

Clinical profile and outcomes of pulmonary nocardiosis in India: a systematic review of individual cases

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SUMMARY

Introduction: Nocardiosis is a common cause of pneumonia in immunocompromised individuals. Limited data regarding its epidemiology, clinical presentations, and outcomes in India are available. This systematic review analysed the clinical profile and outcomes of pulmonary nocardiosis in India.

Methods: We systematically reviewed individual cases of culture-confirmed pulmonary nocardiosis from India published between January 1960 and May 2024 using the PubMed, Embase, and Web of Science databases. Studies lacking microbiological confirmation or detailed clinical data were excluded. Descriptive statistics were used to summarise demographic, clinical, and microbiological data, while chi-square and t-tests assessed differences between mortality and survival groups.

Results: The review included 109 cases from 67 stud-

ies. Male predominance (74.1%) was observed, with a mean age of 49.6 ± 16.9 years. Diabetes (26.6%), steroid use (51.4%), and chronic lung disease (37.8%) were key risk factors. *Nocardia otitidiscaviarum* (38.4%) was the most common species identified. Mortality was noted in 26% of the patients. Cotrimoxazole resistance and lack of cotrimoxazole use for treatment were associated with mortality.

Conclusions: Pulmonary nocardiosis presents diagnostic and therapeutic challenges in India, with high resistance rates and significant mortality. Improved diagnostic methods and region-specific treatment strategies are essential.

Keywords: Nocardia, immunocompromised, antimicrobial resistance, systematic review.

INTRODUCTION

Pulmonary nocardiosis is a rare but severe opportunistic infection caused by *Nocardia* species, ubiquitous in soil and organic matter [1]. *Nocardia* species are Gram-positive, modified acid-fast, saprophytic filamentous bacteria. Of the 100 species of *Nocardia*, more than 50 are of human clinical significance [2]. Identifying the prevalent species in the region is essential, as each species has subtle variations in clinical presentations and

therapeutic challenges [3, 4]. While the infection is primarily hypothesised to occur via inhalation, direct inoculation through the skin and ingestion may also occur [3, 5, 6]. The most common manifestation of nocardial disease is pulmonary nocardiosis, occurring in immunocompromised patients, patients with underlying chronic lung disease, chronic alcoholism, or diabetes mellitus [7-9]. Pulmonary nocardiosis has been described as a subacute or indolent disease, with symptoms present for days to several weeks before presentation. The clinical symptomatology is non-specific, mimicking other pulmonary diseases such as tuberculosis, fungal infections, or malignancies. Chest radiology features include

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unilateral or bilateral infiltrates, nodules, cavitation, and pleural effusions [9]. With an overall paucity of data on speciation, clinical features, and outcomes of pulmonary nocardiosis in the Indian context, there is a need to explore individual patients and their cumulative outcome patterns. This systematic review investigated the epidemiological traits, clinical profiles, antimicrobial resistance patterns, treatment approaches, and patient outcomes of pulmonary nocardiosis in India.

■ METHODOLOGY

The systematic review was started after it was registered in Prospero (Prospero registration number CRD42024543875). Our systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Searches were conducted across three major scientific databases (PubMed, Embase, and Web of Science). The search strategy used the specific string: nocardia* AND (lung OR pulmonary OR thoracic OR mediastinal OR chest OR respiratory) AND India. The review considered studies published over an extended time frame, from January 1960 to May 1, 2024, without imposing language restrictions, allowing for the inclusion of diverse relevant data sources. Studies were included if they reported cases of culture-confirmed pulmonary nocardiosis in India and provided individual case-level data. Studies were excluded if they lacked detailed clinical or microbiological data on individual cases. Additionally, preprints, conference abstracts, and non-human research were excluded.

Two independent reviewers conducted the screening process using the specialised software Rayyan.ai. In cases of disagreement, a third reviewer resolved conflicts. The details of the clinical presentation of the disease, the microbiological diagnoses, the antimicrobial resistance patterns, and the treatment outcomes of the patients were extracted. The data from the included studies were systematically coded and analysed using statistical software (SPSS v26) to generate meaningful insights.

Descriptive statistics were employed to summarise key findings, including calculating frequencies and percentages for categorical variables such as gender distribution, geographic origins (states

and cities), clinical symptoms, and therapeutic interventions. Those studies where the data for a particular variable was mentioned (present or absent) were included in the denominator. Those studies where the variable was not mentioned were excluded from the denominator. Mean and standard deviation or median and interquartile range were calculated for continuous variables such as age and duration of illness. Risk factors between the groups with and without mortality were analysed for comparative analyses. The chi-square test was used to compare categorical variables, while the independent t-test was employed for continuous variables. These statistical tests allowed for the identification of significant associations and patterns. The threshold for statistical significance was set at a p-value of <0.05. The quality and reliability of included case reports and case series were assessed using the JBI Critical Appraisal Tool [10].

■ RESULTS

Selection of articles

Three databases yielded 738 records, of which 386 duplicates were removed. After screening 352 titles and abstracts, 187 were excluded. Of the 165 reports sought for retrieval, 152 reports could be retrieved for full-text screening. After excluding 85 reports [conference abstracts (n=31), not proven on culture (n=18), non-pulmonary samples (n=17), articles not from India (n=9), unavailable individual case details (n=9), and retracted (n=1)], sixty-seven studies with 109 cases were finally included (Figure 1). The summary of the included 109 cases has been presented in Table 1.

Demography and risk factors

One hundred nine cases of pulmonary nocardiosis were included in this systematic review. The geographical distribution of cases highlighted Delhi (21.1%, 23/109), Karnataka (19.3%, 21/109), and Haryana (17.4%, 19/109) as the leading states reporting cases. Most cases involved male patients (69/93, 74.1%). Of the 97 patients whose age was reported, the mean age was 49.6 ± 16.9 years. Risk factors for pulmonary nocardiosis included diabetes mellitus (25/94, 26.6%), steroid use (55/107, 51.4%), and chronic lung diseases (31/82, 37.8%). A history of prior pulmonary tuberculosis (22/83, 26.5%) and Human immunodeficiency virus (HIV)

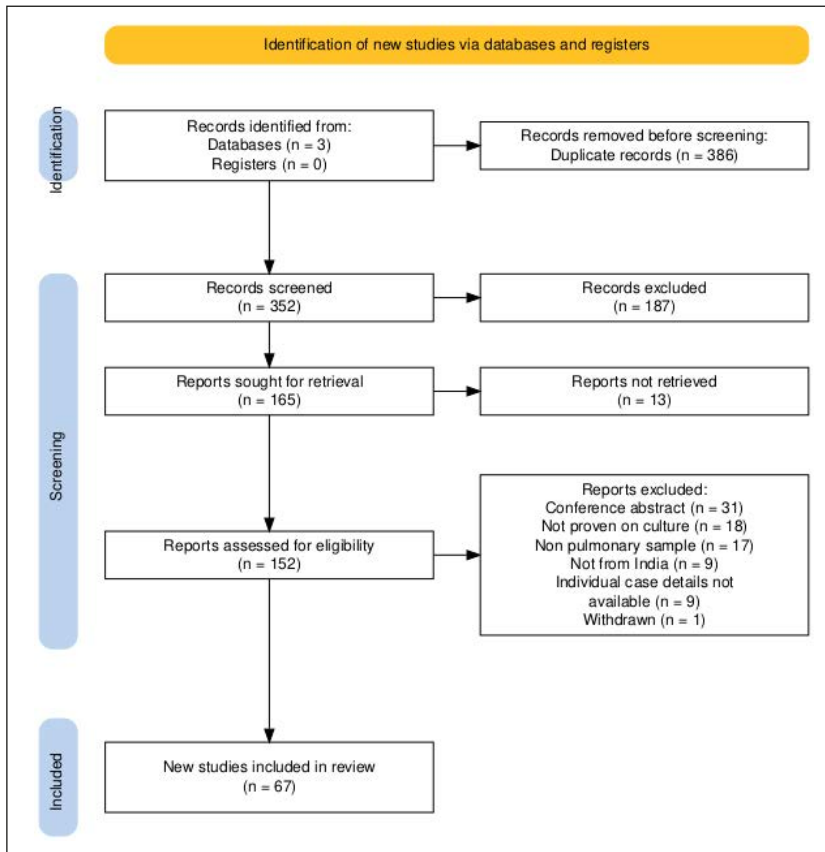


Figure 1
PRISMA flow chart showing screening and inclusion of articles [11].

infection (7/95, 7.4%) were also notable comorbidities. Except for two people, none of the patients were on cotrimoxazole prophylaxis (2.3%, 2/87) at the time of diagnosis of nocardiosis.

