

Original Research Article

Emerging rapidly growing nontuberculous mycobacteria: a retrospective analysis of pulmonary and extrapulmonary isolates and antimicrobial susceptibility

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ABSTRACT

Introduction: Rapidly growing nontuberculous mycobacteria (RGM) account for nearly half of all recognized NTM species and are reported more frequently in Asia than in Western regions. Despite this, data describing RGM infections from North India remain sparse. We evaluated the incidence, species distribution, and antimicrobial susceptibility profiles of pulmonary and extrapulmonary RGM isolates from Delhi, North India.

Methods: A total of 3,624 NTM isolates recovered from pulmonary and extrapulmonary specimens were analyzed. Species identification was performed using MALDI-TOF MS, and antimicrobial susceptibility testing was conducted by broth microdilution in accordance with American Thoracic Society/Infectious Diseases Society of America guidelines. This analysis is limited to culture-positive RGM isolates and does not differentiate colonization from clinically significant disease.

Results: Among 26,475 mycobacterial isolates, 3,624 (12.1%) were identified as NTM, of which 2,115 (58.3%) were RGM. The *Mycobacterium abscessus* complex predominated (80.9%), followed by the *M. fortuitum* group (17.6%); other RGM species were infrequently isolated. RGM were recovered from both pulmonary and extrapulmonary specimens. Antimicrobial susceptibility testing demonstrated the highest in vitro activity for Amikacin, Clarithromycin, and Linezolid, with marked interspecies variability and frequent multidrug resistance, particularly among *M. abscessus* complex isolates.

Conclusions: Despite India being highly endemic for tuberculosis, the epidemiology of NTM particularly RGM remains insufficiently characterized. The findings highlight substantial species diversity and high levels of antimicrobial resistance among RGM isolates in North India, including extensive antimicrobial resistance *M. abscessus*. These data underscore the importance of accurate species-level identification, routine susceptibility testing, and sustained regional surveillance to optimize management and monitor evolving resistance trends.

Keywords: Nontuberculous mycobacteria, Rapidly growing nontuberculous mycobacteria, Antibiotic susceptibility testing, *Mycobacterium tuberculosis* complex, *Mycobacterium abscessus*, *Mycobacterium fortuitum*

INTRODUCTION

Nontuberculous mycobacteria (NTM) have emerged as clinically important opportunistic pathogens worldwide, including in regions where tuberculosis remains endemic.¹⁻⁴ The term “nontuberculous mycobacteria” was

formally adopted by the American Thoracic Society in 1997 and is now standard usage. In India, reported NTM prevalence varies widely (0.7%–34%), reflecting geographic and diagnostic variability.^{2,4,5} These free-living, acid-fast bacilli are ubiquitous in natural and engineered environments, including water, soil, food

sources, and animal reservoirs. Although generally less virulent than Mycobacterium tuberculosis, NTM can cause clinically significant disease in both immunocompromised and immunocompetent hosts and have been recognized as human pathogens since the mid-20th century.^{6,7}

NTM function as facultative intracellular organisms and may represent transient colonizers, contaminants, or true pathogens, complicating clinical interpretation. Their diverse pathogenic potential, variable clinical presentations, and intrinsic antimicrobial resistance underscore the importance of rapid, accurate species-level identification to distinguish infection from colonization and to guide appropriate therapy.^{6,8,9}

Over the past decade, the global burden of NTM disease has increased steadily, highlighting its emerging public health importance. Pulmonary disease remains the predominant manifestation; however, extrapulmonary infections are increasingly recognized, particularly among

older individuals and patients receiving immunosuppressive therapy with chronic, nonhealing lesions.^{2,6,9-11} These manifestations are clinically distinct, with pulmonary disease typically associated with underlying structural lung abnormalities and extrapulmonary infection linked to immune dysfunction or direct inoculation.^{3,6,9,12}

Rapidly growing non-tuberculous mycobacteria account for approximately half of currently recognized non-tuberculous mycobacterial species and represent an important cause of human disease. During the past decade, infections most commonly attributable to Mycobacterium abscessus and *M. fortuitum* have increased substantially, affecting both pulmonary and extrapulmonary sites.^{1-3,6,9,11,13-15} The rapidly growing mycobacteria (RGM) species identified in the laboratory over the study period, along with their taxonomic classification, are summarized in Table 1.⁸

Table 1: Taxonomic classification of RGM.

RGM group	Pigmentation	Representative species
<i>Mycobacterium abscessus</i> / <i>M. chelonae</i> group	Nonchromogenic	<i>M. abscessus</i> , <i>M. massiliense</i> , <i>M. chelonae</i> , <i>M. immunogenum</i>
<i>Mycobacterium fortuitum</i> group	Nonchromogenic	<i>M. fortuitum</i> , <i>M. peregrinum</i> , <i>M. canariense</i> , <i>M. bacteremicum</i> , <i>M. porcinum</i> , <i>M. septicum</i> , <i>M. senegalense</i> , <i>M. salmoniphilum</i> , <i>M. mageritense</i> , <i>M. conceptionense</i> , <i>M. algericum</i>
<i>Mycobacterium mucogenicum</i> group	Nonchromogenic (mucoid colonies)	<i>M. mucogenicum</i> , <i>M. phocaicum</i> , <i>M. aubagnense</i> ,
<i>Mycobacterium smegmatis</i> group	Nonchromogenic	<i>M. smegmatis</i> , <i>M. goodii</i> , <i>M. wolinskyi</i> , <i>M. confluens</i> , <i>M. elephantis</i> , <i>M. duvalii</i> , <i>M. grossiae</i> , <i>M. chubuense</i>
<i>Mycobacterium vaccae</i> / <i>M. parafortuitum</i> group	Scotochromogenic	<i>M. vaccae</i> , <i>M. parafortuitum</i> , <i>M. sarraceniae</i> , <i>M. neoaurum</i> , <i>M. lehmanii</i>
Unclassified / intermediate RGM	Variable	<i>M. monacense</i> , <i>M. saopaulense</i> , <i>M. minnesotense</i>

