Risk Factors and Characteristics of Nontuberculous Mycobacterial Infections

Efraim Güzel[1], *Oya Baydar Toprak*[1]

1 Department of Chest Diseases, Cukurova University, Faculty of Medicine, Adana, Türkiye

Abstract

Aim: Infections caused by nontuberculous Mycobacterium (NTM) are extremely prevalent in nature and challenging to identify and treat. Thus, the purpose of this study was to examine the clinical characteristics and risk factors of NTM infections.

Methods: The present investigation was carried out using 5-year retrospective data in a tertiary university hospital. The study comprised 29 individuals with radiological and clinical signs of NTM infection that were confirmed by microbiological testing. These patients' clinical, laboratory, radiological, and sociodemographic information was documented.

Results: The patients' average age was 58.31 ± 14.31 years, and 62.1% of them were men. Cough, weakness, and fever were the most prevalent symptoms, and hypertension and chronic lung disease were the most prevalent comorbidities. Mycobacteria (M) Kansai, M. Fortuitum, and M. Abscessus were the most commonly isolated NTM species. HIV positivity, treatment type, and treatment duration were determined to be the most significant factors influencing treatment response (p=0.018, p=0.002, p=0.001, respectively). Two (6.9%) of the patients passed away during the follow-up period, and it was discovered that a high sedimentation rate, a high Charlson comorbidity index score, and a lengthy interval between the onset of symptoms and diagnosis were all linked to death (p=0.010, p=0.002, and p=0.000, respectively).

Conclusions: In patients with risk factors, NTM-related clinical, radiological, and laboratory findings should raise suspicion of NTM lung disease; the possibility of contamination should be ruled out; if the pathogen is detected, patients with these findings should receive species-specific and adequate treatment. Treatment should be started as soon as possible, and patients' comorbidities should not be overlooked.

Keywords: *nontuberculous mycobacterium; infections; risk factors; mortality; treatment*

1. Introduction

Non-tuberculous mycobacteria (NTM) are free-living microorganisms that can be found everywhere in nature, but are most commonly found in soil and water sources. Tap water, surface water, dirt, domestic and wild animals, milk, and food products can all include these bacteria, which can dwell on the surfaces of the body or in secretions without producing any disease.[1] It was previously thought that human diseases linked to NTM were mostly contracted through aerosols from contaminated environmental sources; however, a thorough investigation has demonstrated that person-to-person transmission is also a possibility.[2] Human lung disease has been linked to the NTM family, which is believed to include over 170 distinct mycobacterial species. In particular, the *M. avium complex (MAC), M. kansasii, and M. abscessus* species have been implicated in lung disease.[1] Although the precise mode of transmission is yet unknown, environmental factors are the main source of NTM-related human diseases. NTM infections commonly damage the skin, soft tissues, and lymphatic system in addition to the lungs.[3] NTMs' capacity to form biofilms, which offer resistance to antibiotics and disinfectants, is a crucial characteristic. However, these organisms' hydrophobic properties, combined with their resistance to high temperatures and low pH levels, allow them to live longer in the wild. Given these traits, it is not unexpected that the most significant sources of life and infection for NTM are drinking water, home plumbing, soil, swamps, and drainage water.[4] Advanced age, smoking, chronic obstructive pulmonary disease (COPD), pneumoconiosis, bronchiectasis, history of tuberculosis, pulmonary fibrosis following radiation therapy, chronic pulmonary aspiration, cystic fibrosis (CF), immunodeficiency conditions, HIV infection, alcoholism, cancer, and diabetes mellitus (DM) are the most prevalent risk factors for NTM infections, despite the fact that many other risk factors have been found.[5] The need for multimodal diagnosis, such as the identification of consistent radiological and

