Annals of Clinical Microbiology and Antimicrobials

REVIEW

Open Access

# Clinical characteristics and drug resistance of *Nocardia* in Henan, China, 2017–2023

Yungang Han[1,2], Meijin Cheng[1,2], Zheng Li[1,2], Huihui Chen[1,2], Shuang Xia[1,2], Yue Zhao[1,2], Yali Wang[1,2], Wenyi He[1,2] and Wei Wang[1,2*]

## Abstract

**Background** The aim of this study was to investigate the clinical features of *Nocardia* infections, antibiotic resistance profile, choice of antibiotics and treatment outcome, among others. In addition, the study compared the clinical and microbiological characteristics of nocardiosis in bronchiectasis patients and non-bronchiectasis patients.

**Methods** Detailed clinical data were collected from the medical records of 71 non-duplicate nocardiosis patients from 2017 to 2023 at a tertiary hospital in Zhengzhou, China. *Nocardia* isolates were identified to the species level using MALDI-TOF MS and 16S rRNA PCR sequencing. Clinical data were collected from medical records, and drug susceptibility was determined using the broth microdilution method.

**Results** Of the 71 cases of nocardiosis, 70 (98.6%) were diagnosed as pulmonary infections with common underlying diseases including bronchiectasis, tuberculosis, diabetes mellitus and chronic obstructive pulmonary disease (COPD). Thirteen different strains were found in 71 isolates, the most common of which were *N. farcinica* (26.8%) and *N. cyriacigeorgica* (18.3%). All *Nocardia* strains were 100% susceptible to both TMP-SMX and linezolid, and different *Nocardia* species showed different patterns of drug susceptibility in vitro. Pulmonary nocardiosis is prone to comorbidities such as bronchiectasis, diabetes mellitus, COPD, etc., and *Nocardia* is also frequently accompanied by co-infection of the body with pathogens such as *Mycobacterium* and *Aspergillus spp*. Sixty-one patients underwent a detailed treatment regimen, of whom 32 (52.5%) received single or multi-drug therapy based on TMP-SMX. Bronchiectasis was associated with a higher frequency of *Nocardia* infections, and there were significant differences between the bronchiectasis and non-bronchiectasis groups in terms of age distribution, clinical characteristics, identification of *Nocardia* species, and antibiotic susceptibility ($P < 0.05$).

**Conclusions** Our study contributes to the understanding of the species diversity of *Nocardia* isolates in Henan, China, and the clinical characteristics of patients with pulmonary nocardiosis infections. Clinical and microbiologic differences between patients with and without bronchiectasis. These findings will contribute to the early diagnosis and treatment of patients.

**Keywords** *Nocardia*, Identification, Drug susceptibility testing, Treatment, Underlying conditions, Bronchiectasis

## Introduction

*Nocardia*, a Gram-positive filamentous bacterium, is commonly found in soil, water, and air [1, 2]. It can enter the body through inhalation of hyphal fragments, broken skin, or the digestive tract, leading to pneumonia, brain abscesses, and skin and soft tissue infections [1]. Hosts with suppressed immune function, such as those on long-term glucocorticoid therapy, patients undergoing

*Correspondence:
Wei Wang
jyk2785@163.com
[1] Key Laboratory of Medical Laboratory, Henan Provincial Chest Hospital, Affiliated Chest Hospital of Zhengzhou University, Zhengzhou, China
[2] Henan Provincial Medical Key Disciplines (Laboratory Diagnostics), Henan Provincial Chest Hospital, Zhengzhou, China

radiotherapy and chemotherapy for malignant tumors, organ transplantation and hematopoietic stem cell transplantation recipients, and individuals infected with human immunodeficiency virus (HIV), often develop primary pulmonary infections [3]. Non-immunosuppressed hosts primarily suffer from structural lung diseases like cystic fibrosis and bronchiectasis [4, 5].The distribution of *Nocardia* species varies geographically [3]. There is limited research on the clinical characteristics of nocardiosis in mainland China, particularly regarding patient treatment, prognosis, species identification of *Nocardia*, and drug susceptibility testing [6, 7]. To address this knowledge gap, we conducted a retrospective study, collecting detailed clinical data on nocardiosis patients in a tertiary hospital in Henan over a 6-year period. Additionally, we performed species identification of all included *Nocardia* isolates using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) and genetic sequencing, as well as tested their antibiotic susceptibility spectrum. In recent years, the prevalence of pulmonary nocardiosis has significantly increased among patients with bronchiectasis. Although the exact reasons for this increase are not fully understood, they may be attributed to environmental exposure and microbial surveillance, among other factors [5]. Therefore, our study aimed to compare the clinical and microbiological characteristics between nocardiosis patients with and without bronchiectasis. To our knowledge, no studies comparing the characteristics of these two patient groups have been conducted in mainland China.

## Materials and methods

### Collection of bacterial strains

We conducted a retrospective analysis of 71 unique cases of *Nocardia* infection that occurred at Henan Chest Hospital from January 2017 to April 2023. These cases involved patients from 14 different cities in Henan Province. Patient medical records were collected, including demographic information, underlying diseases, co-infections, imaging data, laboratory data, antimicrobial treatment, and prognosis. The inclusion criteria for this study were as follows: *Nocardia* isolation from qualified sputum specimens with at least two positive cultures, or from lung tissue or bronchoalveolar lavage fluid (BALF) obtained under sterile operating conditions, along with the presence of clinical signs of infection and/or radiographic evidence (pulmonary, skin, and soft tissue) of organ involvement. The exclusion criteria included patients with only one positive sputum culture and cases where all *Nocardia* isolates originated from blood agar plate (BAP) culture and BACTEC-MGIT 960 culture system (MGIT960).