Given the rising burden and therapeutic complexity of RGM infections, regional data integrating species-level identification and antimicrobial susceptibility testing are essential to guide clinical management. Accordingly, we conducted a seven-year retrospective analysis to characterize pulmonary and extrapulmonary NTM infections in North India and to define species-specific resistance patterns.

METHODS

This retrospective cohort study was performed at Dr. Lal Path Labs, NRL, New Delhi, India, over a seven-year period (January 2018–December 2024). All patients with culture-confirmed pulmonary and extrapulmonary NTM isolates obtained from clinical specimens were included. Application of the American thoracic society (ATS) diagnostic criteria for NTM pulmonary disease was not

feasible because detailed clinical and radiologic data were unavailable. Species identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) with the MALDI Biotyper Compass/IVD reference library (2023). Antimicrobial susceptibility testing was conducted by broth microdilution using the Sensititre system and interpreted in accordance with Clinical and Laboratory Standards Institute (CLSI) M24-A2 guidelines.¹⁶

Specimen collection and transport

Clinical specimens included sputum, bronchoalveolar lavage (BAL), body fluids (ascitic, pleural, peritoneal, pericardial, and synovial), pus, drain fluids, gastric aspirates, tissue, cerebrospinal fluid, and early-morning urine collected on three consecutive days. Specimens were transported in sterile, leak-proof containers in accordance with standard biosafety protocols.

Specimen processing and culture

All specimens were processed using standard N-acetyl-L-cysteine–sodium hydroxide (NALC–NaOH) digestion, decontamination, and concentration methods. The concentrated sediment was allocated for microscopy and culture. An aliquot was inoculated into the MGIT 960 liquid culture system (Becton Dickinson) and incubated according to the manufacturer’s recommendations. Cultures flagged as positive were examined by Ziehl–Neelsen and Gram staining. Acid-fast bacilli (AFB)–positive cultures were tested for the MPT64 antigen to differentiate *Mycobacterium tuberculosis* complex (MTBC) from NTM. MPT64-negative isolates underwent species identification, whereas MPT64-positive isolates were further assessed for cording on ZN staining and confirmed after subculture on Middlebrook agar by MALDI-TOF mass spectrometry. Cultures flagged positively in the absence of AFB were considered contaminated. MGIT cultures remain negative after 42 days were reported as negative.

A second aliquot was inoculated onto Lowenstein–Jensen (LJ) medium and incubated at 37°C, with daily examination for the first week and weekly monitoring for up to six weeks. Growth was confirmed by ZN staining, and isolates demonstrating visible colonies within ≤7 days were provisionally classified as rapid-growing mycobacteria. A third aliquot was inoculated onto blood agar to detect contamination by non-mycobacterial organisms. Direct smears were prepared from the remaining sediment, stained by the ZN method, and examined for AFB.¹⁷

Protein extraction and MALDI-TOF MS analysis

Mycobacterial isolates were processed using an extended protein extraction protocol prior to MALDI-TOF analysis. Protein extraction was performed using a standardized bead-beating method optimized for mycobacterial cell disruption. Briefly, 2–3 colonies (or a 0.5-ml pellet from MGIT culture) were suspended in 300 µl of distilled water, followed by the addition of 900 µl ethanol for inactivation and lysis. After centrifugation (13,000 rpm, 2 min), the pellet was resuspended in 50 µl of 70% formic acid and 50 µl of acetonitrile and vortexed. Zirconia–silica beads (0.1 mm; 100 µl) were added, and samples were bead-beaten at 30 Hz for 3 min using a Tissue Lyser II. Following centrifugation (13,000 rpm, 2 min), 1 µl of the supernatant was spotted onto an MSP 96 polished steel target plate and overlaid with 1 µl of α-cyano-4-hydroxycinnamic acid matrix (70% acetonitrile, 0.1% trifluoroacetic acid), then air-dried. Spectra were acquired using 240 laser shots per spectrum over a mass range of 2,000–20,000 Da, with automatic calibration performed using the Bruker Bacterial Test Standard. Identification scores were interpreted according to Bruker criteria: log(score) ≥2.0 indicated high-confidence species-level identification; scores of 1.7–1.999 indicated low-confidence species-

genus-level identification requiring manual review; scores of 1.0–1.699 supported genus-level identification only; and scores <1.0 were considered non-identifiable and prompted repeat extraction. Preliminary identification was based on growth characteristics and colony morphology, followed by species-level identification using MALDI-TOF mass spectrometry; subspecies discrimination within the *Mycobacterium abscessus* complex may be limited by assay resolution.

