FACTORS ASSOCIATED WITH NONTUBERCULOUS MYCOBACTERIAL PULMONARY INFECTIONS

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Abstract. The incidence of nontuberculous mycobacterial (NTM) pulmonary infections has increased in Thailand and can be challenging to diagnose. The aim of this study was to determine the clinical features, radiographic findings and species of NTM among patients with NTM pulmonary infection or colonization at Srinagarind Hospital, Khon Kaen, Thailand, from January 2012 to December 2016 in order to inform future efforts for early diagnosis of NTM. The criteria used to diagnose NTM infection and colonization were the Amercican Thoracic Society and the Infectious Disease Society of America (ATS/IDSA) 2007 criteria. The medical records of 263 patients diagnosed at the study hospital during the study period with NTM in the respiratory system were reviewed. Thirty-six subjects had a definite pulmonary NTM infection, 17 had a probable pulmonary NTM infection and 210 had NTM colonization. HIV antibody testing was performed on 32 of the definite/probable pulmonary NTM patients: 2 tested positive. Eight definite/probable pulmonary NTM patients had a positive interferon gamma antibody test, of whom 6 had disseminated NTM infections. The most common co-morbidities seen among subjects with definite/probably NTM infection were having a history of pulmonary tuberculosis and having current bronchiectasis. The most common co-morbidities seen among subjects with NTM colonization were cardiovascular disease and diabetes mellitus. The chest radiographic patterns seen most among subjects with definite/probable pulmonary NTM infection were a reticular infiltration (*n*=31, 58.5%), bronchiectasis (*n*=29, 54.7%) and nodular lesions (*n*=24, 45.3%). The areas on the chest radiograph where infiltrations most commonly seen were in the right upper lobe (*n*=26, 49.1%), right middle lobe (*n*=19, 35.8%), lingular lobe (*n*=17, 32.1%) and left upper lobe (*n*=17, 32.1%). The most common NTM organisms isolated on culture in the subjects with definite/probable pulmonary NTM infection were: *Mycobacterium abscessus* (*n*=21, 39.6%), *M. avium complex* (*n*=19, 35.8%), *M. fortuitum* (*n*=3, 5.7%), *M. scrofulaceum* (*n*= 3, 5.7%), rapid-growing mycobacteria (RGM) (*n*=3, 5.7%), *M. kansasii* (*n*=2, 3.8%) and *M. gordonae* (*n*=2, 3.8%). Five factors were significantly associated with definite/probable pulmonary NTM infection: patient age < 60 years [adjusted OR=2.47; 95% CI: 1.20-5.10], female sex (adjusted OR=2.13; 95% CI: 1.00-4.55), duration of symptoms > 28 days (adjusted OR=3.95, 95% CI: 1.91-8.20), having a bronchiectasis pattern on chest X-ray (adjusted OR=2.56; 95% CI: 1.18-5.53) and isolating *M. abscessus* on culture (adjusted OR=3.25; 95% CI: 1.50-7.02). In conclusion, isolated NTM from respiratory specimens does not necessarily imply infection or require treatment. In our study only twenty percent were denifite/probable pulmonary NTM infection. Early diagnosis and treatment denifite/probable pulmonary NTM

subjects will decrease morbidity and mortality. However, treatment subjects with NTM colonization may increase drug toxicity because of long term of treatment.

Keywords: pulmonary nontuberculous mycobacterium, respiratory specimens

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INTRODUCTION

More than 160 species of nontuberculous mycobacteria (NTM) have been described (Tortoli, 2009; Stout *et al*, 2016). NTM is an environmental organisms frequently isolated from water, soil, dust or plants (Tortoli, 2009). NTM may occasionally cause infection in humans. Transmission of NTM from human to human rarely occurs, which is markedly different from mycobacterium tuberculosis (Tortoli, 2009). The majority of NTM are not pathogenic to humans, but most can colonize humans opportunistically and may occasionally cause disease in certain conditions (Tortoli, 2009).