Clinical and microbiology features

Most patients had isolated pulmonary involvement (92%, 100/109). Additional neurological and skin involvement were present in 2% (n=2) and

Table 1 - Summary of the 109 cases of pulmonary nocardiosis from India.

Variables	Value
Total Patients	109
Mean Age (years)	49.6 ± 16.9
Median duration of illness (days)	15 (IQR: 8.5–52.5)
Risk Factor	Diabetes mellitus (25/94, 26.6%)
Presenting symptoms	Cough (82/88, 93.2%), Fever (66/88, 75%) most common
Chest X-ray Findings	Bilateral infiltrates (49/82, 59.8%) most common
Nocardia Species	<i>N. otitidiscaviarum</i> (15/39, 38.4%) most common
Identification Method	MALDI-TOF MS (15/39, 38.4%)
Susceptibility	linezolid (26/26, 100%), amikacin (38/40, 95%), imipenem (32/35, 91.4%), cotrimoxazole (37/47, 78.7%)
Outcome	Death: 25.5% (26/102)

5% (n=6) of the patients, respectively. The duration of illness was reported in 72 patients. The median duration of the disease was 15 (Interquartile range: 8.5–52.5) days. Cough (82/88, 93.2%) was the most reported symptom, followed by fever (66/88, 75%), dyspnoea (56/87, 64.4%), and hemoptysis (14/88, 15.9%). The infiltrates on CXR were predominantly bilateral (49/82, 59.8%). Cavity, pleural effusion, and hydropneumothorax were noted in 49% (38/77), 21% (16/77), and 4% (3/77) of the patients. Coinfections were observed in thirteen patients: five presenting with concurrent bacterial infections, three with tuberculosis and five with mould infections.

Microscopy was positive in 69/84 (82.1%) cases. Most cases were identified at the genus level, with species-level identification available only for a subset (n=39, 35.7%). Identification methods for species determination were biochemical testing (11/39, 28.2%), MALDI-TOF MS (15/39, 38.4%), and 16S rRNA sequencing (6/39, 15.4%). The susceptibility testing method was reported in 23/109 (21.1%) cases, with disk diffusion (22/109, 20.2%) as the commonest method, followed by the automated minimum inhibitory concentration method (1/109, 0.9%). The sensitivity to common antimicrobials in decreasing order was as follows: linezolid (26/26, 100%), amikacin (38/40, 95%), imipenem (32/35, 91.4%), fluoroquinolone (15/17, 88.2%), cotrimoxazole (37/47, 78.7%), ceftriaxone (11/16, 68.7%), and amoxicillin-clavulanate (6/13, 46.2%).

Treatment regimens

Mechanical ventilation was required in 29% (10/34) of the patients. The details of intravenous (IV) therapy were mentioned in 53 patients, 27 (51%) of which were combination therapy. The most common combination was cotrimoxazole with amikacin or carbapenems. The details of oral therapy were mentioned in 51 patients, 41 (80%) of which were monotherapy, with cotrimoxazole as the commonest oral agent. Of the 15 patients where the mode of administration was not mentioned, 8 (53%) were given as monotherapy. Of the 83 patients where treatment details were mentioned, the following antibiotics were used: cotrimoxazole (n=67, 81%), carbapenems (n=24, 29%), cephalosporins (n=17, 20%), aminoglycosides (n=16, 19%), linezolid (n=16, 19%), tetracyclines (n=12, 14%), amoxicillin-clavulanate (n=3, 4%),

fluoroquinolone (n=3, 4%), and macrolides (n=1, 1%). In the 34 patients where the average IV therapy duration was reported, it was 18 ± 11 days. In the 38 patients where the duration of oral therapy was reported, it was found to be 164 ± 84 days.

Comparison of survivors and non-survivors

Of the 109 cases, 100 had outcome data that could be classified clearly regarding mortality after excluding those lost to follow-up (n=2) or those where no outcome was reported (n=7) (Table 2). There were no differences between the two groups regarding age and comorbidities. Bilateral infiltrates on chest X-rays were present in 71.4% of patients who died as compared to 57% of the survivors. The difference was not significant ($p=0.263$). Cotrimoxazole susceptibility was significantly associated with reduced mortality ($p=0.018$). Other antimicrobial susceptibilities, such as amikacin, imipenem, and linezolid, did not impact survival. Cotrimoxazole use was associated with a significantly lower mortality rate (66.7% in deaths vs. 87.7% in survivors, $p=0.032$). Other treatments (cephalosporins, carbapenems, and aminoglycosides) did not exhibit statistically significant differences. The shorter duration of intravenous ($p=0.002$) and oral treatment ($p=0.004$) and the requirement for mechanical ventilation ($p=0.014$) were associated with mortality.

Cotrimoxazole resistance

The details of the ten patients with resistance to cotrimoxazole have been summarised in Table 3. Most (90%) of these patients had isolated pulmonary involvement, and none were on cotrimoxazole prophylaxis. Additional antibiotic resistance to carbapenems (n=4), fluoroquinolones (n=3), and third-generation cephalosporins (n=2) were also present in some of the cases. Despite resistance, cotrimoxazole was used in four patients. Treatments commonly included carbapenems, amoxicillin-clavulanate, and fluoroquinolones; however, outcomes were poor, with 60% of patients (n=6) succumbing to the infection.

Common species and patterns

N. otitidiscaviarum (15/39, 38.4%), *N. cyriacigeorgica* (6/39, 15.3%), *N. farcinica* (6/39, 15.3%), and *N. brasiliensis* (6/39, 15.3%) were the most frequently reported species (Figure 2). *Nocardia otitidiscaviarum* was the most prevalent species (38.4%), with

Table 2 - Univariate analysis comparing death and no death in patients with pulmonary nocardiosis.

