Epidemiological Characteristics of Nontuberculous Mycobacterial Pulmonary Disease in South Korea: A Meta-analysis of Individual Participant Data

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Geunin Lee, M.D.[1]*[iD], Sol Kim, M.D.[1]*[iD], Shihwan Chang, M.D.[1], Hojoon Sohn, Ph.D., M.P.H.[2], Young Ae Kang, M.D., Ph.D.[1,3] and Youngmok Park, M.D., Ph.D.[1,4][iD]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, [2]Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, [3]Institute of Immunology and Immunological Diseases, Yonsei University College of Medicine, Seoul, [4]Institute for Innovation in Digital Healthcare, Yonsei University, Seoul, Republic of Korea

Abstract

Background: Despite the global increase in nontuberculous mycobacterial pulmonary disease (NTM-PD), clinical characteristics show geographical variations. We investigated the clinical characteristics of patients with NTM-PD in South Korea.

Methods: We systematically reviewed articles concerning patients with NTM-PD in South Korea until February 2022. Individual participant data, regardless of treatment, were collected using a standard case report form.

Results: Data of 6,489 patients from 11 hospitals between 2002 and 2019 were analyzed. The mean age was 61.5±11.7 years, of whom 57.7% were women. *Mycobacterium avium* (41.4%) and *Mycobacterium intracellulare* (38.4%) comprised most of the causative species, followed by *Mycobacterium abscessus* subspecies *abscessus* (8.6%) and *M. abscessus* subspecies *massiliense* (7.8%). Bronchiectasis (59.4%) was the most common pulmonary comorbidity. Although reported cases of NTM-PD increased over the years, the proportions of causative species and radiologic forms remained similar. Distinct clinical characteristics were observed according to age and sex. Men were older at the time of diagnosis (median 63.8 years vs. 59.9 years, p<0.001), and had more cavitary lesions than women (38.8% vs. 21.0%, p<0.001). The older group (≥65 years) had higher proportions of patients with body mass index <18.5 kg/m^2 (27.4% vs. 18.6%, p<0.001) and cavitary lesions (29.9% vs. 27.6%, p=0.009) than the younger group.

Conclusion: We conducted a meta-analysis of the clinical characteristics of patients with NTM-PD in South Korea, and found age- and sex-related differences in disease-specific severity. Further investigation would enhance our comprehension of the nature of the disease, and inherited and acquired host factors.

Keywords: Age; Epidemiology; Nontuberculous Mycobacteria; Sex

Introduction

Nontuberculous mycobacterial pulmonary disease (NTM-PD) has been steadily increasing in incidence and prevalence worldwide[1,2]. In South Korea, the annual prevalence of NTM diseases increased from 11.4 to 56.7 cases per 100,000 population between 2010 and 2021[3]. Moreover, the proportion of patients aged 65

years or older increased by 20%, while during these 12 years, the direct medical expenditure for NTM disease increased nearly six-fold, leading to a significant burden on healthcare systems[3].

NTM-PD is a chronic infectious condition that often challenges clinicians. Treatment is required over 12 months, with a combination of three or four antibiotics[4,5]. Treatment regimens vary by causative species, but a recent randomized clinical trial found that more

than 90% of patients had treatment-related adverse reactions[6]. Overall, treatment outcomes are unfavorable, with treatment success rates reported as 60% for *Mycobacterium avium* complex (MAC) PD, and 45.6% for *Mycobacterium abscessus* PD[7,8]. Even after successful treatment, about 31% to 48% of patients experience reinfection or relapse[9-11].

Geographical variation in NTM-PD by region or nation is well known[12]. Understanding the epidemiology

Table 1. Summary of the 18 articles included for the analysis

Study	Study design (cohort)	Study period	Species (number of patients)	Treatment	Clinical setting
Kim et al. (2014)[17]	Retrospective	2003–2009	MAC (4), MAB (1), unknown (1)	NA	Single center
Jeong et al. (2021)[18]	Retrospective	2014–2019	unknown (4)	NA	Single center
Park et al. (2012)[19]	Retrospective	1992–2007	MAC (14), MAB (1), other (1)	NA	Multicenter
Hong et al. (2015)[20]	Retrospective	2012–2013	MAC (123), MAB (20), other (45)	NA	Single center
Kim et al. (2014)[21]	Retrospective	2006–2012	unknown (30)	NA	Single center
Lee et al. (2019)[22]	Retrospective	2006–2016	MAC (123), MAB (40), other (20)	NA	Single center
Kim et al. (2011)[23]	Retrospective	2005–2008	MAC (42)	Yes	Single center
Hwang et al. (2017)[24]	Retrospective	1998–2011	MAC (420)	Yes or No	Single center
Kwon et al. (2019)[25]	Retrospective	2000–2017	MAC (551)	Yes or No	Single center
Jo et al. (2020)[26]	Retrospective	2012–2018	MAB (241)	Yes or No	Single center
Kwon et al. (2020)[27]	Retrospective	2001–2014	MAC (362)	Yes	Single center
Han et al. (2021)[28]	Retrospective	2002–2013	MAC (859)	Yes or No	Single center
Moon et al. (2019)[29]	Prospective	2003–2013	MAC or MAB (1,021)	Yes or No	Single center
Jhun et al. (2020)[30]	Prospective	1997–2013	MAC (1,142), MAB (303)	Yes	Single center
Kim et al. (2019)[31]	Prospective	2017–2018	MAC (347)	Yes	Single center
Lee et al. (2020)[32]	Prospective	2011–2019	MAC (25), MAB (2), other (4)	Yes or No	Single center
Gu et al. (2021)[33]	Retrospective	2017–2020	MAC (45), MAB (6), other (3)	No	Single center
Park et al. (2020)[16]	Retrospective	2006–2016	MAC (647), MAB (110), other (260)	Yes or No	Single center

