

# Nontuberculous Mycobacterial Infective Endocarditis: A Systematic Review of Clinical Characteristics and Outcomes

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**Background.** Infective endocarditis (IE) due to nontuberculous mycobacteria (NTM) is a rare infection, and several outbreaks have been reported in the last 2 decades. However, the clinical spectrum is still poorly understood. This systematic review aimed to evaluate the clinical characteristics and outcomes in NTM IE.

**Methods.** We searched the major electronic databases (PubMed, Scopus, and Google Scholar) with appropriate keywords to December 2023. We included studies based on predefined diagnostic criteria, and relevant data were collected on clinical presentation and treatment outcomes. The study was registered with PROSPERO (CRD42023492577).

**Results.** A total of 97 studies were reviewed, encompassing 167 patients with NTM IE. The earliest cases were reported in 1975, involving *M chelonae* and *M fortuitum*. *M chimaera* was the most prevalent species (38.9%), though rapidly growing NTM (RGM) were more common than slow-growing NTM (SGM; 59.3% vs 40.7%). Disseminated NTM infection occurred in 84% of cases, with bone marrow infiltration and osteomyelitis as frequent manifestations. Prosthetic valves were the main risk factor, present in 63.5% of cases. In native valve IE, nearly all cases ( $n = 27$ , 96%) were attributed to RGM. The overall mortality rate was 44.9%, with conservative management without surgery associated with poorer outcomes (66.7% vs 30.6%). Mortality was comparable between SGM and RGM IE, although relapses were more common in SGM IE (17.6% vs 1.9%).

**Conclusions.** This review highlights the changing epidemiology of NTM IE with the emergence of RGM IE. Disseminated infections in the setting of prosthetic valves warrant NTM evaluation. The high mortality rate necessitates the role of early surgery.

**Keywords.** infective endocarditis; *M abscessus*; *M chimaera*; nontuberculous mycobacterium; rapid-growing NTM.

The epidemiology of infective endocarditis (IE) has been changing in recent decades. *Staphylococcus aureus* is still the most common cause of IE, but the proportion of opportunistic microorganisms is increasing due to the widespread use of intracardiac devices [1]. Gram-negative bacteria (*Pseudomonas aeruginosa*), fungal infections (*Candida*), and coagulase-negative staphylococci are now emerging as an important cause of IE [2, 3]. Nontuberculous mycobacteria (NTM) as an etiologic agent of IE has been rarely discussed, with previous literature focusing on surgical site infections caused by NTM [4, 5]. However, since the reports of a large outbreak of

*Mycobacterium chimaera*, there is increasing evidence of NTM IE [6–8]. Several cases of *M chimaera* have been reported in the last decade, mainly associated with the use of contaminated heater-cooler units during cardiac surgery [7, 8]. As a result of this outbreak, clinicians have become more aware of *M chimaera*-associated endocarditis, and cases from different parts of the world have been documented [9]. Additionally, new criteria from Duke–International Society for Cardiovascular Infectious Diseases have included NTM as a typical microorganism in the setting of cardiac device use [10].

Notwithstanding, there is a recent change in the epidemiology of NTM cardiac infections, with an increasing number of cases involving rapidly growing NTM (RGM) reported in the last few years [11]. Unlike *M chimaera* cardiac infections, very few of these NTM infections were related to heater-cooler unit contaminations and had other risk factors. NTM IE poses a significant challenge to clinicians due to the lack of guidance regarding management strategies; treatment is largely extrapolated from data on NTM pulmonary infections. Most of the available data consist of anecdotal evidence in the form of individual reports. This systematic review aimed to provide insight into the emerging risk factors, clinical presentation, and treatment outcomes in NTM IE.

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## METHODS

### Protocol and Registration

This systematic review is performed in accordance with the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-analyses; [Supplementary 1](#)) [12] and is registered in the PROSPERO online database (CRD42023492577).