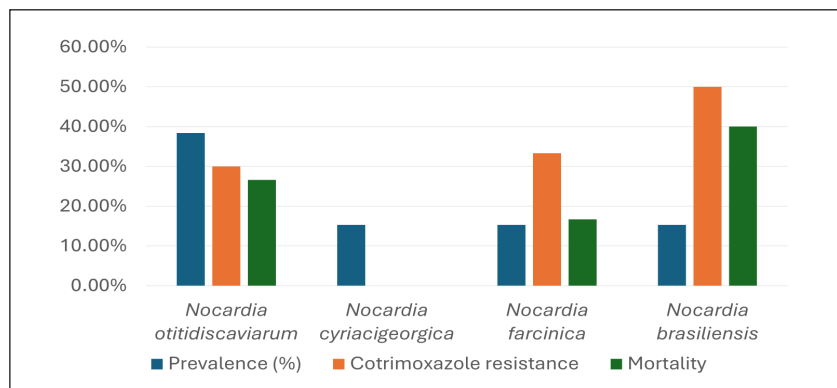
<i>Risk factors</i>	<i>Death (n=26)</i>	<i>Survivors (n=74)</i>	<i>p-value</i>
Age (n=88)	51.7±22.4	48.9±15.1	0.496
Diabetes Mellitus	8/23 (34.8%)	16/64 (25.0%)	0.368
Renal transplant recipient	4/26 (15.4%)	26/74 (35.1%)	0.059
Steroids	14/26 (53.8%)	39/73 (53.4%)	0.97
History of Pulmonary TB	6/22 (27.3%)	15/55 (27.3%)	1
Chronic Lung Diseases	9/21 (42.3%)	20/55 (36.4%)	0.79
Human Immunodeficiency Virus	1/24 (4.2%)	4/64 (6.2%)	0.707
Malignancy	0/24 (0.0%)	1/64 (1.6%)	0.538
Smoking	7/24 (29.2%)	6/64 (9.4%)	0.148
Duration of Illness (n=67)	22.5 (7-30)	15 (10-30)	0.932
Isolated pulmonary involvement	22/26 (84.6%)	69/74 (93.2%)	0.186
Fever	16/24 (66.7%)	44/57 (77.2%)	0.324
Cough	23/24 (95.8%)	52/57 (91.2%)	0.47
Haemoptysis	3/24 (12.5%)	11/57 (19.3%)	0.46
Dyspnoea	18/23 (78.3%)	37/57 (64.9%)	0.244
Bilateral infiltrates on Chest X-ray	15/21 (71.4%)	31/54 (57.4%)	0.263
Cavity	11/20 (55%)	25/52 (48%)	0.599
Pleural Effusion	4/19 (21%)	12/53 (22.6%)	0.886
Nocardia Bacteremia	1/6 (16.7%)	2/11 (18.2%)	0.938
Coinfections	4/26 (15.4%)	8/74 (10.8%)	0.537
<i>Cotrimoxazole Susceptible</i>	9/15 (60%)	27/30 (90%)	0.018
Amikacin Susceptible	11/11 (100.0%)	26/28 (92.9%)	0.363
Imipenem Susceptible	8/10 (80.0%)	24/25 (96.0%)	0.127
Linezolid Susceptible	7/7 (100.0%)	19/19 (100.0%)	1
Fluoroquinolone Susceptible	8/9 (88.9%)	7/7 (100.0%)	0.362
Ceftriaxone Susceptible	5/7 (71.4%)	6/8 (75.0%)	0.876
Amoxycillin clavulanate Susceptible	3/6 (50.0%)	3/7 (42.9%)	0.797
<i>Mechanical Ventilation</i>	6/10 (60%)	4/23 (17.4%)	0.014
<i>Intravenous duration (n=34)</i>	7±4.9	20.8±10.6	0.002
<i>Oral duration (n=37)</i>	2.5±2.1	170.7±75.8	0.004
<i>Cotrimoxazole treatment</i>	14/21 (66.7%)	50/57 (87.7%)	0.032
Cephalosporin treatment	3/21 (14.3%)	13/57 (22.8%)	0.408
Carbapenem treatment	8/21 (38.1%)	14/57 (24.6%)	0.239
Aminoglycoside treatment	4/21 (19.0%)	11/57 (19.3%)	0.98
Linezolid treatment	5/21 (23.8%)	11/57 (19.3%)	0.662
Amoxicillin-clavulanate treatment	1/21 (4.8%)	2/57 (3.5%)	0.799
Fluoroquinolone treatment	1/21 (4.8%)	2/57 (3.5%)	0.799
Macrolides treatment	0/21 (0.0%)	1/57 (1.8%)	0.541
Tetracycline treatment	4/21 (19.0%)	8/57 (14.0%)	0.586

Table 3 - Summary of details of patients with cotrimoxazole resistance.

Sn	Author	Comorbidities	Cot Proph	Isolated Pulmo	Species	Additional Resistance	Treatment	Outcome
1	Bhandari [12]	Renal SOT	No	Yes	<i>Nocardia farcinica</i>	NA	NA	Improved
2	Bhandari [12]	Renal SOT	No	Yes	<i>Nocardia farcinica</i>	NA	NA	Improved
3	Gupta [13]	DM	No	Yes	<i>Nocardia spp</i>	NA	cotrimoxazole, carbapenem, linezolid, minocycline	Improved
4	Saksena [14]		No	Yes	<i>Nocardia otitidiscaviarum</i>	carbapenem, Amoxyclav	cotrimoxazole	Death
5	Saksena [14]	Old PTB	No	Yes	<i>Nocardia otitidiscaviarum</i>	carbapenem, Amoxyclav	cotrimoxazole, carbapenem	Death
6	Princess [15]	Steroids, CLD	No	Yes	<i>Nocardia otitidiscaviarum</i>	Amoxyclav	cotrimoxazole, carbapenem	Death
7	Khare [16]	Steroids, CLD, Old PTB	No	Yes	<i>Nocardia brasiliensis</i>	FQ	carbapenem	Death
8	Prasad [17]	DM	No	No	<i>Nocardia spp.</i>	NA	3GC, FQ	Death
9	Wadhwa [18]	Steroids, CLD	NA	Yes	<i>Nocardia brasiliensis</i>	FQ, 3GC	3GC, AG	NA
10	Pannu [19]	Old PTB, CLD	No	Yes	<i>Nocardia brasiliensis</i>	NA	carbapenem	Death

Abbreviations: Sn- serial number, Cot Proph- Cotrimoxazole prophylaxis, Pulmo- pulmonary involvement, SOT: Solid Organ Transplant, DM: Diabetes Mellitus, CLD: Chronic Lung Disease, PTB: Pulmonary Tuberculosis, Cotrimoxazole (Trimethoprim-Sulfamethoxazole), FQ: Fluoroquinolones, 3GC: Third-Generation Cephalosporins, AG: Aminoglycosides, Amoxyclav: Amoxicillin-clavulanate, NA: Not Available.

Figure 2
Prevalence, resistance and mortality patterns in the common *Nocardia* species.



30% cotrimoxazole resistance and a 26.6% mortality rate. *Nocardia cyriacigeorgica* had no resistance or mortality, while *Nocardia farcinica* showed 33.3% resistance and 16.7% mortality. *Nocardia brasiliensis* had the highest resistance (50%) and mortality (40%).

Critical appraisal of the included cases

Of the 109 cases, 71 (65%) provided complete information on demographics, history, presenta-

tion, diagnosis, treatment, and follow-up. The complete demographic data was missing in 30% of cases, and relevant clinical history was absent in 25%. The diagnostic details were well-documented in 85% of reports, while treatment details were included in 80%. Follow-up information on outcome was present in 90% of cases. We did not analyse the presence of adverse events in the study as it was not aligned with our objectives.

■ DISCUSSION

This systematic review highlights the current epidemiology and diagnostic/management practices of pulmonary nocardiosis in India. The disease predominantly affects middle-aged and older males, often with underlying risk factors such as diabetes, chronic lung diseases, or prolonged steroid use. Its clinical manifestations are non-specific, frequently mimicking other pulmonary conditions like tuberculosis or fungal infections, which can delay diagnosis. The high resistance to cotrimoxazole further complicates treatment, as resistance is associated with poorer outcomes. Despite advancements in diagnostic techniques, including molecular methods, species identification and antimicrobial susceptibility testing remain inconsistent in many cases.

One hundred and nine cases of pulmonary nocardiosis were included in this review. It was noted that most patients were males, possibly related to a higher prevalence of risk factors (e.g. smoking, chronic lung diseases) or higher environmental/occupational exposure. This aligns with most pre-existing literature [3, 10]. The mean age of our study population was 50 years, similar to other studies [21]. Risk factors for pulmonary nocardiosis included diabetes mellitus (26.6%), steroid use (51.4%), and chronic lung diseases (37.8%). In the study by Ninan *et al.*, 82% of the patients with nocardiosis had a history of intake of immunosuppressants [22]. A history of prior pulmonary tuberculosis (21.6%) was notable in this review, similar to the study by Chandrashekar *et al.* [23]. Most patients had isolated pulmonary involvement (92%). Additional neurological involvement was present in only two patients. In a large series of isolates from South India with limited clinical information, 8% of the patients with pulmonary nocardiosis had dissemination to the brain [22]. It is generally recommended to perform neuroimaging in all cases of pulmonary nocardiosis as the treatment in patients with neurological involvement is more intensive and longer. The rarity of neurological involvement in our review questions the need for an expensive investigation in resource-limited settings. It is, however, also possible that asymptomatic neurological involvement was missed in these cases. In a large study, neurological involvement was seen in up to 80% of cases, with approximately 40% of patients remaining asymptomatic

despite central nervous system (CNS) disease [24]. The median duration of illness was 15 (8.5-52.5) days. Classically, nocardiosis has been described as a subacute or chronic disease, but a first quartile of 8.5 days suggests the need to suspect nocardiosis even in patients with a short history. Cough (93.2%) was the most reported symptom, followed by fever (75%), dyspnoea (64.4%), and hemoptysis (15.9%). Bilateral infiltrates and cavities were commonly noted in chest radiology. Coinfections were reported in 13 cases. There was a trend towards higher mortality in cases with coinfections. Although the difference was insignificant, this data highlights the need to incorporate rigorous testing in patients who are not improving on treatment. The differential diagnoses of nocardiosis include tuberculosis, non-tuberculous mycobacteria, melioidosis, mucormycosis, aspergillosis, and pulmonary cryptococcosis. These conditions share common host susceptibility factors and exhibit overlapping clinical and radiological features, often necessitating microbiological confirmation for accurate diagnosis. Nevertheless, certain radiological features can aid in distinguishing fungal infections from nocardiosis. For instance, the presence of an air-crescent sign and vessel invasion leading to wedge-shaped opacities is more suggestive of fungal infections. In contrast, the reversed halo sign is non-specific and may be observed in all the differentials [25].

