

Inflammatory bowel disease and risk of non-tuberculous mycobacterial pulmonary disease: a nationwide retrospective cohort study in Korea

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Background: Inflammatory bowel disease (IBD) is a chronic immune-mediated disorder of the gastrointestinal tract, and patients with IBD are vulnerable to infections. Non-tuberculous mycobacterial pulmonary disease (NTM-PD) is an infection of concern in immunocompromised individuals. However, data on the risk of NTM-PD in IBD patients are limited. This study aimed to investigate the association between IBD and the risk of NTM-PD using nationwide data in Korea.

Methods: We conducted a population-based matched cohort study involving 6,869 adults aged ≥ 20 years with IBD, using data acquired from the Korean National Health Insurance Service-National Sample Cohort (NHIS-NSC) database between 2002 and 2019. Multivariable Cox proportional hazards regression analyses were performed to estimate the hazard ratio (HR) and corresponding 95% confidence interval (CI) for incident NTM-PD in the overall IBD and IBD subtype cohorts (Crohn's disease and ulcerative colitis) compared to their respective 1:4 age-, sex-, and health insurance-matched cohorts. Fine-Gray subdistribution hazard models were additionally applied to account for competing risks.

Results: Over a median follow-up duration of 13.1 [interquartile range (IQR), 10.3–16.3] years, the incidence rate of NTM-PD was not significantly different, showing 54.82 and 43.21 per 100,000 person-years (PY) in the overall IBD and matched cohorts, respectively. In multivariable Cox-regression analysis, the risk of NTM-PD was not significantly increased in the IBD cohort compared to the matched controls (adjusted HR = 1.12, 95% CI: 0.82–1.54). Also, in Fine-Gray model, the risk of NTM-PD was not significantly increased in the IBD cohort compared to the matched controls (adjusted HR = 1.16, 95% CI: 0.85–1.59). Neither Crohn's disease nor ulcerative colitis was associated with increased risk of NTM-PD (adjusted HR = 0.98, 95% CI: 0.52–1.84 for Crohn's; adjusted HR = 1.26, 95% CI: 0.88–1.81 for ulcerative colitis *vs.* respective matched cohorts).

Conclusions: In this nationwide, large, longitudinal study, IBD was not associated with increased risk of NTM-PD.

Keywords: Inflammatory bowel disease (IBD); non-tuberculous mycobacterial pulmonary disease (NTM-PD); risk

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Introduction

Inflammatory bowel disease (IBD), which includes ulcerative colitis and Crohn's disease, is a chronic, immune-mediated disorder of the gastrointestinal tract (1,2). Patients with IBD are inherently susceptible to infections due to both systemic immune dysregulation and the frequent use of immunosuppressive agents such as corticosteroids, thiopurines, and biologics (3-5).

While tuberculosis has traditionally been a major infectious concern in IBD patients, particularly in tuberculosis-prevalent countries (6,7), increasing attention has been drawn to non-tuberculous mycobacterial pulmonary disease (NTM-PD) (8,9). NTM-PD is caused by environmental mycobacteria and is becoming more prevalent globally, especially among individuals with underlying pulmonary diseases or compromised

immunity (10-12). Despite this, the epidemiology and risk profile of NTM-PD in the IBD population remain poorly characterized. Currently, studies have focused on tuberculosis in IBD patients, and few studies focused on NTM-PD (6-9). This gap in knowledge is particularly concerning given the immunosuppressive status of patients with IBD (13).

Therefore, in this study, we aimed to evaluate the risk of incident NTM-PD in individuals with IBD, using representative nationwide database. We also evaluate the risk of NTM-PD according to IBD subtype (Crohn's disease and ulcerative colitis). We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-2026-0585/rc>).

Methods

Data source

This study utilized data from the Korean Health Insurance Service-National Sample Cohort (NHIS-NSC), a nationally representative retrospective cohort in Korea. The NHIS-NSC database encompasses data on (I) demographic variables (age and sex); (II) socioeconomic variables (e.g., type of insurance, residential area); (III) healthcare utilization (outpatient department visit, emergency room visit, and hospitalization); (IV) health screening examination findings [e.g., body mass index (BMI), smoking status, and alcohol consumption]; and (V) disease diagnoses based on the International Classification of Diseases, Tenth Revision (ICD-10), medical treatment, procedures, and surgery (14). This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of Chungbuk National University Hospital (IRB No. 2025-02-024). The requirement for informed consent was waived because the NHIS database was constructed after

Highlight box

Key findings

- Inflammatory bowel disease (IBD) was not associated with increased risk of non-tuberculous mycobacterial pulmonary disease (NTM-PD).

