

Comparison of Computed Tomography Findings of Tuberculosis and Non-Tuberculous Mycobacterial Lung Infections

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Background: The treatment of non-tuberculous mycobacterial infections, which are becoming increasingly common, is different and longer than tuberculosis. Correct diagnosis and subtyping are vital for patient management.

Purpose: To determine the radiological findings of mycobacterial infections, detect differences, and contribute to the most accurate and rapid diagnosis.

Materials and Methods: This retrospective and single-center study included a total of 264 patients diagnosed with mycobacterial lung infections, comprising 152 cases of tuberculosis and 112 cases of non-tuberculous mycobacterial infections. Patient demographics (age and gender), the specific subtypes of non-tuberculous mycobacteria, and detailed computed tomography findings were systematically evaluated.

Results: Mean age of the patients was 45.84±16.84 (min 14, max 87). More than half of the mycobacteria infections (54.5%) were in the patient group aged 35–65. As the patient's age decreased, the incidence of tuberculosis increased, and as the patient's age increased, the incidence of non-tuberculous mycobacteria infections increased. 85.9% of patients in the <35 age group were infected with tuberculosis, and 64.3% of patients in the >65 age group were infected with non-tuberculous mycobacteria. Male patients were the majority in all mycobacteria infections, but male dominance was especially evident in non-tuberculous mycobacteria infections ($p<0.001$ for both). Tree-in-bud and pleural effusion were more common in tuberculosis; while cavity, bronchiectasis, and sequela fibrotic changes were more common in non-tuberculous mycobacteria infections ($p<0.05$). The cavitation wall was thicker in tuberculosis ($p=0.015$). In addition, the anterior segment of the left upper lobe was more frequently affected in tuberculosis patients ($p=0.018$).

Conclusion: It is necessary to know the radiological findings well and to guide clinicians in terms of possible non-tuberculous mycobacterial infection, especially in cases resistant to treatment. Accurate differentiation between tuberculosis and non-tuberculous infections is essential, as it has a direct impact on the treatment algorithm. Multi-center studies with larger patient populations may provide additional contributions to our current knowledge.

Plain Language Summary: This study compares lung infections caused by tuberculosis and by non-tuberculous mycobacteria. Although both infections can look similar on CT scans, they are different diseases and require different treatments. To help clinicians tell them apart, we examined CT scan results from 264 patients; 152 with tuberculosis and 112 with non-tuberculous mycobacterial infections. We found that certain features on the CT scans differed between the two groups. By understanding these differences, clinicians can more easily and accurately diagnose the type of infection and select the appropriate treatment. This may help patients receive the correct care more quickly and improve their outcomes.

Keywords: tuberculosis, non-tuberculous mycobacteria, computed tomography

Introduction

Tuberculosis (TB) continues to be a major public health problem today, and as of 2023, with the COVID-19 infection losing its lethal effect, it has once again taken its place as the number one cause of infection-related deaths in the world.

The regions with the highest TB incidence and mortality worldwide are Africa and Southeast Asia. According to the Global Tuberculosis Reports, Turkey's estimated incidence rate has been reported as 15 per 100,000 population. Although this disease, caused by *Mycobacterium tuberculosis*, is preventable and treatable, according to the World Health Organization (WHO), 10 million people are infected, and 1.5 million people die annually. Adults constitute 90% of patients and it is more common in men than in women. While the mortality rate is almost 50% when tuberculosis is not treated, 85% of patients can be cured with 4–6 months of treatment with anti-tuberculosis drugs as recommended by the WHO.¹ Only a portion of infected individuals develop active disease. Others have asymptomatic latent infection, and it is thought that latent infection constitutes approximately one-fourth of the total population. However, in these individuals, there is a risk of developing active TB in cases of immunosuppression caused by various reasons, which occurs more frequently in the first 18 months of infection, and the disease is activated in approximately 5% of patients with latent infection.²

