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Evaluation of the clinical, radiological, and microbiological characteristics of patients with non-tuberculosis mycobacteria (NTM) growth in respiratory tract samples culture

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ABSTRACT

Aims: This study aimed to look at the clinical, imaging, and microbiological features of patients with non-tuberculosis mycobacteria (NTM) growth in respiratory samples and to identify the factors that might help in distinguishing the difference between infection and colonization.

Methods: This retrospective study included 85 patients with NTM growth in respiratory tract samples (sputum, bronchial lavage/bronchoalveolar lavage) between January 2017 and March 2025. Demographic data, comorbidities, radiological findings, and microbiological results were analyzed. The diagnosis of NTM infection was made based on the ATS/ERS/ESCMID/IDSA clinical practice guidelines, which consider clinical, radiological, and microbiological criteria.

Results: Among the 85 patients, 55.3% were diagnosed with infection and 44.7% with colonization. The most common comorbidities were chronic obstructive pulmonary disease (COPD) (47.1%), bronchiectasis (37.6%), and hypertension (31.8%). Radiological findings included infiltration (51.8%), nodules (50.6%), bronchiectasis (37.6%), and cavitation (20%). Infiltration (p=0.013) and cavitation (p=0.012) were significantly more frequent in the infection group, while bronchiectasis (p=0.010) and asthma (p=0.045) were more prevalent in the colonization group. Inhaled corticosteroid (ICS) use showed no significant difference between groups.

Conclusion: In line with previous literature, this study confirms that NTM infections are commonly associated with structural lung diseases such as COPD and bronchiectasis. Radiological findings, particularly cavitation and infiltration, play an important role in the diagnosis of infection. A comprehensive evaluation of clinical, radiological, and microbiological data is essential for differentiating NTM infection from colonization. Distinguishing colonization from active infection prevents unnecessary treatments. It reduces healthcare costs. It protects patients from the possible side effects of antibiotics.

Keywords: Non-tuberculosis mycobacteria, radiologic images, comorbidities

INTRODUCTION

Mycobacterial species other than the *Mycobacterium tuberculosis* complex (TB) and *Mycobacterium leprae* are referred to as non-tuberculous mycobacteria (NTM). NTMs are environmental organisms commonly found in environments such as soil, natural water sources, tap water, and animals. It is generally transmitted to humans by reaching the respiratory system through aerosol; however, person-to-person transmission has been rarely reported.[1]

NTM can lead to either transient colonization or active infection in the respiratory system, depending on various factors, such as the species of mycobacteria, its virulence, the duration of exposure, and the immune status of the host.[2] Today, more than 190 NTM species have been identified. *Mycobacterium avium* complex (MAC), *Mycobacterium kansasii, Mycobacterium xenopi,* and *Mycobacterium abscessus* are the most frequently clinically isolated species.[3]

NTMs may cause lung infections in individuals with conditions such as chronic obstructive pulmonary disease (COPD), cystic fibrosis, bronchiectasis, pneumoconiosis, previous tuberculosis, and immunosuppression. In addition, they can cause skin, lymph node, soft tissue, bone, and disseminated infections.[4-6]

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The most common clinical pulmonary symptoms include chronic cough, sputum production, hemoptysis, and shortness of breath, while systemic symptoms are fatigue, loss of appetite, weight loss, sweating, and fever. Radiologically, fibrotic cavitary lesions, nodular infiltrations, and bronchiectasis may be detected.[7,8]

Due to the widespread prevalence of NTMs, their isolation from respiratory specimens does not always indicate infection. Therefore, the distinction between NTM infection and NTM colonization is critical for the clinical decision-making process. For a definitive infection diagnosis, in addition to the presence of appropriate clinical symptoms, radiological findings and microbiological isolation of "the same species of NTM" in more than one sputum culture or bronchoalveolar lavage (BAL) sample or tissue biopsy are required. Isolation of NTM in a single sputum sample in asymptomatic individuals is generally accepted as colonization.[9]