The laboratory diagnosis of nocardiosis has evolved from microscopy to advanced molecular methods. For the diagnostic pathway to be initiated, one requires strong suspicion from the physician. This is essential so that measures can be taken to improve the recognition and recovery of the organism. Modified acid-fast stains and Gram stains help provide rapid presumptive diagnosis while awaiting the results of the culture [26]. In our review, microscopy was positive in 82.1% of cases. Although *Actinomyces* can mimic *Nocardia* on gram stain due to its filamentous structure, these two organisms differ in that *Nocardia* is acid-fast, while *Actinomyces* is not. The smooth, chalky white colonies of nocardiosis may take 2 to 14 days to appear, suggesting the need for extended incubation [24]. Species-level data were absent from most of the included cases. We did not consider the isolates identified as *Nocardia asteroides* complex separate species because it is an outdated term for all clinically relevant nocardiosis. After

molecular advancements, they have been re-classified into separate species. In our review, *N. otitidiscaviarum*, *N. cyriacigeorgica*, *N. farcinica*, and *N. brasiliensis* were the most frequently reported species. In a study from Manipal (South India), *N. otitidiscaviarum* (23%) was the most common species [23]. In another study from Vellore (South India), *N. cyriacigeorgica* (35.4%) and *N. farcinica* (29%) were the most common species [22]. The review could not include both studies because of the lack of individual patient-level data.

Identifying *Nocardia* species is crucial for predicting antimicrobial susceptibility and guiding appropriate therapy. For instance, *Nocardia farcinica*, often associated with CNS involvement, is frequently resistant to third-generation cephalosporins [27]. Similarly, *Nocardia otitidiscaviarum* can be resistant to imipenem, as seen in some of the cases in our review [28]. The preferred method for antimicrobial susceptibility testing is broth microdilution [29]. It should be noted that micro broth dilution is unreliable for cotrimoxazole, and confirmation with disc diffusion is recommended [30]. In our review, disk diffusion (20.2%) was the most common susceptibility testing method. The significant resistance in cotrimoxazole mirrored the Manipal study's findings [23]. Various studies reveal cotrimoxazole resistance ranging from 2-60% [31-35]. Our review's *Nocardia* spp associated with cotrimoxazole resistance included *N. farcinica*, *N. otitidiscaviarum* and *N. brasiliensis*. Among the 10 patients with cotrimoxazole resistance, none were on cotrimoxazole prophylaxis. Despite resistance, cotrimoxazole was used in four patients. Only three patients with cotrimoxazole resistance improved, highlighting the high mortality associated with these resistant infections, particularly in individuals with significant comorbidities. High resistance to ceftriaxone and amoxicillin-clavulanate was noted in this review. However, it should be noted that false resistance to ceftriaxone and imipenem has been reported, especially with *N. cyriacigeorgica*, *N. wallacei* and *N. brasiliensis* [30].

We did not find any difference in age, risk factors, or clinical presentation between those who died and those who survived. Cotrimoxazole susceptibility was significantly associated with reduced mortality ($p=0.018$). Cotrimoxazole-treated patients had a significantly lower mortality rate. Other antimicrobial susceptibilities or treatments did not exhibit statistically significant differences.

Managing nocardiosis is complex due to the need for prolonged antibiotic therapy, potential drug interactions, and adverse effects [31]. Given varying resistance patterns, it is recommended to provide multidrug combination therapy in severe nocardiosis [32-35]. Resistance to cotrimoxazole, renal dysfunction, and neurological involvement further complicate the formulation of effective combination therapy. The adverse effects associated with cotrimoxazole and its interactions with commonly prescribed drugs make the management even more challenging. Despite reports of resistance, cotrimoxazole remains the drug of choice for mild infections and a part of combination therapy. Severe pulmonary disease needs treatment from 6-12 months. While both cotrimoxazole and linezolid have good CNS penetration, the side effects of linezolid might preclude long-term use [4, 33, 36]. However, in settings with high resistance to cotrimoxazole and uniform susceptibility to linezolid, it is prudent to keep linezolid in the treatment regimen. The optimal duration of treatment for nocardiosis remains undefined, although prolonged antibiotic courses are generally recommended, particularly for immunocompromised patients, those with neurological involvement, or infections caused by *Nocardia farcinica*. Recent studies indicate that patients with non-severe, isolated pulmonary disease can be effectively treated with a short course of antibiotics (3 months) without increased risk of relapse or mortality [37]. Individualised regimens are needed based on factors such as antibiotic resistance, disease severity, dissemination, and the degree of underlying immunosuppression.

The limitations of this systematic review include the inability to evaluate alcohol use as a potential risk factor due to inconsistent or missing data in the included studies. Additionally, species-level identification of *Nocardia* was mostly unavailable, limiting the analysis of species-specific variations in clinical presentation and outcomes. Micro broth dilution susceptibility testing was not performed in many reports, potentially impacting data accuracy on antimicrobial resistance patterns. Furthermore, CNS screening was inconsistently conducted in many cases, potentially underestimating the prevalence of CNS involvement. These limitations underscore the need for standardised reporting in future research.

In conclusion, the non-specific clinical and radio-

logical features, the apparent absence of neurological involvement, the need for invasive sampling, difficulties in isolation, speciation and antimicrobial susceptibility present significant diagnostic and therapeutic challenges in India. The considerable proportion of resistance to cotrimoxazole and its association with mortality makes it prudent to routinely test cotrimoxazole susceptibility and develop region-specific management approaches. There is a need to improve access to antimicrobial susceptibility testing, especially for micro broth dilution. Ongoing research and clinical trials are critical to optimising treatment regimens and understanding the long-term outcomes of this disease.

Conflict of interest

None.

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SUPPLEMENTARY TABLES

Supplementary Table 1 - Summary of demographic details and risk factors of patients with pulmonary nocardiosis.