Non-tuberculous mycobacteria (NTM), on the other hand, are common in nature, but rarely cause disease. Although they are less virulent than *M. tuberculosis*, they can cause disease in both immunocompromised and immunocompetent individuals.³ Although there are more than 200 NTM species in nature,⁴ only a few, including *M. avium complex* (MAC), *M. kansasii*, and *M. abscessus*, often cause pulmonary disease.⁵ There may be an underlying structural lung disease such as cystic fibrosis, but sometimes it can affect individuals with no risk factors.⁶ The most affected organ is the lungs, and this condition is defined as non-tuberculous mycobacteria-associated pulmonary disease (NTM-PD) in many sources. *Mycobacterium avium complex* is the most frequently detected NTM and is also the most associated with chronic lung disease.⁷ NTMs are more resistant to drugs and disinfectants due to their cellular structure. Although there are many subtypes, they can be generally classified as rapidly growing mycobacteria (<7 days) and slowly growing mycobacteria (≥7 days). Although there are rapid molecular tests to detect NTMs and their subtypes, in many countries where tuberculosis is common, they are considered drug-resistant tuberculosis and are tried to be treated. The sensitivity of NTMs to anti-tuberculosis drugs is also quite variable and they are mostly resistant to them. The treatment period is also usually longer than TB. Species identification is required and sometimes, in the presence of chronic changes such as underlying bronchiectasis, surgical treatment, which may include resection of the affected lung segment and is a part of the treatment, may be required.⁸

To provide timely and correct treatment to patients, it is important to have a good knowledge of the radiological findings of TB and NTM infections for radiological diagnosis in addition to clinical and microbiological diagnosis. Due to the considerable radiological overlap between tuberculosis (TB) and non-tuberculous mycobacterial (NTM) infections, early distinction remains challenging. Currently, definitive diagnosis often relies on culture-based methods, which are time-consuming and delay treatment decisions. The aim of this study is to describe the radiological findings and differences between the two groups.

Materials and Methods

The study is retrospective and single-centered. A total of 264 patients diagnosed and treated at our hospital between 2017–2024 were included. 152 patients were infected with *M. tuberculosis* and 112 patients with non-tuberculous mycobacteria. The study's ethics committee approval is available with the protocol code 2024–2 by Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital's ethics committee. The requirement for informed consent was waived by the institutional ethics committee, as the retrospective design of the study was disclosed during the ethics application process and approved accordingly. Patient data included in the study are kept confidential, and the study was conducted in accordance with the Declaration of Helsinki.

Inclusion Criteria

- Patients with tuberculosis and non-tuberculous mycobacteria infection
- Patients who underwent thoracic CT in our hospital

Exclusion Criteria

- Non-mycobacteria infections

HIV-positive and immunosuppressed patients
Extrapulmonary involvement

The demographic data and radiological findings of the patients were evaluated. Demographic and clinical information was obtained from our hospital information system, and radiological images were obtained from Picture Archiving and Communication Systems (PACS). Computed tomography (CT) findings were evaluated by a radiologist with 6 years of thoracic radiology and infectious pulmonary diseases experience. Radiological evaluations in this study were performed by a single radiologist due to institutional structure.

Radiologically Evaluated Parameters

Bilateral-unilateral involvement
Percentage prevalence of parenchymal involvement
Cavitation
Tree-in-bud
Ground glass
Consolidation
Miliary involvement
Bronchiectasis
Sequelae/fibrotic changes
Nodule/granuloma
Parenchymal calcification
Mediastinal lymphadenopathy
Pleural effusion
Pleural thickening/calcification
Involved lobes and segments

Statistical Analysis

Commercial statistical package SPSS® 22.0 (IBM Corporation, Armonk, New York, United States) was used. Continuous variables were presented as mean $\pm$ standard deviation (SD) or as median (minimum–maximum), depending on the distribution of the data. Categorical variables were expressed as frequencies and percentages.

