patients with newly diagnosed TB and the number of person-years at risk of developing TB (per 1,000). The Kaplan–Meier analysis was used to calculate the cumulative TB incidence according to alcohol consumption categories. A multivariate Cox proportional hazards model was used to evaluate the effect of risk factors on the time-to-event of TB development. The proportional hazards assumption was checked using the Schoenfeld residuals test. Model 1 was nonadjusted. In Model 2, the covariates included age and sex. Model 3 included the covariates in Model 2 and BMI, income, cigarette smoking (non, former, current), regular exercise, hypertension, and dyslipidemia. Model 4 (the main analysis model) contained the covariates in Model 3 and FBG concentration, CKD (DM-related renal complication), T2DM duration (<5 vs. ≥5 years), numbers of OHAs (<3 vs. ≥3), and insulin. The last covariates were included as surrogate markers for DM severity, which was also associated with the risk of developing TB [20]. Subgroup analysis stratified by age and smoking status was performed for Model 4. In the multivariate analyses, age, BMI, and FBG concentration were included as continuous variables. All *P* values were two-tailed, and statistical significance was set at $P<0.05$. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, United States), and the PHREG procedure was used for the Cox proportional hazards model.

Results

Baseline characteristics

Table 1 shows the baseline characteristics of the study population according to alcohol consumption categories. The mean age of all participants was 57.3 ± 12.3 years, with men accounting for 59.7%. Nonalcohol drinkers were predominantly women (61.3%) and never smokers (75.8%), whereas heavy drinkers were predominantly men (96.9%) and current smokers (54.0%).

Risk of TB development according to alcohol consumption

Table 2 demonstrates the associations between alcohol consumption and TB development. Mild-to-moderate drinkers had a lower risk of TB development (adjusted hazard ratio [aHR] 0.92, 95% confidence interval [CI] 0.89–0.96), whereas heavy drinkers had a higher risk of TB development (aHR 1.21, 95% CI 1.16–1.27) than nonalcohol drinkers. The cumulative TB incidence exhibited consistent results in the Kaplan–Meier analysis (Fig. 2).

We further categorized alcohol intake by 5 g/day to evaluate the dose–response effects of alcohol consumption on TB development (Fig. 3). Alcohol drinkers of <5 g/day had the lowest risk for TB development (aHR 0.85, 95% CI 0.81–0.90) compared with that of nonalcohol drinkers. The risk increased with alcohol amounts, and an alcohol intake of ≥20 g/day was the threshold for the risk of TB development (20≤…<25 g/day, aHR 1.09, 95% CI 1.02–1.16). This dose–response effect was more prominent among men than among women.

Risk of TB development according to alcohol consumption stratified by age and current smoking status

In the stratified analysis by age, mild-to-moderate alcohol consumption showed a significant inverse association with TB development only in individuals aged ≥ 65 years (aHR 0.85, 95% CI 0.81–0.89), but no such association was evident for younger individuals (age < 40 years, aHR 1.00, 95% CI 0.85–1.18; age 40–64 years, aHR 0.99, 95% CI 0.94–1.03). When stratified by smoking status, mild-to-moderate alcohol consumption was associated with decreased TB risk among noncurrent smokers (aHR 0.85, 95% CI 0.81–0.89) but increased TB risk among current smokers (aHR, 1.08, 95% CI 1.01–1.14). Heavy alcohol consumption was associated with an increased risk of TB among current smokers (aHR 1.36, 95% CI 1.27–1.46),