The objective of this study was to evaluate the clinical, radiological, and microbiological characteristics of patients with NTM growth from respiratory samples between 2017 and 2025 and to reveal the factors that may be effective in distinguishing between infection and colonization. Distinguishing colonization from active infection prevents unnecessary treatments. Using antibiotics wisely reduces healthcare costs. Protecting the patients from the possible side effects of antibiotics is the primary target of a doctor. By focusing on appropriate treatment strategies, healthcare providers can improve patient outcomes while simultaneously minimizing the risk of antibiotic resistance. Education on the proper use of antibiotics is essential for both practitioners and patients to ensure a more effective approach to managing infections.

METHODS

This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Samsun University (Date: 19.02.2025, Decision No: 2025/4/1).

This study was conducted by retrospectively evaluating the data of 87 patients with NTM growth in respiratory tract samples (sputum, bronchial lavage/BAL) between January 2017 and March 2025 in the chest diseases clinic of Samsun Training and Research Hospital. The study included a total of 85 patients, as we were unable to reach the data for two patients (**Figure 1**).

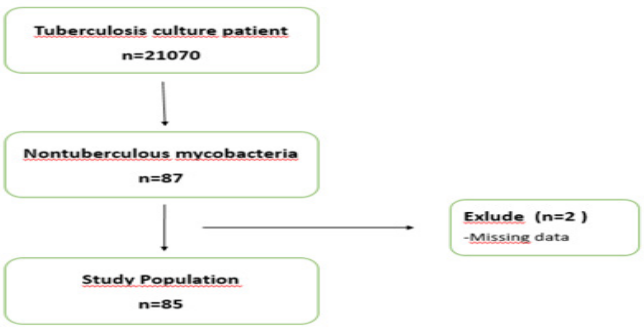

Figure 1. Flowchart

Sputum and bronchial lavage/BAL samples from the lungs were stained with the Ziehl-Neelsen (ZN) method to check for acid-fast bacilli (AFB), and cultures were done using the BACTEC 460 TB system. The patients with TB growth were excluded from the study.

The diagnosis of non-tuberculous mycobacterial infection was established according to the ATS/ERS/ESCMID/IDSA Clinical Practice Guideline based on the presence of respiratory or systemic symptoms along with radiological findings (such as cavitation, nodules, or bronchiectasis), and the following:

1. NTM growth in two or more sputum cultures obtained at different times, or
2. NTM growth in bronchial lavage/BAL culture, or
3. The presence of mycobacterial histological findings, such as granulomatous inflammation or AFB, in transbronchial or other lung biopsies, along with the growth of NTM in culture or NTM culture positivity in at least one sputum or bronchial lavage sample, indicates a diagnosis.[3]

The diagnosis of non-tuberculous mycobacteria colonization was established only in cases where NTM growth was detected in a single sputum sample, and there was no evidence in favor of infection with clinical/radiological findings.[3] Demographic data (age, gender), accompanying diseases, and thoracic tomography findings (nodule, cavitation, bronchiectasis, normal) of the patients were obtained from the patient files and the information processing system of our hospital (**Figure 2, 3, 4**).

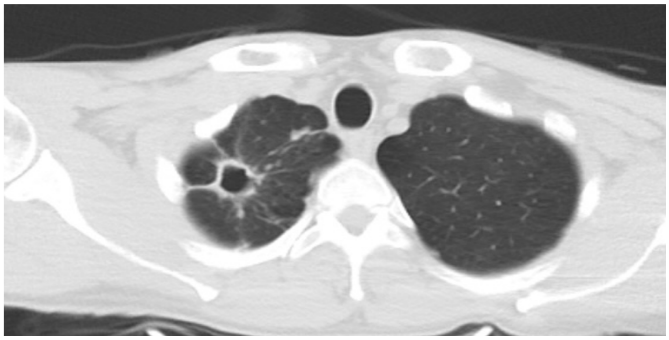

Figure 2. The figure represents a sample of a radiologic image of a "cavity" in a thoracic CT of an NTM patient
CT: Computed tomography, NTM: Non-tuberculosis mycobacteria