### Search Strategy and Information Sources

A systematic search was conducted to identify all cases of IE caused by various NTM species in the existing literature. We searched major electronic databases of English literature (PubMed/Medline, Scopus, and Google Scholar) for published data, including case reports, case series, and original articles containing information about individual cases, from the earliest literature records until December 2023. The search terms and keywords used in this systematic review included “NTM” or “non-tuberculous mycobacteria” or “*mycobacterium abscessus*” or “*mycobacterium chimaera*” or “*mycobacterium fortuitum*” or “rapid growing mycobacterium,” combined with “endocarditis” or “infective endocarditis” or “cardiac device infections” or “prosthetic valve endocarditis” or “native valve endocarditis” or “pacemaker endocarditis” or “cardiac surgery” ([Supplementary 2](#)).

### Study Selection: Case Definition and Inclusion Criteria

This systematic review includes 167 cases of NTM IE. The 2023 IE criteria from Duke–International Society for Cardiovascular Infectious Diseases was used as the standard diagnostic criteria for case definition [10]. We considered only studies that provided detailed descriptions of clinical presentation, diagnostic procedures, and treatment methods. Pediatric and adult cases were included. Cases with surgical site infections or pacemaker infections without evidence of endocarditis were excluded. Additionally, cases with NTM isolation as contaminants, unclear treatment, and insufficient follow-up were excluded. For NTM disease, antibiotic therapy and therapeutic response are prolonged, so we analyzed a follow-up of at least 3 months after initiation of antibiotics in the surviving group. We excluded conference papers (abstract/posters), review articles, animal studies, and editorials. Disseminated NTM was defined as involvement of  $\geq 2$  noncontagious sites with at least 1 site involving endocardium. The mean duration of illness was defined as the time from the onset of symptoms until the first presentation or hospital admission. Relapse was defined as the occurrence—after culture conversion to negative and completion of a full course of treatment—of  $\geq 2$  positive culture results with same NTM species as the index IE. Early prosthetic valve endocarditis is defined as an infection of a prosthetic heart valve occurring within 12 months of valve implantation.

### Data Extraction and Qualitative Assessment

The clinical details from the selected cases were independently extracted by 2 authors (D. S. M. and G. K. B.). The online

software for systematic review (COVidence; Veritas Health Innovation) was used for data extraction. To remove duplicate records, we used reference management software (COVidence) for automated detection based on title, author, year, and DOI. We then performed a manual check to catch any remaining duplicates missed by the software. Gathered data encompassed risk factors, clinical presentation, diagnostic methods (microbiology and cardiac imaging), treatment strategies, and outcomes within a 90-day follow-up period. In the event of discrepancies between the authors, agreement was achieved through discussions with other reviewers (D. K., N. M., and M. K. G.). A risk bias assessment was carried out with the standardized critical appraisal tool proposed by the Joanna Briggs Institute [13]. The institute’s critical appraisal checklist can be found in [Supplementary 3](#).

### Statistical Analysis

We used SPSS software version 29.0 (IBM Corp) for data analysis. Descriptive statistics for continuous variables were presented as mean  $\pm$  SD or median (IQR), while categorical variables were displayed as number (percentage). We used the chi-square test to compare categorical data between the groups (survived and died) and the Student *t* test to analyze mean differences in quantitative data. *P* < .05 was considered statistically significant.