Table 1 Baseline characteristics of the study population

		Alcohol consumption		
	Total	**None**	**Mild-to-moderate**	**Heavy**
	***N*=2,437,443**	***n*=1,392,994**	***n*=802,138**	***n*=242,311**
Age, years	57.3±12.3	60.6±11.8	52.9±11.7	52.3±10.9
<40 years	188,964 (7.8)	59,752 (4.3)	102,015 (12.7)	27,197 (11.2)
40–64 years	1,528,160 (62.7)	780,024 (56.0)	565,823 (70.5)	182,313 (75.2)
≥65 years	720,319 (29.6)	553,218 (39.7)	134,300 (16.7)	32,801 (13.5)
Male sex	1,454,818 (59.7)	539,167 (38.7)	680,982 (84.9)	234,669 (96.9)
Income, lowest Q1	512,357 (21.0)	308,281 (22.1)	158,298 (19.7)	45,778 (18.9)
BMI, kg/m^2	25.1±3.4	25.1±3.5	25.1±3.3	25.3±3.3
Smoking status				
Non	1,360,148 (55.8)	1,055,693 (75.8)	260,344 (32.5)	44,111 (18.2)
Former	444,654 (18.2)	161,890 (11.6)	215,320 (26.8)	67,444 (27.8)
Current	632,641 (26.0)	175,411 (12.6)	326,474 (40.7)	130,756 (54.0)
Regular exercise	501,240 (20.6)	265,344 (19.1)	183,407 (22.9)	52,489 (21.7)
Hypertension	1,378,039 (56.5)	827,697 (59.4)	413,364 (51.5)	136,978 (56.5)
Dyslipidemia	1,017,535 (41.8)	641,565 (46.1)	290,598 (36.2)	85,372 (35.2)
Chronic kidney disease	276,399 (11.3)	206,786 (14.8)	57,040 (7.1)	12,573 (5.2)
DM duration ≥5 years	738,263 (30.3)	502,277 (36.1)	184,630 (23.0)	51,356 (21.2)
Insulin usage	203,048 (8.3)	148,533 (10.7)	42,501 (5.3)	12,014 (5.0)
Fasting glucose, mg/dL	144.8±46.8	141.4±46.8	148.3±45.8	153.3±47.9

Data are expressed as mean±standard deviation or number (%), unless otherwise indicated

BMI: body mass index, DM: diabetes mellitus

Table 2 Effect of alcohol consumption on tuberculosis development

Alcohol consumption	***n***	**TB**	**Duration (PY)**	**IR (per 1,000 PY)**	**Adjusted hazard ratio (95% confidence interval)**			
					Model 1	**Model 2**	**Model 3**	**Model 4**
None	1,392,994	12,524	9,540,124.90	1.31	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
Mild-to-moderate	802,138	6,209	5,545,466.42	1.12	0.85 (0.83, 0.88)	0.92 (0.89, 0.95)	0.89 (0.86, 0.92)	0.92 (0.89, 0.96)
Heavy	242,311	2,542	1,658,904.16	1.53	1.17 (1.12, 1.22)	1.24 (1.19, 1.30)	1.17 (1.12, 1.23)	1.21 (1.16, 1.27)

Model 1: nonadjusted

Model 2: adjusted for age and sex

Model 3: adjusted for age, sex, BMI, income, smoking, regular exercise, hypertension, and dyslipidemia

Model 4: adjusted for age, sex, BMI, income, smoking, regular exercise, hypertension, dyslipidemia, fasting glucose, CKD, DM duration (<5 vs.≥5 years), OHA (<3 vs.≥3), and insulin usage

TB: tuberculosis; PY: person-year; IR: incidence rate; Ref.: reference

which was higher compared to current nonsmokers (aHR 1.14, 95% CI 1.06–1.22, Table 3).

Discussion

In this nationwide population-based retrospective cohort study including more than two million individuals with T2DM, we examined the association between alcohol consumption and TB development. Heavy alcohol consumption was associated with an increased risk of TB development, whereas mild-to-moderate alcohol consumption was associated with a decreased risk of TB development. Individuals who consumed less than 5 g of alcohol per day had the lowest risk of developing TB, even lower than those who did not drink alcohol. As alcohol intake increased, the risk of TB also increased, resulting in a J-shaped curve. Nevertheless, even mild-to-moderate alcohol consumption was associated with an increased risk of TB development among current smokers.

Heavy alcohol intake (>30–40 g/day) and alcohol use disorder are well-established risk factors for active TB and poor treatment outcome [7–11]. Our study also showed that heavy alcohol consumption was associated with an increased TB risk. Alcohol use impairs the alveolar macrophage function and increases oxidative stress in the alveolar space, thus mitigating host defense and facilitating *Mycobacterium tuberculosis* growth [30]. Moreover, alcohol use disorder affects unhealthful behaviors, including delay in accessing healthcare facilities, decreased treatment adherence, and nutritional deficiencies [30]. Hence, reducing alcohol intake is essential for the national healthcare policy in the aspect of TB control.

Our study demonstrated that mild-to-moderate drinking was not generally associated with increased TB risk.