NTM infections are classified into four clinical syndromes: pulmonary disease, lymphadenitis, cutaneous disease and disseminated disease (Tortoli, 2009). The incidence of pulmonary disease cause by NTM has increased in the past 2-3 decades (Stout *et al*, 2016). In South Korea, India, China, Thailand and Taiwan, 31% of isolated NTM from respiratory specimens were considered to be pulmonary NTM infections according to Amercican Thoracic Society and the Infectious Disease Society of America (ATS/IDSA) diagnostic criteria (Griffith *et al*, 2007; Simon *et al*, 2011). A 2005 study from Japan estimated the national prevalence of pulmonary NTM infection to be 33-65 cases per 100,000 population, which is nearly 10 times higher than in America and Europe (Morimoto *et al*, 2014). The annual mortality rate of patients with newly diagnosed pulmonary NTM in Japan is estimated to be 1-2% (Morimoto *et al*, 2014).

Thailand has a high prevalence of tuberculosis (WHO, 2015). Patients with sputum positive for acid-fast bacilli (AFB) are presumed to have tuberculosis and are treated for it (Thanachartwet *et al*, 2014). NTM pulmonary infection is often only diagnosed after lung disease progression has occurred, increasing the risk for greater morbidity and mortality (Thanachartwet *et al*, 2014). Even when NTM is identified from a respiratory specimen, NTM lung disease still requires differentiation from contamination or colonization (Griffith *et al*, 2007). Because of the above factors, diagnosing NTM pulmonary infection can be challenging.

The objective of this study was to determine the clinical features, radiographic findings and types of NTM species among patients with NTM pulmonary infection or colonization of the respiratory tract at the study hospital during the study period in order to inform future efforts for early diagnosis of NTM infection, which could result in better outcomes with lower morbidity and mortality as the final goal.

MATERIALS AND METHODS

Study group

We conducted this cross-sectional study of NTM pulmonary infection at

Srinagarind Hospital, Khon Kaen, Thailand, from January 2012 to December 2016. Inclusion criteria for study subjects were all patients aged ≥15 years with mycobacterial respiratory specimen cultures showing NTM. Exclusion criteria were those with extrapulmonary NTM infections. Subjects were classified as having NTM infection or NTM colonization following the criteria of the ATS/IDSA (Griffith *et al*, 2007).

The study was approved by the Research Ethics Committee, Khon Kaen University (approval no. HE601027).

Study design

We conducted a retrospective review of the medical records of all patients meeting inclusion criteria and exclusion criteria during the study period. The data recorded form with record were: patient age, sex, occupation, signs and symptoms of NTM infection, history of underlying disease, HIV status, chest radiograph results, sputum AFB smear results, mycobacterium culture results, type of respiratory specimen, diagnosis of definite, probable infection or colonization with NTM. The infection was defined as localized or disseminated and the treatment regimen and outcome were also recorded.

A definite pulmonary NTM infection was defined as: 1) having respiratory symptoms and an abnormal chest radiograph or high resolution computed tomography (HRCT) and 2) having a culture positive for NTM from at least two different expectorated sputum samples or a culture positive for NTM from at least one bronchial washing or lavage specimen and 3) exclusion of other diagnoses (Griffith *et al*, 2007). A probable NTM pulmonary infection was defined as having respiratory symptoms, an abnormal chest radiograph or HRCT and one positive culture from an expectorated sputum sample and improvement in symptoms with specific NTM treatment. Colonization was defined as having one NTM positive culture from an expectorated sputum sample but having neither symptoms nor an abnormal chest radiograph.

Statistical analysis

Descriptive statistics were used to analyze demographic data. Means, standard deviations (SD), medians and interquartile ranges (IQR) were calculated for continuous data and numbers and percentages were used for categorical data. To analyze differences between groups, the χ^2 test, Fisher's exact test, Mann–Whitney *U* test or independent *t*-test were used, depending on the data. A p-value < 0.05 was considered statistically significant. Univariate and multivariate analyses were used to assess if a factor was significantly associated with a confirmed or probable case of NTM pulmonary infection and results were presented as crude and adjusted odds ratios (adjusted OR). The Pearson correlation was used to control for collinearity between independent variables; if a correlation had a rho ≥ 0.9, the variable was not used. The Hosmer-Lemeshow goodness-of-fit statistic was used to assess the model fit. Statistical analysis was performed using STATA, version 10.1 (StataCorp, College Station, TX).