MAC: *Mycobacterium avium* complex; MAB: *Mycobacterium abscessus*; NA: not available.

of NTM-PD in Korea might identify the manageable features of the disease, which would lead to the improvement of treatment outcomes. However, unlike tuberculosis (TB), there is no obligation to report NTM-PD in many countries, including South Korea. Therefore, previous epidemiologic studies investigating NTM-PD have relied on single-center data, which lack generalizability, or national insurance claim data, which lack information about causative species, radiologic findings, or disease severity. We therefore conducted a systematic review combined with a meta-analysis of individual participant data, aiming to elucidate the disease-specific characteristics of NTM-PD in South Korea.

Materials and Methods

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[13]. The protocol was registered with PROSPERO (registration number: CRD42022343306).

1. Study design and population
We systematically reviewed studies of patients with NTM-PD in South Korea through February 2022. We used the MEDLINE, Embase, Cochrane Library, and KoreaMed databases. The search terms were adapted

Figure 1. Flowchart of article selection and individual participant data integration. IPD: individual participant data.
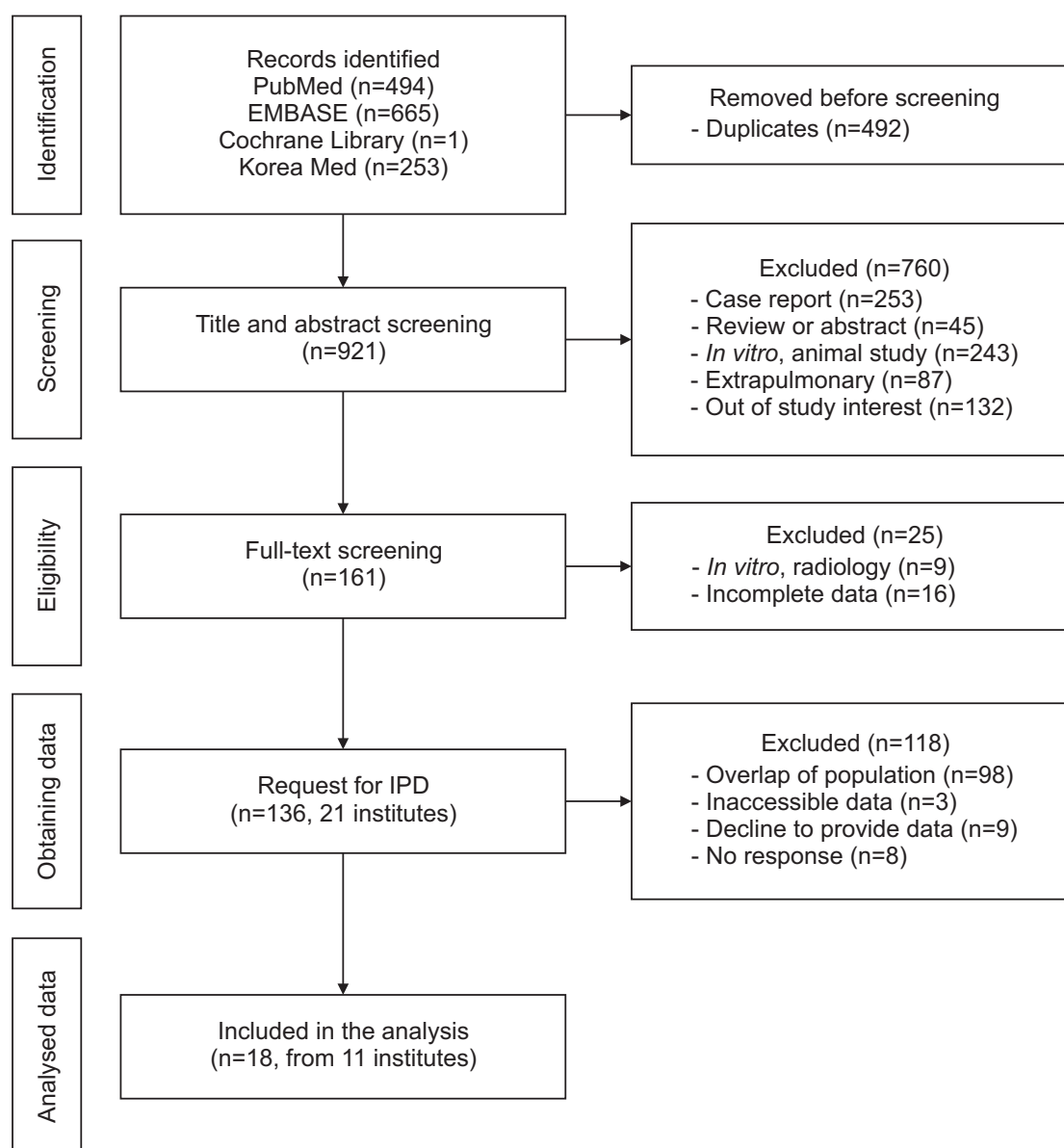
from MEDLINE, and modified to suit each database (Supplementary Table S1). Two investigators (Kim S and Park Y) independently screened the articles by title and abstract for initial eligibility, followed by a detailed full-text review. Discrepancies or uncertainties were resolved through adjudication by a third author (Kang YA).