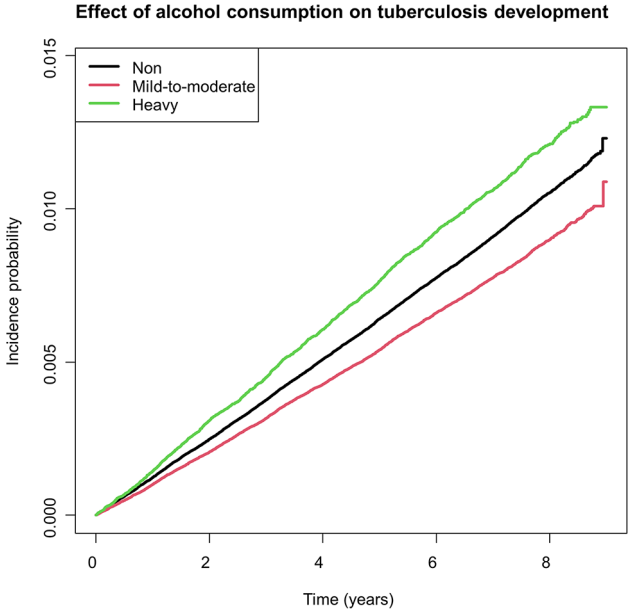

Fig. 2 Cumulative incidence of tuberculosis by alcohol consumption category plotted using the Kaplan–Meier curve

Alcohol consumption of <10 g/day was associated with decreased TB risk, whereas >20 ~ 30 g/day was associated with increased TB risk compared with that among nondrinkers, suggesting a J-shaped association. Our results are generally consistent with a previous prospective cohort study conducted in Singapore [12].

Our results may be explained as follows: First, mild drinking itself would be protective against TB. A previous epidemiologic study reported that infrequent and mild-to-moderate alcohol consumption were inversely associated with mortality from all causes, chronic lower respiratory tract diseases, influenza, and pneumonia [31]. Mild-to-moderate consumption of polyphenol-rich alcoholic beverages, such as wine and beer, might exert a protective effect on immune function [32]. Another experimental study suggested that a brief exposure to mild alcohol concentrations stimulates mucociliary clearance and bronchodilation and attenuates airway inflammation in airway diseases [33]. Other studies have also demonstrated that mild-to-moderate alcohol drinkers had better lung function (1-s forced expiratory volume and forced vital capacity) than nondrinkers [34, 35]. Better lung function was also associated with increased muscle mass and strength [34] and wine intake [35]. These data suggest that the beneficial effect of mild alcohol consumption results from other healthful lifestyle behaviors that could not be measured completely, such as regular exercise and healthy diet, rather than a possible beneficial effect from alcohol itself. In this context, our results should also be cautiously interpreted, because risk reduction due to mild-to-moderate alcohol consumption was observed among noncurrent smokers, but not among current smokers.

Second, some nondrinkers might not drink or quit drinking due to their poor health status, which might not be fully accounted for in our analyses, and they may have increased susceptibility to TB infection. In our stratified analyses by age, an inverse association was evident only in individuals aged ≥ 65 years. Considering that those who maintain mild-to-moderate alcohol consumption in this age group might have fewer health problems and may engage in more social activity, reverse causality would also partially explain the lower risk of TB development in mild-to-moderate alcohol drinkers.

Although our study suggests that mild-to-moderate drinking does not significantly increase TB risk in general, our subgroup analysis showed that even mild-to-moderate drinking was associated with increased TB risk among current smokers (aHR 1.08, 95% CI 1.01–1.14) but decreased TB risk among nonsmokers (aHR 0.85, 95% CI 0.81–0.89). This result is also consistent with that reported by the study conducted in Singapore, which demonstrated that noncurrent smokers with monthly-to-weekly alcohol intake had decreased TB risk (aHR 0.70, 95% CI 0.55–0.89) compared with that among nondrinkers; however, this risk reduction with low-dose alcohol drinking was not observed among current smokers [12]. This suggests the synergistic effect of alcohol consumption and cigarette smoking on TB development. Cigarette smoking increases the risk of TB infection, active TB, severity of TB, TB treatment failure, and recurrence of TB after successful treatment [26]. A prospective cohort study described a synergistic effect of alcohol consumption and smoking on TB treatment outcomes, wherein former and current smokers with alcohol dependence had the highest risk of composite outcomes compared with that in individuals who never smoked nor had alcohol use disorder [10]. Moreover, current smokers may have poorer overall health compared to nonsmokers, a factor that could not be fully evaluated in our analyses. Our results suggest that even mild drinking can increase TB risk particularly in current smokers. Hence, it is necessary to further clarify the synergistic effects of alcohol consumption and smoking on TB.