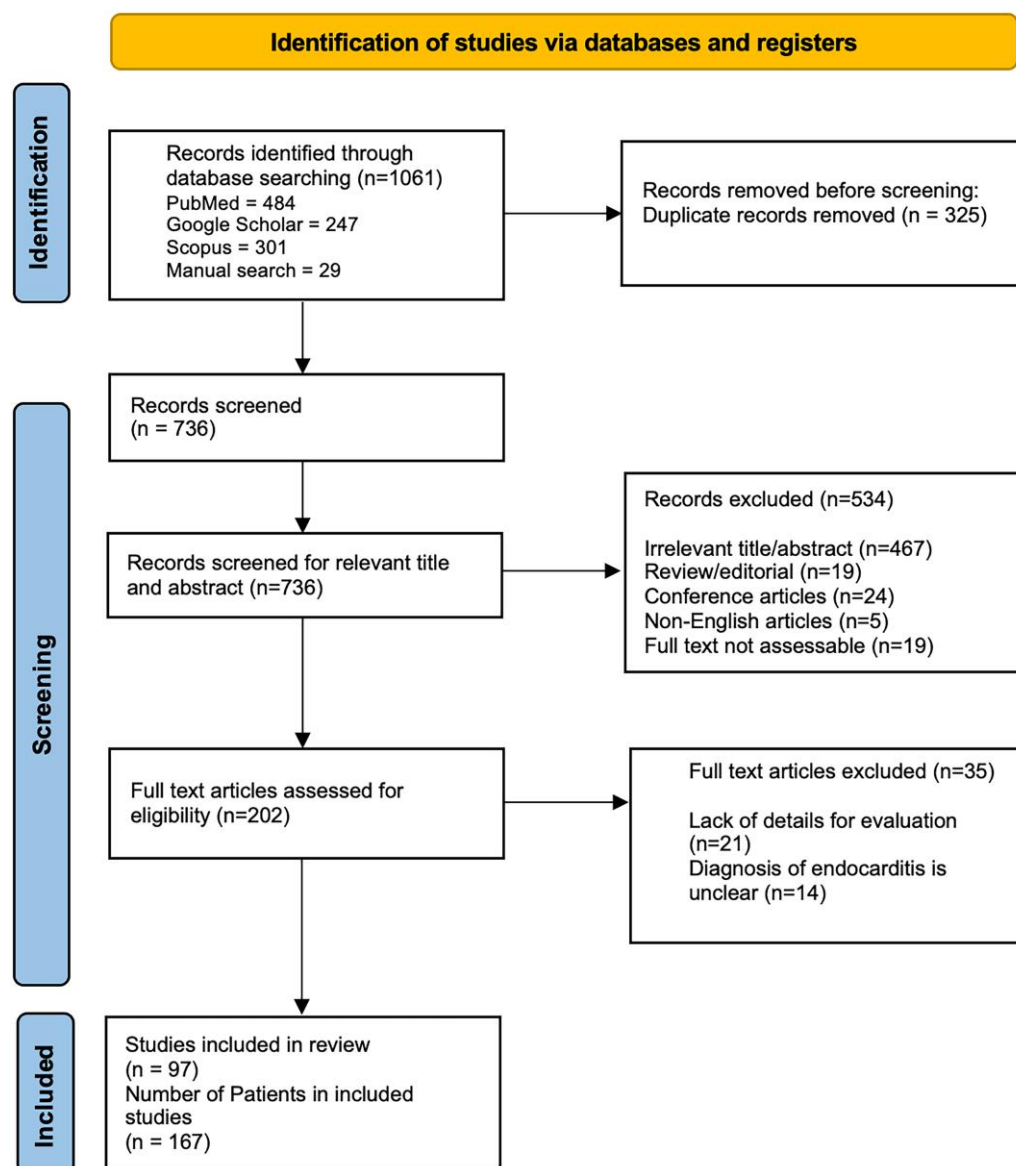
## RESULTS

A preliminary literature search identified 1061 case records, which were further analyzed for inclusion. After removal of any duplicate case records, 736 articles were reviewed for final inclusion. Finally, 167 patients from 97 studies were included in the systematic review ([Figure 1](#)). Of these 167 patients, 90 were from case series (20 studies), and the remaining 77 were individual cases. The reference list for all the studies included in this review can be found in [Supplementary 4](#).

The earliest mention of NTM IE in the literature dates back to 1975, with 2 studies on *M chelonae* and *M fortuitum* IE [14, 15]. However, the number of reported cases was limited before 2000, with only 13 cases, while the last 10 years have seen an increase with 122 reported cases. In total, 56 cases (33.5%) were related to an NTM endocarditis outbreak.