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microbiological evidence in patients with vague symptoms like cough and weight loss, makes diagnosing NTM infection challenging. However, prompt detection of these people stops the condition from getting worse and minimizes the need for recurrent medications.[6, 7] Standard therapy for tuberculosis (drug-sensitive), until culture results are available, is a combination therapy of isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (ETH) for at least six months. However, more antibiotics are needed for a longer duration of time when treating instances of extensively drug-resistant (XDR) and multidrug-resistant (MDR) tuberculosis. On the other hand, anti-tuberculous (TB) medications typically have little effect in NTM .[8] NTM infections are treated according to certain protocols that depend on the type of bacteria causing the infection and necessitate species identification. Treatment for NTM disease requires more various combinations based on different species than for TB.[3] The significance of NTM in human diseases has grown as a result of advancements in modern microbiological techniques and the reduction in the worldwide burden of tuberculosis brought about by efficient diagnostic and treatment techniques. The current study's objectives were to, on the one hand, raise awareness of NTM infection and, on the other, characterize the clinical traits and risk factors of NTM.

2. Materials and Methods

2.1. *Study design and participants*

The study that is being reported is a retrospective analysis of patient data from August 2021 to March 2025 from the pulmonology outpatient clinic at Cukurova University Faculty of Medicine Balcalı Hospital, a tertiary care university hospital. Patients over the age of 18 with appropriate clinical symptoms (fever, fatigue, cough) and radiological findings (bronchiectasis, cavities, reticulonodular infiltration, tree-in-bud pattern, etc.) who had NTM growth in sputum (2 times) and/or bronchoscopic lavage (at least once) spicemens. The study included 29 participants in all who satisfied our requirements.

2.2. Ethical Approval

According to the 1964 Helsinki Declaration's tenets and hospital ethics regulations, the study was carried out with ethical approval from the Cukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee on March 7, 2025 (42/153).

2.3. Data

The data of participants in the study was obtained retrospectively from the hospital database. Information including sociodemographic data such as age, gender, height, body weight, body mass index, and smoking history; clinical characteristics such as symptoms, comorbidities, and medications used in treatment; radiological findings; diagnostic methods applied to identify the NTM subtype; and laboratory results were extracted from the hospital database and recorded using a form. Comorbidities were categorized as "0 points low risk, 1-2 points moderate risk, 3-4 points high risk, and 5 points and above very high risk", in accordance with the Charlson Comorbidity Index.[9]

2.4. Pathogen detection and identification

Samples submitted for pathogen detection in this study included sputum and bronchoalveolar lavage fluid (BAL). Pathogen diagnosis and identification was performed in one of the following three ways.

1) Mycobacterial culture: A fully automated BACTEC MGIT 960 mycobacterial culture system (BD, Franklin Lakes, NJ) in our hospital's in-house microbiology laboratory was used to culture mycobacteria. If mycobacteria were present in the samples, the result was usually reported within 2-4 weeks. For culture positive specimens, smear microscopy was performed to confirm positive results and real-time PCR was used to differentiate TB from NTM. If there were no positive results 45 days after culture, the result was reported as negative.

2) Acid-fast staining: Samples were processed and evaluated in the microbiology laboratory of our hospital. The specimens were first spread and then stained with concentrated petrolatum compound red under heating, colored with hydrochloric acid alcohol and then counterstained with methylene blue solution. Acid-fast mycobacteria were stained red. Acid-fast staining could be detected by morphological analysis by microscopy by an experienced observer, but no clear distinction between TB or NTM could be made. Culture results were followed up at this stage.

3) National Tuberculosis Diagnostic and Confirmatory Laboratory: All samples were simultaneously sent to the national tuberculosis diagnosis and confirmation laboratory. Here, microbiological analyses and mycobacteria culture cultures were performed, and we were informed through the national hospital communication network as a result of the evaluation. The system worked as follows; first, a warning was generated in the data recording system as "growth of tuberculous or non-tuberculous mycobacteria was detected", and then it resulted in subtyping for non-tuberculous mycobacteria.