What is known and what is new?

- IBD is an immune-mediated disorder affecting the gastrointestinal tract. Patients with IBD are susceptible to infections such as tuberculosis, due to systemic immune dysregulation inherent to the disease itself, as well as the frequent use of immunosuppressants for its management.
- Unlike tuberculosis, patients with IBD did not have a significantly higher incidence of NTM-PD.

What is the implication, and what should change now?

- While the use of immunosuppressive agents in patients with IBD may raise concerns about a potential risk of NTM-PD, routine screening or intensified surveillance for NTM-PD solely based on an IBD diagnosis, in the absence of other risk factors, appears to be less warranted than that for tuberculosis.

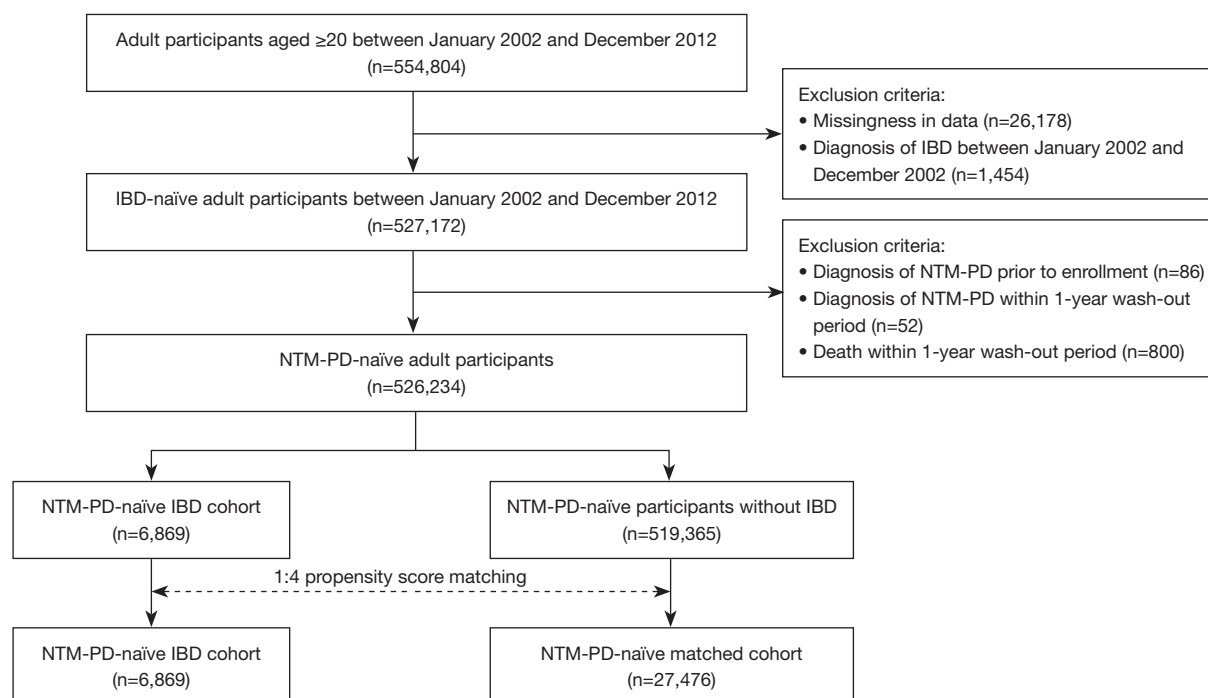


Figure 1 Flow chart of the study design. IBD, inflammatory bowel disease; NTM-PD, non-tuberculous mycobacterial pulmonary disease.

anonymization.