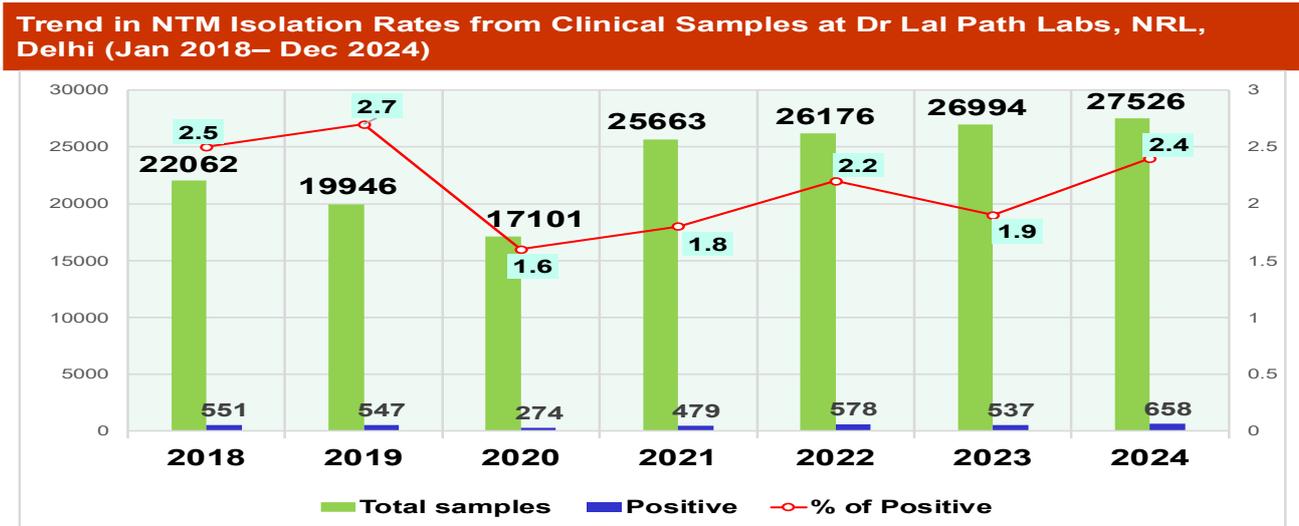
Statistical analysis

Descriptive statistical analysis was performed using Microsoft Excel, with results expressed as frequencies and percentages.

RESULTS

Of the 165,468 clinical specimens processed, 18.2% (n=30,099) were positive for acid-fast bacilli (AFB) in culture. The *Mycobacterium tuberculosis* complex (MTBC) constituted 87.9% (n=26,475) of the positive cultures, whereas nontuberculous mycobacteria (NTM) accounted for 12.1% (n = 3,624). The overall positivity rates were 16.0% for MTBC and 2.2% for clinically significant NTM. Among the NTM isolates, 58.4% (2,115/3,624) were rapid-growing mycobacteria and 41.6% (1,509/3,624) were slow-growing mycobacteria, with *Mycobacterium abscessus* being the most frequently isolated NTM species. In the pre-pandemic years, positivity rates were comparable in 2018 (2.5%) and 2019 (2.7%). During the COVID-19 period, a marked decline was observed in 2020, with positivity decreasing to 1.6%, coinciding with reduced healthcare access, diagnostic prioritization for SARS-CoV-2, and lower sample volumes. Although testing increased in 2021, the positivity rate remained suppressed at 1.8%, suggesting a persistent pandemic-related impact. Post-pandemic recovery was evident from 2022 onward, with a gradual increase in positivity (2.2% in 2022 and 1.9% in 2023), reaching near pre-pandemic levels by 2024 (2.4%). These findings highlight the transient but significant effect of the COVID-19 pandemic on MOTT detection, followed by restoration of diagnostic yield in the post-pandemic period.

A total of 2,115 Rapidly growing non-tuberculous mycobacteria isolates were identified from clinical specimens. Respiratory samples predominated, with BAL accounting for 590 isolates (27.9%) and sputum for 572 (27.0%). Among extrapulmonary specimens, pus (254; 12.0%) and tissue samples (211; 9.9%) were the most frequent sources. Body fluids contributed 151 isolates (7.1%), while samples categorized as others comprised 171 isolates (8.1%). Endometrial specimens yielded 68 isolates (3.2%), followed by urine (62; 2.9%) and menstrual blood (23; 1.1%). Colonoscopy-derived specimens represented the smallest proportion, with 13 isolates (0.6%).



The proportion of NTM-positive isolates varied between 2018 and 2024, reflecting changes in testing volume and potential impacts of the COVID-19 pandemic; these observations are descriptive and do not imply causality.

Figure 1: Yearly trends in total samples, positives, and positivity rates for NTM at Dr Lal path labs, NRL, Delhi (2018–2024).