2.5. Confirmation of NTM Lung Disease

The diagnostic criteria for NTM specified in the ATS/IDSA guidelines are based on the proof of the NTM subtype microbiologically, in addition to consistent findings in clinical and radiological analyses. The isolation of the pathogen from body fluids, particularly sputum, at least twice, and at least once from effectively performed bronchial lavage fluid, is of particular importance. Since NTMs are very common in the environment, their possible colonization and transmission also affect diagnosis and treatment approaches. However, while the initiation of treatment in all patients suspected of having NTM lung disease remains controversial, a "wait and see" approach, particularly with close monitoring, is accepted for a subset of patients.[3]

2.6. Evaluation of Treatment Response

During the study period, patient data was collected via the hospital data recording system and the national inter-hospital data network. Retrospective data was examined, and the clinical, radiologic, laboratory-microbiologic, and treatment responses of the patients during the diagnosis-therapy and follow-up periods were evaluated. The response to treatment was evaluated by pulmonologists at a tertiary care university hospital and concluded in accordance with the literature data. If the right combination therapy was given, insufficient treatment was defined as treatment that did not satisfy the ATS/IDSA guidelines[3] for the duration and dosage for each kind of NTM in patients with an NTM infection. Recurrence was allowed if the causative agent was found in the relevant samples again within a year, even after receiving treatment tailored to the type and for a long enough duration. Inadequate recovery, recurrence, and all-cause death as a result of negative results were reported as negative treatment responses, whereas improvement in clinical and radiological findings and recovery with culture negativity were recorded as positive treatment responses.

2.7. Statistical analysis

SPSS 22 program was used for data analysis. Kolmogorov Smirnov test was used as normal distribution test. T-test, Mann-Whitney U test, Chi-square test were used in the analysis. $p<0.05$ value was considered statistically significant.

3. Results

The mean age of the patients who took part in the presented study was 58.31 ± 14.31 years, and 62.1% of them were male. The most typical initial symptoms were fever, weakness, and cough. The two most prevalent comorbidities among our patients were hypertension (17.2%) and chronic pulmonary illnesses (20.7%). We had two individuals with acquired immunodeficiency syndrome and four patients undergoing immunosuppressive treatment. Table 1 displays our patients' sociodemographic information. Bronchiectasis and lung nodules were the most often observed radiological imaging abnormalities, followed by cavities and a ground-glass appearance.

Table 1

Sociodemographic Features of Patients

Characteristics		n (%) or mean ± SD
Age		58.31 ± 14.31
Sex	Male	18 (62.1)
	Female	11 (37.9)
Symptoms		
Cough	Yes	26 (89.7)
	No	3 (10.3)
Sputum	Yes	16 (55.2)
	No	13 (44.8)
Dyspnea	Yes	4 (13.8)
	No	25 (86.2)
Haemoptysis	Yes	12 (41.4)
	No	17 (58.6)
Fever	Yes	17 (58.6)
	No	12 (41.4)
Weakness	Yes	18 (62.1)
	No	11 (37.9)
Comorbidity		
Hypertension	Yes	5 (17.2)
	No	24 (82.8)
Diabetes Mellitus	Yes	2 (6.9)
	No	27 (93.1)
Heart Disease	Yes	3 (10.3)
	No	26 (89.7)
Chronic Lung Disease	Yes	6 (20.7)
	No	23 (79.3)
Rheumatological Disease	Yes	2 (6.9)
	No	27 (93.1)
Neurological Disease	Yes	4 (13.8)
	No	25 (86.2)
Leukemia	Yes	1 (3.4)
	No	28 (96.6)
Lung Cancer	Yes	1 (3.4)
	No	28 (96.6)
Human Immunodeficiency Virus	Yes	2 (6.9)
	No	27 (93.1)
Charlson Comorbidity Index	Mild	10 (34.5)
	Moderate	13 (44.8)
	High	5 (17.2)
	Very High	1 (3.4)
Immunosupressive treatment	Yes	4 (13.8)
	No	25 (86.2)