Study population

Between 1 January 2002 and 31 December 2012, the database recorded data for 554,804 adults aged ≥20 years. From this database, 26,178 individuals with any missing data on health screening examinations, 1,454 individuals with IBD between 1 January 2002 and 31 December 2002, 86 individuals with a prior diagnosis of NTM-PD, 52 individuals diagnosed with NTM-PD within a 1-year wash-out period, and 800 individuals who died during the wash-out period were excluded. Consequently, a total of 526,234 individuals was included in the final analysis. The index date was defined as the date of first health screening examination between January 1, 2002, and December 31, 2012. Of these, 6,869 were identified as having IBD (IBD cohort) and 519,365 were not (controls). A 1:4 matching was performed to construct a matched cohort, matching individuals with IBD to controls without IBD based on age, sex, and type of insurance, resulting in 27,476 individuals in the matched cohort (Figure 1). For analysis of IBD subtypes, each individual with Crohn's disease or ulcerative colitis was matched with four controls based on age, sex, and type of insurance.

Exposure

IBD was defined as the presence of either a major or minor diagnostic code corresponding to ICD-10 code K50 for Crohn's disease or K51 for ulcerative colitis, along with the special codes (V130 for Crohn's disease and V131 for ulcerative colitis) assigned through the Rare Intractable Diseases (RID) program, an aspect of the NHIS (15,16).

Outcome

The primary outcome was incident NTM-PD. In the first operational definition, NTM-PD was defined as the presence of at least one ICD-10 code (A31.0, A31.8, or A31.9) recorded as either a primary or secondary diagnosis. In the second operational definition, NTM-PD was defined as the presence of these ICD-10 codes on at least two occasions as either a primary or secondary diagnosis (17,18). In the third operational definition, NTM-PD was defined as the presence of these ICD-10 codes on at least two occasions as either a primary or secondary diagnosis, together with claims for acid-fast bacilli smears or mycobacterial cultures (procedure codes B4052, B4054, or B4055) (19-23). Participants in the IBD and matched cohorts were followed until death, diagnosis of NTM-PD,

or 31 December 2019, whichever came first.

Covariates

BMI was calculated as the weight (kg) divided by height squared (m^2) and categorized as underweight ($<18.5 \text{ kg/m}^2$), normal ($18.5\text{--}22.9 \text{ kg/m}^2$), overweight ($23.0\text{--}24.9 \text{ kg/m}^2$), or obese ($\geq 25.0 \text{ kg/m}^2$) according to the recommended classification for Asians (24). Household income levels were categorized as low ($<40^{\text{th}}$ percentile), middle ($40^{\text{th}}\text{--}80^{\text{th}}$ percentile), and high ($80^{\text{th}}\text{--}100^{\text{th}}$ percentile). The type of insurance was classified as self-employed health insurance or employee health insurance. Participants were classified as never, former or current smokers. Alcohol consumption and physical activity were evaluated according to the weekly frequency of drinking and exercise. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI), based on diagnoses recorded during the previous year (25,26). Use of 5-aminosalicylic acid, corticosteroids, and immunomodulators (azathioprine, mercaptopurine, cyclosporine, tacrolimus, and methotrexate) within 1 year before the follow-up start date was included.

Baseline comorbidities were identified using claims data when at least one record with the relevant ICD-10 code was listed as the primary diagnosis during the baseline period. The following conditions were included: asthma (J45–J46) (27–30); chronic obstructive pulmonary disease (COPD) [J42–J44, except J43.0 (unilateral emphysema)] (31–35); bronchiectasis (J47) (36,37); cerebrovascular disease (G45–G46, I60–I69); cardiovascular disease including hypertension (I10–I15); angina or myocardial infarction (I20, I21–I22 and I25.2) and heart failure (I43, I50, I09.9, I11.0, I25.5, I13.0, I13.2, I42.0, I42.5–I42.9 and P29.0) (38,39); diabetes mellitus (E10–E14) (40); and connective tissue diseases (M05–M06, M32–M34, M31.5, M35.1, M35.3, and M36.0) (41–46).

Statistical analysis

Categorical variables were summarized as counts and percentages. Group differences were assessed using the χ^2 test for categorical variables and either the *t*-test or the Mann-Whitney U-test for continuous variables, depending on the data distribution.

The incidence rate of NTM-PD was estimated as the number of newly identified cases divided by the total person-years (PY) of follow-up (per 100,000 PY). Cumulative incidence curves were constructed to compare

the incidence of NTM-PD between the IBD and matched cohorts, and differences between groups were assessed using Gray's test.