The inclusion criteria encompassed all studies with Korean patients with NTM-PD diagnosed according to the comprehensive guidelines disseminated by the American Thoracic Society and the Infectious Diseases Society of America[14]. No restrictions were placed on the type of study design, data collection methods (prospective or retrospective), number of study participants, or treatment modality. We excluded *in vitro* experimental studies, animal studies, and radiologic studies without or with minimal clinical information on patients with NTM-PD.

2. Data acquisition and integration
We requested that the corresponding or first authors provide data on individual participants. A standardized case report form was used to obtain information on age, sex, year of diagnosis, height, weight, history of TB, history of NTM treatment, comorbidities, smear positivity, causative species, and radiologic forms at the time of diagnosis.

In instances of multiple publications from a single institution, the most representative study was selected as the primary reference, and data pertaining to the article were specifically requested. If two or more primary studies emanated from one institution, consolidated cohort-wide data were used to prevent duplication within the study population.

We divided patients into three subgroups by age, sex, and healthcare institution, with a comparison of four major tertiary referral centers (Samsung Medical Center, Asan Medical Center, Seoul National University Hospital, and Severance Hospital, selected by the size of the NTM-PD clinics) with other institutions.

The BACES score, comprising body mass index (BMI), age, cavity presence, erythrocyte sedimentation rate (ESR), and sex, is designed to predict mortality in patients with NTM-PD[15]. Due to the unavailability of ESR data, we calculated the BACS score in this study, which omits ESR, to evaluate disease severity and prognosis indirectly.

3. Statistical analysis
Numerical data were analyzed using t-tests, while categorical data were analyzed using chi-squared tests and the Cochran-Armitage trend test. p-values <0.05 were considered statistically significant.

Results

1. Clinical characteristics of patients with NTM-PD
A database search identified 1,413 articles. After the eligibility screening, we found 136 articles from 21 institutions. We contacted first/corresponding authors of the 21 institutions, and received responses from 16. Three authors replied with the discarded data, and two authors were unable, or refused, to provide the data. Finally, the data of 6,489 patients from 18 primary refer-

Figure 2. Reported numbers of patients with nontuberculous mycobacterial pulmonary disease by diagnosis year.
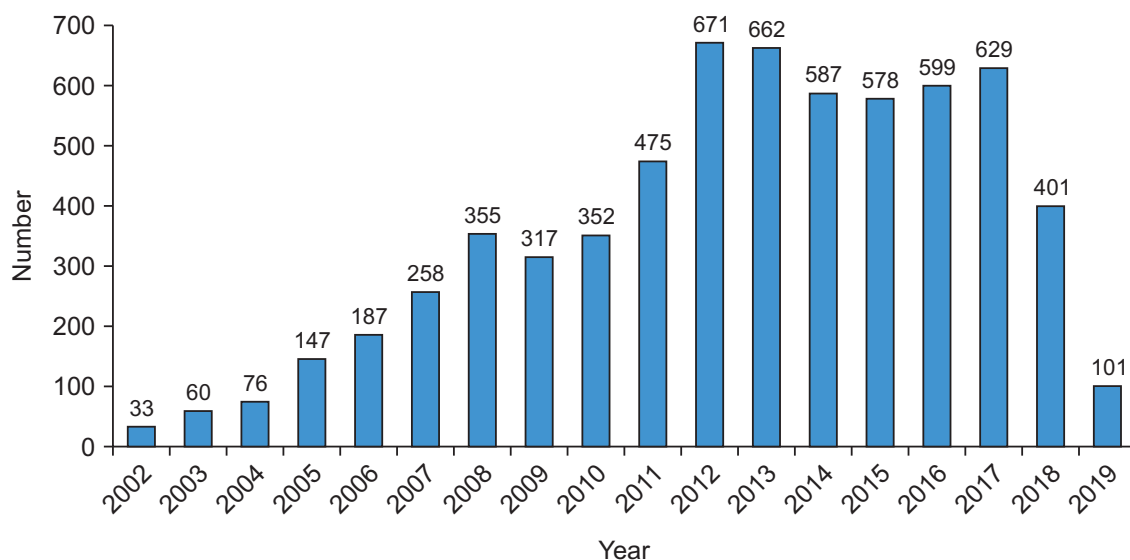
Table 2. Clinical characteristics of patients with nontuberculous mycobacterial pulmonary disease