For comparisons between the two groups, the independent samples *t*-test was used for continuous variables with normal distribution, and the Mann–Whitney *U*-test was applied for non-normally distributed variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, when appropriate. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated to assess the strength. *P* values < 0.05 was accepted as statistically significant.

Results

Of a total of 264 patients with 152 tuberculosis and 112 non-tuberculous diagnoses, 85 were female (32.2%) and 179 were male (67.8%). Mean age was 45.84 ± 16.84 (min 14, max 87). While the causative agent of mycobacterial infections in patients younger than 35 years was tuberculosis (OR: 4.48), non-tuberculosis mycobacterial infections were more common in patients over 65 years of age (OR: 2.44). 67.8% of all mycobacterial infections were male, but especially in the NTM group, the vast majority of patients were male (80.4%) ($\chi^2=14.044$, $p<0.001$) (Table 1).

The most common species detected in NTM-LD were *M. avium complex* (MAC) (41.9%), *M. kansasii* (29.4%), and *M. abscesses* (17.8%). Other than three of these species, three *M. fortuitum* and *M. chelonae*, two *M. lentiflavum*, and one *M. mageritense*, *M. chimaera*, *M. triplex* and *M. parascrofulaceum* were detected.

Radiologically, there was mostly bilateral involvement in both groups, and rarely more than 50% of the parenchyma was involved. No significant difference was found in terms of ground glass, consolidation, miliary pattern, nodule, calcification, enlarged mediastinal lymph node, and pleural thickening in both groups. Tree-in-bud appearance and

Table 1 Demographic Data of Patients

Variables		TB (n, %)	NTM (n, %)	Total (n, %)	p
Total		152 (57.6)	112 (42.4)	264 (100)	
Age	< 35	67 (44.1)	11 (9.8)	78 (29.5)	<0.001
	35-65	70 (46.1)	74 (66.1)	144 (54.5)	
	> 65	15 (9.9)	27 (24.1)	42 (15.9)	
Gender	Male	89 (58.6)	90 (80.4)	179 (67.8)	<0.001
	Female	63 (41.4)	22 (19.6)	85 (32.2)	

pleural effusion were more common in tuberculosis patients ($\chi^2=12.555$, $p=0.002$ and $\chi^2=9.809$, $p=0.001$, respectively); cavitation, bronchiectasis, and sequela fibrotic changes were more common radiological findings in patients infected with non-tuberculous mycobacteria ($\chi^2=18.589$, $\chi^2=13.282$, and $\chi^2=12.245$; $p<0.001$ for all) (Figure 1). In both groups, the cavitory lesion with the thickest wall was most commonly the largest cavity. The wall thickness of cavitory lesions was significantly greater in the tuberculosis group compared to non-tuberculous mycobacterial infections ($p=0.015$). Left upper lobe anterior segment involvement was also more common in TB ($p=0.018$). The right upper lobe apical segment, right middle lobe, and left upper lobe lingula involvement was higher in NTM-LD than in TB, but it was not statistically significant ($p>0.05$). No difference was found between other lobe and segmental involvements (Table 2).

Discussion

While *M. tuberculosis* is transmitted by inhalation of bacilli released into the air by active tuberculosis patients, the interpersonal transmission of NTM infections is not an expected finding and is mostly transmitted through environmental routes such as soil and water. Acid-fast bacilli (AFB) staining is a practical and cheap method used routinely in sputum samples, especially in regions where TB is common, but its sensitivity is low, and it is a disadvantage that it cannot distinguish between TB and NTM. Microbiological diagnosis is very important in all mycobacterial infections. In this way, both *M. tuberculosis* and NTM distinction and NTM species distinction can be made. However, since it takes weeks to detect mycobacteria grown in culture, which is considered the gold standard, the importance of radiological findings is