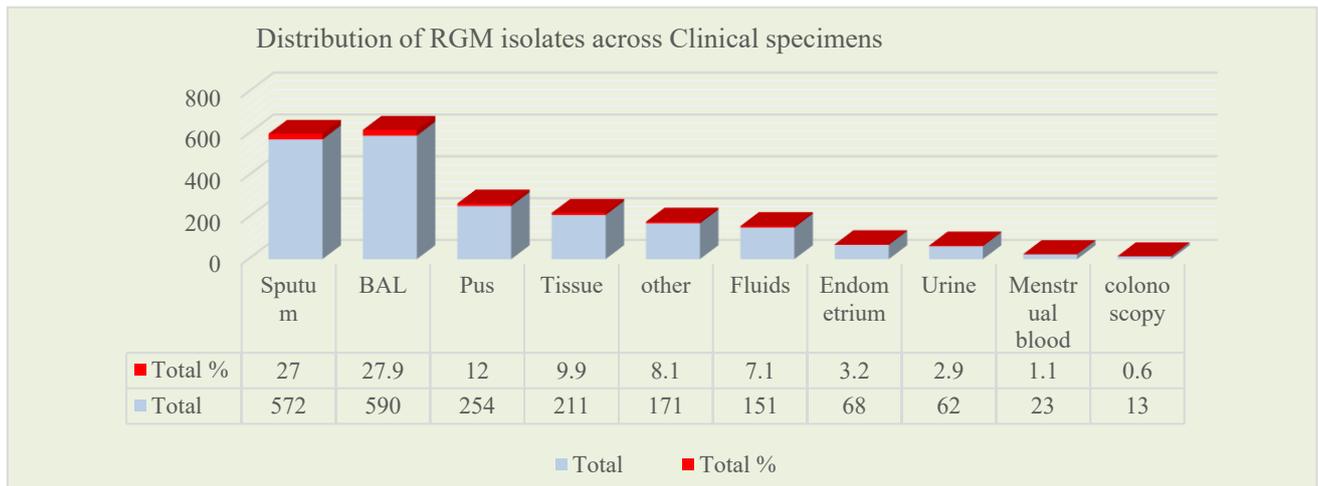


Figure 2: Distribution of rapidly growing nontuberculous mycobacteria isolates across clinical specimen types.

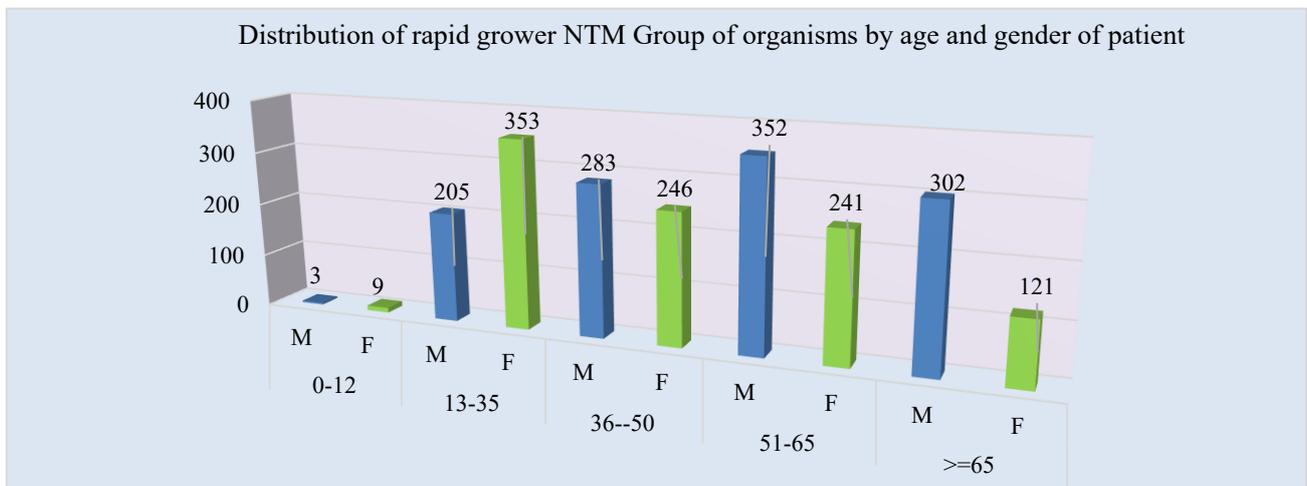


Figure 3: Distribution of rapid grower NTM group of organisms by age and gender of patient.

Cumulative interpretation of susceptibility pattern of Rapid Grower NTM species in diverse samples during Jan 2018 to Dec 2024.