Characteristic	Total (n=6,489)	Men (n=2,741)	Women (n=3,745)	p-value
Age, yr (NA=8)	61.5±11.7	63.8±11.8	59.9±11.6	<0.001
Sex, women (NA=3)	3,745 (57.7)			
Height, cm (NA=108)	161.1±8.0	165.2±7.9	158.2±6.8	<0.001
Weight, kg (NA=103)	53.8±9.6	56.8±10.3	51.7±8.4	<0.001
BMI, kg/m^2 (NA=109)	20.7±3.0	20.7±3.1	20.6±2.9	0.192
BMI <18.5 kg/m^2 (NA=109)	1,462 (22.9)	623 (23.1)	803 (21.8)	0.212
Ever smoker (NA=101)	1,829 (28.6)	1,405 (52.0)	423 (11.5)	<0.001
History of tuberculosis (NA=22)	2,502 (38.7)	1,146 (42.0)	1,335 (36.3)	<0.001
History of NTM treatment (NA=4)	767 (11.8)	331 (12.1)	436 (11.6)	0.591
Comorbidity				
Asthma (NA=3,353)	122 (3.9)	50 (3.5)	72 (4.2)	0.296
Bronchiectasis (NA=1,558)	2,929 (59.4)	897 (46.9)	2,031 (67.4)	<0.001
COPD (NA=193)	658 (10.4)	401 (15.1)	256 (7.0)	<0.001
ILD (NA=1,528)	151 (3.0)	79 (3.7)	72 (2.5)	0.017
Diabetes (NA=10)	656 (10.1)	365 (13.4)	290 (7.7)	<0.001
Hypertension (NA=3,596)	695 (24.0)	342 (25.2)	353 (23.0)	0.176
CKD (NA=131)	129 (2.0)	65 (2.4)	64 (1.7)	0.056
CHD (NA=133)	531 (8.4)	281 (10.5)	250 (6.8)	<0.001
CLD (NA=90)	401 (6.3)	200 (7.4)	201 (5.4)	0.001
Transplantation (NA=235)	77 (1.2)	38 (1.4)	39 (1.1)	0.197
Cancer (NA=10)	1,033 (15.9)	518 (19.0)	514 (13.7)	<0.001
Connective tissue disease (NA=53)	194 (3.0)	72 (2.7)	122 (3.3)	0.154
Smear positivity (NA=247)	2,969 (47.5)	1,464 (55.4)	1,505 (41.9)	<0.001
Species (NA=56)				
Mycobacterium avium	2,574 (41.4)	1,118 (41.2)	1,454 (39.1)	0.090
M. intracellulare	2,385 (38.4)	1,088 (40.1)	1,296 (34.8)	<0.001
M. abscessus sub. *abscessus*	535 (8.6)	170 (6.3)	364 (9.8)	<0.001
M. abscessus sub. *massiliense*	484 (7.8)	124 (4.6)	360 (9.7)	<0.001
*M. abscessus**	7 (0.1)	2 (0.1)	5 (0.1)	0.465
M. fortuitum	31 (0.5)	16 (0.6)	15 (0.4)	0.287
M. kansasii	130 (2.1)	93 (3.4)	37 (1.0)	<0.001
Mixed multi-species	223 (3.5)	66 (2.4)	147 (4.2)	<0.001
Radiologic type (NA=1)				<0.001
Non-cavitary NB	4,185 (64.5)	1,458 (53.2)	2,727 (72.8)	<0.001
Cavitary NB	1,431 (22.0)	861 (31.4)	570 (15.2)	<0.001
Fibrocavitary	420 (6.5)	203 (7.4)	217 (5.8)	0.009
Others[†]	449 (6.9)	218 (8.0)	231 (6.2)	0.010
BACS score[‡] (NA=117)				<0.001
0	1,628 (25.5)	0	1,628 (44.2)	
1	2,007 (31.5)	637 (23.7)	1,370 (37.2)	
2	1,797 (28.3)	1,230 (45.7)	567 (15.4)	
3	763 (12.0)	645 (24.0)	118 (3.2)	
4	177 (2.8)	177 (6.6)	0	

Values are presented as mean±standard deviation or number (%).
*Subspecies not clarified. [†]Consolidation, single nodule, or indeterminate type. [‡]BACS score is derived from the BACES score without erythrocyte sedimentation rate data.
NA: not available; BMI: body mass index; NTM: nontuberculous mycobacteria; COPD: chronic obstructive pulmonary disease; ILD: interstitial lung disease; CKD: chronic kidney disease; CHD: chronic heart disease; CLD: chronic liver disease; NB: nodular bronchiectatic.

ences across 11 institutions were included in the analysis (Table 1 and Figure 1)[16-33]. Supplementary Table S2 presents detailed information of the institutions and study designs.

Figure 2 illustrates the increasing numbers of patients with NTM-PD reported in the studies. Smaller numbers were noted in 2018 and 2019, likely due to the database search cutoff in February 2022.