The association between IBD and incident NTM-PD was evaluated using Cox proportional hazards regression analyses. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated through univariable and multivariable models for the overall IBD cohort and for subgroups with Crohn's disease or ulcerative colitis, each compared with matched cohorts. The association between IBD and incident NTM-PD was additionally evaluated using the Fine-Gray competing-risk model, considering death as a competing event. Model 1 was a crude model. Model 2 was adjusted for household income, BMI, smoking status, alcohol consumption, physical activity, comorbidities (asthma, COPD, cerebrovascular disease, hypertension, angina or myocardial infarction, congestive heart failure, diabetes mellitus, and connective tissue diseases), and CCI. Model 3 was additionally adjusted for medication use (5-aminosalicylic acid, corticosteroids, and immunomodulators).

A two-sided *P* value <0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

The baseline characteristics of the individuals, including age, sex, and type of insurance, exhibited a well-balanced distribution between the two cohorts (Table 1). Among 34,345 individuals, the IBD cohort had a higher rate of individuals with high household income (35.5% *vs.* 33.1%, $P<0.001$), non-smokers (65.4% *vs.* 63.1%, $P<0.001$), non-alcohol drinkers (54.3% *vs.* 52.1%, $P=0.006$), connective tissue diseases (4.7% *vs.* 3.8%, $P<0.001$), and medications such as 5-aminosalicylic acid (1.8% *vs.* 0.1%, $P<0.001$), corticosteroid (5.5% *vs.* 4.0%, $P<0.001$), immunomodulator (0.7% *vs.* 0.2%, $P<0.001$) than the matched cohort.

Risk of NTM-PD in the overall IBD *vs.* matched controls

During a median follow-up of 13.1 years [interquartile range (IQR), 10.3–16.3], among the 27,476 individuals in the matched cohort, according to the first operational

Table 1 Baseline characteristics of the study individuals

Variable	Total (n=34,345)	IBD cohort (n=6,869)	Matched cohort (n=27,476)	P value
Age (years)				>0.99
20–29	4,550 (13.3)	910 (13.3)	3,640 (13.3)	
30–39	4,720 (13.7)	944 (13.7)	3,776 (13.7)	
40–49	9,370 (27.3)	1,874 (27.3)	7,496 (27.3)	
50–59	7,445 (21.7)	1,489 (21.7)	5,956 (21.7)	
60–69	5,785 (16.8)	1,157 (16.8)	4,628 (16.8)	
≥70	2,475 (7.2)	495 (7.2)	1,980 (7.2)	
Sex				>0.99
Male	18,670 (54.4)	3,734 (54.4)	14,936 (54.4)	
Female	15,675 (45.6)	3,135 (45.6)	12,540 (45.6)	
Type of insurance				>0.99
Self-employed health insurance	11,925 (34.7)	2,385 (34.7)	9,540 (34.7)	
Employee health insurance	22,420 (65.3)	4,484 (65.3)	17,936 (65.3)	
Household income				<0.001
Low	6,166 (18.0)	1,186 (17.3)	4,980 (18.1)	
Middle	16,639 (48.5)	3,245 (47.2)	13,394 (48.8)	
High	11,540 (33.6)	2,438 (35.5)	9,102 (33.1)	
Body mass index				0.26
Underweight	1,341 (3.9)	277 (4.0)	1,064 (3.9)	
Normal	13,087 (38.1)	2,679 (39.0)	10,408 (37.9)	
Overweight	8,411 (24.5)	1,667 (24.3)	6,744 (24.6)	
Obese	11,506 (33.5)	2,246 (32.7)	9,260 (33.7)	
Smoking status				<0.001
Never smoker	21,834 (63.6)	4,495 (65.4)	17,339 (63.1)	
Ex-smoker	3,346 (9.7)	711 (10.4)	2,635 (9.6)	
Current smoker	9,165 (26.7)	1,663 (24.2)	7,502 (27.3)	
Alcohol consumption (days/week)				0.006
None	18,054 (52.6)	3,727 (54.3)	14,327 (52.1)	
1–4	14,907 (43.4)	2,867 (41.7)	12,040 (43.8)	
≥5	1,384 (4.0)	275 (4.0)	1,109 (4.0)	
Physical activity (days/week)				0.40
None	20,288 (59.1)	4,079 (59.4)	16,209 (59.0)	
1–4	11,247 (32.8)	2,209 (32.2)	9,038 (32.9)	
≥5	2,810 (8.2)	581 (8.5)	2,229 (8.1)	