Table 2

Radiological, Microbiological and Laboratory Findings in the Diagnostic Process

Characteristics		n (%) or mean ± SD
Cavity	Yes	7 (24.1)
	No	22 (75.9)
Bronchiectasis	Yes	10 (34.5)
	No	19 (65.5)
Ground Glass	Yes	6 (20.7)
	No	23 (79.3)
Consolidation	Yes	4 (13.8)
	No	25 (86.2)
Nodules	Yes	10 (34.5)
	No	19 (65.5)
Tree in bud	Yes	4 (13.8)
	No	25 (86.2)
Reticulonodular infiltration	Yes	5 (17.2)
	No	24 (82.8)
Sequelae	Yes	2 (6.9)
	No	27 (83.1)
Time from first symptom to diagnosis	<3 month	18 (62.1)
	3-6 month	8 (27.6)
	>6 month	3 (10.3)
Diagnostic Method	Sputum	17 (58.6)
	Bronchoalveolar lavage	12 (41.4)
ARB	Positive	8 (27.6)
	Negative	21 (72.4)
Type of nontuberculous mycobacteria	Undetermined type	7 (24.1)
	M. Kansasii	5 (14.2)
	M. Simiae	4 (13.8)
	M. Chelonae	1 (3.4)
	M. Fortuitum	5 (14.2)
	M. Abscessus	5 (14.2)
	M. Species	1 (3.4)
	M. Intercellulare	1 (3.4)
WBC (*103 / mm3)		7.46 ± 2.41
Neutrophil (*103 / mm3)		4.91 ± 1.91
Lymphocyte (*103 / mm3)		1.61 ± 0.83
CRP		31.91 ± 58.11
Sedimentation		29.90 ± 15.20
LCR		255.50 ± 272.53
NLR		4.08 ± 3.16

Abbrevations: ARB: acid-fast/resistant bacilli, M.: Mycobacteria, WBC: white blood cell, CRP: C-Reactive Protein, LCR: Lymphocyte/CRP ratio, NLR: Neutrophil/Lymphocyte ratio, LSR: Lymphocyte/Sedimentation ratio

The most prevalent method of diagnosis was the creation of microorganisms from sputum culture, and in about 62.1% of the patients, the diagnosis was made within three months after the onset of symptoms. Only 27.6% of patients had an acid-fast/resistant bacillus (ARB) positive. The most prevalent mycobacterial species were *M. kansasii* (17.2%), *M. fortuitum* (17.2%), *M. abscessus* (17.2%), and *M. simiae* (13.8%), but NTM subspecies were not found in 24.1% of the patients. Table 2 displays the results of the laboratory, microbiology, and radiologic tests.

Of the diagnosed patients, 62.1% received normal antituberculosis medications, 17.2% received treatment specific to NTM, and 20.7% were followed without treatment. Treatment was initiated in patients with positive symptoms, radiological findings, and microbiological findings, confirming the diagnosis of NTM lung

disease. However, in patients without radiological or symptomatic findings, the positive microbiological results were considered to be infection, and treatment was not initiated in this group of patients, who were monitored without treatment. 55.2% of patients received treatment for less than six months, and 24.1% received treatment for more than six months. It is clear that NTM treatment is long-term, but in patients receiving short-term treatment, there were reasons for discontinuing treatment, such as bacterial growth in tuberculosis cultures sometime after NTM, patients discontinuing treatment of their own accord, and side effects caused by the medication. Table 3 displays the patients' treatment characteristics.