### Demography and Risk Factors

In this systematic review, we analyzed 167 cases of NTM IE. The median age of patients was 53 years, ranging from 6 months to 85 years. Only 5.4% (*n* = 9) were pediatric (<18 years), and 75% overall were male ([Table 1](#)). Most NTM IE cases were reported from the United States (39%), followed by Europe (33%). RGM accounted for the majority of cases (59%). Among the RGM IE cases, *M abscessus* (30%, *n* = 30) and *M chelonae* (28%, *n* = 28) were the most prevalent, while



**Figure 1.** Flowchart of article selection according to the PRISMA guideline.

*M chimaera* was the leading cause among slow-growing NTM (SGM). Specific details about other species can be found in Table 1. Overall, the proportion of *M chimaera* IE was the highest in this review (39%, n = 65).

The study found that 82% (n = 137) of patients with IE had at least 1 predisposing factor. Prosthetic valve was the most common risk factor for NTM IE (63.5%; Table 2). Furthermore, 84% of prosthetic valve IE cases were associated with SGM, while 96% of native valve IE cases were RGM related, mostly *M abscessus* (17/28). Intravenous drug use and history of IE were the other significant risk factors for NTM IE. Intravenous drug use was the major risk factor in native valve IE due to NTM (10/28). The heater-cooler unit was identified as the outbreak source for NTM in 56 cases (33.5%), with most

outbreaks being *M chimaera* related (53 cases) and the rest being *M massiliense* (2 cases) and *M chelonae* (1 case). Among comorbidities, immunodeficiency (16.8%) and diabetes mellitus (8.4%) were common. HIV and idiopathic CD4 lymphocytopenia were each found in 1 patient with NTM IE.

The average duration of illness, from the onset of symptoms to the first hospital presentation, was 80 days. Fever was the most common presenting feature (80%), followed by weight loss/constitutional symptoms (48%) and shortness of breath (29%). When compared with vascular events, immunologic events were infrequent (Table 3). Disseminated NTM disease was present in 84.4% (n = 141) of the patients. Among these cases, NTM bacteremia, bone marrow infiltration, and osteomyelitis were the most common manifestations.

**Table 1. Demographic and Etiologic Characteristics of Patients With NTM Endocarditis (N = 167)**

Characteristic	Patients, No. (%)
Age, y	
Mean $\pm$ SD (range)	51 $\pm$ 18 (6 mo–85 y)
Median (IQR)	53 (42–63)
Gender	
Male	125 (74.8)
Female	42 (25.2)
Geographic distribution	
United States	65 (38.9)
Europe	55 (32.9)
Asia	28 (16.8)
South America	16 (9.6)
Oceania	3 (1.8)
<b>Isolation of NTM species in endocarditis</b>	
Slow-growing NTM	68 (40.7)
<i>M chimaera</i>	65 (95.5)
<i>M gordonae</i>	1 (1.5)
<i>M malmoense</i>	1 (1.5)
<i>M kansasii</i>	1 (1.5)
Rapid-growing NTM	99 (59.3)
<i>M abscessus</i>	30 (30.3)
<i>M chelonae</i>	28 (28.3)
<i>M fortuitum</i>	21 (21.2)
<i>M wolinskyi</i>	4 (4)
<i>M massiliense</i>	3 (3)
<i>M bolletii</i>	2 (2)
<i>M neoaurum</i>	2 (2)
<i>M goodii</i>	2 (2)
<i>M mageritense</i>	1 (1)
<i>M canariense</i>	1 (1)
Species unidentified	5 (5.1)

Abbreviation: NTM, nontuberculous mycobacteria.

