



## The Association between Behavioral Risk Factors and Nontuberculous Mycobacterial Pulmonary Disease

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**Purpose:** We aimed to determine the relationship between environmental exposure and nontuberculous mycobacterial pulmonary disease (NTM-PD) in Korea.

**Materials and Methods:** A group of 150 patients with NTM-PD and a control group of 217 patients with other respiratory diseases were prospectively enrolled between June 2018 and December 2020 in Seoul, Korea. They were surveyed with a standardized questionnaire, and their medical records were reviewed. Odds ratio (OR) and 95% confidence intervals (CI) were calculated with multivariate logistic regression analysis.

**Results:** The mean ages of the NTM-PD and control groups were similar (63.8±9.2 years vs. 63.5±10.0 years;  $p=0.737$ ), and most patients were female (76.0% vs. 68.7%;  $p=0.157$ ) and nonsmokers (82.0% vs. 72.8%;  $p=0.021$ ). *Mycobacterium avium* (49.3%) was the most commonly identified strain among NTM-PD patients, followed by *M. intracellulare* (32.0%) and *M. abscessus* subspecies *massiliense* (12.7%). There were no differences in housing type or frequency of soil- or pet-related exposure between the case and the control groups. However, in subgroup analysis excluding patients with *M. intracellulare* infection, more case patients frequently visited public baths ≥1 time/week (35.3% vs. 19.4%,  $p=0.003$ ); this remained significant after multivariate analysis (OR, 2.84; 95% CI, 1.58–5.17).

**Conclusion:** Frequent exposure to water at public baths might affect the odds of contracting NTM-PD, excluding individuals infected with *M. intracellulare* strains.

**Key Words:** Nontuberculous mycobacteria, nontuberculous mycobacterium infection, environmental exposure

### INTRODUCTION

Nontuberculous mycobacteria (NTM) are widely distributed

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throughout the environment.<sup>1</sup> NTM are generally acquired from the environment via ingestion, inhalation, and dermal contact, which results in lymphadenitis, pulmonary and disseminated infections, and skin and soft tissue infections.<sup>2,3</sup> Although estimating the incidence of NTM pulmonary disease (NTM-PD) is difficult because it is not a reportable disease, recent increases in the incidence and prevalence of NTM-PD are a global phenomenon.<sup>4-6</sup> Several presumed causes have been discussed, including 1) an increase of mycobacterial infection sources in the environment, 2) an increase in susceptible individuals, 3) improvements in laboratory detection techniques, and 4) increased awareness of NTM diseases among physicians.<sup>7</sup>

For preventing and treating NTM-PD, it is essential to identify the infection sources and the role of individual behaviors that may increase the risk of NTM exposure in the environ-

ment. Previous studies have suggested a correlation between environmental and behavioral risk factors and the incidence of NTM-PD. Maekawa, et al.<sup>8</sup> reported that *Mycobacterium avium* complex pulmonary disease (MAC-PD) was associated with aerosol-generating soil activities, but not with water-related activities, in Japan. Prevots, et al.<sup>9</sup> reported an additional effect from atmospheric conditions, rather than individual behaviors: indoor swimming was associated with incident NTM infections in patients with cystic fibrosis.

In Korea, the prevalence and incidence of NTM infection have increased, similar to other countries.<sup>10,11</sup> However, the role of individual behaviors in relation to environmental exposure to NTM has not been evaluated. Therefore, we performed a case-control study to investigate the role of individual behaviors that might increase exposure to NTM during housing-, water-, soil-, and pet-related activities.

## MATERIALS AND METHODS

The study protocol was approved by the Institutional Review Board of Severance Hospital (4-2018-0444), and written informed consent was obtained from all participants.

### Study participants

Both case and control participants were prospectively recruited between June 2018 and December 2020 at Severance Hospital, a tertiary referral hospital in Seoul, South Korea. Case participants comprised patients with NTM-PD who visited the respiratory clinic at Severance Hospital; the control group comprised patients who visited the same clinic for respiratory diseases other than NTM-PD. We purposefully sampled the control participants to establish similar age and sex composition. All patients with NTM-PD were diagnosed according to the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) 2007 guidelines.<sup>12</sup> A reverse-hybridization line probe assay based on the *rpoB* gene,<sup>13</sup> conducted at Seoul Clinical Laboratories (Yongin, Korea), was used for NTM species identification.