<i>Sn</i>	<i>Author</i>	<i>State</i>	<i>Age</i>	<i>Gender</i>	<i>DOI (days)</i>	<i>DM</i>	<i>Renal</i>	<i>Steroids</i>	<i>Old PTB</i>	<i>CLD</i>	<i>HIV</i>	<i>Mx</i>	<i>Smoking</i>
1	Marak [38]	Bihar	36	M	X	N	Y	Y	X	X	N	N	N
2	Marak [38]	Bihar	36	F	X	N	Y	Y	X	X	N	N	N
3	Marak [38]	Bihar	48	F	X	N	Y	Y	X	X	N	N	N
4	Marak [38]	Bihar	62	M	X	Y	Y	Y	X	X	N	N	N
5	Marak [38]	Bihar	50	M	X	Y	Y	Y	X	X	N	N	N
6	Marak [38]	Bihar	66	M	X	Y	Y	Y	X	X	N	N	N
7	Marak [38]	Bihar	31	M	X	Y	Y	Y	X	X	N	N	N
8	Gupta [13]	Maharashtra	56	M	1	N	N	N	Y	N	N	N	Y
9	Bhat [39]	Karnataka	71	M	X	Y	N	Y	N	X	N	N	N
10	Vaddepally [40]	Telangana	70	M	14	N	N	Y	N	X	N	N	N
11	Sachdeva [41]	Haryana	66	M	21	N	N	N	Y	Y	N	N	N
12	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
13	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
14	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
15	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
16	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
17	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
18	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
19	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
20	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
21	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
22	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
23	Bhandari [12]	Delhi	X	X	X	X	Y	Y	X	X	X	X	X
24	Sekar [42]	Haryana	0.66	M	30	X	N	N	N	N	N	N	N
25	Shabeen [43]	Kerala	59	M	90	N	Y	Y	N	N	N	N	N
26	Bansal [44]	Haryana	45	M	X	N	N	Y	X	Y	N	N	N
27	Bansal [44]	Haryana	31	F	X	N	N	Y	X	X	N	N	N
28	Bansal [44]	Haryana	55	F	X	Y	N	N	X	X	N	N	N
29	Bansal [44]	Haryana	42	M	X	N	N	N	N	Y	N	N	Y
30	Bansal [44]	Haryana	71	M	X	N	N	N	N	Y	N	N	Y
31	Bansal [44]	Haryana	72	M	X	N	N	Y	N	N	N	N	Y
32	Bansal [44]	Haryana	50	F	X	N	N	Y	N	Y	N	N	N
33	Reddy [45]	Telangana	54	M	30	Y	N	Y	N	N	N	N	N
34	Shah [46]	Gujarat	57	M	15	N	N	N	Y	N	N	N	N
35	Raj [47]	Karnataka	59	M	15	Y	N	N	N	N	N	N	N
36	Dutta [48]	West Bengal	42	M	60	N	Y	Y	N	N	N	N	N
37	Prabhudev [49]	Karnataka	38	F	14	N	N	N	N	Y	N	N	N
38	Gupta [50]	Karnataka	72	M	25	Y	N	N	N	N	N	N	Y
39	Saksena [14]	Delhi	70	F	30	N	N	N	N	N	N	N	N
40	Saksena [14]	Delhi	72	M	7	N	N	N	Y	N	N	N	Y
41	Meena [51]	Rajasthan	46	F	60	N	N	N	Y	Y	N	N	N
42	Chauhan [52]	Rajasthan	62	M	5	N	N	N	Y	Y	N	N	N
43	Princess [15]	Tamil Nadu	51	M	15	N	N	Y	N	Y	N	N	N
44	Singh [53]	Uttar Pradesh	36	F	7	N	N	N	N	N	N	N	N
45	Kumar [54]	Karnataka	70	M	10	N	N	N	N	Y	N	N	N
46	Thirouvengadame [55]	Puducherry	66	M	90	N	N	N	N	N	N	N	N
47	Arjun [56]	Kerala	61	M	21	N	N	N	N	N	N	Y	N
48	Balasubramanian [57]	Delhi	62	M	4	N	N	Y	N	Y	N	N	Y
49	Taneja [58]	Delhi	55	F	14	N	N	N	Y	N	N	N	N
50	Shariff [59]	Delhi	76	X	5	N	N	N	Y	Y	N	N	Y
51	Shariff [59]	Delhi	70	X	14	N	N	X	Y	Y	N	N	Y
52	Shariff [59]	Delhi	70	X	90	N	N	N	Y	N	N	N	N
53	Shariff [59]	Delhi	42	X	60	N	N	N	Y	N	N	N	N
54	Aggarwal [60]	Haryana	50	F	15	N	N	N	Y	Y	N	N	N
55	Aggarwal [60]	Haryana	72	M	90	N	N	Y	N	Y	N	N	Y
56	Aggarwal [60]	Haryana	42	M	20	N	N	Y	N	Y	N	N	N
57	Barve [61]	Maharashtra	52	M	30	Y	N	N	X	X	N	N	N
58	Meena [62]	Uttar Pradesh	45	M	10	N	N	N	N	Y	N	N	N
59	Soman [63]	Maharashtra	52	M	14	N	Y	Y	N	N	N	N	N
60	Qureshi [64]	Uttar Pradesh	49	M	60	Y	N	Y	N	Y	N	N	Y
61	Praharaj [65]	Tamil Nadu	30	M	60	N	N	Y	N	N	N	N	Y
62	Paty [66]	Odisha	18	M	356	N	N	N	Y	N	N	N	N
63	Misra [67]	Uttar Pradesh	37	M	6	Y	N	Y	N	N	N	N	N
64	Das [68]	Delhi	70	F	30	N	N	N	X	X	N	N	N
65	Khare [16]	Uttar Pradesh	85	M	10	N	N	Y	Y	Y	N	N	N
66	Patel [69]	Gujarat	50	M	15	Y	Y	Y	N	N	N	N	N
67	Patil [70]	Karnataka	47	M	4	Y	N	N	N	Y	N	N	N
68	Mali [71]	Maharashtra	46	F	8	N	N	Y	N	N	N	N	N
69	Shah [72]	Gujarat	43	M	75	N	N	N	N	N	Y	N	N
70	Prasad [17]	Uttar Pradesh	57	M	7	Y	N	N	N	N	N	N	N
71	Hathur [73]	Karnataka	60	M	30	N	N	Y	N	Y	N	N	Y
72	Ramamoorthi [74]	Karnataka	36	F	14	N	N	N	N	N	N	N	N
73	Rawat [75]	Uttarakhand	65	M	60	N	N	N	N	Y	N	N	N
74	Reddy [76]	Andhra Pradesh	36	M	10	Y	N	N	Y	N	Y	N	N
75	Parande [77]	Karnataka	27	M	150	N	N	N	N	N	Y	N	N
76	Gowrinath [78]	Karnataka	32	F	14	Y	Y	Y	N	N	N	N	N
77	Chawla [79]	Karnataka	23	M	30	N	Y	Y	N	N	N	N	N
78	Chawla [79]	Karnataka	17	M	7	N	Y	Y	N	N	N	N	N
79	Chawla [79]	Karnataka	57	M	3	N	N	N	Y	N	N	N	N
80	Chawla [79]	Karnataka	58	M	30	N	N	N	Y	N	N	N	N
81	Chawla [79]	Karnataka	35	F	30	N	N	N	N	N	Y	N	N
82	Chawla [79]	Karnataka	62	F	5	N	N	N	Y	Y	N	N	N
83	Chawla [79]	Karnataka	36	M	30	N	N	N	Y	N	N	N	N
84	Chandrashekar [80]	Karnataka	35	F	30	N	N	N	N	N	Y	N	N
85	Chaudhury [81]	Madhya Pradesh	45	F	90	N	N	N	N	N	N	Y	N
86	Tilak [82]	Uttar Pradesh	32	F	600	N	N	N	Y	N	N	N	N
87	Gowrinath [83]	Karnataka	23	M	10	N	Y	Y	N	N	N	N	N
88	Gowrinath [83]	Karnataka	17	M	7	Y	Y	Y	N	N	N	N	N
89	Wadhwa [18]	Delhi	42	M	5	N	N	Y	N	Y	N	N	N
90	Gowrinath [84]	Tamil Nadu	47	M	60	Y	N	N	N	N	N	N	N
91	Venugopal [85]	Tamil Nadu	57	M	X	X	X	X	X	X	N	N	N
92	Venugopal [85]	Tamil Nadu	35	M	X	X	X	X	X	X	N	N	N
93	Dhanasekar [86]	Tamil Nadu	67	M	10	N	N	N	N	N	N	N	N
94	George [87]	Karnataka	48	M	120	N	N	N	N	N	Y	N	N
95	Shah [88]	Maharashtra	63	F	10	N	N	Y	Y	N	N	N	N
96	Subhash [89]	Tamil Nadu	27	M	60	N	N	N	N	N	Y	N	N
97	Shivaprakash [90]	Haryana	40	F	X	Y	Y	Y	N	N	N	N	N
98	Shivaprakash [90]	Haryana	26	M	X	N	N	Y	N	N	N	N	N
99	Shivaprakash [90]	Haryana	64	M	X	N	N	Y	N	Y	N	N	N
100	Shivaprakash [90]	Haryana	45	M	X	Y	N	Y	N	N	N	N	N
101	Shivaprakash [90]	Haryana	11	M	X	N	N	Y	N	N	N	N	N
102	Manoharan [91]	Tamil Nadu	40	M	X	N	N	Y	N	Y	N	N	N
103	Manoharan [91]	Tamil Nadu	28	F	X	N	N	N	N	Y	N	N	N
104	Mohanty [92]	Uttarakhand	62	F	4	Y	N	N	N	N	N	N	N
105	Pannu [19]	Haryana	65	M	7	N	N	N	Y	Y	N	N	Y
106	Ranjan [93]	Haryana	75	M	30	Y	N	N	N	N	N	N	N
107	Sharma [94]	Delhi	70	M	5	Y	N	Y	N	Y	N	N	N
108	Kanakan [95]	Uttar Pradesh	75	M	20	Y	N	N	N	Y	N	N	N
109	Gandham [96]	Maharashtra	41	M	X	N	Y	Y	N	N	N	N	N

Abbreviations: Sn-Serial number, Y-Yes, N-No, X- No data available, DOI- Duration of illness, Renal- Renal transplant recipient, DM- Diabetes mellitus, Mx- Malignancy, CLD- Chronic Lung disease, HIV- Human Immunodeficiency Virus.