### Microbiological Diagnosis and Echocardiography Findings

Blood culture, vegetation culture, and molecular methods were the different modalities used for IE diagnosis. Blood culture showed positive results in 127 of 167 cases (76%; Table 4). The blood culture yield was higher in RGM vs SGM (83% vs 66%). Among RGM, *M abscessus* had the highest blood culture positivity rate at 97% (29/30). Molecular methods were used for diagnosis in 43% (n = 72) of cases, primarily through polymerase chain reaction (PCR)-based tests such as the sequencing of 16S rRNA and *hsp65* genes (68/72). The diagnosis of NTM IE was confirmed with metagenomic next-generation sequencing in 4 patients [13, 16–18]. In 53 of 72 patients, the source for molecular diagnosis was identified as valvular tissue or vegetation. Among them, 15 patients had negative blood culture results, and the diagnosis was established solely through molecular testing. We also collected data regarding the antibiotic susceptibility rate for different NTM species in IE (Supplementary Table 1).

Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were the primary cardiac imaging

**Table 2. Predisposing Factors and Comorbidities Associated With NTM Endocarditis (N = 167)**

Variable	Patients, No. (%)
<b>Predisposing factors for endocarditis</b>	
Cardiac devices	137 (82)
Prosthetic valve	106 (63.5)
Aortic graft	12 (7.2)
Stent	9 (5.4)
Pacemaker	6 (3.6)
AICD	6 (3.6)
Left ventricular assist device	4 (2.4)
RA-PA conduit	1 (0.6)
Intravenous drug users	15 (9)
History of endocarditis	11 (6.6)
Previous valve disease <sup>a</sup> /rheumatic heart disease	9 (5.4)
Congenital heart disease <sup>b</sup>	8 (4.8)
<b>Comorbidities</b>	
Immunocompromised/taking immunosuppressants	28 (16.8)
Mellitus	14 (8.4)
Hypertension	12 (7.2)
Chronic kidney disease/end-stage renal disease	7 (4.2)
Malignancy	6 (3.6)
Chronic liver disease/cirrhosis	6 (3.6)
Chronic obstructive pulmonary disease	6 (3.6)
HIV	1 (0.6)
Idiopathic CD4 lymphocytopenia	1 (0.6)

Abbreviations: AICD, automatic implantable cardioverter defibrillator; NTM, nontuberculous mycobacteria; RA-PA, right atrial-pulmonary artery.

<sup>a</sup>Degenerative valve disease, mitral valve prolapses, aortic sclerosis.

<sup>b</sup>Ventricular septal defect, 5 cases; atrial septal defect, 1 case; tetralogy of Fallot, 1 case; patent ductus arteriosus, 1 case.

methods used to detect vegetation. In this review, the sensitivity of TTE for detecting IE was 44% (48/110), while TEE was able to diagnose 83% (64/77) of the cases (Table 4). The sensitivity of TTE for detecting native and prosthetic valve vegetations was 77% (21/27) and 32% (27/83). In contrast, the sensitivity of TEE for detecting native and prosthetic valve IE was 100% (12/12) and 80% (52/65). The average vegetation size was 13.7 mm, with most NTM vegetations (63%) being large ( $\geq 10$  mm). Vegetations in RGM infections were larger than those in SGM infections, though the difference was not statistically significant (14.5 vs 11 mm,  $P = .415$ ). Similarly, native valve vegetations were larger than prosthetic valve vegetations (18 vs 10 mm,  $P = .04$ ). Cardiac computed tomography and positron emission tomography-computed tomography were used for diagnosis in 16 and 5 patients. Except for 1 patient, all of these cases involved prosthetic valve IE. The aortic and mitral valves were the most commonly affected (62% and 33%). Eight patients had multivalvular disease. Isolated right-side IE was documented in 16 patients.