This study had some remarkable strengths. First, the large sample size and long-term follow-up of a nationwide population-based cohort improved the statistical power to describe the association between alcohol consumption and TB development in individuals with T2DM. Second, using the national health examination data, we could evaluate a daily alcohol intake amount to describe the dose–response relationship between alcohol consumption and TB risk. Third, due to the current mandatory reporting system, the RID registry provided a highly accurate TB diagnosis among the

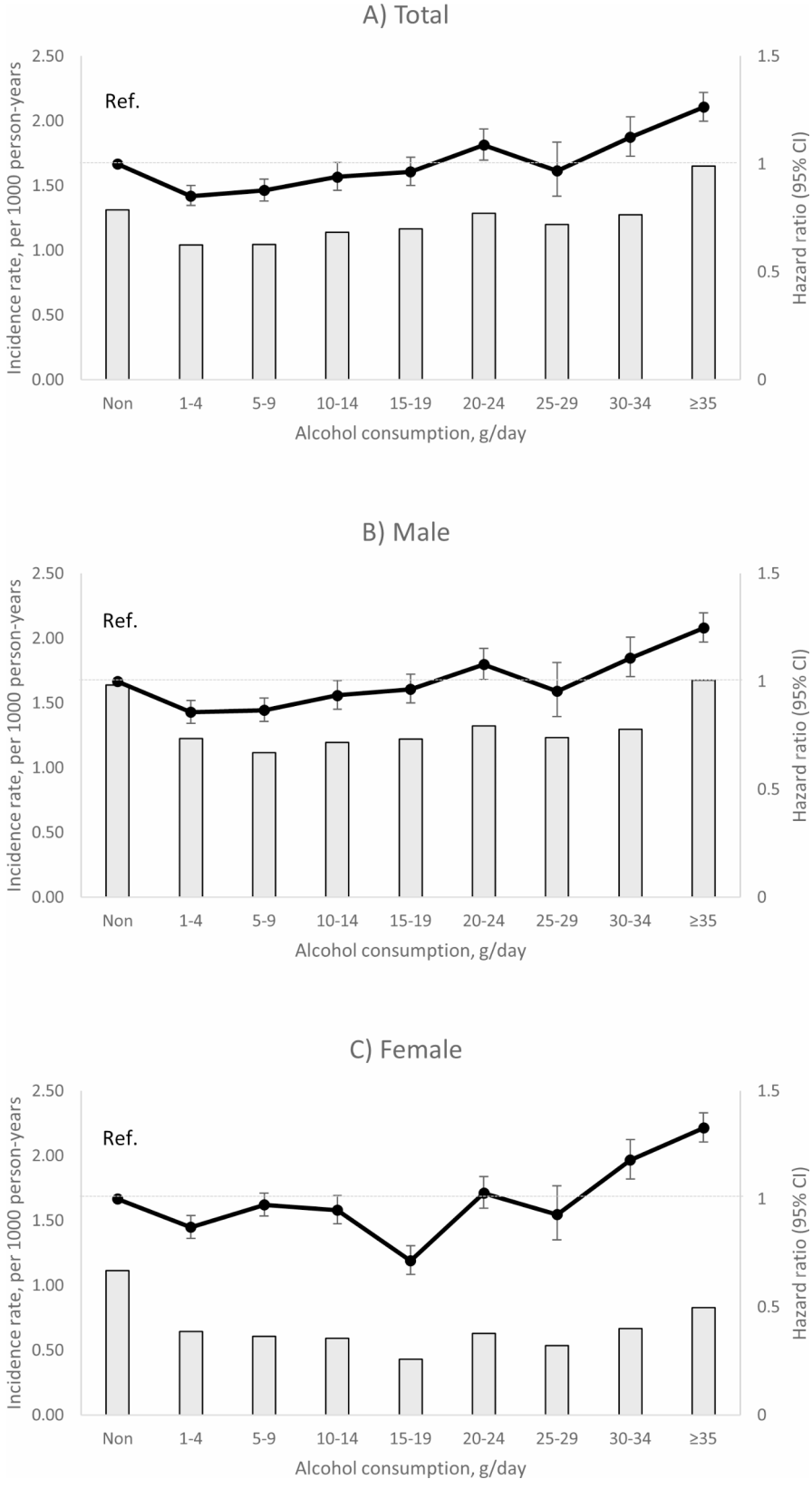

Fig. 3 Incidence rates and adjusted hazard ratios of developing tuberculosis categorized by alcohol intake of 5 g/day. **(A)** Total. **(B)** Male. **(C)** Female

Table 3 Effect of alcohol consumption on tuberculosis development stratified by age and current smoking in model 4