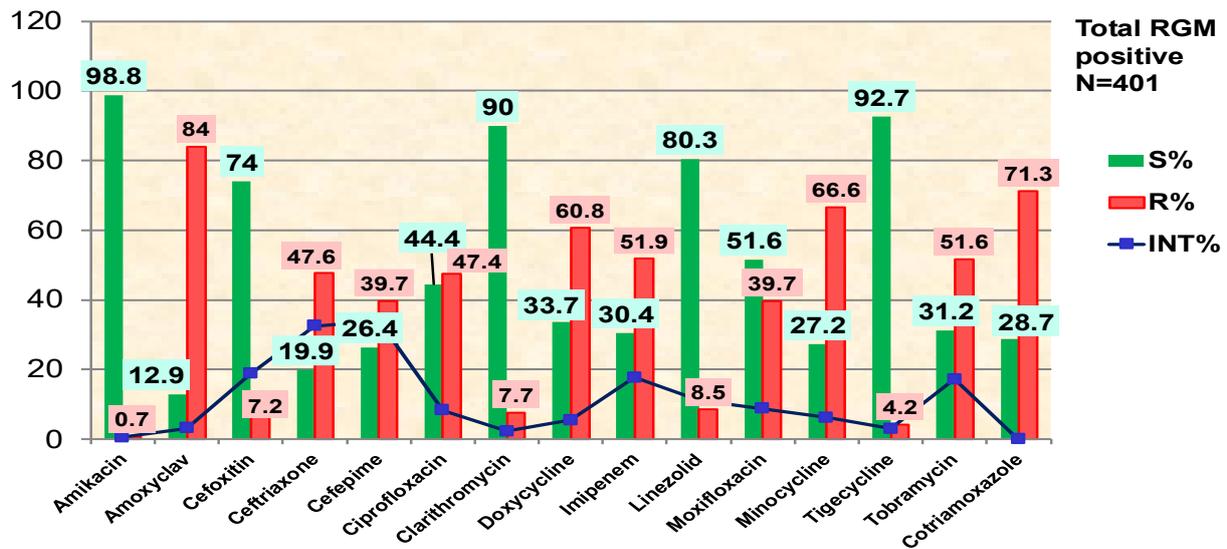


Figure 4: Cumulative interpretation of antimicrobial susceptibility (%) among rapidly growing nontuberculous mycobacteria (RGM) group of organisms in diverse samples.

A total of 2,115 rapid-growing nontuberculous mycobacterial isolates were identified during the study period, including 1,162 (54.9%) from pulmonary specimens and 953 (45.1%) from extrapulmonary sources. Although rapid-growing species were slightly more frequent in pulmonary infections, a substantial proportion also involved extrapulmonary sites.

The *Mycobacterium abscessus*/ *M. chelonae* was the dominant species group, comprising 80.9% (1,711/2,115) of all isolates. The *M. fortuitum* group was the next most common, contributing 17.6% (372/2,115). Other species were identified far less frequently, including the *M. smegmatis* group (0.8%), the *M. parafortuitum-vaccae* group (0.3%), and the *M. mucogenicum* group (0.2%). A small proportion of isolates (0.1%) remained unclassified among the rapid growers. This, pattern suggests a broad clinical distribution rather than site-specific restriction. Overall, the findings underscore the marked dominance of the *M. abscessus/chelonae* group among clinical RGM infections in Delhi, North India.

The age- and sex-wise distribution of NTM isolates is depicted in Figure 3. Among 2,115 culture-positive cases, the highest proportion occurred in individuals aged 51–65 years (n = 593; 28%), followed by those aged 13–35 years (n = 558; 26.4%), 36–50 years (n=529; 25%), and ≥66 years (n = 423; 20%).

Children aged 0–12 years accounted for a negligible fraction of cases (n=12; 0.56%). The 51–65-year age group constituted the largest cohort and demonstrated male predominance, whereas females were more frequently represented in the 13–35-year group. In contrast, males

predominated across the older age groups (36–50, 51–65, and ≥66 years).

This study describes the distribution of rapidly growing non-tuberculous mycobacteria (RGM) across a wide range of clinical specimens, including respiratory and extrapulmonary sources. Among 2,115 RGM isolates, respiratory specimens (sputum and bronchoalveolar lavage) accounted for the majority; however, a substantial proportion were recovered from extrapulmonary sites, including pus, tissue, and body fluids. *Mycobacterium abscessus* was the most prevalent species, predominating in respiratory samples and frequently isolated from multiple extrapulmonary specimens, reflecting its broad pathogenic potential. Isolates belonging to the *M. abscessus*–*M. chelonae* group showed a similarly wide distribution across specimen types.

M. fortuitum was the next most common species, followed by several moderately prevalent RGM species such as *M. mageritense*, *M. senegalense*, *M. porcinum*, and *M. salmoniphilum* with mixed respiratory and soft-tissue involvement. Several additional other rapidly growing nontuberculous mycobacterial species were identified at low frequency, each contributing minimally to the overall isolate burden. Interpretation of these rare identifications is limited by the absence of molecular confirmation.

Overall, RGM recovery was highest from respiratory specimens, followed by pus, tissue, body fluids, urine, and other infrequent sample types. Antimicrobial susceptibility testing demonstrated marked inter-drug variability with a limited number of agents retaining reliable activity. Amikacin showed the highest activity in vitro, with 98.8%

of isolates susceptible and minimal resistance (1.2%). Tigecycline (92.7% susceptible) and Clarithromycin (90.0% susceptible) also exhibited excellent activity, followed by Linezolid, which remained active against 80.3% of isolates.

Among cephalosporins, cefoxitin demonstrated moderate activity (74% susceptible) with a considerable intermediate category (18.8%), whereas ceftriaxone and cefepime showed limited efficacy, characterized by low susceptibility rates (19.9% and 26.4%, respectively) and high intermediate proportions (32.5% and 33.9%), alongside substantial resistance (47.6% and 39.7%).

Fluoroquinolones exhibited variable activity, with susceptibility rates of 51.6% for moxifloxacin and 44.4% for ciprofloxacin. High resistance was observed to amoxicillin–clavulanate (84%), cotrimoxazole (71.3%), Minocycline (66.6%), doxycycline (60.8%), imipenem (51.9%), and tobramycin (51.6%). Overall, amikacin, tigecycline, Clarithromycin, and Linezolid remained the most consistently active agents, while cephalosporins showed substantial intermediate and resistant profiles, limiting their reliability for empirical therapy.