Table 1 (continued)

Table 1 (continued)

Variable	Total (n=34,345)	IBD cohort (n=6,869)	Matched cohort (n=27,476)	P value
Comorbidities				
Pulmonary comorbidities				
Asthma	3,104 (9.0)	600 (8.7)	2,504 (9.1)	0.33
Chronic obstructive pulmonary disease	1,518 (4.4)	312 (4.5)	1,206 (4.4)	0.58
Bronchiectasis	292 (0.9)	62 (0.9)	230 (0.8)	0.60
Cerebrovascular disease	1,076 (3.1)	195 (2.8)	881 (3.2)	0.12
Cardiovascular disease				
Hypertension	6,149 (17.9)	1,211 (17.6)	4,938 (18.0)	0.51
Angina or myocardial infarction	1,728 (5.0)	352 (5.1)	1,376 (5.0)	0.69
Congestive heart failure	705 (2.1)	123 (1.8)	582 (2.1)	0.09
Diabetes mellitus	3,418 (10.0)	665 (9.7)	2,753 (10.0)	0.41
Connective tissue diseases	1,364 (4.0)	321 (4.7)	1,043 (3.8)	<0.001
CCI				0.23
0–1	31,593 (92.0)	6,343 (92.3)	25,250 (91.9)	
≥2	2,752 (8.0)	526 (7.7)	2,226 (8.1)	
Medication				
5-aminosalicylic acid	151 (0.4)	124 (1.8)	27 (0.1)	<0.001
Corticosteroid	1,475 (4.3)	380 (5.5)	1,095 (4.0)	<0.001
Immunomodulator	106 (0.3)	46 (0.7)	60 (0.2)	<0.001

Data are presented as number (%). CCI, Charlson comorbidity index; IBD, inflammatory bowel disease.

definition (at least one ICD-10 code as a primary or secondary diagnosis), a total of 153 incident cases of NTM-PD were identified, of which 53 occurred among the 6,869 individuals in the IBD cohort. The incidence rate of NTM-PD was not statistically different between the IBD and matched cohorts (54.8 *vs.* 43.2 per 100,000 PY) (Table 2). The cumulative incidence plot showed similar results (Gray's test, $P=0.31$) (Figure 2). In multivariable Cox-regression analysis, the risk of NTM-PD was not significantly increased in the IBD cohort compared to the matched controls in the first operational definition (adjusted HR =1.12, 95% CI: 0.82–1.54), second operational definition (adjusted HR =1.17, 95% CI: 0.80–1.71), nor third operational definition (adjusted HR =1.31, 95% CI: 0.87–1.98). In Fine-Gray model, the risk of NTM-PD was not also significantly increased in the IBD cohort compared to the matched controls in the first operational definition (adjusted HR =1.16, 95% CI: 0.85–1.59), second

operational definition (adjusted HR =1.21, 95% CI: 0.83–1.78), nor third operational definition (adjusted HR =1.36, 95% CI: 0.89–2.08) (Table 2). As shown in Table S1, subgroup analyses showed that age, sex, type of insurance, BMI, smoking status, alcohol consumption, and physical activity did not significantly modify the association between IBD and the risk of NTM-PD (all P values for interaction >0.05 in Model 2).

Risk of NTM-PD in the IBD subtype cohorts vs. matched controls

As shown in Table 3, the risk of each IBD subtype cohort had no statistical difference compared to their matched controls in Cox proportional hazards model (adjusted HR =0.98, 95% CI: 0.52–1.84 for Crohn's cohort; adjusted HR =1.26, 95% CI: 0.88–1.81 for ulcerative colitis cohort) and Fine-Gray model (adjusted HR =1.00, 95% CI: 0.54–1.86

Table 2 Incidence rates and risk for NTM-PD in IBD and matched cohorts

Variable	Number of patients	Incidence rate (/100,000 PY)	Cox PH model			Fine-Gray model		
			Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
NTM-PD operational definition 1: at least one ICD-10 code as the primary or secondary diagnosis								
Overall								
Matched cohort	27,476	153	43.21	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
IBD cohort	6,869	53	54.82	1.18 (0.86, 1.61)	0.31	1.13 (0.83, 1.55)	0.45	1.12 (0.82, 1.54)
NTM-PD operational definition 2: at least twice ICD-10 code as the primary or secondary diagnosis								
Overall								
Matched cohort	27,476	103	29.05	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
IBD cohort	6,869	37	38.24	1.22 (0.83, 1.77)	0.31	1.16 (0.80, 1.69)	0.44	1.17 (0.80, 1.71)
NTM-PD operational definition 3: at least twice ICD-10 code as the primary or secondary diagnosis with microbial culture and identification test								
Overall								
Matched cohort	27,476	79	22.28	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
IBD cohort	6,869	32	33.07	1.38 (0.92, 2.09)	0.12	1.31 (0.87, 1.98)	0.20	1.31 (0.87, 1.98)