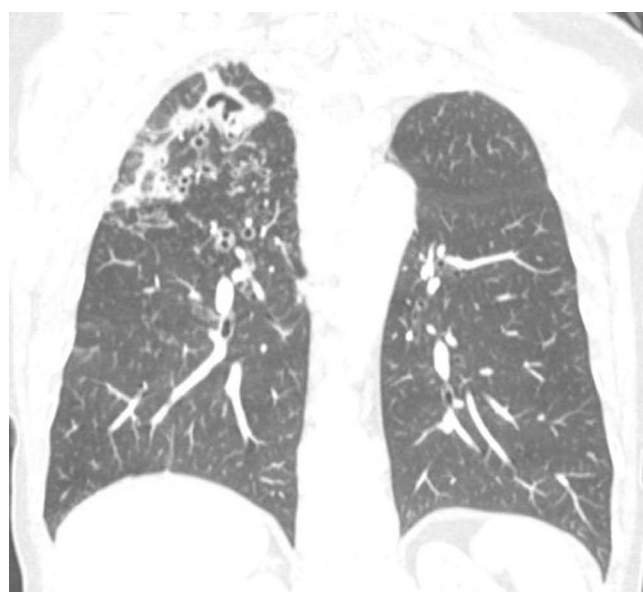


Figure 1 Cavitation and bronchiectasis in the right upper lobe. Caused by *M. avium*.

Table 2 Radiographic Characteristics of Patients

Variables		TB (n, %)	NTM (n, %)	Total (n, %100)	OR (95% CI)	p
Radiological involvement	Bilateral	92 (60.5)	76 (67.9)	168 (63.6)	0.73 (0.44–1.22)	0.245
	Unilateral	60 (39.5)	36 (32.1)	96 (36.5)	1.38 (0.83–2.30)	
Radiological involvement	<25%	90 (59.2)	53 (47.3)	143 (54.2)		0.182
	25-50%	43 (28.3)	46 (41.1)	89 (33.7)		
	50-75%	15 (9.9)	10 (8.9)	25 (9.5)		
	>75%	4 (1.5)	3 (1.1)	7 (2.7)		
Radiological lesions	Cavity	71 (46.4)	82 (73.2)	153 (58)	0.32 (0.18–0.57)	<0.001
	Tree-in-bud	126 (82.9)	73 (65.2)	199 (75.4)	2.59 (1.52–4.39)	0.002
	Ground glass	25 (16.4)	17 (15.2)	42 (15.9)	1.10 (0.56–2.14)	0.865
	Consolidation	65 (42.8)	38 (33.9)	103 (39)	1.45 (0.87–2.41)	0.161
	Miliary pattern	4 (2.6)	3 (2.7)	7 (2.7)	0.98 (0.22–4.44)	0.634
	Bronchiectasis	66 (43.4)	74 (66.1)	140 (53)	0.39 (0.23–0.66)	<0.001
	Sequela changes	82 (53.9)	84 (75)	166 (62.9)	0.39 (0.23–0.66)	<0.001
	Nodule	81 (53.3)	73 (65.2)	154 (58.3)	0.61 (0.36–1.04)	0.059
	Calcification	52 (34.2)	35 (31.3)	87 (33)	1.14 (0.68–1.91)	0.691
	Mediastinal lymph node enlargement	24 (15.8)	12 (10.7)	36 (13.6)	1.56 (0.73–3.29)	0.278
	Pleural effusion	28 (18.4)	6 (5.4)	34 (12.9)	3.99 (1.58–9.96)	0.001
	Pleural thickening	37 (24.7)	38 (33.9)	75 (28.6)	0.63 (0.37–1.08)	0.128
Right upper lobe		102 (67.1)	80 (71.4)	182 (68.9)		0.502
	Apical	49 (32.2)	50 (44.6)	99 (37.5)	0.59 (0.36–0.97)	0.053
	Posterior	80 (52.6)	67 (59.8)	147 (55.7)		0.261
	Anterior	49 (32.2)	37 (33)	86 (32.6)		0.895
Right middle lobe		39 (25.7)	40 (35.7)	79 (29.9)	0.62 (0.36–1.05)	0.102
	Medial	29 (19.1)	32 (28.6)	61 (23.1)		0.078
	Lateral	30 (19.7)	27 (24.1)	57 (21.6)		0.450
Right lower lobe		85 (55.9)	64 (57.1)	149 (56.4)		0.900
	Superior	65 (42.8)	48 (42.9)	113 (42.8)		0.544
	Lateral	21 (13.8)	18 (16.1)	39 (14.8)		0.604
	Anterior	32 (21.1)	26 (23.2)	58 (22)		0.764
	Posterior	33 (21.7)	22 (19.6)	55 (20.8)		0.760
Left upper lobe		100 (65.8)	85 (75.9)	185 (70.1)		0.079
	Apicoposterior	76 (50)	56 (50)	132 (50)		0.550
	Anterior	44 (28.9)	18 (16.1)	62 (23.5)	2.13 (1.15–3.93)	0.018
	Lingula	58 (38.2)	51 (45.5)	109 (41.3)	0.74 (0.45–1.21)	0.256