RESULTS

During January 2012 - December 2016, 321 patients were diagnosed with having NTM infection at the study hospital. The complete medical records of 263 of these were available and reviewed: 36 met criteria for a definite pulmonary NTM infection, 17 met criteria for a probable pulmonary NTM infection, and 210 met criteria

for NTM colonization. The mean age of the 263 subjects was 58.3 years [standard deviation (SD) = 16.7]; 145 (55.1%) were male. Twenty-five point eight percent of patients were agricultural workers. The median duration of symptoms prior to diagnosis was 28 days. The most common clinical symptom was chronic cough (58.2%), followed by weight loss (35%), fever (30%), productive sputum (25.5%), anorexia (20.5%) and hemoptysis (15.6%). When the medical characteristics of the definite/probable pulmonary NTM infection group and NTM colonization group were compared, patients in the former group were younger, more likely to be female, have a longer duration of symptoms prior to diagnosis and more likely to have hemoptysis (Table 1).

Of the 263 study subjects, 244 specimens (92.8%) were from the sputum, 19 (7.2%) from bronchial washings, 2 (0.8%) were from pleural fluid, 11 (4.2%) were from a lymph node, 1 (0.4%) was from pus on the skin and 1 (0.4%) was from pleural biopsy tissue (Table 2).

Table 1
Characteristics of study subjects with definite/probable pulmonary nontuberculous mycobacterial infection and colonization.

Characteristics	Definite/probable infection (n = 53)	Colonization (n = 210)	p-value
Age in years, mean (SD)	54.4 (13.9)	59.3 (17.2)	0.03
Sex (Male : Female)	22 : 31	123 : 87	0.03
Occupations, n (%)			
Agriculture	12 (22.6)	56 (26.7)	0.55
Government service	13 (24.5)	16 (7.6)	< 0.01
Merchant	5 (9.4)	9 (4.3)	0.14
Employee	4 (7.5)	12 (5.7)	0.62
Monk	2 (3.8)	11 (5.2)	0.66
Other	12 (22.6)	42 (20)	0.67
Duration of symptoms in days, median (q1, q3)	84 (28, 224)	28 (7, 60)	< 0.01
Symptoms, n (%)			
Cough	35 (66)	118 (56.2)	0.19
Weight loss	17 (32.1)	75 (35.7)	0.62
Fever	13 (24.5)	65 (31)	0.36
Productive sputum	11 (20.8)	56 (26.7)	0.38
Anorexia	12 (22.6)	42 (20)	0.67
Hemoptysis	13 (24.5)	28 (13.3)	0.045
Dyspnea	4 (7.5)	27 (12.9)	0.28
Night sweat	0 (0)	5 (2.4)	0.26
Malaise	0 (0)	3 (1.4)	0.38
Disseminate NTM, n (%)	12 (22.6)	0 (0)	< 0.01
Sweet syndrome, n (%)	3 (5.6)	0 (0)	< 0.01

SD, standard deviation; NTM, nontuberculous mycobacteria; q1, first quartile; q3, third quartile.

Twelve of the definite/probable pulmonary NTM infection cases had disseminated NTM infection, 11 had pulmonary and lymph node infections and 1 had both a pulmonary and skin infection. Skin lesions of Sweet's syndrome were found in 3 definite/probable pulmonary NTM patients. Seven cases of definite/probable pulmonary NTM infection had co-infections with other organisms: tuberculosis (n = 4, 7.5%) and cryptococcosis (n = 3, 5.7%). A smoking history was present in 25 patients in the definite/probable pulmonary NTM infection group; of these, 2 were current smokers. Seven were past smokers and 16 were non-smokers. HIV antibody testing was performed on 32 of the definite/probable pulmonary NTM patients: 2 tested positive. Eight definite/probable pulmonary NTM patients (15.1%) had a positive interferon gamma (IFNγ) antibody test; of whom, 6 had disseminated NTM infections.

Seventy-five percent of patients had underlying disease, the most common being old pulmonary tuberculosis (19.4%), cardiovascular disease (17.9%), bronchiectasis (16.3%) and diabetes mellitus (14.1%). The most common co-morbidities seen in the patients with definite/probable pulmonary NTM infection were pulmonary tuberculosis and current bronchiectasis. The most common co-morbidities seen in the patients with NTM colonization were cardiovascular disease and diabetes mellitus (Table 3).