Table 3

Treatment Characteristics of Patients

Characteristics		n (%)
Treatment type	Follow-up without treatment	6 (20.7)
	Standard Antituberculosis treatment	18 (62.1)
	Type Specific Treatment	5 (17.2)
	No treatment	6 (20.7)
Total treatment time	6 months and less	16 (55.2)
	>6 months	7 (24.1)
Drug resistance	Rifampicin	3 (10.3)
	Ethambutol	6 (20.7)
	Trimethoprim-Sulfomethoxazole	15 (51.7)
	Ciprofloxacin	8 (27.6)
	Doxycycline	9 (31)
	Clarithromycin	1 (3.4)
	Streptomycin	1 (3.4)
	Cefoxitin	4 (13.8)
	Tobramycin	1 (3.4)
Treatment Responses	Treatment success	21 (72.4)
	Treatment failure	8 (27.6)
Final status following follow-up	Exitus	2 (6.9)
	Recovery	27 (83.1)

In our treatment response analysis, we found that presence of HIV, treatment type (follow-up prior to treatment initiation, non-species-specific treatment regimens), and insufficient treatment duration negatively affected treatment response (respectively; p=0.018, p=0.002, p=0.001). Detailed evaluation is presented in Table 4.

In the 5-year data, it was determined that 2 (6.9%) of the patients included in the study died for various reasons. One of the deceased patients had chronic lung disease, while the other had lung cancer. One patient had the NTM subtype *M. fortuitum*, while the other patient's NTM subtype could not be determined. In the analyses, a high Charlson comorbidity index score, high sedimentation rate, and long interval between symptom onset and diagnosis were found to be associated with mortality (p=0.010, p=0.002, and p=0.000, respectively). Table 5 provides a detailed presentation of the findings and their correlation with mortality.

Table 4

Treatment Responses According to Patient Characteristics

Characteristics		n (%) or mean ± SD Treatment success	Treatment failure	p
Age		59.67 ± 15.14	54.75 ± 12.01	0.235
Sex	Male	15 (51.7)	3 (10.3)	0.092
	Female	6 (20.7)	5 (17.2)	
Charlson Comorbidity Index	Mild	8 (27.6)	2 (6.9)	0.330
	Moderate	10 (34.5)	3 (10.3)	
	High	3 (10.3)	2 (6.9)	
	Very High	0	1 (3.4)	
HIV	Yes	0	2 (6.9)	0.018
	No	21 (72.4)	6 (20.7)	
	Undetermined	6 (20.7)	1 (3.4)	
Type of nontuberculous mycobacteria	M. Kansasi	5 (17.2)	0	0.905
	M. Simiae	4 (13.8)	0	
	M. Chelonae	1 (3.4)	0	
	M. Fortuitum	4 (13.8)	1 (3.4)	
	M. Abscessus	5 (17.2)	0	
	M. Species	1 (3.4)	0	
	M. Intercellulare	1 (3.4)	0	
Time from first symptom to diagnosis	<3 month	12 (41.4)	6 (20.7)	0.533
	3-6 month	7 (24.1)	1 (3.4)	
	>6 month	2 (6.9)	1 (3.4)	
	No treatment	1 (3.4)	5 (17.2)	
Treatment type	Standard AntiTb	15 (51.7)	3 (10.3)	0.002
	Type Specific	5 (17.2)	0	
	No treatment	1 (3.4)	5 (17.2)	
Total treatment time	6 months and less	16 (55.2)	0	0.001
	>6 months	4 (13.8)	3 (10.3)	
Cavity	Yes	5 (17.2)	2 (6.9)	0.947
	No	16 (55.2)	6 (20.7)	
Bronchiectasis	Yes	7 (24.1)	3 (10.3)	0.833
	No	14 (48.4)	5 (17.2)	
Ground Glass	Yes	4 (13.8)	2 (6.9)	0.724
	No	17 (58.6)	6 (20.7)	
Consolidation	Yes	3 (10.3)	1 (3.4)	0.901
	No	18 (62.1)	7 (24.1)	
Nodules	Yes	7 (24.1)	3 (10.3)	0.833
	No	14 (48.4)	5 (17.2)	
Tree in bud	Yes	4 (13.8)	0	0.184
	No	17 (58.6)	8 (27.6)	
Reticulonodular infiltration	Yes	4 (13.8)	1 (3.4)	0.677
	No	17 (58.6)	7 (24.1)	
Sequelae	Yes	2 (6.9)	0	0.366
	No	19 (65.5)	8 (27.6)	
WBC (*103 / mm3)		7.95 ± 2.42	6.17 ± 1.95	0.074
Neutrophil (*103 / mm3)		5.28 ± 2.01	3.95 ± 1.24	0.094
Lymphocyte (*103 / mm3)		1.67 ± 0.82	1.41 ± 0.87	0.455
CRP		29.09 ± 56.87	39. 28± 64.87	0.681
Sedimentation		30.38 ± 16.55	28.63 ± 11.75	0.787
LCR		301.14 ± 295.21	135.67 ± 159.49	0.147
NLR		4.16 ± 3.49	3.88 ± 2.21	0.835