(Continued)

Table 2 (Continued).

Variables		TB (n, %)	NTM (n, %)	Total (n, %100)	OR (95% CI)	p
Left lower lobe		86 (56.6)	63 (56.3)	149 (56.4)		0.528
	Superior	64 (42.1)	44 (39.3)	108 (40.9)		0.704
	Anteromedial	30 (19.7)	18 (16.1)	48 (18.2)		0.519
	Lateral	24 (15.8)	22 (19.6)	46 (17.4)		0.418
	Posterior	36 (23.7)	28 (25)	64 (24.2)		0.885
Total		152 (57.6)	112 (42.4)	264 (100)		

Note: Chi-square Test.

very important for correct diagnosis and treatment in the early period. Therefore, a multidisciplinary approach is essential for correct diagnosis and treatment.⁹ CT findings alone may not be sufficient for definitive diagnosis or differentiation between TB and NTM infections. Clinical correlation, including patient history, microbiological tests, and laboratory data, is essential to accurately interpret radiological features and guide appropriate management.

The primary imaging method in every patient suspected of lung infection is chest radiography. Although data as detailed as CT cannot be obtained, alveolar infiltrates, cavitation, lymphadenopathy, bronchiectasis, nodules, calcifications, and pleural effusions can be detected with X-ray. Nevertheless, CT is generally required to detect more subtle and thin lesions.^{10,11} There are some difficulties encountered in clinical practice in the radiological diagnosis of mycobacterial infections. Findings such as nodules and cavitations can be frequently seen on both direct radiography and CT images. Although findings such as tree-in-bud are much more selected on CT in addition to radiography, no radiological findings are specific and pathognomonic for mycobacterial infections. In addition, no definitive radiological finding has been defined for the distinction between TB and NTM-LD. However, today, with the introduction of Artificial Intelligence (AI) in addition to conventional imaging and evaluation methods, successful results are reported in some cases where the distinction is difficult. In one study, it was reported that TB and NTM-LD can be successfully distinguished using deep transfer learning in X-ray images.¹² Techniques such as radiomics and machine learning can extract and analyze quantitative imaging features beyond visual assessment, potentially identifying subtle patterns that are not discernible to radiologists. Although not utilized in the present study, we believe that future research incorporating AI-based tools could enhance early and accurate differentiation, thereby supporting more targeted clinical decision-making.

The incidence of NTM infections is increasing today.¹³ In addition, while the incidence of tuberculosis decreases as the patient age increases, the incidence of NTM increases.¹⁴ There are recent studies that associate NTM infections with poor treatment outcomes in an elderly population with comorbidities, as the frequency of structural lung diseases and impaired immunity increases as the patient's age increases.⁹ In our study, similar to the literature, we found a significant relationship between patient age and mycobacteria species. As patient age increased, the incidence of NTM infections also increased. In addition, in our study, male patients were more common in all mycobacteria infections, and the male patient dominance was much more pronounced, especially in NTM-LD. However, there are also studies that state that the rate of women is higher in NTM infections.^{15,16}

While symptoms such as cough, night sweats, and weight loss may have a more acute onset in tuberculosis, underlying bronchiectasis and chronic obstructive pulmonary disease (COPD) and related chronic symptoms may be described more frequently by patients in NTM-LD. Since it is a predominant factor, the possibility of NTM should be kept in mind in patients with accompanying bronchiectasis.¹⁷ In many studies, bronchiectasis, cavitation, and pulmonary nodules are the most frequently described radiological findings in NTM-LD. It has been reported that cavitations in NTM-LD have thinner and more even walls than those in TB¹⁸ (Figure 2).