### Radiologic evaluation

The radiological patterns of NTM-PD were classified according to chest radiography and computed tomography findings.<sup>12</sup> The fibrocavitary type was defined as the presence of cavitary opacities in the upper lobes, either with or without consolidation and pleural thickening. The nodular bronchiectatic type was defined as the presence of bilateral bronchiectasis with multiple nodules and tree-in-bud opacities. The unspecified type was defined as either the absence of the evident characteristics of these two types or the presence of consolidation or solitary nodules.

### Measurement of NTM exposure

All participants completed a standardized questionnaire surveying environmental exposure in the most recent 6–12 months: soil exposure from farming or gardening; water exposure from baths, showering, washing dishes, or swimming; and pet exposure (Supplementary Material, only online). We also collected data on underlying diseases, age at menopause, and smoking status. Information related to NTM-PD, such as NTM species, radiological information, and treatment, was analyzed.

The date of NTM-PD diagnosis was defined as the earliest of the following: 1) the first date of NTM recovery from a respiratory specimen in the study hospital, 2) the first date of NTM recovery recorded in the medical records of referring hospitals, and 3) the initial date of NTM-PD treatment at referring hospitals.

We excluded patients with *M. intracellulare* from analysis of water exposure because *M. intracellulare* lung disease is not associated with household water use.<sup>14</sup>

### Statistical analysis

Categorical variables were analyzed using Pearson's chi-squared test or Fisher's exact test, while continuous variables were analyzed with Student's t-test. After adjusting for age, sex, body mass index, smoking, history of tuberculosis, and history of gastroesophageal reflux disease, multivariate logistic regression analyses were performed to calculate odds ratios (OR) and 95% confidence intervals (CI) for NTM-PD. All statistical analyses were performed using R version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria), and a two-tailed  $p < 0.05$  was considered statistically significant.

## RESULTS

### Participant characteristics

The case group comprised 150 patients with NTM-PD; the control group had 217 patients with other respiratory diseases. The characteristics of the study participants are shown in Table 1. The mean ages of patients in both groups were similar: 63.8±9.2 years in the NTM-PD group and 63.5±10.0 years in the control group. Female and nonsmokers were predominant in both groups. Patients with NTM-PD were leaner (body mass index, 20.8 kg/m<sup>2</sup> vs. 23.0 kg/m<sup>2</sup>,  $p < 0.001$ ) and more frequently had gastroesophageal reflux disease (as a comorbidity) and a history of tuberculosis. Those in the control group more frequently had interstitial lung disease. Many female had post-menopausal status in both groups, with no difference in age at menopause. Family history of tuberculosis was more frequent in the NTM-PD group than in the control group (18.0% vs. 9.7%,  $p = 0.030$ ). Conversely, family histories of NTM-PD were similar between the two groups (3.3% vs. 0.5%,  $p = 0.086$ ).

Table 2 shows the characteristics of patients with NTM-PD. Among the NTM-PD group, 74 (49.3%) patients had *M. avium*,

**Table 1.** Baseline Characteristics of the Study Groups

	NTM-PD (n=150)	Control (n=217)	p value
Age, yr	63.8±9.2	63.5±10.0	0.737
Sex, female	114 (76.0)	149 (68.7)	0.157
Height, cm	160.1±7.2	159.8±7.4	0.720
Weight, kg	53.3±8.0	58.8±9.9	<0.001
Body mass index, kg/m <sup>2</sup>	20.8±2.6	23.0±3.1	<0.001
Smoking			0.021
Current	1 (0.7)	12 (5.5)	
Ex-smoker	26 (17.3)	47 (21.7)	
Never	123 (82.0)	158 (72.8)	
Pack-year	27.1±21.0	24.9±21.2	0.639
Comorbidities			
Bronchiectasis	68 (45.3)	77 (35.5)	0.074
History of TB	42 (28.0)	40 (18.4)	0.042
GERD	39 (26.0)	32 (14.7)	0.011
COPD	20 (13.3)	35 (16.1)	0.556
Asthma	11 (7.3)	23 (10.6)	0.380
Diabetes mellitus	10 (6.7)	25 (11.5)	0.169
Interstitial lung diseases	2 (1.3)	22 (10.1)	0.002
Lung cancer	1 (0.7)	10 (4.6)	0.062
Menopause	103 (90.4)	130 (87.2)	0.556
Age at menopause, yr	49.9±4.7	49.3±6.6	0.394
Family history of TB	27 (18.0)	21 (9.7)	0.030
Family history of NTM	5 (3.3)	1 (0.5)	0.086

COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; NTM, nontuberculous mycobacteria; NTM-PD, nontuberculous mycobacterial pulmonary disease; TB, tuberculosis.

Data are presented as numbers (%) or means±standard deviation.

**Table 2.** Characteristics of the Patients with NTM-PD (n=150)

NTM species	
<i>Mycobacterium avium</i>	74 (49.3)
<i>M. intracellulare</i>	48 (32.0)
<i>M. abscessus</i> subspecies <i>massiliense</i>	19 (12.7)
<i>M. abscessus</i> subspecies <i>abscessus</i>	12 (8.0)
Others*	8 (5.3)
CAT score, median (IQR)	11 (6–17)
AFB smear, positive	17 (11.3)
Radiologic finding	
NB type without cavity	101 (67.3)
NB type with cavity	32 (21.3)
Fibrocavitary type	9 (6.0)
Unclassified	8 (5.3)
Time between diagnosis and survey, months (IQR)	20.5 (8.0–56.8)
Treatment during the survey	70 (46.7)

AFB, acid-fast bacilli; CAT, chronic obstructive pulmonary disease assessment test; IQR, interquartile range; NB, nodular bronchiectatic; NTM, nontuberculous mycobacteria; NTM-PD, nontuberculous mycobacterial pulmonary disease.

Data are presented as numbers (%) unless otherwise indicated.

\**M. kansasii*, *M. fortuitum*, and unclassified.

**Table 3.** Comparison of Housing, Soil, and Pet Exposure between the Two Groups

	NTM-PD (n=150)	Control (n=217)	p value	OR* (95% CI)
Housing			0.113	
Apartment building	126 (84.0)	119 (54.8)		Reference
Detached house	24 (16.0)	50 (23.0)		0.61 (0.33–1.09)
Soil exposure				
Farming	23 (15.3)	26 (12.0)	0.440	1.36 (0.71–2.63)
≥1 time/week	18 (12.0)	21 (9.7)	0.591	1.42 (0.68–2.94)
Duration, yr	16.5±18.5	20.8±18.6	0.425	
Flowerbed	27 (18.0)	43 (19.8)	0.764	0.87 (0.49–1.55)
≥1 time/week	11 (7.3)	27 (12.4)	0.160	0.63 (0.28–1.34)
Duration, yr	12.0±10.1	15.9±15.3	0.204	
Flowerpot	53 (35.3)	80 (36.9)	0.849	1.04 (0.64–1.67)
≥1 time/week	6 (4.0)	7 (3.2)	0.915	1.40 (0.40–4.75)
Duration, yr	14.4±10.6	18.6±12.1	0.040	
Any soil activity	72 (48.0)	111 (51.2)	0.626	0.94 (0.60–1.50)
≥1 time/week	27 (18.0)	43 (26.1)	0.113	0.62 (0.33–1.15)
Pet exposure				
Pet	25 (16.8)	30 (13.8)	0.530	1.31 (0.69–2.48)
Dog	18 (72.0)	25 (83.3)	0.071	
Cat	5 (20.0)	2 (6.7)		
Fish	0 (0.0)	3 (10.0)		
Other†	2 (8.0)	0 (0.0)		
Duration, yr	11.5±5.6	11.3±11.0	0.926	

CI, confidence interval; NTM-PD, nontuberculous mycobacterial pulmonary disease; OR, odds ratio.

Data are presented as numbers (%) or means±standard deviation.

\*Adjusted for age, sex, body mass index, smoking, history of tuberculosis, and history of gastroesophageal reflux disease, †Both dogs and cats.