Figure 3. Proportions of causative species of nontuberculous mycobacterial pulmonary disease by year of diagnosis. Cochrane-Armitage trend test was used, p for trend >0.05.
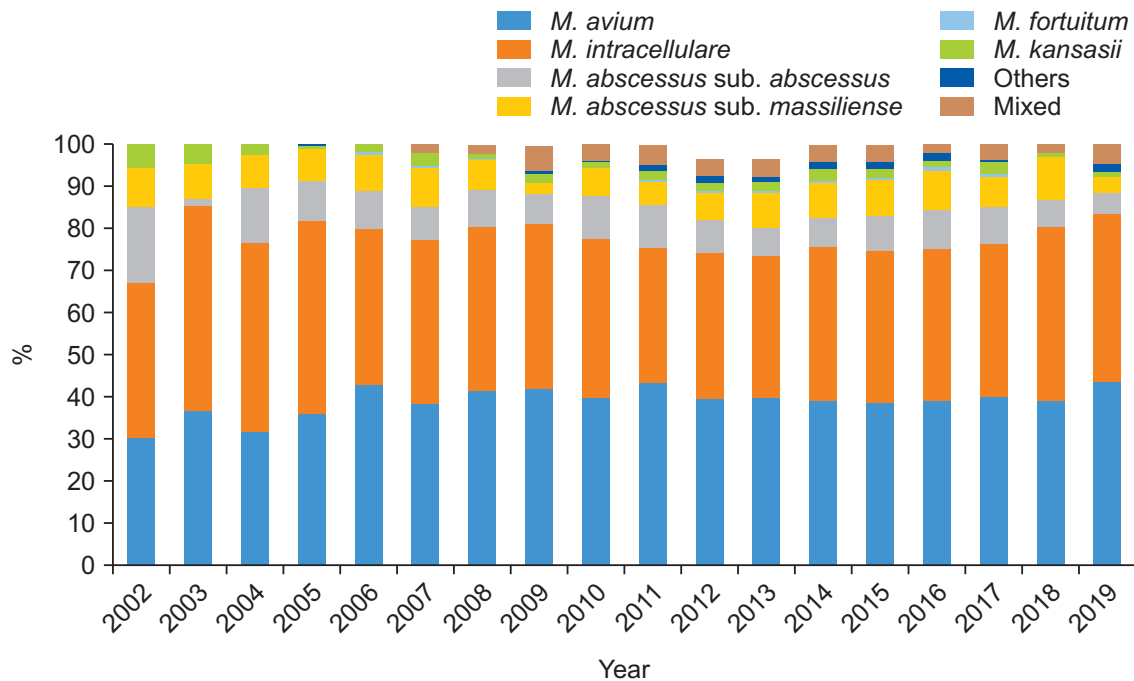

Figure 4. Proportions of radiologic types of nontuberculous mycobacterial pulmonary disease by year diagnosis. Cochrane-Armitage trend test was used, p for trend >0.05. NB: nodular bronchiectatic.
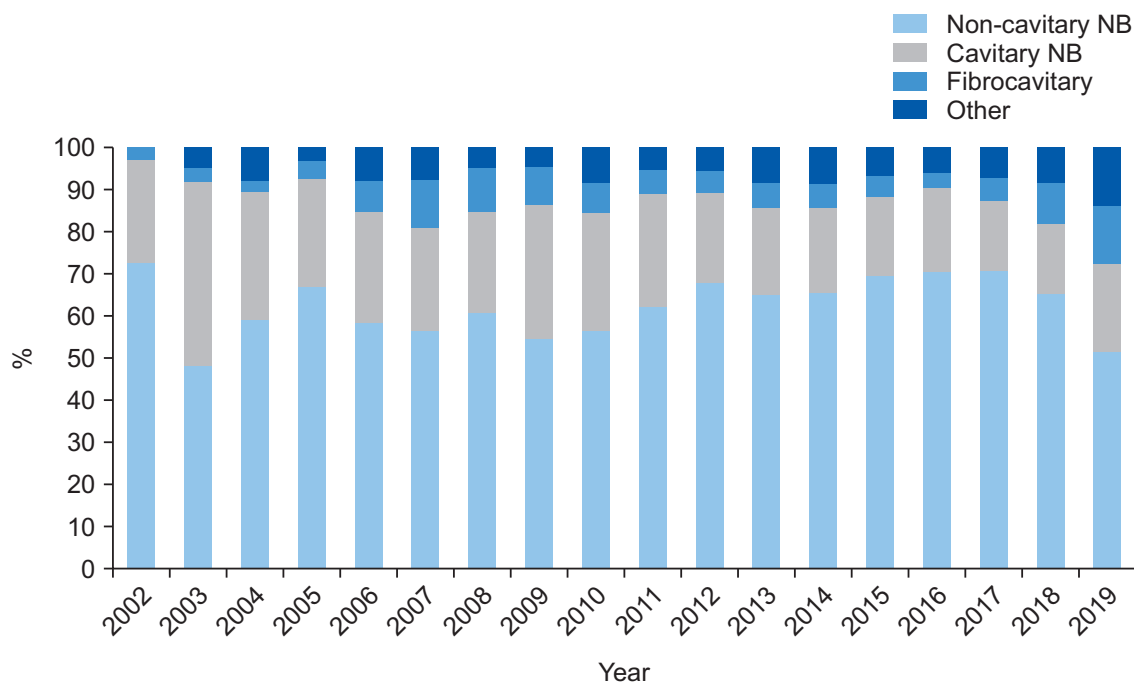
Table 2 describes the integrated clinical characteristics of patients with NTM-PD in South Korea. The mean age was 61.5±11.7 years, of whom 57.7% were women. A history of TB and NTM treatment were noted in 38.7% and 11.8% of patients, respectively. Bronchiectasis was the most prevalent pulmonary comorbidity (59.4%), followed by chronic obstructive pulmonary disease (COPD; 10.4%). Positive sputum acid-fast bacillus smears were found in 47.5% of patients, while the non-cavitary nodular bronchiectatic form was observed in 64.5%. The causative species of NTM-PD were predominantly MAC (79.8%), and *M. abscessus* (16.5%). No significant changes in age, sex, or proportion of low BMI, causative species, or radiologic forms of NTM-PD were observed over the study period (all p for trend >0.05) (Figures 3, 4 and Supplementary Figure S1).