In both diseases, the upper lobes and superior segments of the lower lobes are most frequently involved, but NTM-LD should be suspected when the middle lobe and lingula are involved.¹⁹ Our results were also consistent with the literature, and in addition, we found involvement in the anterior segment of the left upper lobe to be more common in TB.

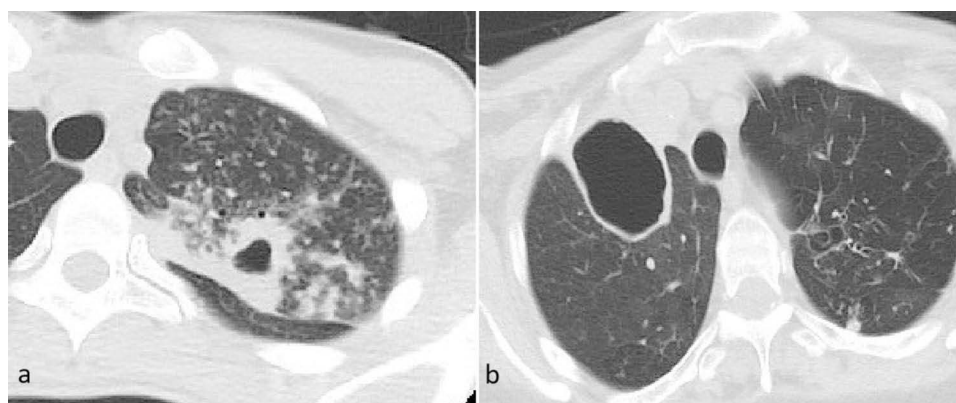


Figure 2 Thick-walled cavity and tree-in-bud appearances in a patient diagnosed with tuberculosis (a). Thin-walled cavity in the right upper lobe, and bronchiectasis in the left upper lobe in a patient diagnosed with *M. abscessus* microbiologically (b).

Our study has several limitations. First, it is a retrospective single-center study with a relatively small number of patients. Second, radiological assessments were performed by a single observer, and the lack of inter-observer validation may have introduced interpretation bias. Third, detailed sociodemographic data (eg, marital status, occupation, area of residence) were not available due to the retrospective nature of the study. Fourth, the presence of different types within the NTM group may affect the lesion characteristics. Finally, among immunocompetent patients, chronic diseases such as diabetes and COPD were not excluded in both groups.

Conclusion

Correctly differentiating tuberculosis, which is still a widespread public health problem, from NTM infections, which are increasingly common, and providing appropriate treatment is of vital importance for patients. At this point, for radiologists and clinicians to work in harmony with a multidisciplinary approach, radiologists should be well aware of the radiological features of mycobacterial infections and, when necessary, be able to warn clinicians about the possibility of NTM infection.

Abbreviation

TB, Tuberculosis; WHO, World Health Organization; NTM, Non-tuberculous mycobacteria; MAC, *M. avium* complex; NTM-PD, Non-tuberculous mycobacteria-associated pulmonary disease; PACS, Picture Archiving and Communication Systems; CT, Computed tomography; AFB, Acid-fast bacilli; AI, Artificial Intelligence; COPD, Chronic obstructive pulmonary disease.

Data Sharing Statement

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

The study's ethics committee approval is available with the protocol code 2024-2 by Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital's ethics committee.

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Disclosure

The author(s) report no conflicts of interest in this work.

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