### Outcomes

The majority of patients (61.5%, n = 103) received a combination treatment of antibiotics and valvular surgery, while the rest

**Table 3. Clinical Manifestations and Complications in NTM Endocarditis (N = 167)**

Variables	No. (%)
Fever	134 (80.2)
Weight loss/constitutional symptoms	80 (47.9)
Dyspnea	48 (28.7)
Heart murmur	43 (25.7)
Splenomegaly	39 (23.4)
<b>Immunologic phenomena</b>	
Osler node	8/79 (10.1)
Roth spots	4/79 (5.1)
Glomerulonephritis	3/31 (9.6)
Positive rheumatoid factor	4/34 (11.76)
<b>Vascular phenomena</b>	
Embolism	35 (20.9)
Stroke	23 (13.8)
Mycotic aneurysm	12 (7.2)
Janeway lesion	4/79 (5.1)
<b>Complication/extracardiac manifestation</b>	
Sepsis	38 (22.8)
Heart failure	38 (22.8)
Stroke	27 (16.2)
Acute kidney injury	23 (13.8)
HLH	3 (1.8)
<b>Disseminated NTM disease<sup>a</sup></b>	
Bacteremia	127 (76)
Bone marrow	25 (14.9)
Osteomyelitis	17 (10.2)
Pulmonary disease	14 (8.4)
Liver granuloma	6 (3.6)
Renal	6 (3.6)
CNS NTM infection	5 (3)
Spleen	1 (0.6)

Abbreviations: CNS, central nervous system; HLH, hemophagocytic lymphohistiocytosis; NTM, nontuberculous mycobacteria.

<sup>a</sup>Disseminated NTM was defined as either bacteremia or involvement of  $\geq 2$  noncontiguous sites.

were treated with antibiotics alone. Various antibiotic combinations for NTM species are summarized in [Supplementary Table 2](#). The average duration of antibiotic therapy for surviving patients was 278 days, with the mean duration of injectable antibiotics being 93 days. The overall case fatality rate in NTM IE was 44.9% (n = 75). A higher mortality rate was observed in patients treated without surgery (66.7% vs 30.6%), likely because surgery is often reserved for those with a better prognosis. Additionally, 5 patients received indefinite chronic suppressive antibiotic therapy [19–23]. The relapse rate in NTM IE was 7.9%. Except for 1 case of *M abscessus*, all cases of relapse were related to *M chimaera*. Paravalvular complications were documented in 31.5% of cases, and other cardiac and extracardiac complications are summarized in [Table 3](#).

#### Comparison Between SGM (*M chimaera*) and RGM IE

In this review, we compared the demographics, clinical characteristics, and outcomes of SGM and RGM IE, as depicted in

**Table 4. Diagnostic Modalities in Patients With NTM Endocarditis: Microbiological, Molecular, and Echocardiography Findings**

Variables	Patients, No. (%)
<b>Blood culture positivity</b>	
Slow-growing NTM	45/68 (66.2)
Rapidly growing NTM	82/99 (82.8)
<b>NTM species</b>	
<i>M chimaera</i>	42/65 (64.6)
<i>M abscessus</i>	29/30 (96.7)
<i>M chelonae</i>	18/28 (64.3)
<i>M fortuitum</i>	18/21 (85.7)
<b>Molecular diagnosis</b>	
16S rRNA, <i>hsp65</i> , <i>rpoB</i>	72/167 (43.1)
Metagenomic next-generation sequencing	68/72 (94.4)
Line probe assay	4
MALDI-TOF	1
Vegetation culture	76/91 (83.5)
<b>Diagnostic imaging in NTM endocarditis</b>	
Transthoracic echo	48/110 (43.6)
Transesophageal echo	64/77 (83.1)
Cardiac CT	16/16 (100)
FDG PET-CT	5/5 (100)
<b>Distribution of NTM IE according to valvular involvement</b>	
Aortic valve	144
Mitral valve	89 (61.8)
Tricuspid valve	47 (32.6)
Pulmonary valve	13 (9)
Multivalvular disease	3 (2.1)
	8 (5.6)

Abbreviations: CT, computed tomography; FDG, fluorodeoxyglucose; IE, infective endocarditis; MALDI-TOF, matrix-assisted laser desorption–ionization time of flight; NTM, nontuberculous mycobacteria; PET, positron emission tomography.