Model 1 is a crude model. Model 2 is adjusted for household income, body mass index, smoking status, alcohol consumption, physical activity, comorbidities, and CCI. Model 3 is adjusted for household income, body mass index, smoking status, alcohol consumption, physical activity, comorbidities, CCI, and medications. CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease; ICD-10, International Classification of Diseases, 10th Revision; NTM-PD, non-tuberculous mycobacterial pulmonary disease; PH, proportional hazards; PY, person-years; ref, reference.

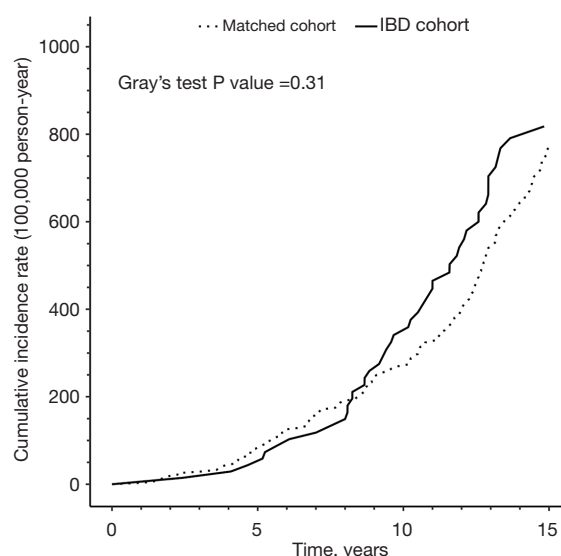


Figure 2 Cumulative incidence probability of NTM-PD (/100,000 person-years) in IBD and matched cohorts. IBD, inflammatory bowel disease; NTM-PD, non-tuberculous mycobacterial pulmonary disease.

for Crohn's cohort; adjusted HR =1.30, 95% CI: 0.90–1.89 for ulcerative colitis cohort). Among the 8,836 individuals in the matched cohort, 42 developed NTM-PD, compared with 13 cases among 2,209 individuals in the Crohn's disease cohort. In the ulcerative colitis cohort, 42 cases of NTM-PD were identified among 4,858 individuals, while 107 cases occurred among 19,432 matched controls.

Discussion

In this large-scale nationwide cohort study, we found that patients with IBD did not have a significantly higher incidence of NTM-PD compared to a matched control cohort. Even when evaluated by IBD subtype, neither Crohn's disease nor ulcerative colitis show an increased risk of NTM-PD, suggesting no significant association between IBD and risk of NTM-PD. The incidence rates observed in our study were generally consistent with those reported in previous nationwide Korean studies (47), supporting the validity of our findings.

Regarding associations between IBD and mycobacterial pulmonary diseases, previous studies have shown a significantly increased risk of tuberculosis in patients with IBD (6,7). However, information regarding the risk of NTM-PD in patients with IBD is scarce, leaving important clinical questions unanswered (8,9). Meeting this need, our study showed that the risk of NTM-PD incidence was

not significantly increased in IBD patients, regardless of subtype.

The reasons why these two pathogens elicited different results in patients with IBD cannot be clearly explained by our study. One reason for this phenomenon might be different immunological responses to *Mycobacterium tuberculosis* (MTB) and NTM. NTM, unlike MTB, does not cause latent infection. Thus, reactivation of latent infection under immunosuppressive status might explain a higher risk of tuberculosis in IBD, but not for NTM-PD. Second, the immune dysregulation in IBD may impair tuberculosis-specific responses (e.g., Th1/IFN- γ pathways) more than those needed to control NTM (48,49). However, since our study is observational, future basic studies explaining this phenomenon are needed.