The most common NTM organisms found on culture in definite/probable pulmonary NTM infection cases were: *M. abscessus* (n=21, 39.6%), *M. avium complex* (n=19, 35.8%), *M. fortuitum* (n=3, 5.7%), *M. scrofulaceum* (n= 3, 5.7%), rapid-growing mycobacteria (RGM) (n=3, 5.7%), *M. kansasii* (n=2, 3.8%) and *M. gordonae* (n=2, 3.8%). The most common NTM organisms found on culture in the colonization group were *M. avium complex* (n=98, 46.7%), *M. abscessus* (n=30, 14.3%), *M. fortuitum* (n=24, 11.4%), *M. scrofulaceum* (n= 14, 6.7%), *M. gordonae* (n=12, 5.7%), *M. simiae* (n=12, 5.7%), and other nontuberculous mycobacteria (Table 4).

Table 2
Specimen sources among patients with definite/probable pulmonary nontuberculous mycobacterial infection and colonization.

Specimen sources	Definite/probable infection[a] (n = 53) n (%)	Colonization[b] (n = 210) n (%)	Total (n = 263) n (%)
Sputum	47 (89)	197 (93.8)	244 (92.8)
Bronchial wash or lavage	5 (9.4)	14 (6.7)	19 (7.2)
Pleural fluid	2 (3.8)	0 (0)	2 (0.8)
Lymph node	11 (21)	0 (0)	11 (4.2)
Pus from skin	1 (1.9)	0 (0)	1 (0.4)
Pleural tissue	1 (1.9)	0 (0)	1 (0.4)

[a]Twelve patients in the definite/probable infection group had disseminated infections; [b]1 patient in the colonization group had culture results from the sputum and bronchoalveolar lavage, but different organisms.

Table 3
Co-morbidities of study subjects with definite/probable pulmonary nontuberculous mycobacterial infection and colonization.

Co-morbidities	Definite/probable infection (n = 53) n (%)	Colonization (n = 210) n (%)	p-value
Underlying disease	38 (71.7)	159 (75.7)	0.55
Old pulmonary tuberculosis	17 (32.1)	34 (16.2)	< 0.01
Cardiovascular disease	4 (7.5)	43 (20.5)	0.03
Bronchiectasis	12 (22.6)	31 (14.8)	0.17
Diabetes mellitus	3 (5.7)	34 (16.2)	0.05
Connective tissue disease	2 (3.8)	22 (10.5)	0.13
Interferon gamma deficiency	8 (15.1)	0 (0)	< 0.001
Lung cancer	0 (0)	13 (6.2)	0.06
Liver disease	0 (0)	9 (4.3)	0.12
Renal disease	1 (1.9)	6 (2.9)	0.70
COPD	2 (3.8)	5 (2.4)	0.57
Asthma	0 (0)	2 (1)	0.48
Hematologic malignancy	0 (0)	5 (2.4)	0.26
Old CVA	1 (1.9)	2 (1)	0.57
Immunosuppressive drug	2 (3.8)	25 (12)	0.08
Old pulmonary NTM	2 (3.8)	2 (1)	0.13

HIV, human immunodeficiency virus; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular disease; NTM, nontuberculous mycobacteria.

The radiographic findings are shown in Table 5. The most common chest radiological patterns found among definite/probable pulmonary NTM infection cases were reticular infiltration (n=31, 58.5%), bronchiectasis (n=29, 54.7%) and nodular lesions (n=24, 45.3%). The most common locations for an infiltration seen on a chest radiograph were right upper lobe (n=26, 49.1%), right middle lobe (n=19, 35.8%), lingular lobe (n=17, 32.1%), and left upper lobe (n=17, 32.1%). Chest computed tomography (CT) was performed in 26 of the 53 patients with definite/probable NTM infection. The commonest chest CT findings seen were bronchiectasis (n=19, 73.1%), reticular lesions (n=17, 65.4%), and nodular lesions (n=16, 61.5%). The commonest infiltrate locations seen on chest CT were right lower lobe (16, 61.5%) and right middle lobe (15, 57.7%).