2. Subgroup analysis by sex
We found distinct disease-related characteristics between men and women in patients with NTM-PD. Men were diagnosed with NTM-PD at an older age than women (63.8±11.8 years vs. 59.9±11.6 years, p<0.001) (Table 2). Figure 5 shows the age distribution of the patients with NTM-PD at diagnosis. Most men were in their 60s and early 70s, whereas most women were in their 50s and early 60s.

MAC was the predominant causative species in both men and women; however, *M. abscessus* was more prevalent in women than men (19.4% vs. 10.7%, p< 0.001) (Table 2). The composition of the causative species remained consistent throughout the study period in both men and women (all p for trend >0.05) (Supplementary Figures S2-S5).

Cavitary lung lesions were more common in men than women (38.8% vs. 21.0%, p<0.001). BACS scores indicated higher disease severity in men, although the clinical significance was not ascertainable, because by the definition of the score, men were given 1 point (Table 2).

3. Subgroup analysis by age
Clinical characteristics varied between patients aged <65 and ≥65 years (Table 3). Those aged ≥65 had a higher proportion of patients with BMIs <18.5 kg/m^2 (27.4% vs. 18.6%, p=0.002), and a higher prevalence of cavitary lesions (29.9% vs. 27.6%, p=0.009). Consequently, the BACS score tended to be higher in the older group, although the clinical significance could not be evaluated, because by the definition of the score, they received 1 point. Additionally, underlying comorbidities were more common in the older group, except bronchiectasis (52.9% vs. 63.9%, p<0.001).

Figure 5. Distribution of age at diagnosis for patients with nontuberculous mycobacterial pulmonary disease, by sex, from 2002 to 2019.
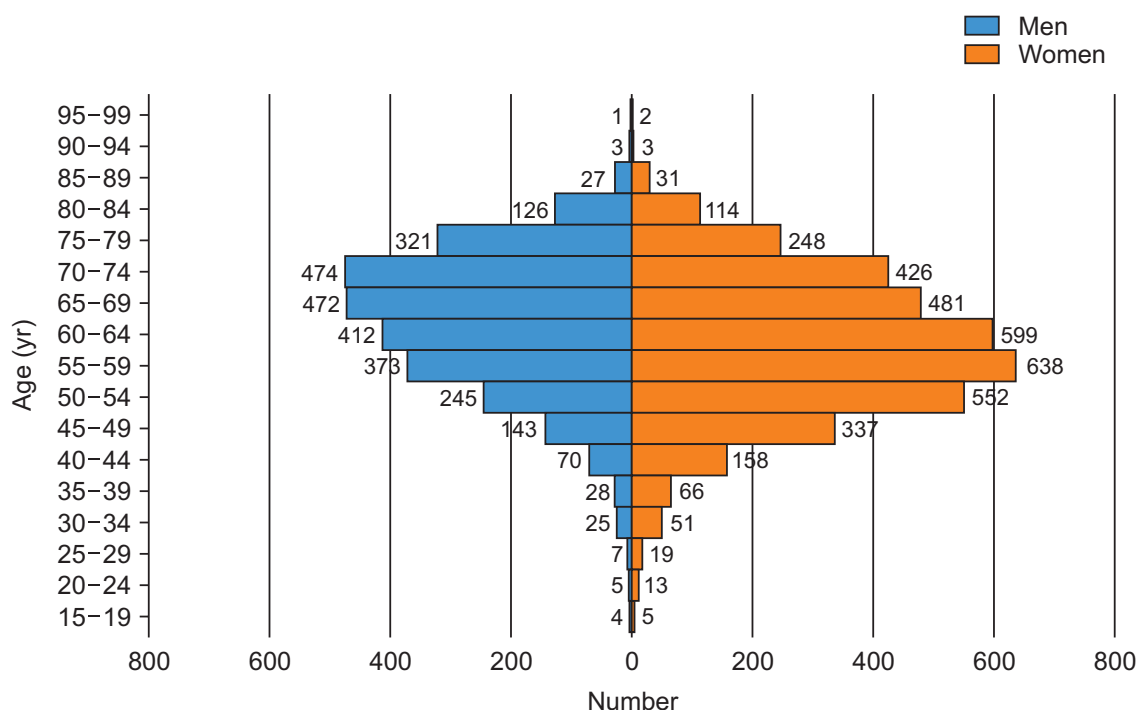
Table 3. Clinical characteristics of patients with nontuberculous mycobacterial pulmonary disease according to age