Abbrevations: AntiTb: Antituberculosis, ARB: acid-fast/resistant bacilli, M.: Mycobacteria, WBC: white blood cell, CRP: C-reactive protein, LCR: Lymphocyte/CRP ratio, NLR: Neutrophil/Lymphocyte ratio, LSR: Lymphocyte/Sedimentation ratio

Table 5

Relationship between Patient Characteristics and Mortality

Characteristics		n (%) or mean ± SD		p
		Lives	Exitus	
Age		58.11 ± 14.76	61.00 ± 7.07	0.235
Sex	Male	17 (58.6)	1 (3.4)	0.715
	Female	10 (34.5)	1 (3.4)	
Charlson Comorbidity Index	Mild	10 (34.5)	0	0.002
	Moderate	12 (41.4)	1 (3.4)	
	High	5 (17.2)	0	
	Very High	0	1 (3.4)	
HIV	Yes	2 (6.9)	0	0.690
	No	25 (86.2)	2 (6.9)	
	Undetermined	6 (20.7)	1 (3.4)	
Type of nontuberculous mycobacteria	M. Kansasi	5 (17.2)	0	0.905
	M. Simiae	4 (13.8)	0	
	M. Chelonae	1 (3.4)	0	
	M. Fortuitum	4 (13.8)	1 (3.4)	
	M. Abscessus	5 (17.2)	0	
	M. Species	1 (3.4)	0	
	M. Intercellulare	1 (3.4)	0	
Time from first symptom to diagnosis	<3 month	18 (62.1)	0	0.000
	3-6 month	8 (27.6)	0	
	>6 month	1 (3.4)	2 (6.9)	
Treatment type	No treatment	5 (17.2)	1 (3.4)	0.168
	Standard AntiTb	18 (62.1)	0	
	Type Specific	4 (13.8)	1 (3.4)	
Cavity	Yes	7 (24.1)	0	0.408
	No	20 (69)	2 (6.9)	
Bronchiectasis	Yes	10 (34.5)	0	0.288
	No	17 (58.6)	2 (6.9)	
Ground Glass	Yes	5 (17.2)	1 (3.4)	0.289
	No	22 (75.9)	1 (3.4)	
Consolidation	Yes	3 (10.3)	1 (3.4)	0.124
	No	24 (82.8)	1 (3.4)	
Nodules	Yes	9 (31)	1 (3.4)	0.632
	No	18 (62.1)	1 (3.4)	
Tree in bud	Yes	4 (13.8)	0	0.558
	No	23 (79.3)	2 (6.9)	
Reticulonodular infiltration	Yes	4 (13.8)	1 (3.4)	0.204
	No	23 (79.3)	1 (3.4)	
Sequelae	Yes	2 (6.9)	0	0.690
	No	25 (86.2)	2 (6.9)	
WBC (*103 / mm3)		7.18 ± 2.09	11.25 ± 4.31	0.121
Neutrophil (*103 / mm3)		4.73 ± 1.79	7.41 ± 1.98	0.874
Lymphocyte (*103 / mm3)		1.55 ± 0.76	2.25 ± 1.77	0.073
CRP		29.34 ± 59.91	66.50 ± 42.28	0.867
Sedimentation		29.67 ± 15.74	33.00 ± 0.00	0.010
LCR		272.07 ± 275.42	31.81 ± 6.85	0.196
NLR		4.07 ± 3.04	4.25 ± 2.46	0.867