Univariate analysis was performed to determine factors associated with definite/probable pulmonary NTM. Patient age < 60 years, female gender, duration of symptoms > 28 days, past history of pulmonary tuberculosis, having hemoptysis, a bronchiectasis pattern on radiography, reticular infiltration on radiography, and those who had *M. abscessus* isolated on culture were significantly more likely to have definite/probable pulmonary NTM (Table 6). Multiple logistic regression analysis revealed 5 factors significantly associated

Table 4
Species of nontuberculous mycobacteria among subjects with definite/probable pulmonary nontuberculous mycobacterial infection and colonization.

Species	Definite/probable infection (n = 53) n (%)	Colonization (n = 210) n (%)	p-value
M. abscessus	21 (39.6)	30 (14.3)	<0.01
M. avium complex	19 (35.8)	98 (46.7)	0.16
M. fortuitum	3 (5.7)	24 (11.4)	0.22
Rapid-growing mycobacteria	3 (5.7)	6 (2.9)	0.32
M. scrofulaceum	3 (5.7)	14 (6.7)	0.79
M. kansasii	2 (3.8)	5 (2.4)	0.57
M. gordonae	2 (3.8)	12 (5.7)	0.57
M. simiae	0 (0)	12 (5.7)	0.08
M. asiaticum	0 (0)	3 (1.4)	0.38
M. chelonae	0 (0)	1 (0.5)	0.62
M. genavensae	0 (0)	6 (2.9)	0.21
M. interjectum	0 (0)	4 (1.9)	0.31
M. lentiflavum	0 (0)	6 (2.9)	0.21
M. malmoense	0 (0)	2 (1.0)	0.48
M. mucogenicum	0 (0)	2 (1.0)	0.48
M. palustre	0 (0)	3 (1.4)	0.38
M. saskatchewanense	0 (0)	1 (0.5)	0.62
M. szulgai	0 (0)	2 (1.0)	0.48

M, mycobacteria.

with definite/probable pulmonary nontuberculous mycobacterial infection: patient age < 60 years [adjusted odds ratio (OR): 2.47; 95% confidence interval (CI): 1.20-5.10], female sex (adjusted OR=2.13; 95% CI: 1.00-4.55), duration of symptoms > 28 days (adjusted OR=3.95; 95% CI: 1.91-8.20), having a bronchiectasis pattern on chest X-ray (adjusted OR=2.56; 95% CI: 1.18-5.53), and having *M. abscessus* isolated on culture (adjusted OR=3.25; 95% CI: 1.50-7.02) (Table 6). No collinearity was found among independent variables (rho < 0.9). The Hosmer-Lemeshow goodness-of-fit test for the logistic regression model gave a p-value = 0.75, indicating a good fit.

Forty-two of the 53 definite/probable pulmonary NTM infection patients received treatment at Srinagarind Hospital. According to the species of NTM infection, the drugs prescribed for *M. abscessus* infection were: macrolides, fluoroquinolones, doxycycline, imipenem, and amikacin; for *M. avium complex* were: macrolides, rifampicin, ethambutol, and linezolid; for *M. scrofulaceum* were: macrolides, isoniazid, rifampicin, and ethambutol; for rapid-growing mycobacterial infections were: macrolides, fluoroquinolones, and doxycycline; for *M. kansasii* were: isoniazid, rifampicin, ethambutol, and fluoroquinolones; for *M. scrofulaceum* were: macrolides,

Table 5
Radiographic findings among study subjects with definite/probable pulmonary non-tuberculous mycobacterial infection and colonization.

Radiology results	Definite/probable infection (n = 53) n (%)	Colonization (n = 210) n (%)	p-value
Abnormal CXR	53 (100)	182 (86.7)	< 0.01
Pattern			
Bronchiectasis	29 (54.7)	57 (27.1)	< 0.01
Reticular infiltration	31 (58.5)	89 (42.4)	0.04
Nodular lesion	24 (45.3)	79 (37.6)	0.31
Patchy alveolar infiltration	12 (22.6)	47 (22.4)	0.97
Pleural effusion	5 (9.4)	23 (11)	0.75
Cavitary formation	4 (7.5)	17 (8.1)	0.90
Emphysema	4 (7.5)	10 (4.8)	0.42
Miliary infiltration	0 (0)	2 (1)	0.48
Lymphadenopathy	0 (0)	3 (1.4)	0.38
Location in lung			
Right upper lobe	26 (49.1)	75 (35.7)	0.07
Right middle lobe	19 (35.8)	51 (24.3)	0.09
Right lower lobe	16 (30.2)	73 (34.8)	0.53
Left upper lobe	17 (32.1)	72 (34.3)	0.76
Lingular	17 (32.1)	47 (22.4)	0.14
Left lower lobe	15 (28.3)	69 (32.9)	0.52

CXR, chest radiograph.