Characteristic	Age <65 (n=3,752)	Age ≥65 (n=2,729)	p-value
Age, yr (NA=8)	53.7±8.1	72.4±5.4	<0.001
Sex, women (NA=3)	2,439 (65.0)	1,304 (47.8)	<0.001
Height, cm (NA=108)	161.4±7.7	160.8±8.5	0.003
Weight, kg (NA=103)	54.3±9.2	53.2±10.1	<0.001
BMI, kg/m^2 (NA=109)	20.8±2.8	20.5±3.2	0.002
BMI <18.5 kg/m^2 (NA=109)	668 (18.6)	735 (27.4)	<0.001
Ever smoker (NA=101)	761 (20.6)	1,064 (39.6)	<0.001
History of tuberculosis (NA=22)	1,385 (37.0)	1,114 (40.8)	0.001
History of NTM treatment (NA=4)	443 (11.8)	321 (11.8)	0.982
Comorbidity			
Bronchiectasis (NA=1,558)	1,897 (63.9)	1,057 (52.9)	<0.001
ILD (NA=1,528)	41 (1.4)	108 (5.4)	<0.001
COPD (NA=193)	263 (7.2)	394 (15.0)	<0.001
Asthma (NA=3,353)	53 (3.2)	69 (4.7)	0.031
Diabetes (NA=10)	228 (6.1)	428 (15.7)	<0.001
Hypertension (NA=3,596)	229 (14.9)	466 (34.3)	<0.001
CKD (NA=131)	36 (1.0)	92 (3.5)	<0.001
CHD (NA=133)	169 (4.6)	362 (13.6)	<0.001
CLD (NA=90)	235 (6.3)	166 (6.2)	0.857
Transplantation (NA=235)	51 (1.4)	26 (1.0)	0.188
Cancer (NA=10)	494 (13.2)	538 (19.8)	<0.001
Connective tissue disease (NA=53)	119 (3.2)	75 (2.8)	0.376
Smear positivity (NA=247)	1,673 (46.2)	1,293 (49.5)	0.001
Species (NA=56)			<0.001
Mycobacterium avium	1,594 (42.7)	974 (36.2)	<0.001
M. intracellulare	1,187 (31.8)	1,196 (44.4)	<0.001
M. abscessus sub. *abscessus*	352 (9.4)	182 (6.8)	<0.001
M. abscessus sub. *massiliense*	340 (9.1)	144 (5.3)	<0.001
M. abscessus*	5 (0.1)	2 (0.1)	0.712
M. fortuitum	15 (0.4)	16 (0.6)	0.195
M. kansasii	90 (2.4)	40 (1.5)	<0.001
Others	35 (0.9)	33 (1.2)	0.171
Mixed multi-species	118 (3.2)	105 (3.9)	0.050
Radiologic type (NA=1)			<0.001
Non-cavitary NB	2,491 (66.4)	1,692 (62.0)	<0.001
Cavitary NB	835 (22.3)	595 (21.8)	<0.001
Fibrocavitary	199 (5.3)	220 (8.1)	<0.001
Others[†]	227 (6.1)	221 (8.1)	<0.001
BACS score[‡] (NA=117)			<0.001
0	1,628 (44.1)	0	
1	1,280 (34.7)	727 (27.1)	
2	638 (17.3)	1,159 (43.2)	
3	145 (3.9)	618 (23.1)	
4	0	177 (6.6)	

Values are presented as mean±standard deviation or number (%).
*Subspecies not clarified. [†]Consolidation, single nodule, or indeterminate type. [‡]BACS score is derived from the BACES score without erythrocyte sedimentation rate data.
NA: not available; BMI: body mass index; ILD: interstitial lung disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; CHD: chronic heart disease; CLD: chronic liver disease; NB: nodular bronchiectatic.

4. Subgroup analysis by healthcare institution

Patients were divided according to the reporting institutions (Supplementary Table S3). While the four major referral hospitals accounted for 93% of the patients (6,056 individuals), those from the other institutions tended to have higher disease severity, as indicated by the BACS scores (p for trend <0.001).

Discussion

This study synthesized clinical and disease-related data from 6,489 patients diagnosed with NTM-PD between 2002 and 2019 in South Korea. We observed variations in clinical characteristics according to age and sex. Men were generally older than women at diagnosis, and exhibited a higher prevalence of cavitary disease. Additionally, patients aged ≥65 years presented with a lower BMI, and a greater incidence of cavitary disease. To the best of our knowledge, this is the first comprehensive study to integrate the clinical characteristics and disease-specific features of NTM-PD in South Korea.

Geographical variation in the epidemiology of NTM is well recognized. The distribution of NTM species varies by country and climate. A 2008 study across six continents and 30 countries found MAC to be the most isolated NTM species from pulmonary samples globally (47%), followed by *Mycobacterium gordonae* (11%), and *Mycobacterium xenopi* (8%)[12]. In Asia, MAC was the predominant species (54%), but important geographical differences were noted among rapidly growing mycobacteria, accounting for 27% of NTM isolates in Asia, compared to 14%–17.9% in Western countries. Within Asia, the proportions varied significantly: Tokyo (Japan) had 6.6%, Taiwan 50%, and South Korea 28.7%[12]. A separate study reported that the incidence rate of NTM-PD varied by region within Japan, likely influenced by climatic factors[34]. Hence, understanding the local epidemiology is crucial for NTM-PD management.

The diagnosis of NTM-PD does not necessitate immediate treatment; thus, identifying risk factors for poor prognosis is a clinical priority[35]. The BACES score is used to predict 5-year mortality in NTM-PD patients. In this context, we analyzed the study group by age and sex, two components of the score, to investigate the clinical characteristics associated with these risk factors.