Supplementary Table 2 - Summary of clinical profile of patients with pulmonary nocardiosis.

<i>Sn</i>	<i>Author</i>	<i>Fever</i>	<i>Cough</i>	<i>Haemoptysis</i>	<i>Dyspnoea</i>	<i>CXR</i>
1	Gupta [13]	Y	Y	N	Y	B/L
2	Bhat [39]	Y	Y	N	Y	B/L
3	Vaddepally [40]	Y	Y	N	Y	U/L
4	Sachdeva [41]	Y	Y	N	Y	B/L
5	Sekar [42]	Y	Y	N	Y	X
6	Shabeen [43]	Y	Y	N	Y	U/L
7	Bansal [44]	Y	Y	N	Y	X
8	Bansal [44]	Y	Y	N	Y	X
9	Bansal [44]	Y	Y	N	N	B/L
10	Bansal [44]	Y	Y	N	N	B/L
11	Bansal [44]	Y	Y	N	N	U/L
12	Bansal [44]	N	Y	N	Y	X
13	Bansal [44]	N	Y	N	Y	B/L
14	Reddy [45]	Y	Y	N	N	U/L
15	Shah [46]	Y	Y	N	Y	U/L
16	Raj [47]	Y	Y	N	Y	B/L
17	Dutta [48]	Y	Y	N	Y	B/L
18	Prabhudev [49]	Y	Y	N	Y	B/L
19	Gupta [50]	Y	Y	N	Y	B/L
20	Saksena [14]	Y	Y	N	Y	B/L
21	Saksena [14]	Y	Y	N	Y	B/L
22	Meena [51]	Y	Y	N	Y	B/L
23	Chauhan [52]	Y	Y	N	Y	B/L
24	Princess [15]	Y	Y	N	Y	B/L
25	Singh [53]	Y	N	Y	Y	U/L
26	Kumar [54]	N	Y	N	Y	B/L
27	Thirouvengadame [55]	N	Y	N	Y	B/L
28	Arjun [56]	Y	Y	Y	N	B/L
29	Balasubramanian [57]	Y	Y	N	Y	B/L
30	Taneja [58]	Y	Y	Y	N	B/L
31	Shariff [59]	N	Y	N	Y	B/L
32	Shariff [59]	Y	Y	N	Y	B/L
33	Shariff [59]	Y	Y	N	Y	U/L
34	Shariff [59]	Y	Y	N	N	U/L
35	Aggarwal [60]	N	Y	N	Y	B/L
36	Aggarwal [60]	N	Y	N	Y	B/L
37	Aggarwal [60]	Y	Y	N	Y	B/L
38	Barve [61]	Y	Y	N	X	B/L
39	Meena [62]	Y	Y	N	Y	U/L
40	Soman [63]	Y	Y	N	N	U/L
41	Qureshi [64]	Y	Y	N	Y	B/L
42	Praharaj [65]	Y	Y	N	Y	U/L
43	Paty [66]	N	Y	Y	N	U/L
44	Misra [67]	N	N	N	N	B/L
45	Das [68]	Y	Y	N	Y	X
46	Khare [16]	Y	Y	N	Y	B/L
47	Patel [69]	Y	Y	N	N	U/L
48	Patil [70]	Y	Y	N	N	U/L
49	Mali [71]	N	Y	N	Y	B/L
50	Shah [72]	Y	Y	N	Y	B/L
51	Prasad [17]	Y	Y	N	N	U/L
52	Hathur [73]	N	Y	N	Y	B/L
53	Ramamoorthi [74]	Y	Y	Y	Y	U/L
54	Rawat [75]	Y	Y	N	N	U/L
55	Reddy [76]	Y	Y	N	N	U/L
56	Parande [77]	N	Y	N	N	U/L
57	Gowrinath [78]	Y	Y	N	Y	U/L
58	Chawla [79]	N	Y	N	N	B/L
59	Chawla [79]	N	Y	Y	Y	B/L
60	Chawla [79]	N	N	Y	N	U/L
61	Chawla [79]	N	N	Y	Y	U/L
62	Chawla [79]	N	N	N	Y	U/L
63	Chawla [79]	Y	Y	Y	Y	B/L
64	Chawla [79]	Y	Y	Y	N	U/L
65	Chandrashekar [80]	Y	Y	N	Y	B/L
66	Chaudhury [81]	N	Y	N	N	U/L
67	Tilak [82]	N	Y	Y	Y	U/L
68	Gowrinath [83]	Y	Y	N	N	B/L
69	Gowrinath [83]	Y	Y	N	Y	B/L
70	Wadhwa [18]	Y	Y	N	Y	B/L
71	Gowrinath [84]	N	Y	N	N	U/L
72	Dhanasekar [86]	Y	Y	N	N	U/L
73	George [87]	Y	Y	N	N	B/L
74	Shah [88]	Y	Y	N	N	U/L
75	Subhash [89]	Y	Y	N	N	U/L
76	Shivaprakash [90]	N	Y	N	N	B/L
77	Shivaprakash [90]	Y	Y	Y	N	B/L
78	Shivaprakash [90]	Y	Y	N	Y	B/L
79	Shivaprakash [90]	Y	Y	N	Y	U/L
80	Shivaprakash [90]	Y	Y	Y	N	U/L
81	Manoharan [91]	Y	Y	Y	N	B/L
82	Manoharan [91]	Y	N	N	Y	B/L
83	Mohanty [92]	N	Y	N	Y	X
84	Pannu [19]	Y	Y	N	Y	B/L
85	Ranjan [93]	Y	Y	N	Y	B/L
86	Sharma [94]	Y	Y	N	Y	B/L
87	Kanakan [95]	Y	Y	N	Y	U/L
88	Gandham [96]	Y	Y	N	N	B/L

Abbreviations: Sn-Serial number, Y-Yes, N-No, X- No data available, CXR- Chest X-ray, U/L- Unilateral, B/L-Bilateral.

Supplementary Table 3 - Summary of culture and identification of patients with pulmonary nocardiosis