Table 6
Crude and adjusted odds ratios of factors associated with definite/probable pulmonary nontuberculous mycobacterial infection.

Studied factors	Crude OR (95% CI)	Adjusted OR (95% CI)
Age < 60 years	2.36 (1.24-4.50)	2.47 (1.20-5.10)
Female sex	1.99 (1.08-3.67)	2.13 (1.00-4.55)
Duration of symptom >28 days	3.11 (1.68-5.78)	3.95 (1.91-8.20)
History of pulmonary tuberculosis	2.44 (1.23-4.84)	1.78 (0.71-4.42)
Hemoptysis	2.11 (1.00-4.43)	1.72 (0.71-4.16)
Bronchiectasis	3.24 (1.74-6.03)	2.56 (1.18-5.53)
Reticular infiltration	1.91 (1.04-3.53)	1.54 (0.72-3.30)
Right upper lobe lesion	1.73 (0.94-3.18)	1.50 (0.70-3.22)
Right middle lobe lesion	1.74 (0.91-3.32)	1.02 (0.44-2.37)
Lingular lobe lesion	1.64 (0.84-3.17)	1.17 (0.49-2.80)
M. abscessus isolated on culture	3.93 (2.01-7.71)	3.25 (1.50-7.00)

fluoroquinolones, and amikacin; and for *M. gordonae* were macrolides, fluoroquinolones, and ethambutol. Sixteen subjects (38.1%) were cured, 11 (26.2%) were receiving ongoing treatment, 3 (7.1%) failed treatment, 9 (21.4%) were lost to follow-up, and 3 (7.1%) were referred out. All patients with interferon gamma deficiency were receiving ongoing treatment and one patient with disseminated infection was cured.

DISCUSSION

Nontuberculous mycobacterium (NTM) infections are increasing in prevalence worldwide (Stout *et al*, 2016). The diagnosis of true pulmonary NTM infection is challenging. NTM are frequently found in the environment, unlike *M. tuberculosis*, which is an obligate human pathogen (Tortoli, 2009). NTM can be considered as a pathogen when isolated from sterile sites, such as lymph nodes, pleural fluid, bones and joints, bone marrow and blood (Tortoli, 2009). However, when isolated from respiratory specimens (non-sterile sites), which is the most common site from which it is recovered, NTM may be either colonizing that site or may be a true pathogen (Tortoli, 2009). Diagnosing true pulmonary NTM infection requires clinical, radiographical, and bacteriological evidence following ATS/IDSA criteria (Griffith *et al*, 2007).

A study from South Korea during 2002-2003 found 1,548 NTM respiratory isolates in 794 subjects; of these, 17% met criteria for definite NTM pulmonary infection and 8% met criteria for probable infection (Koh *et al*, 2006). In our study, 14% of patients met criteria for definite NTM pulmonary infection and 6% met criteria for probable NTM pulmonary infection. Our finding is lower than the 31% reported by a previous study (Simons *et al*, 2011) which included data from Japan, Taiwan, South Korea, Thailand, Hong Kong, India, and Singapore covering a study period of 1971-2007.

The most common pathogen found in our study was *M. abscessus*; unlike a study from South Korea where the most common pathogen was *M. avium complex* (Koh *et al*, 2006). The organisms isolated in our study causing pulmonary NTM infection were: *M. abscessus*, *M. avium complex*, *M. fortuitum*, *M. scrofulaceum*, rapid-growing mycobacterium (RGM), *M. kansasii*, and *M. gordonae*. The other NTM organisms identified in our study were considered to be colonizing. Simon *et al* (2011) reported the five most common species of NTM isolated causing pulmonary infection were *M. avium complex*, *M. abscessus*, *M. chelonae*, *M. kansasii*, and *M. scrofulaceum*. The most common isolates from NTM pulmonary infection patients from China were *M. abscessus* (42%) and *M. intracellulare* (34%) (Chu *et al*, 2015), similar to our study. In the past, *M. abscessus* was not considered a major pathogen in South Korea or Taiwan and was not considered a pathogen at all in Thailand (Simons *et al*, 2011). In the past in Thailand, most NTM pulmonary infections occurred in HIV-infected patients (Saritsiri *et al*, 2006; Ratanasuwan *et al*, 2002). The most common true pulmonary NTM pathogen among HIV-negative patients in our study was *M. abscessus*. *M. abscessus* is becoming an increasingly most common cause of pulmonary NTM lung disease (Chu *et al*, 2015; McShane and Glassroth, 2015).