48 (32.0%) had *M. intracellulare*, 19 (12.7%) had *M. abscessus* subspecies *massiliense*, and 12 (8.0%) had *M. abscessus* subspecies *abscessus*. The median time between the diagnosis of NTM-PD and survey was 20.5 months (interquartile range 8.0–56.8), and 70 patients (46.7%) were receiving ongoing treatment for NTM-PD during the survey.

### Environmental exposure to NTM

Table 3 shows the environmental risk factors for NTM exposure in each group. Apartments were the primary type of housing in the NTM-PD and control groups (84.0% vs. 54.8%,  $p=0.113$ ), and living in a detached house did not influence the odds of NTM-PD (OR, 0.61; 95% CI, 0.33–1.09). The frequencies of soil- or pet-related activities were similar between the two groups, and these did not affect the odds of NTM-PD (any soil activities ≥1 time/week, OR, 0.62; 95% CI, 0.33–1.15; pet exposure, OR, 1.31; 95% CI, 0.69–2.48).

Table 4 shows the results for water exposure between the patients with NTM-PD, excluding those infected with *M. intracellulare*, and the controls. The case group had more frequent exposure to water from public baths than those in the control group (public bath ≥1 time/week, 35.3% vs. 19.4%,  $p=0.003$ ). In

**Table 4.** Comparison of Water Exposure between the Two Groups

	NTM-PD* (n=102)	Control (n=217)	p value	OR <sup>†</sup> (95% CI)
Shower, ≥1 time/day	56 (54.9)	130 (59.9)	0.469	0.96 (0.57–1.64)
Public bath	63 (61.8)	119 (54.8)	0.296	1.76 (1.04–3.04)
≥1 time/week	36 (35.3)	42 (19.4)	0.003	2.84 (1.58–5.17)
Hot tub	46 (45.1)	85 (39.2)	0.378	1.69 (0.99–2.91)
≥1 time/week	24 (23.5)	35 (16.1)	0.152	2.17 (1.13–4.17)
Wet sauna	41 (40.2)	73 (33.6)	0.310	1.76 (1.02–3.05)
≥1 time/week	15 (14.7)	24 (11.1)	0.457	1.89 (0.87–4.04)
Swimming	9 (8.8)	17 (7.8)	0.935	1.59 (0.61–3.93)
≥1 time/week	8 (7.8)	11 (5.1)	0.470	2.27 (0.79–6.34)
Duration, yr	8.1±7.5	16.7±18.0	0.097	
Dishwashing	90 (88.2)	185 (85.3)	0.585	1.05 (0.40–2.82)
≥1 time/day	80 (88.9)	164 (88.6)	>0.999	0.67 (0.21–2.11)
Humidifier at home	17 (16.7)	31 (14.3)	0.699	1.16 (0.57–2.29)
≥1 time/week	15 (14.7)	24 (11.1)	0.457	1.34 (0.63–2.80)

CI, confidence interval; NTM-PD, nontuberculous mycobacterial pulmonary disease; OR odds ratio.

Data are presented as numbers (%) or means±standard deviation.

\*NTM-PD patients with *M. intracellulare* infection were excluded, <sup>†</sup>Adjusted for age, sex, body mass index, smoking, history of tuberculosis, and history of gastroesophageal reflux disease.

multivariate analysis, frequent use of public baths increased the odds of contracting NTM-PD (OR, 2.84; 95% CI, 1.58–5.17). There were no significant differences in the frequencies of showering, swimming, dishwashing, and humidifier use at home between the two groups.

## DISCUSSION

This is the first study to evaluate environmental exposure to NTM in Korea. Water exposure from public baths was more common in patients with NTM-PD, except for those with *M. intracellulare* infection, compared to the control group. Moreover, public bath use increased the odds of contracting NTM-PD, whereas water exposure from showering, swimming, dishwashing, or humidifier use did not increase the odds of NTM-PD. Soil exposure from farming or gardening activities or pet caring activities was also similar in both groups.