Abbrevations: AntiTb: Antituberculosis, ARB: acid-fast/resistant bacilli, M.: Mycobacteria, WBC: white blood cell, CRP: C-reactive protein, LCR: Lymphocyte/CRP ratio, NLR: Neutrophil/Lymphocyte ratio, LSR: Lymphocyte/Sedimentation ratio

4. Discussion

Since NTM infections are difficult to detect, treatment and monitor, it is difficult to arrive at clear conclusions about their incidence. Nevertheless, different results have been recorded in different regions. The first incidence estimates of NTM disease were reported as 5.7 per 100,000 in Oregon in 2012, with a 3-4 times higher risk, especially in people over 70 years of age.[10] Between 1995 and 2012, a comprehensive study showed that the incidence of NTM culture-positive isolates increased nearly eightfold in England, Wales and Northern Ireland, from 0.9 per 100,000 in 1995 to 7.6 per 100,000 in 2012.[11, 12] In another study, Prevots et al. reported an increase in the prevalence of pulmonary NTM cases in people over 60 years of age from 19.6 cases/100,000 person-years between 1994 and 1996 to 26.7 cases/100,000 person-years between 2004 and 2006.[13] A meta-analysis in sub-Saharan Africa reported that the prevalence of NTMs in probable TB cases ranged from 1.7% to 15.1%.[14] In our study, we identified a total of 29 NTM infections, but we were unable to determine the incidence with certainty. From the hospital data portal, we learned that an average of 80,000 patients with respiratory symptoms suspected of NTM present to hospitals each year. Based on these data, we estimate that the annual incidence of NTM is approximately 7 per 100,000 based on our total case count. We would also like to remind you that this measurement may not be entirely reliable and is only an estimate.

Many different studies on Mycobacterium subtypes have been published. A recent review emphasized that the most frequently isolated Mycobacterium species in NTM infections in South Africa was *MAC*, followed by *M. kansassii* and *M. fortuitum*, but the 2nd and 3rd most common agents may vary depending on regional differences.[15] Prevots et al. reported that *MAC* (80.1%) was the most common species isolated from patients with definite disease, followed by *M. chelonae* and *M. abscessus* (12.1%), *M. fortuitum* (5.6%) and *M. kansasii* (5.5%).[13] A study evaluating NTM infections in immunocompromised patients showed a significant reduction in the incidence of *MAC* cases in HIV patients after effective antiretroviral therapies. On the other hand, the same study linked common NTM infection with *M. kansasii*, which causes lung disease in more than 50% of AIDS patients.[16] In a review of the epidemiology, diagnosis and treatment of TB and NTM infections, it was reported that MAC was isolated in 61% of cystic fibrosis patients, *M. abscessus* in 39% and other NTMs in 21%, and that more than one NTM species was isolated in approximately 19% of these patients.[17] In our study, the most frequently isolated species were *M. kansasii, M. fortuitum* and *M. abscessus*, while *M. intercellulare (MAC)* was very rare. Since the test results detected in our hospital laboratory have also been confirmed by the national microbiology laboratory, we believe that the results we have obtained regarding NTM subtypes reflect the truth. Contrary to many studies in the literature, the low number of *MAC* cases in our study was attributed to the low number of HIV-positive or immunosuppressive patients in the patient group, as well as climatic and geographical conditions.

In the diagnosis of active NTM disease, the most important indicators are clinical symptoms along with radiological findings such as pulmonary nodules, cavitary opacities, multifocal bronchiectasis, and scattered multiple small nodules.[3] A study conducted in the UK presented case-supported findings showing that the most common radiological findings of NTM are associated with pulmonary nodular infiltrates with various characteristics, cavitary opacities, bronchiectasis, thickening of the bronchial wall, mucus plugs, and fibrotic sequelae of lung structures.[18] In our study, the most common radiological findings were nodular opacities and bronchiectasis. In addition to these findings, cavities, ground-glass opacities, reticulonodular infiltrates, and consolidation were also notable radiological

findings and were consistent with data in the literature.