<i>Sn</i>	<i>Author</i>	<i>Stain</i>	<i>Species</i>	<i>Method of Species ID</i>
1	Marak [38]	Positive	<i>Nocardia farcinica</i>	MALDI-TOF MS
2	Marak [38]	Positive	<i>Nocardia</i>	MALDI-TOF MS
3	Marak [38]	Positive	<i>Nocardia</i>	MALDI-TOF MS
4	Marak [38]	Positive	<i>Nocardia</i>	MALDI-TOF MS
5	Marak [38]	Positive	<i>Nocardia</i>	MALDI-TOF MS
6	Marak [38]	Positive	<i>Nocardia</i>	MALDI-TOF MS
7	Marak [38]	Positive	<i>Nocardia cyriacigeorgica</i>	MALDI-TOF MS
8	Gupta [13]	Positive	<i>Nocardia otitidiscaviarum</i>	MALDI-TOF MS
9	Bhat [39]	Negative	<i>Nocardia</i>	X
10	Vaddepally [40]	Positive	<i>Nocardia</i>	X
11	Sachdeva [41]	Positive	<i>Nocardia otitidiscaviarum</i>	MALDI-TOF MS
12	Bhandari [12]	X	<i>Nocardia</i>	X
13	Bhandari [12]	X	<i>Nocardia</i>	X
14	Bhandari [12]	X	<i>Nocardia</i>	X
15	Bhandari [12]	X	<i>Nocardia</i>	X
16	Bhandari [12]	X	<i>Nocardia</i>	X
17	Bhandari [12]	X	<i>Nocardia</i>	X
18	Bhandari [12]	X	<i>Nocardia</i>	X
19	Bhandari [12]	X	<i>Nocardia</i>	X
20	Bhandari [12]	X	<i>Nocardia farcinica</i>	MALDI-TOF MS
21	Bhandari [12]	X	<i>Nocardia cyriacigeorgica</i>	MALDI-TOF MS
22	Bhandari [12]	X	<i>Nocardia farcinica</i>	MALDI-TOF MS
23	Bhandari [12]	X	<i>Nocardia wallacei</i>	MALDI-TOF MS
24	Sekar [42]	X	<i>Nocardia pseudobrasiliensis</i>	Molecular
25	Shabeen [43]	Negative	<i>Nocardia</i>	X
26	Bansal [44]	Positive	<i>Nocardia otitidiscaviarum</i>	Molecular
27	Bansal [44]	Negative	<i>Nocardia</i>	X
28	Bansal [44]	Positive	<i>Nocardia</i>	X
29	Bansal [44]	Positive	<i>Nocardia</i>	X
30	Bansal [44]	Negative	<i>Nocardia</i>	X
31	Bansal [44]	Positive	<i>Nocardia</i>	X
32	Bansal [44]	Positive	<i>Nocardia</i>	X
33	Reddy [45]	Positive	<i>Nocardia</i>	X
34	Shah [46]	Negative	<i>Nocardia</i>	X
35	Raj [47]	Negative	<i>Nocardia</i>	X
36	Dutta [48]	Positive	<i>Nocardia cyriacigeorgica</i>	MALDI-TOF MS
37	Prabhudev [49]	Positive	<i>Nocardia</i>	X
38	Gupta [50]	Positive	<i>Nocardia</i>	MALDI-TOF MS
39	Saksena [14]	Positive	<i>Nocardia otitidiscaviarum</i>	MALDI-TOF MS
40	Saksena [14]	Positive	<i>Nocardia otitidiscaviarum</i>	MALDI-TOF MS
41	Meena [51]	Positive	<i>Nocardia</i>	X
42	Chauhan [52]	Positive	<i>Nocardia</i>	X
43	Princess [15]	Positive	<i>Nocardia otitidiscaviarum</i>	MALDI-TOF MS
44	Singh [53]	Positive	<i>Nocardia</i>	X
45	Kumar [54]	Positive	<i>Nocardia</i>	X
46	Thirouvengadame [55]	Positive	<i>Nocardia otitidiscaviarum</i>	Molecular
47	Arjun [56]	Positive	<i>Nocardia cyriacigeorgica</i>	MALDI-TOF MS
48	Balasubramanian [57]	Positive	<i>Nocardia</i>	X
49	Taneja [58]	Positive	<i>Nocardia otitidiscaviarum</i>	Biochemical
50	Shariff [59]	Positive	<i>Nocardia</i>	X
51	Shariff [59]	Positive	<i>Nocardia</i>	X
52	Shariff [59]	Positive	<i>Nocardia</i>	X
53	Shariff [59]	Positive	<i>Nocardia</i>	X
54	Aggarwal [60]	Positive	<i>Nocardia</i>	X
55	Aggarwal [60]	Negative	<i>Nocardia</i>	X
56	Aggarwal [60]	Negative	<i>Nocardia</i>	X
57	Barve [61]	Negative	<i>Nocardia</i>	X
58	Meena [62]	Positive	<i>Nocardia farcinica</i>	Molecular
59	Soman [63]	Positive	<i>Nocardia</i>	X
60	Qureshi [64]	Positive	<i>Nocardia</i>	X
61	Praharaj [65]	Positive	<i>Nocardia</i>	Biochemical
62	Paty [66]	Positive	<i>Nocardia</i>	Biochemical
63	Misra [67]	Negative	<i>Nocardia</i>	X
64	Das [68]	Positive	<i>Nocardia</i>	X
65	Khare [16]	Positive	<i>Nocardia brasiliensis</i>	Biochemical
66	Patel [69]	Positive	<i>Nocardia</i>	X
67	Patil [70]	Negative	<i>Nocardia</i>	X
68	Mali [71]	Positive	<i>Nocardia</i>	Biochemical
69	Shah [72]	Positive	<i>Nocardia</i>	Biochemical
70	Prasad [17]	Negative	<i>Nocardia</i>	Biochemical
71	Hathur [73]	Positive	<i>Nocardia</i>	X
72	Ramamoorthi [74]	Negative	<i>Nocardia otitidiscaviarum</i>	Biochemical
73	Rawat [75]	Positive	<i>Nocardia brasiliensis</i>	Biochemical
74	Reddy [76]	Positive	<i>Nocardia</i>	X
75	Parande [77]	Positive	<i>Nocardia farcinica</i>	X
76	Gowrinath [78]	Positive	<i>Nocardia farcinica</i>	X
77	Chawla [79]	X	<i>Nocardia otitidiscaviarum</i>	Biochemical
78	Chawla [79]	X	<i>Nocardia otitidiscaviarum</i>	Biochemical
79	Chawla [79]	X	<i>Nocardia</i>	Biochemical
80	Chawla [79]	X	<i>Nocardia</i>	Biochemical
81	Chawla [79]	X	<i>Nocardia</i>	Biochemical
82	Chawla [79]	X	<i>Nocardia otitidiscaviarum</i>	Biochemical
83	Chawla (48)	X	<i>Nocardia otitidiscaviarum</i>	Biochemical
84	Chandrashekar [80]	Positive	<i>Nocardia</i>	X
85	Chaudhury [81]	Positive	<i>Nocardia</i>	X
86	Tilak [82]	Positive	<i>Nocardia</i>	X
87	Gowrinath [83]	Negative	<i>Nocardia otitidiscaviarum</i>	Biochemical
88	Gowrinath [83]	Positive	<i>Nocardia otitidiscaviarum</i>	Biochemical
89	Wadhwa [18]	Positive	<i>Nocardia brasiliensis</i>	Biochemical
90	Gowrinath [84]	Positive	<i>Nocardia</i>	Biochemical
91	Venugopal [85]	Positive	<i>Nocardia</i>	Biochemical
92	Venugopal [85]	Positive	<i>Nocardia</i>	Biochemical
93	Dhanasekar [86]	Positive	<i>Nocardia</i>	X
94	George [87]	Positive	<i>Nocardia</i>	X
95	Shah [88]	Positive	<i>Nocardia</i>	X
96	Subhash [89]	Positive	<i>Nocardia</i>	X
97	Shivaprakash [90]	X	<i>Nocardia brasiliensis</i>	X
98	Shivaprakash [90]	X	<i>Nocardia</i>	X
99	Shivaprakash [90]	X	<i>Nocardia</i>	X
100	Shivaprakash [90]	X	<i>Nocardia brasiliensis</i>	X
101	Shivaprakash [90]	X	<i>Nocardia</i>	X
102	Manoharan [91]	Positive	<i>Nocardia cyriacigeorgica</i>	X
103	Manoharan [91]	Positive	<i>Nocardia beijingensis</i>	X
104	Mohanty [92]	Positive	<i>Nocardia araoensis</i>	MALDI-TOF MS
105	Pannu [19]	Positive	<i>Nocardia brasiliensis</i>	X
106	Ranjan [93]	Positive	<i>Nocardia wallacei</i>	Molecular
107	Sharma [94]	Negative	<i>Nocardia</i>	X
108	Kanakan [95]	Positive	<i>Nocardia amamiensis</i>	Molecular
109	Gandham [96]	Positive	<i>Nocardia cyriacigeorgica</i>	MALDI-TOF MS

Abbreviations: Sn-Serial number, Y-Yes, N-No, X- No data available, ID-identificaton.

Supplementary Table 4 - JBI checklist of case series and case reports.