Among the 401 rapidly growing mycobacterial (RGM) isolates, *Mycobacterium abscessus* was predominant (n=336), with the remaining isolates comprising other RGM species (n=65). Antimicrobial susceptibility testing was performed for only a limited subset of isolates, restricted to cases in which such testing was requested; consequently, susceptibility data were available for fewer isolates than those identified by culture.

Among *Mycobacterium abscessus* isolates, the highest in vitro susceptibility was observed to Amikacin (98.5%), Tigecycline (92.5%), Clarithromycin (88.6%), and linezolid (79.7%). Cefoxitin demonstrated moderate activity, with a notable proportion of isolates categorized as intermediate (20.2%). Extended incubation to detect inducible macrolide resistance was not routinely performed; therefore, clarithromycin susceptibility results should be interpreted with caution, particularly for *M. abscessus*.

Fluoroquinolones exhibited limited and variable activity. High resistance was observed to amoxicillin–clavulanate, tetracyclines, trimethoprim–sulfamethoxazole and extended-spectrum cephalosporins. In contrast, other RGM species demonstrated broader susceptibility, with universal susceptibility to Amikacin and high activity of Tigecycline, Clarithromycin, Linezolid, and Cefoxitin, although resistance to β-lactams and several parenteral agents remained common.

Overall, *M. abscessus* exhibited a more resistant phenotype than other RGM, underscoring the importance of species-level identification and susceptibility-guided therapy.

The limited activity of broad-spectrum β-lactams (Amoxiclav, Ceftriaxone, Cefepime) and older oral agents (Doxycycline, TMP–SMX), and certain parenteral drugs (Imipenem, Tobramycin) highlights the need for NTM-specific antimicrobial selection, particularly in severe or invasive disease.

Table 2: Pulmonary vs. extrapulmonary distribution of rapid-growing NTM Isolates (2018–2024).

NTM species (rapid grower)	Pulmonary (n=1162) (54.9%)	Extra pulmonary (n= 953) (45.1%)	Total (n=2115) (%)
<i>M. abscessus/M. chelonae complex group</i>	941	770	1711 (80.9)
<i>M. fortuitum group</i>	207	165	372 (17.6)
<i>M. smegmatis group.</i>	9	8	17 (0.8)
<i>M. parafortuitum–vaccae group</i>	2	5	7 (0.3)
<i>M. mucogenicum group</i>	1	4	5 (0.2)
<i>Unclassified/ intermediate rapid growers</i>	2	1	3(0.1)

Table 3: Specimen-wise distribution of rapid-growing NTM species: pulmonary and extrapulmonary sources.

Rapidly growing non-tuberculous mycobacteria (RGM)	Sputum	BAL	Pus	Fluid	Tissue	Urine	Menstrual blood	Endo-metrium	other	Colono-scropy	Total
<i>M. abscessus</i>	423	475	186	116	164	56	21	63	127	13	1644
<i>M. chelonae</i>	14	9	3	1	4	*	*	2	6	*	39
<i>M. immunogenum</i>	10	9	2		3	*	*	*	3	*	27
<i>M. massiliense</i>	*	1	*	*	*	*	*	*	*	*	1
<i>M. abscessus/M. chelonae group</i>	447	494	191	117	171	56	21	65	136	13	1711
<i>M. fortuitum</i>	86	61	39	16	22	6	2	2	24	*	258
<i>M. mageritense</i>	11	9	2	3	5	*	*	*	*	*	30

Continued.