In our study, the majority of patients with true pulmonary NTM infection were female, similar to previous studies (Griffith *et al*, 2007; Bodle *et al*, 2008; Chien *et al*, 2014). Most of our subjects were non-smokers, similar to a study of Koh *et al* (2006). A previous study re-

ported NTM lung infections were more common among slender women without a history of immune deficiency, supporting the theory that abnormal expression of sex hormones and/or TGF-β may play an important role in susceptibility to pulmonary NTM infection (Chan and Iseman, 2010). In our study, subjects with true pulmonary NTM infection were more likely to be aged < 60 (mean: 54.4) years. NTM is indolent, with the majority of our subjects having an incubation period of > 28 days. The diagnosis of pulmonary NTM infection is frequently delayed because the symptoms are nonspecific (Stout *et al*, 2016). In HIV-negative patients, the disease is undistinguishable from tuberculosis and is characterized by slow progression (Tortoli, 2009). In our study, hemoptysis was the only symptom more common in true infection than in the colonization group. In a previous study, the most common symptoms of NTM pulmonary infection were chronic cough (76%), non-massive hemoptysis (36%), fever and weight loss (Koh *et al*, 2006). Patients with chronic lung disease, such as pulmonary tuberculosis or bronchiectasis may be more likely to develop NTM pulmonary infections (Andréjak *et al*, 2010; Honda *et al*, 2015; Stout *et al*, 2016), as was seen in our study. Isolation of NTM from respiratory specimens in older patients who have underlying cardiovascular disease or diabetes mellitus may indicated colonization rather than true infection, as was seen in our study.

Radiological imaging is important when NTM lung disease is suspected. The two major radiographic patterns previously reported to be found in pulmonary NTM infections are nodular bronchiectatic forms and fibrocavitary lesions (Griffith *et al*, 2007; Stout *et al*, 2016). However in our study, in which most of the patients were HIV negative, the most common radiograph patterns seen were bronchiectasis, reticular infiltration, and nodular lesions. In our study, only 7% of subjects had cavitary formation. Chest computed tomography (CT) was performed in half of our patients: the most common radiologic abnormalities seen in pulmonary NTM infection patients were bronchiectasis and reticular infiltration and the most common locations where radiologic abnormalities seen were the right lower lobe and the right middle lobe. Chest CT scans were significantly more sensitive than plain chest radiography for detecting bronchiectasis and pulmonary nodules (Stout *et al*, 2016). A study from China comparing chest imaging between non-tuberculous and tuberculous mycobacteria found bronchiectasis was significantly more common in those with NTM pulmonary disease; the most common lung area with radiologic abnormalities seen were the right middle lobe and left lingular segment (Chu *et al*, 2015).

Treatment regimens and response rates differ by NTM species. Better molecular identification of NTM species and drug susceptibilities tests are needed to select optimal treatment (Cowman *et al*, 2016; Ryu *et al*, 2016). *Mycobacterium abscessus* was the most common pathogen isolated in our study and the most drug resistant, resulting in limited therapeutic options and high treatment failure rates (Koh *et al*, 2014; Stout *et al*, 2016).

In conclusion, the isolated of NTM from respiratory specimens does not necessarily imply infection or require treatment. In this study only twenty percent were denifite/probable pulmonary NTM infection. Five factors were significantly associated with denifite/probable pulmonary NTM infection were age < 60 years, female sex, duration of symptoms > 28

days, having a bronchiectasis pattern on chest X-ray, and isolating of *M. abscessus* on culture. Early diagnosis and treatment denifite/probable pulmonary NTM subjects will decrease morbidity and mortality. However, treatment subjects with NTM colonization, may increase drug toxicity because of long term of treatment.

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