In a review of patients infected with *M. kansasii*, the most common risk factors for NTM were found to be smoking, chronic obstructive pulmonary disease (COPD), alcohol abuse, previous tuberculosis (TB), and HIV infection.[19] In a review published in the UK on NTM management, the following factors were identified: alcohol abuse, biological agents, chronic kidney disease, diabetes, female gender, gastroesophageal reflux disease, immunosuppression (primary or secondary due to disease or drug treatment), inhaled corticosteroids, low body mass index, pneumoconiosis, and underlying structural lung disease (e.g., bronchiectasis and COPD (chronic obstructive pulmonary disease) are the most important risk factors for the development of pulmonary NTM disease.[18] In a recent study examining comorbid factors associated with 2,990 NTM-related deaths using death certificate data from 1999 to 2010, it was found that 2% of these were related to primary immunodeficiency, 1.1% to lymphoma and hematological malignancies, and 0.5% to human immunodeficiency virus (HIV).[20] A 2017 review emphasized that the presence of cavitary disease is associated with higher mortality in NTM cases and that these patients require urgent treatment, whereas cases with nodular or bronchiectasis disease may progress more slowly and early treatment may not be recommended.[21] In addition to these risk factors, treatment of NTM diseases follows specific guidelines based on the nature of the infecting bacteria, requires species identification, and generally takes longer than standard treatment.[3] However, it should also be noted that a diagnosis of NTM lung disease does not necessarily require the initiation of antibiotic treatment against NTM species.[3] A recent review published in 2024 found that adding rifampicin to the M. kansasii treatment regimen reduced relapses and increased recovery rates.[22] In this study, we found that the most common comorbidities associated with NTM were chronic lung disease and hypertension. Given that these are among the most common diseases in the community, this result did not surprise us. Additionally, only two of our patients were HIV-positive, and the presence of HIV, non-adherence to treatment, and treatment practices not specific to the NTM subtype were found to negatively affect the response to treatment. These results were consistent with data in the literature.

Another focus of our study was mortality data in NTM patients. There is limited data on mortality in the literature. In a 2018 review of 14 *MAC*-based studies, although significant heterogeneity was observed in mortality, the overall mortality rate was found to be approximately 27%. The same study also noted that male gender, the presence of comorbidities, and advanced age are common risk factors for mortality.[23] The mortality rate in our study was 6.9%, and we found that high sedimentation rate, high Charlson comorbidity score, and long time between symptom onset and diagnosis were associated with mortality. However, we believe that our mortality data should be evaluated considering the small sample size and only two cases of death.

Despite our important findings, the study has some limitations. One important limitation was the small sample size. This limited the ability to conduct in-depth analyses, particularly multivariate analyses, resulting in limited data on risk factors. Additionally, the retrospective nature of the study, its conduct at a single center, its dependence on the data recording system for results, and the variability in follow-up duration are among the other important limitations.

5. Conclusion

Although the results of the presented study are consistent with the literature, we believe that it is a unique study due to the presence of HIV, untreated follow-up, insufficient treatment duration, and non-species-specific treatment practices affecting treatment success, as well as findings such as low *MAC* rates . It should also be noted that although NTMs can live in a wide variety of natural environments and spread easily to humans, they are difficult to detect. However, in patients with compatible clinical and radiological findings, microbiological identification of the causative agent should be considered in terms of treatment needs. After confirming NTM lung disease, identifying NTM subtypes, and ruling out contamination, risk factors such as HIV and immunosuppression should also be identified, and patients should be started on species-specific treatment, which should be continued for an adequate period of time.

Statement of ethics

The study received approval from the Cukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee on March 7, 2025 (42/153).

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

This Data and materials are available to the researchers.

Author contributions

Both authors contributed equally to the article. Both authors read and approved the final manuscript.

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