Rapidly growing non-tuberculous mycobacteria (RGM)	Sputum	BAL	Pus	Fluid	Tissue	Urine	Menstrual blood	Endo-metrium	other	Colono-scopy	Total
<i>M. senegalense</i>	9	0	6	4	2	*	*	*	7	*	28
<i>M. porcinum</i>	8	6	2	6	2	*	*	*	*	*	24
<i>M. salmoniphilum</i>	3	7	1	1	*	*	*	*	2	*	14
<i>M. peregrinum</i>	*	*	*	*	1	*	*	*	*	*	1
<i>M. septicum</i>	*	*	*	1	*	*	*	*	*	*	1
<i>M. houstonense</i>	*	*	1	*	*	*	*	*	*	*	1
<i>M. canariasense,</i>	*	*	1	*	*	*	*	*	*	*	1
<i>M.algericum</i>	*	2	*	2	*	*	*	*	*	*	4
<i>M. brisbanense</i>	1		1	*	*	*	*	*	*	*	2
<i>M. bacteremicum</i>		*	1	*	*	*	*	*	*	*	1
<i>M. conceptionense</i>	3	1	*	*	*	*	*	*	*	*	4
<i>M.novocastrense</i>	*	*	2	*	1	*	*	*	*	*	3
<i>M. fortuitum group</i>	121	86	56	33	33	6	2	2	33	**	372
<i>M. mucogenicum</i>	*	*	1	*		*	*	*	*	*	1
<i>M. phocaicum</i>	*	*	1	*	*	*	*	*	1	*	2
<i>M. aubagnense</i>	*	1	*	*	1	*	*	*	*	*	2
<i>M. mucogenicum group</i>	*	1	2	*	1	*	*	*	1	*	5
<i>M. elephantis</i>	2	2	1	1	1	*	*	1	*	*	8
<i>M. goodii</i>	1	1	*	*	*	*	*	*	*	*	2
<i>M. wolinskyi</i>	*	*	*	*	2	*	*	*	*	*	2
<i>M. confluentis</i>	*	*	*	*	*	*	*	*	1	*	1
<i>M. duvalii</i>	*	1	*	*	*	*	*	*	*	*	1
<i>M. chubuense</i>	*	1	1	*	*	*	*	*	*	*	2
<i>M.grossiae</i>	*	1		*	*	*	*	*	*	*	1
<i>M. smegmatis group</i>	3	6	2	1	3	*	*	1	1	*	17
<i>M. vaccae</i>	--	--	1	--	1	*	*	*	*	*	2
<i>M.parafortuitum</i>	1		*	*	*	*	*	*	*	*	1
<i>M. sarraceniae</i>	*	1	*	*	*	*	*	*	*	*	1
<i>M. lehmannii</i>	*	*	*	*	1	*	*	*	*	*	1
<i>M. neoaurum</i>	*	*	1		1	*	*	*	*	*	2
<i>M. parafortuitum vaccae group</i>	1	1	2		3	*	*	*	*	*	7
<i>M. minnesotense</i>	*	1	*	*	*	*	*	*	*	*	1
<i>M. monacense</i>	*	1	*	*	*	*	*	*	*	*	1
<i>M. saopaulense</i>	*		1	*	*	*	*	*	*	*	1
Unclassified/ intermediate rapid growers	*	2	1	*	*	*	*	*	*	*	3
Total	572	590	254	151	211	62	23	68	171	13	2115

Table 4: Cumulative interpretation of antimicrobial susceptibility (%) among rapidly growing nontuberculous mycobacteria (RGM) group of organisms in diverse samples.

Antibiotic	RGM: <i>M. Absessus</i> (n=336)						Other RGM (n=65)						Total RGM (n=401)					
	S	S%	INT	INT%	R	R%	S	S%	INT	INT%	R	R%	S	S%	INT	INT%	R	R%
Amikacin	331	98.5	2	0.5	3	0.8	65	100	0	0	0	0	396	98.8	2	0.5	3	0.7
Amoxyclav	43	12.7	9	2.7	284	84.5	9	13.8	3	4.7	53	81.5	52	12.9	12	3.1	337	84
Cefoxitin	241	71.7	68	20.2	27	8	56	86.1	7	10.8	2	3.1	297	74	75	18.8	29	7.2
Ceftriaxone	73	21.7	126	37.5	137	40.7	7	10.8	4	6.2	54	83.1	80	19.9	130	32.5	191	48
Cefepime	100	29.7	125	37.2	111	33	6	9.2	11	16.9	48	73.8	106	26.4	136	33.9	159	40
Ciprofloxacin	157	46.7	30	8.9	149	44.3	21	32.3	3	4.6	41	63.1	178	44.4	33	8.2	190	47

Continued.

	RGM: <i>M. Abscessus</i> (n=336)				Other RGM (n=65)				Total RGM (n=401)									
Clarithro- mycin	298	88.6	9	2.7	29	8.6	63	96.9	0	0	2	3.1	361	90	9	2.3	31	7.7
Doxycycline	114	33.9	22	6.5	200	59.5	21	32.3	0	0	44	67.7	135	33.7	22	5.5	244	61
Imipenem	110	32.7	67	19.9	159	47.3	12	18.4	4	6.2	49	75.4	122	30.4	71	17.7	208	52
Linezolid	268	79.7	38	11.3	30	8.9	54	83.1	7	10.8	4	6.2	322	80.3	45	11.2	34	8.5
Moxifloxacin	173	51.4	35	10.4	128	38.1	34	52.3	0	0	31	47.7	207	51.6	35	8.7	159	40
Minocycline	93	27.6	25	7.4	218	64.8	16	24.6	0	0	49	75.4	109	27.2	25	6.2	267	67
Tigecycline	311	92.5	12	3.5	13	3.8	61	93.8	0	0	4	6.2	372	92.7	12	3	17	4.2
Tobramycin	112	33.3	63	18.8	161	47.9	13	20	6	9.3	46	70.7	125	31.2	69	17.2	207	52
Cotriamo- xazole	91	27.1	0	0	245	72.9	24	36.9	0	0	41	63.1	115	28.7	0	0	286	71

S: Sensitive, R: Resistant, INT: Intermediate

DISCUSSION

NTM are increasingly recognized as clinically relevant pathogens, particularly in chronic pulmonary disease. Reported incidence in high-income countries ranges from 1.0 to 15.5 per 100,000 population, and global analyses show that NTM-associated mortality doubled between 2000 and 2022, highlighting their growing public health significance.¹⁸ Rising NTM burden is driven by expanding immunocompromised populations, improved diagnostics, and heightened clinical awareness. Once considered environmental saprophytes, NTM are now established pathogens capable of causing pulmonary and extrapulmonary disease that can closely mimic tuberculosis.^{1,4,17} In TB-endemic regions such as India, NTM infections remain underdiagnosed due to overlapping clinical presentations, limited laboratory capacity, and restricted access to species-level identification, leading to potential misclassification and inappropriate therapy.^{14,19}