Figure 3. The figure represents a sample of a radiologic image of "infiltrations" in a thoracic CT of an NTM patient
CT: Computed tomography, NTM: Non-tuberculosis mycobacteria

Figure 4. This image shows an example of "nodular infiltration" in a chest CT scan of a patient with NTM
CT: Computed tomography, NTM: Non-tuberculosis mycobacteria

Microscopic examination of some samples as a result of AFB staining may not show sufficient bacilli in the examination areas. Even if bacilli are found in the samples, they may not be seen in the areas examined by microscopy; the number of bacilli may be very low, but there may be growth in culture. For this reason, it is imperative to perform a microscopic examination of all specimens taken after AFB staining and then cultivate them in culture to see if there will be growth even if bacilli are not observed. Because the gold standard method in the diagnosis of tuberculosis is whether there will be growth in culture.

Statistical Analysis

The data were analyzed using the SPSS 23.0 (SPSS Inc., Chicago, IL, USA) program. Categorical variables were defined by frequency and percentage values, while numerical variables were defined by mean±standard deviation (SD). The relationship between categorical variables was evaluated by the chi-square test, and a p-value of <0.05 was considered statistically significant.

RESULTS

Of the 85 patients with NTM growth, 22 were female and 63 were male. The mean age of the patients was 58.6±17.5 years. It was calculated as 60.1±16.2 in women and 58.1±18.1 in men. Of the culture samples, 65 (76.5%) were obtained from sputum and 20 (23.5%) from bronchial lavage/BAL. AFB positivity was detected in 74 patients (87.1%) with EZN staining. While AFB staining was negative in 11 patients (12.9%), growth was observed in tuberculosis culture.

Of the 85 patients with growth in tuberculosis cultures, 47 (55.3%) were infected patients and 38 (44.7%) were evaluated as colonization. AFB staining was found to be positive in 38 cases (80.8%) in the patient group and 36 cases (94.7%) in the colonization group. In 73 (85.9%) of the patients, at least one comorbidity was present. The most common comorbidities were detected to be COPD by 40 (47.1%), bronchiectasis by 32 (37.6%), and hypertension by 27 (31.8%), respectively.

When thoracic computed tomography (CT) findings were examined, it was observed that 44 patients (51.8%) had infiltration, 43 patients (50.6%) had nodules, 32 patients (37.6%) had bronchiectasis, and 17 patients (20%) had cavitation. In 8 patients (9.4%), thoracic CT findings were normal (Table 1).

Table 1. General characteristics of NTM patients

Demographic features	
Age	58.6±17.5
Female	60.1±16.2
Male	58.1±18.1
Gender	
Female n (%)	22 (25.9)
Male n (%)	63 (74.1)
Culture	
Sputum	65 (76.5)
Bronchial/bronchoalveolar lavage	20 (23.5)
Disease n (%)	47 (55.3)
ARB positive	38 (80.8)
ARB negative	9 (19.2)
Colonization n (%)	38 (44.7)
ARB positive	36 (94.7)
ARB negative	2(5.3)
Co-morbidity and risk factors n (%)	73 (85.9)
COPD	40 (47.1)
Bronchiectasis	32 (37.6)
Hypertension	27 (31.8)
Ischemic heart disease	17 (20)
Diabetes	14 (16.5)
Asthma	11 (12.9)
Chronic kidney failure	9 (10.6)
Malignancy	8 (9.4)
History of chemotherapy	6 (7.1)
Cerebrovascular disease	4 (4.7)
Corticosteroid treatment history	3 (3.5)
HIV-infected	3 (3.5)
Chest deformity	2 (2.4)
Dialysis	2 (2.4)
Anti-TNF treatment history	1 (1.2)
ICS (inhale corticosteroid)	
Yes	51 (60)
No	34 (40)
Thoracic tomography findings	
Infiltration	44 (51.8)
Nodule	43 (50.6)
Bronchiectasis	32 (37.6)
Cavitation	17 (20)
Normal	8 (9.4)