The findings of this nationwide cohort study carry meaningful clinical implications for the care of patients with IBD. Given that NTM-PD is a chronic mycobacterial infection and that IBD patients often receive immunosuppressive therapies, clinicians may harbor heightened concerns about the potential risk of NTM-PD in this population. However, our results demonstrate that IBD, including both Crohn's disease and ulcerative colitis, is not associated with a significantly increased risk of NTM-PD compared to matched controls. This evidence suggests that such concerns may be unnecessary in the absence of other risk factors. Consequently, routine screening or

Table 3 Incidence rates and HR for NTM-PD according to type of IBD

Variable	Number of patients	Cases	Incidence rate /100,000 PY	Cox PH model			Fine-Gray model		
				Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
				HR (95% CI) P value	HR (95% CI) P value	HR (95% CI) P value	HR (95% CI) P value	HR (95% CI) P value	HR (95% CI) P value
Crohn's disease									
Matched cohort	8,836	42	36.88	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Crohn's disease cohort	2,209	13	41.47	1.04 (0.56,1.94)	0.97 (0.52,1.82)	0.98 (0.52,1.84)	1.06 (0.57,1.96)	0.99 (0.54,1.84)	1.00 (0.54,1.86)
Ulcerative colitis									
Matched cohort	19,432	107	42.49	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Ulcerative colitis cohort	4,858	42	61.65	1.35 (0.94,1.93)	1.30 (0.91,1.86)	1.26 (0.88,1.81)	1.37 (0.96,1.97)	1.34 (0.93,1.93)	1.30 (0.90,1.89)

Model 1 is a crude model. Model 2 is adjusted for household income, body mass index, smoking status, alcohol consumption, physical activity, comorbidities, and CCI. Model 3 is adjusted for household income, body mass index, smoking status, alcohol consumption, physical activity, comorbidities, CCI, and medications. CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease; NTM-PD, non-tuberculous mycobacterial pulmonary disease; PH, proportional hazards; PY, person-years; ref, reference.

intensified surveillance for NTM-PD solely based on an IBD diagnosis may not be warranted. These findings can help alleviate undue anxiety among clinicians and patients and support more balanced decision-making regarding immunosuppressive treatment strategies. Nonetheless, individualized assessment remains essential, particularly in patients with additional risk factors or in regions with high environmental exposure to NTM.

The major advantage of our study is that we considered demographic as well as personal habits in the evaluation of NTM-PD risk in patients with IBD. By matching demographics and adjusting for other potential confounding factors, our results provide convincing evidence in this field. However, there are several limitations in our study. First, only individuals who underwent health screening examination were included. Thus, there might be biases associated with healthy behaviors. Second, there is a potential risk of over- or underestimating NTM-PD because we defined it using ICD-10 codes. In Korea, tuberculosis is a legally notifiable communicable disease and must be reported, whereas NTM is not. Consequently, unlike tuberculosis, data on NTM are not systematically collected, and the possibility of underdiagnosis cannot be excluded. Third, given the relatively small number of incident NTM-PD cases, the statistical power of the study may have been limited. Therefore, although the HRs were consistently greater than 1, the lack of statistical significance should be interpreted with caution, and a modest increase in the risk of NTM-PD among patients with IBD cannot be completely excluded. Fourth, we defined IBD based on ICD-10 codes and thus, detailed information on disease severity and inflammatory burden could not be provided. Because treatment strategies for IBD vary according to disease severity and immunosuppressive treatment could increase the risk of NTM infection, these factors may have influenced our results. Consequently, future studies incorporating detailed clinical and treatment-related information are warranted to determine whether the risk of NTM-PD differs according to IBD severity and therapeutic exposure. Fifth, since this study was conducted using data from the Korean population, directly applying the findings to other populations requires caution. This is because environmental exposure to NTM, genetic susceptibility, and healthcare systems may differ across regions. Therefore, further studies are needed to generalize the results to other countries. Finally, although we adjusted for several potential confounders, unmeasured factors-such as regional, environmental, and occupational exposures-may still have

influenced the observed associations.

Conclusions

In conclusion, this nationwide longitudinal cohort study demonstrated that the risk of NTM-PD was not higher in individuals with IBD than in those without IBD.

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None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-2026-0585/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of Chungbuk National University Hospital (IRB No. 2025-02-024). The requirement for informed consent was waived because the NHIS database was constructed after anonymization.

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