Global isolation rates of nontuberculous mycobacteria have risen steadily over the past two decades, with significant increases reported across North America, Europe, and Asia.^{1,5,7,8,12,13,18} Distinct geographic patterns have been observed, with the *Mycobacterium avium* complex predominating in Western countries, while *Mycobacterium abscessus* has demonstrated a rapidly increasing incidence in Asian regions, a trend that is consistent with our findings.^{3,6-8,11,13,18}

In this laboratory-based study provides comprehensive insight into the epidemiology and antimicrobial resistance patterns of rapidly growing nontuberculous mycobacteria in North India. The overall NTM positivity rate of 2.2% aligns with reports from TB-endemic settings and reinforces the growing recognition of NTM as clinically relevant pathogens rather than incidental laboratory findings.^{10,17}

Consistent with global trends, pulmonary disease predominated, particularly among older individuals and males.^{8,9,15,18,19} The striking dominance of *M. abscessus*,

accounting for over 80% of rapid-growing mycobacterium isolates, exceeds proportions reported in many Western studies but mirrors observations from India and other parts of Asia, where *M. abscessus* has emerged as a leading cause of NTM disease.^{7,8,13} In some high-income regions, NTM isolation now surpasses that of *Mycobacterium tuberculosis*.^{2,6,7,9,10,12,18} The burden of pulmonary NTM disease continues to rise, driven by environmental exposures and aging populations.^{7,8,17}

In our study, pulmonary specimens accounted for the highest isolation rate of rapidly growing nontuberculous mycobacteria (58.6%), followed by pus (10.3%) and tissue samples (8.3%), consistent with prior studies, although geographic and healthcare-related variability has been noted.^{1,3,5-8,11-14,20} The notable proportion of extrapulmonary RGM infections underscores the expanding clinical spectrum of NTM disease beyond the respiratory tract. Recovery from pus, tissue, body fluids, and genitourinary specimens indicates the relevance of direct inoculation, surgical procedures, and device-associated infections, particularly in immunocompromised or medically complex patients.¹⁰⁻¹² These patterns likely reflect regional differences in environmental exposure, host susceptibility, and healthcare infrastructure.

In this study, species diversity was high, with 36 NTM species recovering. While *M. abscessus* predominated, other RGM including the *M. fortuitum* group and less common species were detected across pulmonary and extrapulmonary specimens, suggesting that clinical manifestations are influenced by host factors and exposure rather than strict species tropism.^{3,7,11,14,15,19,20}

The antimicrobial susceptibility profiles observed in this study highlight the substantial therapeutic challenges associated with rapidly growing mycobacteria, particularly *Mycobacterium abscessus*. Amikacin demonstrated the most consistent in vitro activity, followed by tigecycline and clarithromycin, findings that are concordant with regional and international studies.^{1-3,5,6,8,9,13-15} However, the clinical utility of amikacin is limited by parenteral

administration and potential dose-limiting toxicity. Linezolid and cefoxitin showed moderate activity; however, resistance rates exceeding 20–30% limit their reliability as standalone therapeutic options.^{1,2,6} In contrast, reduced susceptibility was observed for Amoxicillin–clavulanate, Cephalosporins, Fluoroquinolones, Tobramycin, Minocycline, and Trimethoprim–sulfamethoxazole, underscoring pronounced geographic variability and the limited role of these agents in empirical treatment strategies.^{1,5,6,10}

Moreover, the potential for inducible macrolide resistance in *M. abscessus* necessitates cautious interpretation of clarithromycin susceptibility results, particularly in the absence of extended incubation or molecular characterization of *erm* genes. Collectively, these findings reinforce the inadequacy of empirical treatment strategies and emphasize the critical importance of accurate species-level identification and susceptibility-guided therapy in the management of rapidly growing mycobacterial infections.

M. abscessus displayed extensive resistance across most antimicrobial classes, with Linezolid and amikacin among the few retained options, reflecting the narrow therapeutic window and limited treatment options.⁶ In contrast, other RGM such as *M. fortuitum* exhibited broader susceptibility, permitting more flexible therapy.³

Overall, these findings highlight the emergence of extensively drug-resistant RGM in North India, particularly *M. abscessus*, highlights the need for early microbiological diagnosis, robust laboratory capacity individualized susceptibility-guided treatment strategies to mitigate the clinical and public health impact of these infections.

CONCLUSION

India remains highly endemic for tuberculosis; however, the epidemiology of nontuberculous mycobacteria (NTM) is incompletely defined. NTM are increasingly recognized as pathogens in both immunocompromised and immunocompetent hosts, contributing to a growing burden of pulmonary and extrapulmonary disease. In this study, we demonstrate substantial taxonomic diversity and high antimicrobial resistance among rapid-growing NTM in Delhi, North India, including emerging extensive antimicrobial resistance, particularly within the *M. abscessus*. Marked interspecies variability in antimicrobial susceptibility underscores the importance of accurate species-level identification and routine susceptibility testing. Strengthening diagnostic capacity, standardizing testing practices, and implementing susceptibility-guided therapy are essential to address therapeutic challenges. Ongoing regional surveillance is critical to monitor evolving resistance patterns, guide empirical therapy, and mitigate the increasing burden of NTM disease in high-endemic settings such as India.

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