NTM: Non-tuberculosis mycobacteria, COPD: Chronic obstructive pulmonary disease

When the disease and colonization groups were compared, infiltration (36.8% vs. 63.8%; p=0.013) and cavitation (7.9% vs. 29.8%; p=0.012) were observed significantly and more frequently in the disease group. Colonization was significantly higher in the patients diagnosed with bronchiectasis (25.5% vs. 52.6%; p=0.010) and asthma (6.4% vs. 21.1%; p=0.045) (Table 2). Of the patients, 60% (n=51) were using inhaled corticosteroids (ICS), and ICS doses were moderate to high in these patients. Colonization was detected in 60.5% (n=23) of the ICS users, and disease was observed in 59.6% (n=28). No significant difference was found between the two groups in terms of ICS use.

Table 2. Comparison of underlying diseases and thorax tomography findings in cases evaluated as NTM infection and colonization

	Disease n=47	Colonization n=38	p
Infiltration	30 (63.8)	14 (36.8)	0.013
Cavitation	14 (29.8)	3 (7.9)	0.012
Bronchiectasis	12 (25.5)	20 (52.6)	0.010
Asthma	3 (6.4)	8 (21.1)	0.045

NTM: Non-tuberculosis mycobacteria

DISCUSSION

This study was designed as a retrospective, descriptive, and cross-sectional cohort study. In our study, we evaluated the clinical, radiological, and microbiological characteristics of cases with NTM growth in respiratory tract samples. Infection was detected in 55.3% (n=47) of the patients, while colonization was detected in 44.7% (n=38) of the patients. While infiltrative and cavitary radiological findings were more commonly observed in the infection group, structural lung diseases such as bronchiectasis and asthma were found to be more associated with colonization.

The misclassification of cases with colonization as infection leads to unnecessary treatment and possible side effects. There is an increase in morbidity and mortality due to unnecessary treatment. Legal consequences may also arise due to malpractice. Resistance to antibiotics used in the treatment of tuberculosis may develop. It is important for clinicians to develop awareness on this issue.

Numerous studies related to NTM infections have reported similar results in the literature. In a 10-year prevalence study conducted by Bents et al.,[10] where 59.724 cases were evaluated, the prevalence of NTM in individuals over 65 years of age was found to be 20 per 100.000, and bronchiectasis, COPD, gastroesophageal reflux, asthma, and diabetes were among the most common comorbidities. In the study of Veziris et al.,[11] which examined 4447 NTM patients, researchers found that bronchiectasis, HIV, steroid use, and COPD were significantly more common in the patient group than in the control group. In the study of Adzic-Vukicevic et al.,[8] COPD (40%), diabetes (13%), previous tuberculosis (13%), and immunosuppressive therapy (9%) were among the most common comorbidities, while Jones et al. detected COPD in 67.8%, malignancy in 37.2%, and bronchiectasis in 7% of 2.367 NTM patients.[12] These data support that COPD and bronchiectasis are important structural disorders that pave the way for NTM infection. Similarly, in our study, COPD (47.1%) and bronchiectasis (37.6%) were among the most commonly observed conditions.