**Table 5.** Patients with *M chimaera* IE were older and experienced a significantly prolonged course of illness as compared with those with RGM IE. Right-sided IE was found exclusively with RGM. The proportion of aortic valve and prosthetic valve involvement was also higher in *M chimaera* as compared with other NTM species (71% vs 51% and 84% vs 49%). Early prosthetic valve infections (within a year of the implant) were more common in RGM IE. The mortality rate did not differ between the groups; however, the relapse rate was significantly higher in *M chimaera* endocarditis ( $P = .009$ ).

## DISCUSSION

NTM are emerging as a significant cause of nosocomial IE, a rare manifestation of disseminated NTM that may occur even in patients who are nonimmunocompromised. Most data on NTM IE are from case reports or clusters, with treatment generally adapted from pulmonary NTM guidelines [24]. *M chimaera*, first identified in 2004, attracted attention after IE outbreaks were traced to contaminated heater-cooler units (Stockert 3T) used in open-heart surgery [25]. Although *M chimaera* outbreaks are well reported, overall RGM species



**Table 5. Clinical Characteristics, Risk Factors, and Outcomes of Slow-Growing and Rapidly Growing NTM Endocarditis**

Variable	NTM Endocarditis, No. (%)		P Value
	Slow Growing (n = 68)	Rapidly Growing (n = 99)	
Gender	58/68 (85.3)	67/99 (67.7)	.010
Mean $\pm$ SD			
Age, y	56 $\pm$ 14	47 $\pm$ 18	.001
Duration of illness, d	140 $\pm$ 21	60.7 $\pm$ 41.1	.005
C-reactive protein, mg/dL	67 $\pm$ 14.8	84 $\pm$ 13	.408
Endocarditis			
Right side	0/68 (0)	15/80 (18.75)	<.001
Aortic valve	48/68 (70.6)	41/80 (51.2)	.016
Valve IE			
Prosthetic	57/68 (83.8)	49/99 (49.5)	<.001
Early prosthetic	22/57 (38.6)	31/49 (63.3)	.011
Native	1/28 (3.6)	27/28 (96.4)	<.001
Paravalvular complications	16/68 (23.5)	32/86 (37.2)	.068
Peripheral emboli	15/68 (22.1)	24/99 (24.2)	.743
Disseminated disease	59/68 (86.8)	82/99 (82.8)	.490
Mean $\pm$ SD			
Vegetation size, mm	11 $\pm$ 4.8	14.5 $\pm$ 10.8	.415
Duration of antibiotics, d	357 $\pm$ 49	219 $\pm$ 89	.012
Surgery for IE	46/66 (69.7)	55/99 (55.6)	.067
Relapse	6/34 (17.6)	1/52 (1.9)	.009
Mortality	28/68 (41.2)	47/99 (47.5)	.421

Abbreviations: IE, infective endocarditis; NTM, nontuberculous mycobacteria.

predominate in NTM IE. Subsequent outbreak investigations further substantiated the association of *M. chimaera* IE with contaminated heater-cooler units (Stockert 3T) [26, 27]. Aerosolized transmission from the contaminated water in heater-cooler units is the main mode of NTM spread [7, 8]. The warm water environment favors the colonization of NTM, making them more likely to be aerosolized [28]. Additionally, the propensity of NTM for biofilm formation makes it resistant to disinfectants [29]. Despite efforts to mitigate heater-cooler unit-related *M. chimaera* infections, more than two-thirds of overall NTM IE cases have been reported in the last decade; however, most are related to RGM. The colonization/contamination of the bioprosthetic valve during manufacture or storage could be another hypothesis for NTM endocarditis. Most cases have been reported from developed countries; yet, this is expected to change with the increase in cardiac procedures in developing nations and rising awareness.