<i>Sn</i>	<i>Author</i>	<i>Demography</i>	<i>History</i>	<i>Presentation</i>	<i>Diagnosis</i>	<i>Treatment</i>	<i>Follow-up</i>	<i>Adverse event</i>
1	Marak [38]	No	No	No	Yes	No	Yes	NA
2	Marak [38]	No	No	No	Yes	No	Yes	NA
3	Marak [38]	No	No	No	Yes	No	Yes	NA
4	Marak [38]	No	No	No	Yes	No	Yes	NA
5	Marak [38]	No	No	No	Yes	No	Yes	NA
6	Marak [38]	No	No	No	Yes	No	Yes	NA
7	Marak [38]	No	No	No	Yes	No	Yes	NA
8	Gupta [13]	Yes	Yes	Yes	Yes	Yes	Yes	NA
9	Bhat [39]	No	Yes	Yes	Yes	Yes	Yes	NA
10	Vaddepally [40]	Yes	Yes	Yes	Yes	Yes	Yes	NA
11	Sachdeva [41]	Yes	Yes	Yes	Yes	Yes	Yes	NA
12	Bhandari [12]	No	No	No	No	No	Yes	NA
13	Bhandari [12]	No	No	No	No	No	Yes	NA
14	Bhandari [12]	No	No	No	No	No	Yes	NA
15	Bhandari [12]	No	No	No	No	No	Yes	NA
16	Bhandari [12]	No	No	No	No	No	Yes	NA
17	Bhandari [12]	No	No	No	No	No	Yes	NA
18	Bhandari [12]	No	No	No	No	No	Yes	NA
19	Bhandari [12]	No	No	No	No	No	Yes	NA
20	Bhandari [12]	No	No	No	No	No	Yes	NA
21	Bhandari [12]	No	No	No	No	No	Yes	NA
22	Bhandari [12]	No	No	No	No	No	Yes	NA
23	Bhandari [12]	No	No	No	No	No	Yes	NA
24	Sekar [42]	No	Yes	No	No	No	Yes	NA
25	Shabeen [43]	Yes	Yes	Yes	Yes	Yes	Yes	NA
26	Bansal [44]	No	Yes	No	Yes	Yes	Yes	NA
27	Bansal [44]	No	Yes	No	Yes	Yes	Yes	NA
28	Bansal [44]	No	Yes	Yes	Yes	Yes	No	NA
29	Bansal [44]	No	Yes	Yes	Yes	Yes	Yes	NA
30	Bansal [44]	No	Yes	Yes	Yes	Yes	No	NA
31	Bansal [44]	No	Yes	No	Yes	Yes	Yes	NA
32	Bansal [44]	No	Yes	Yes	Yes	Yes	Yes	NA
33	Reddy [45]	Yes	Yes	Yes	Yes	Yes	Yes	NA
34	Shah [46]	Yes	Yes	Yes	Yes	Yes	Yes	NA
35	Raj [47]	Yes	Yes	Yes	Yes	Yes	Yes	NA
36	Dutta [48]	Yes	Yes	Yes	Yes	Yes	Yes	NA
37	Prabhudev [49]	Yes	Yes	Yes	Yes	Yes	Yes	NA
38	Gupta [50]	Yes	Yes	Yes	Yes	Yes	Yes	NA
39	Saksena [14]	Yes	Yes	Yes	Yes	Yes	Yes	NA
40	Saksena [14]	Yes	Yes	Yes	Yes	Yes	Yes	NA
41	Meena [51]	Yes	Yes	Yes	Yes	Yes	Yes	NA
42	Chauhan [52]	Yes	Yes	Yes	Yes	Yes	Yes	NA
43	Princess [15]	Yes	Yes	Yes	Yes	Yes	Yes	NA
44	Singh [53]	Yes	Yes	Yes	Yes	Yes	Yes	NA
45	Kumar [54]	Yes	Yes	Yes	Yes	Yes	Yes	NA
46	Thirouvengadame [55]	Yes	Yes	Yes	Yes	Yes	Yes	NA
47	Arjun [56]	Yes	Yes	Yes	Yes	Yes	Yes	NA
48	Balasubramanian [57]	Yes	Yes	Yes	Yes	Yes	Yes	NA
49	Taneja [58]	Yes	Yes	Yes	Yes	Yes	Yes	NA
50	Shariff [59]	Yes	Yes	Yes	Yes	Yes	Yes	NA
51	Shariff [59]	Yes	Yes	Yes	Yes	Yes	Yes	NA
52	Shariff [59]	Yes	Yes	Yes	Yes	Yes	Yes	NA
53	Shariff [59]	Yes	Yes	Yes	Yes	Yes	Yes	NA
54	Aggarwal [60]	Yes	Yes	Yes	Yes	Yes	Yes	NA
55	Aggarwal [60]	Yes	Yes	Yes	Yes	Yes	Yes	NA
56	Aggarwal [60]	Yes	Yes	Yes	Yes	Yes	Yes	NA
57	Barve [61]	Yes	Yes	Yes	Yes	Yes	Yes	NA
58	Meena [62]	Yes	Yes	Yes	Yes	Yes	Yes	NA
59	Soman [63]	Yes	Yes	Yes	Yes	Yes	Yes	NA
60	Qureshi [64]	Yes	Yes	Yes	Yes	Yes	Yes	NA
61	Praharaj [65]	Yes	Yes	Yes	Yes	Yes	Yes	NA
62	Paty [66]	Yes	Yes	Yes	Yes	Yes	Yes	NA
63	Misra [67]	Yes	Yes	Yes	Yes	Yes	Yes	NA
64	Das [68]	Yes	Yes	No	Yes	Yes	Yes	NA
65	Khare [16]	Yes	Yes	Yes	Yes	Yes	Yes	NA
66	Patel [69]	Yes	Yes	Yes	Yes	Yes	Yes	NA
67	Patil [70]	Yes	Yes	Yes	Yes	Yes	Yes	NA
68	Mali [71]	Yes	Yes	Yes	Yes	Yes	Yes	NA
69	Shah [72]	Yes	Yes	Yes	Yes	Yes	Yes	NA
70	Prasad [17]	Yes	Yes	Yes	Yes	Yes	Yes	NA
71	Hathur [73]	Yes	Yes	Yes	Yes	Yes	Yes	NA
72	Ramamoorthi [74]	Yes	Yes	Yes	Yes	Yes	Yes	NA
73	Rawat [75]	Yes	Yes	Yes	Yes	Yes	Yes	NA
74	Reddy [76]	Yes	Yes	Yes	Yes	Yes	Yes	NA
75	Parande [77]	Yes	Yes	Yes	Yes	Yes	Yes	NA
76	Gowrinath [78]	Yes	Yes	Yes	Yes	Yes	Yes	NA
77	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
78	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
79	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
80	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
81	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
82	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
83	Chawla [79]	Yes	Yes	Yes	Yes	Yes	Yes	NA
84	Chandrashekar [80]	Yes	Yes	Yes	Yes	Yes	Yes	NA
85	Chaudhury [81]	Yes	Yes	Yes	Yes	No	No	NA
86	Tilak [82]	Yes	Yes	Yes	Yes	No	Yes	NA
87	Gowrinath [83]	Yes	Yes	Yes	Yes	Yes	Yes	NA
88	Gowrinath [83]	Yes	Yes	Yes	Yes	Yes	Yes	NA
89	Wadhwa [18]	Yes	Yes	Yes	Yes	Yes	No	NA
90	Gowrinath [84]	Yes	Yes	Yes	Yes	Yes	Yes	NA
91	Venugopal [85]	No	No	No	Yes	No	No	NA
92	Venugopal [85]	No	No	No	Yes	No	No	NA
93	Dhanasekar [86]	Yes	Yes	Yes	Yes	Yes	Yes	NA
94	George [87]	Yes	Yes	Yes	Yes	No	No	NA
95	Shah [88]	Yes	Yes	Yes	Yes	Yes	No	NA
96	Subhash [89]	Yes	Yes	Yes	Yes	Yes	No	NA
97	Shivaprakash [90]	No	Yes	Yes	Yes	Yes	Yes	NA
98	Shivaprakash [90]	No	Yes	Yes	Yes	Yes	Yes	NA
99	Shivaprakash [90]	No	Yes	Yes	Yes	Yes	Yes	NA
100	Shivaprakash [90]	No	Yes	Yes	Yes	Yes	Yes	NA
101	Shivaprakash [90]	No	Yes	Yes	Yes	Yes	Yes	NA
102	Manoharan [91]	No	Yes	Yes	Yes	Yes	Yes	NA
103	Manoharan [91]	No	Yes	Yes	Yes	Yes	Yes	NA
104	Mohanty [92]	Yes	Yes	No	Yes	Yes	Yes	NA
105	Pannu [19]	Yes	Yes	Yes	Yes	Yes	Yes	NA
106	Ranjan [93]	Yes	Yes	Yes	Yes	No	Yes	NA
107	Sharma [94]	Yes	Yes	Yes	Yes	Yes	Yes	NA
108	Kanakan [95]	Yes	Yes	Yes	Yes	Yes	Yes	NA
109	Gandham [96]	No	Yes	Yes	Yes	Yes	Yes	NA