Characteristic radiological findings have an important place in the diagnosis process of NTM infections. In the literature, the most commonly reported finding is bronchiectasis. It is stated to be detected in 60-80% of NTM cases.[13] Cavitation is particularly common in the fibro-cavitary form and is reported to be 30-60% in this form.[14] Nodular infiltrations, "tree-in-bud" appearance, and micronodules are common radiological findings in the nodular-bronchiectatic form.[15] Both fibro-cavitary and nodular forms can exhibit consolidation and diffuse infiltration findings, particularly in cases of MAC infections.[16] In the study of Jeong et al.,[14] where 22 patients diagnosed with NTM from surgical samples were evaluated, nodular infiltration and bronchiectasis were reported in 91% of all cases. Koh et al.[17] found that among 36 patients they looked at, 61% had bronchiolitis with bronchiectasis, 51% had nodular lesions, 61% had lobular consolidation, and 47% had cavitation. Dailloux et al.[18] observed infiltration, nodules, and cavitation in 36%, 25%, and 15% of their patients, respectively. Our study found that infiltration, nodules, and bronchiectasis were the most common radiological findings, occurring in 51.8%, 50.6%, and 37.2% of cases, respectively, which matches what other studies have reported.

Isolation of NTM from respiratory tract samples does not always indicate clinical infection. Therefore, distinguishing between infection and colonization is critical for both treatment decisions and patient management. In the literature, there are many studies evaluating this distinction, and the findings reveal that radiological, clinical, and microbiological criteria should be evaluated together for the diagnosis of infection.

In the study conducted by Chien et al.,[19] it was revealed that both NTM infection and colonization were more common in male individuals; the rate of males in the infection group was 57.6% and 59.6% in the colonization group. However, Hernández-Garduño et al.[20] reported that female gender and advanced age were significant risk factors in terms of NTM colonization. This suggests that the effect of gender on NTM pathogenesis may vary based on the region and patient population. Our study found no significant difference in gender distribution between the infection and colonization groups.

In studies where radiological findings were examined comparatively, it was revealed that findings such as cavitation, infiltration, and consolidation were at the forefront in the infection group. In the study by Szturmowicz et al.[21] on COPD patients, cavitation and infiltration were seen in the infection group, but these were not found in the colonization group. Similarly, in the study conducted by Mencarini et al.,[22] cavity (26%) and bronchiectasis (53%) rates were found to be significantly higher in the infection group compared to the colonized group. In the study by Chen et al.,[23] 127 patients diagnosed with NTM disease were compared with 37 colonized cases, and bronchiectasis was reported to be significantly more common in the disease group (35% vs. 16%). However, no significant difference was found in terms of COPD and asthma rates. In the same study, radiological findings such as cavitation, consolidation, ground-glass opacity, nodules, and patchy opacity were observed at similar rates in both groups, indicating that these findings alone were not sufficient to distinguish infection.[23] Garcia et al.[24] reported a more widespread distribution of bronchiectasis in the patient group, whereas the colonization group had a higher number of affected lobes and more frequent cystic bronchiectasis. When the infection and colonization groups were evaluated in terms of comorbidity in the study conducted by Andréjak et al.[25] on 1.282 patients, it was revealed that structural lung diseases such as COPD, asthma, and bronchiectasis were associated with both infection and colonization; however, these rates were higher in the infection group. In our study, infiltrative and cavitary radiological findings were detected more frequently in the infection group, while structural lung diseases such as bronchiectasis and asthma were detected more in the colonization group.

Limitations

Our study has certain limitations. First of all, the small sample size, the single-center design, and the retrospective nature of the study limit the generalizability of the findings. Moreover,

molecular diagnostic methods were not used, and non-tuberculous mycobacteria were not identified at the species level. This prevented the evaluation of clinical and radiological characteristics of specific NTM types. Finally, since the long-term follow-up data of the patients could not be reached, the clinical courses of the cases diagnosed with infection and evaluated as contamination could not be compared.

CONCLUSION

As a result, in line with the literature, our study reveals that NTM infections are frequently associated with structural lung diseases such as COPD and bronchiectasis, and radiological findings, especially cavitation and infiltration, contribute to the diagnosis of infection. In cases with a potential risk of contamination, findings such as bronchiectasis should be evaluated more cautiously, and clinical, radiological, and microbiological findings should be considered as a whole when diagnosing infection.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Samsun University (Date: 19.02.2025, Decision No: 2025/4/1).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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