As NTM are ubiquitous in nature and human-made environments, high exposure to soil and water has been considered a risk factor for the development of NTM-PD. Many studies have reported the isolation of MAC and other NTM species from showerheads, bathrooms, tap water, drinking water distribution systems, soil, and dust.<sup>1,3,15–18</sup> However, the sources of NTM and the behaviors related to developing NTM-PD are still unclear. Maekawa, et al.<sup>8</sup> first reported high soil exposure, defined as farming and gardening more than twice weekly, in patients with MAC-PD, compared with that in bronchiectasis patients, in Japan. Several studies followed, trying to identify behavioral

risks associated with environmental exposure of NTM in various populations; however, the results were inconsistent. In the United States, a population-based case-control study by Dirac, et al.<sup>19</sup> was conducted to determine the risk behaviors associated with MAC-PD. Therein, aerosol-generating activities in water and soil were not correlated with an increased risk of the disease. Prevots, et al.<sup>9</sup> reported a relationship between indoor swimming and incident NTM infection in cystic fibrosis patients. These inconsistencies might have resulted from differences in the study populations, geography, or measurement tools for environmental exposure. Likewise, in our study, we were unable to find a hazardous or protective individual behavior linked to NTM-PD other than exposure to water at public baths.

Aerosolized water droplets are an important portal through which NTM enter the human airway.<sup>20</sup> Public bath use is a common behavior in Korea. Aerosolized and humidified water at public baths can more easily penetrate the human body than water at home. Thus, water exposure at public baths might be associated with NTM-PD in susceptible populations in Korea.

On the contrary, we did not find an association between soil exposure and NTM-PD in our study. There might be a few explanations for this. Identifying the risk of a particular behavior is limited by the precision of the tools measuring it. The standardized questionnaire used in this study to assess NTM exposure might be insufficient for estimating an accurate intensity of exposure, especially for soil-related activities. We developed a standard questionnaire based on previous studies conducted in Japan and the USA.<sup>8,9,19</sup> However, it would be necessary to include detailed information regarding the intensity of exposure, not merely the frequency. In addition, participants may not recall their lifestyle accurately.

A few limitations of this study warrant consideration. First, differences in residence and individual behaviors might be too small in the modernized era. Most participants in our study lived in a metropolitan area, where the housing environment and lifestyle regarding soil-related activities might be similar. Therefore, the small differences in NTM exposure in urban areas might be insufficient to prove a relationship.<sup>9</sup> Second, the heterogeneity of participants could be another confounder. All patients with NTM-PD were diagnosed according to ATS/IDSA guidelines, but they had infections caused by different NTM species and different comorbidities. Even though they were recruited from the same respiratory clinic, patients in the control group were heterogeneous, had a higher incidence of interstitial lung disease, and a lower incidence of tuberculosis history. Because host susceptibility is one of the known factors for the development of NTM-PD, the heterogeneity of participants could affect our results. Third, the time between the diagnosis of NTM-PD and the survey might be another confounding factor. As this institution is a tertiary referral hospital, many of the cases were referred from another center. The time interval between the diagnosis and the survey in this study was

a median of 20.5 months (interquartile range 8.0–56.8), over which changes in individual behaviors could have occurred.

In conclusion, frequent exposure to water at public baths might be a risk factor of NTM-PD, except for infections with *M. intracellulare* strains, in Korea. Otherwise, we could not identify other individual behaviors causally related to environmental exposure to NTM. To determine risk behaviors affecting NTM-PD, we need to perform further studies in a homogenous susceptible group, with a more in-depth standard questionnaire and complementary environmental sampling.