Individuals aged 65 and older showed a higher proportion of men, and a higher proportion of patients with BMI <18.5 kg/m^2 (Table 3), indicative of a poorer NTM-PD prognosis. Given the anticipated worse out-comes in the older demographic[36], proactive treatment consideration is critical. Notably, treatment-related adverse events are commonly reported among NTM-PD patients[37], and those over 65 in our study also exhibited a higher prevalence of underlying respiratory (COPD, asthma, and interstitial lung disease) and non-respiratory (hypertension, diabetes, chronic kidney diseases, and chronic heart disease) conditions, necessitating vigilant monitoring for drug-related adverse events during treatment.

A few studies have reported sex-related differences in the clinical characteristics of NTM-PD[16,34,38,39]. Our study observed that men were diagnosed at an older age, and had a higher incidence of cavitary lesions. This aligns with data from Korea's National Health Insurance Service, which also indicates a later diagnosis in men[3]. A Japanese study found a higher prevalence and incidence among women with younger age at diagnosis[34]. Possible explanations for these sex-related disparities include physiological processes influenced by estrogen, adipokines, and growth factor-β. Slender, older women may be more prone to NTM, due to a relative estrogen deficit, and abnormal expression of adipokines and transforming growth factor-β[40]. In addition, the incidence of NTM-PD tends to be higher in women who undergo hormone replacement therapy for longer periods, indicating the possible role of sex hormones in the development of NTM-PD[41]. Underlying respiratory conditions could be another explanation. A recent meta-analysis highlighted bronchiectasis as a significant risk factor for NTM-PD, followed by history of TB, interstitial lung disease, and COPD[42]. In our study, the prevalence of respiratory comorbidities differed by sex; bronchiectasis was more prevalent in women, whereas COPD and a history of TB were more frequent in men, mirroring findings from Japan[34]. The underlying mechanisms for sex-related differences in NTM-PD remain uncertain. To understand the sex-related differences in the clinical characteristics of NTM-PD, further research is warranted to investigate the nature of disease and host susceptibility, considering the complex interplay in NTM-PD development between environmental factors, host genetics, and microbial characteristics[43].

The strength of this study lies in its comprehensive analysis of NTM-PD severity, causative species, and radiologic presentations in Korea, providing vital clinical insights. However, several limitations should be considered. First, the included studies primarily involved patients from tertiary medical centers, which might introduce selection bias, due to these centers treating more severe cases. Second, it was not possible to aggregate all patient data from the reported

literature, potentially limiting the representativeness of the Korean NTM-PD population in the study. Third, due to the absence of ESR data, the BACES score could not be calculated; therefore, the BACS score was alternatively used for indirect assessment of disease severity. Fourth, as data were requested from different institutions, there was a high rate of missing values for key variables (e.g., bronchiectasis). However, we chose not to impute the missing values for possible distortion; this could lead to an overestimation or underestimation of the characteristics of the actual patient population. Fifth, the risk of bias in individual studies was not assessed. Although we identified 136 studies from 21 institutions, data from only 18 primary articles across 11 institutions were synthesized, with cohort-wide data collected to prevent duplication from single institutions; this precluded an evaluation of individual study biases. In South Korea, the NTM research and patient cohorts were predominantly concentrated in a few institutions. Therefore, applying the analytic methods of conventional individual participants data meta-analysis, including publication bias or sensitivity analysis, was not feasible. Sixth, the patient information only reflects the characteristics of the patient group at the time of NTM-PD diagnosis, thus not accounting for changes in characteristics as the disease progresses. Lastly, while it was possible to minimize patient overlap within institutions, patients might overlap between institutions.

In conclusion, we analyzed the clinical characteristics of NTM-PD in South Korea, highlighting the variable impact of the disease across different ages and sexes, which may influence clinical outcomes. Ongoing research into these characteristics and their association with treatment responses is vital to developing targeted therapies and improving patient prognosis.

Authors' Contributions

Conceptualization: Kang YA, Park Y. Methodology: Kang YA, Park Y. Formal analysis: all authors. Data curation: Kim S, Chang S, Park Y. Writing - original draft preparation: Lee G, Kim S. Writing - review and editing: all authors. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Material

Supplementary material can be found in the journal homepage (http://www.e-trd.org).

Supplementary Table S1. MEDLINE search terms and results.

Supplementary Table S2. List of institutions and research information of the selected articles.

Supplementary Table S3. Clinical characteristics of patients with nontuberculous mycobacterial pulmonary disease between healthcare facilities.

Supplementary Figure S1. Proportions of elderly, women, and low body mass index (BMI) in patients with nontuberculous mycobacterial pulmonary disease by year of diagnosis.

Supplementary Figure S2. Causative species of nontuberculous mycobacterial pulmonary disease by year of diagnosis in men.

Supplementary Figure S3. Radiologic types of nontuberculous mycobacterial pulmonary disease by year of diagnosis in men.

Supplementary Figure S4. Causative species of nontuberculous mycobacterial pulmonary disease by year of diagnosis in women.

Supplementary Figure S5. Radiologic types of nontuberculous mycobacterial pulmonary disease by year of diagnosis in women.

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