Subgroup		Alcohol consumption	*n*	TB	Duration (PY)	IR (per 1,000 PY)	Adjusted hazard ratio (95% confidence interval)
Age	< 40	None	59,752	223	417,225.21	0.53	1 (Ref.)
		Mild-to-moderate	102,015	423	710,431.41	0.60	1.00 (0.85, 1.18)
		Heavy	27,197	125	190,248.79	0.66	1.10 (0.88, 1.37)
	40–64	None	780,024	4,672	5,483,652.40	0.85	1 (Ref.)
		Mild-to-moderate	565,823	3,841	3,942,624.81	0.97	0.99 (0.94, 1.03)
		Heavy	182,313	1,785	1,256,504.00	1.42	1.35 (1.27, 1.43)
	≥ 65	None	553,218	7,629	3,639,247.28	2.10	1 (Ref.)
		Mild-to-moderate	134,300	1,945	892,410.21	2.18	0.85 (0.81, 0.89)
		Heavy	32,801	632	212,151.36	2.98	1.06 (0.97, 1.15)
							p for interaction < 0.0001
Current smoking	No	None	1,217,583	10,652	8,369,698.43	1.27	1 (Ref.)
		Mild-to-moderate	475,664	3,211	3,309,516.34	0.97	0.85 (0.81, 0.89)
		Heavy	111,555	1,015	770,993.59	1.32	1.14 (1.06, 1.22)
	Yes	None	175,411	1,872	1,170,426.47	1.60	1 (Ref.)
		Mild-to-moderate	326,474	2,998	2,235,950.07	1.34	1.08 (1.01, 1.14)
		Heavy	130,756	1,527	887,910.57	1.72	1.36 (1.27, 1.46)
							p for interaction < 0.0001

Model 4: adjusted for age, sex, BMI, income, smoking, regular exercise, hypertension, dyslipidemia, fasting glucose, CKD, DM duration (<5 vs. ≥5 years), OHA (<3 vs. ≥3), and insulin usage

TB: tuberculosis; PY: person-year; IR: incidence rate; Ref.: reference

Korean population. Furthermore, T2DM diagnosis provided a high diagnostic accuracy, which was based on the combination of insurance claims with ICD-10 codes, medication records, and laboratory data in the health examination [19]. Fourth, we could include certain clinical parameters, such as DM duration and CKD, as covariates in the multivariate analysis to adjust DM severity, which might be confounders for TB risk [20].

This study also had some limitations. First, because we determined alcohol consumption according to baseline health examination data, there might exist a considerable time interval between the health examination and TB diagnosis. Nonetheless, because the national health examination is voluntary participation, many of the study population lack the health examination data at the time of TB diagnosis. Second, the self-reported questionnaire during the health examination might result in a recall bias. Third, voluntary participation in health examinations might cause a selection bias. Fourth, the types of alcohol beverages, such as wine and beer, could not be categorized because of the limitations of source data. Fifth, because this was an observational study, the association between alcohol consumption and TB risk might not be causal. Sixth, since the level of alcohol consumption that minimizes harm across various health outcomes was 0 standard drink per week, the lower TB risk observed among mild-to-moderate drinkers may reflect complex interactions between alcohol consumption and other social and lifestyle factors that may not be fully accounted for in our analysis [36]. Finally, because this study was conducted in South Korea, caution is required when the results are applied to other ethnicities, particularly those with a lower TB prevalence.

In conclusion, heavy alcohol drinkers with T2DM had increased risks for TB development. Mild-to-moderate alcohol drinkers with T2DM had decreased risks for TB development. Alcohol intake of ≥ 20 g/day was a threshold that substantially increases TB risk. Even mild-to-moderate alcohol consumption was associated with increased TB risk among current smokers. These data suggest that a small amount of alcohol drinking exerts a complicated effect on TB development associated with other social behaviors such as smoking.

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Author contributions
Chiwook Chung, Kyu Na Lee, Kyungdo Han, Junhee Park, Dong Wook Shin, and Sei Won Lee conceived and designed the study. Kyu Na Lee, Kyungdo Han, and Junhee Park contributed to the data collection and data analysis. Chiwook Chung, Dong Wook Shin, and Sei Won Lee contributed to data interpretation and drafted the manuscript. All authors revised and approved the final manuscript. All authors accept responsibility for the accuracy of the content in the final manuscript. Generative artificial intelligence was not used in any portion of the manuscript writing.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study protocol was approved by the Institutional Review Board of Samsung Medical Center, Seoul, Republic of Korea (approval No. SMC 2022-07-072). The requirement for informed consent was waived, as it was a retrospective study and the data used were anonymized. This study complied with the guidelines stipulated in the Declaration of Helsinki, and all methods were performed in accordance with the relevant guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The funder did not have any role in the design of the study, in the collection, analysis, and interpretation of data, and in writing the manuscript.

Clinical trial number
Not applicable.

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