Disseminated NTM infections are typically associated with immunodeficient states such as HIV [30]. However, this review found that only 17% of the cases were linked to immune deficiency. Furthermore, only 1 patient in this IE cohort had HIV [31]. This suggests that immune deficiency is not a requirement for NTM IE, which is also supported by previous literature [8]. In this review, we found the exclusive association of

native valve IE with RGM. These patients had other risk factors, such as intravenous drug use, a history of endocarditis, and an immunocompromised state. Aging is a well-established risk factor for IE, especially in the context of opportunistic microorganisms such as NTM. Immunosenescence, comorbidities, and increased interventions with aging are the contributing factors for IE [32]. Two-thirds (n = 101) of the patients with IE in this review were >50 years old. *M. chimaera* IE is an indolent infection, and many patients present very late (mean duration of illness >4 months). Yet, we found a relatively rapid progressive course of endocarditis in RGM species. Similarly, early prosthetic valve IE was predominant in RGM infections. This finding could be crucial for choosing antibiotic regimens when species identification is not available.

If NTM is isolated from a single blood culture, it may indicate contamination. However, isolation from  $\geq 2$  blood cultures could strongly suggest NTM IE [10]. Most patients with IE in this review were diagnosed via blood culture, with *M. abscessus* and *M. fortuitum* showing the highest culture yields, consistent with prior studies [33, 34]. Molecular methods, particularly PCR, have proven essential for diagnosing blood culture-negative cases, especially for *M. chimaera*, with 19 of 40 negative cases confirmed via PCR. Given that NTM IE primarily affects prosthetic valves, the role of TEE is crucial [35]. RGM vegetations tend to be larger than those of SGM, likely due to RGM's aggressive nature. Additionally, 70% of native valve IE cases presented with large vegetations (>10 mm), possibly due to delayed diagnosis from low suspicion of IE in native valve IE.

Clear guidelines for treating NTM IE are lacking and often extrapolated from severe or disseminated NTM disease. Combination antibiotic therapy, typically with 3 or 4 drugs, is the cornerstone to counteract drug resistance and manage severe infections [36, 37]. While the recommended duration for disseminated NTM disease is generally 6 to 12 months, no consensus exists for IE. Lifelong suppressive therapy is suggested in cases where source control is unattainable. Mortality in NTM IE is notably high (45%) as compared with pulmonary NTM disease (12%–20%) [38, 39], likely due to high bacterial load, biofilm formation, and challenges with source control. Our review shows improved outcomes in patients who underwent valve surgery. However, the results should be interpreted cautiously due to heterogeneous data and selection bias. Patients who underwent surgery might have had a better clinical status, which was not assessed in this review. Nonetheless, the difference in mortality with surgery was significant ( $P < .0001$ ), which emphasizes the role of expeditious surgery in NTM IE.

This study has a few important limitations. The retrospective nature of the data and the individual cases make it difficult to evaluate the outcomes. Although most data on NTM IE are available in the form of individual cases, some data from original articles are still missing, which is also an important limitation of the study. Furthermore, key information essential for

long-term therapy was not available, such as antibiotic minimum inhibitory concentration data, therapeutic drug monitoring, and adverse effect profile. Additionally, the assessment of relapse could have been improved with long-term follow-up (3–5 years), which was not available.

## CONCLUSIONS

NTM are a rare cause of endocarditis, which carries substantial mortality. We want to emphasize the emerging role of RGM in endocarditis, especially in cases of early prosthetic valve IE and even in the setting of native valve disease. Valvular surgery is imperative to improve outcomes. Failure to achieve this may necessitate chronic suppressive antibiotic therapy. Although mortality rates remain the same, relapses are more common with SGM and require periodic follow-up.

## Supplementary Data

**Supplementary materials** are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

**Author contributions.** D. S. M. and D. K. conceived the study. D. S. M., D. K., and G. K. B. designed the study protocol and methodology. D. S. M., G. K. B., D. K., M.K.G., and N. M. analyzed the data and drafted the manuscript. All authors critically revised the manuscript for critical content. All authors read and approved the final manuscript.

**Availability of data and materials.** The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate.** Not required.

**Patient consent statement.** This study does not include factors necessitating patient consent.

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