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## AUTHOR CONTRIBUTIONS

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## REFERENCES

- Falkinham JO 3rd. Environmental sources of nontuberculous mycobacteria. *Clin Chest Med* 2015;36:35-41.
- Thomson R, Tolson C, Carter R, Coulter C, Huygens F, Hargreaves M. Isolation of nontuberculous mycobacteria (NTM) from household water and shower aerosols in patients with pulmonary disease caused by NTM. *J Clin Microbiol* 2013;51:3006-11.
- Falkinham JO 3rd. Ecology of nontuberculous mycobacteria--where do human infections come from? *Semin Respir Crit Care Med* 2013;34:95-102.
- Adjemian J, Olivier KN, Seitz AE, Falkinham JO 3rd, Holland SM, Prevots DR. Spatial clusters of nontuberculous mycobacterial lung disease in the United States. *Am J Respir Crit Care Med* 2012;186:553-8.
- Thomson RM; NTM working group at Queensland TB Control Centre and Queensland Mycobacterial Reference Laboratory. Changing epidemiology of pulmonary nontuberculous mycobacteria infections. *Emerg Infect Dis* 2010;16:1576-83.
- Prevots DR, Shaw PA, Strickland D, Jackson LA, Raebel MA, Blosky MA, et al. Nontuberculous mycobacterial lung disease prevalence at four integrated health care delivery systems. *Am J Respir Crit Care Med* 2010;182:970-6.
- Shah NM, Davidson JA, Anderson LE, Lalor MK, Kim J, Thomas HL, et al. Pulmonary Mycobacterium avium-intracellulare is the main driver of the rise in non-tuberculous mycobacteria incidence in England, Wales and Northern Ireland, 2007-2012. *BMC Infect Dis* 2016;16:195.
- Maekawa K, Ito Y, Hirai T, Kubo T, Imai S, Tatsumi S, et al. Environmental risk factors for pulmonary Mycobacterium avium-intracellulare complex disease. *Chest* 2011;140:723-9.
- Prevots DR, Adjemian J, Fernandez AG, Knowles MR, Olivier KN. Environmental risks for nontuberculous mycobacteria. Individual exposures and climatic factors in the cystic fibrosis population. *Ann Am Thorac Soc* 2014;11:1032-8.
- Park SC, Kang MJ, Han CH, Lee SM, Kim CJ, Lee JM, et al. Prevalence, incidence, and mortality of nontuberculous mycobacterial infection in Korea: a nationwide population-based study. *BMC Pulm Med* 2019;19:140.
- Lee H, Myung W, Koh WJ, Moon SM, Jhun BW. Epidemiology of nontuberculous mycobacterial infection, South Korea, 2007-2016. *Emerg Infect Dis* 2019;25:569-72.
- Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007;175:367-416.
- Lee H, Bang HE, Bai GH, Cho SN. Novel polymorphic region of the rpoB gene containing Mycobacterium species-specific sequences and its use in identification of mycobacteria. *J Clin Microbiol* 2003;41:2213-8.
- Wallace RJ Jr, Iakhiaeva E, Williams MD, Brown-Elliott BA, Vasireddy S, Vasireddy R, et al. Absence of Mycobacterium intracellulare and presence of Mycobacterium chimaera in household water and biofilm samples of patients in the United States with Mycobacterium avium complex respiratory disease. *J Clin Microbiol* 2013;51:1747-52.
- Lande L, Alexander DC, Wallace RJ Jr, Kwiat R, Iakhiaeva E, Williams M, et al. Mycobacterium avium in community and household water, suburban Philadelphia, Pennsylvania, USA, 2010-2012. *Emerg Infect Dis* 2019;25:473-81.
- Feazel LM, Baumgartner LK, Peterson KL, Frank DN, Harris JK, Pace NR. Opportunistic pathogens enriched in showerhead biofilms. *Proc Natl Acad Sci U S A* 2009;106:16393-9.
- De Groote MA, Pace NR, Fulton K, Falkinham JO 3rd. Relationships between Mycobacterium isolates from patients with pulmonary mycobacterial infection and potting soils. *Appl Environ Microbiol* 2006;72:7602-6.
- Nishiuchi Y, Maekura R, Kitada S, Tamaru A, Taguri T, Kira Y, et al. The recovery of Mycobacterium avium-intracellulare complex (MAC) from the residential bathrooms of patients with pulmonary

MAC. Clin Infect Dis 2007;45:347-51.

19. Dirac MA, Horan KL, Doody DR, Meschke JS, Park DR, Jackson LA, et al. Environment or host?: a case-control study of risk factors for Mycobacterium avium complex lung disease. Am J Respir Crit

Care Med 2012;186:684-91.

20. Hamilton LA, Falkinham JO. Aerosolization of Mycobacterium avium and Mycobacterium abscessus from a household ultrasonic humidifier. J Med Microbiol 2018;67:1491-5.