### Identification of strains

Suspected *Nocardia* specimens found in smear microscopy of clinical samples were inoculated onto BAP and incubated in a (35 ± 2) °C incubator for 1–7 days, with daily observations of growth. *Nocardia* identification was carried out based on colony morphology on the culture medium, positive Gram stain (Gram-positive branching, moniliform, and filamentous bacilli), acid-fast staining, and modified acid-fast staining for preliminary presumptive identification. Further species identification was performed using MALDI-TOF MS. In cases where MALDI-TOF MS failed to provide species-level identification, final identification was achieved through polymerase chain reaction (PCR) amplification and sequencing of the full length of the 16S rRNA gene. The 16S rRNA primers used were: forward primer (5'-AGA GTTTGATCCTGGCTCAG-3'), reverse primer (5'-CGG TTACCTTGTTACGACTT-3'), with an amplification length of approximately 1500 bp. The amplified products were purified by Sangon Biotech (Shanghai, China) and sequenced using an ABI 3730XL gene sequencer. At the species level, the identity of the PCR products was confirmed by searching the 16S rRNA gene sequence in the NCBI GenBank using BLAST software (http://www.ncbi.nlm.nih.gov). *Nocardia* isolates were considered identified at the species level when similarity values ≥ 99.0% were obtained.

### Antimicrobial susceptibility testing

Antibiotic susceptibility testing (AST) was performed using the microbroth dilution method provided by Thermo Fisher (USA). In brief, colonies growing on BAP were collected using a swab and suspended in deionized water. The turbidity was adjusted to a 0.5 McFarland standard by visual inspection or with the help of a Sensititre® Turbidimeter. Next, 50μL of the bacterial suspension was transferred into a test tube containing cation-adjusted Mueller–Hinton broth medium with TES buffer added, and mixed thoroughly. Subsequently, 100 μL of the bacterial suspension was transferred onto a drug susceptibility plate and incubated at 35℃ for 72 h. The results were then observed and the minimum inhibitory concentration (MIC) was determined based on the instructions provided on the drug susceptibility plate. Interpretations of the results were made according to clinical and laboratory standards institute (CLSI) recommendations for *Nocardia*. Quality control strains, *Staphylococcus aureus* ATCC29213 and *Escherichia coli* ATCC35218, were included in the testing. The MIC was defined as the lowest concentration of a drug that inhibited visible growth.

### Comparison between drug sensitivity data

Accurate identification of *Nocardia* species provides the potential to partially predict antimicrobial susceptibility and helps in the selection of appropriate therapeutic approaches, for this reason we we reviewed the literature with drug susceptibility data between 2014–2023, from which we chose four representative papers (large size, large number, reliable drug susceptibility methods, etc.) to do a cross-sectional comparative study with our findings and with CLSI M62 in the The results were compared with our study in a cross-sectional study and with the CLSI M62 drug susceptibility patterns of different *Nocardia* species to find out the similarities and differences between them.

### Statistical analysis

The MIC data for each antibiotic were recorded and analyzed using WHONET 5.6 software. The MIC50 and MIC90 were calculated as well. Additionally, data analysis was performed using SPSS 25.0 statistical software. Normally distributed measurement data were presented as mean ± standard deviation (x ± s), while non-normally distributed measurement data were presented as the median. A comparison was made between patients with bronchiectasis and those non-bronchiectasis in terms of the distribution, drug susceptibility, and clinical characteristics of *Nocardia* strains. Categorical variables were compared using the $x^2$ test or Fisher exact test.

## Results

### Demographic characteristics and geographical distribution

A total of 71 cases of nocardiosis were collected, with ages ranging from 18 to 85 years and an average age of 56 years. Among these cases, 31 (43.6%) were aged 60 years or older, including 42 males and 29 females. The majority of the patients were farmers (67.6%, 48), and the main department involved was respiratory medicine (60.6%, 43). The most common specimen sources were sputum (52.1%, 37) and alveolar lavage fluid (46.5%, 33). Please refer to Table 1 for more details. The geographical distribution of *Nocardia* is depicted in Fig. 1. The city with the highest number of sources was Zhengzhou (21), followed by Zhoukou (12), Zhumadian (9), Shangqiu and Xuchang (6 strains each), and the classification of *Nocardia* species in various municipalities shows different.

### Clinical characteristics

Among patients infected with *Nocardia*, 23.9% had a history of smoking, and 12.7% had a history of alcohol consumption. Out of 71 patients, 90.1% had at least one underlying disease. These included bronchiectasis (39), tuberculosis(16), type 2 diabetes (12), chronic obstructive

**Table 1** Basline characteristics of included patients

| Characteristics | N | (%) |
|---|---|---|
| Mean age (range) (ys) | 56(18–85) | |
| < 40 | 13/71 | 18.3 |
| 40–60 | 27/71 | 38 |
| ≥ 60 | 31/71 | 43.6 |
| Male sex | 42/71 | 59.2 |
| Occupational distribution | | |
| Farmer | 48/71 | 67.6 |
| Male sex | 29/48 | 60.4 |
| Urban workers | 18/71 | 25.4 |
| Others | 5/71 | 7 |
| Departmental distribution of isolated strains | | |
| Respiratory department | 43/71 | 60.6 |
| Tuberculosis departmen | 17/71 | 23.9 |
| Thoracic surgery | 6/71 | 8.5 |
| Outpatient | 4/71 | 5.6 |
| Cardiology department | 1/71 | 1.4 |
| Infection types and sample sources | | |
| Pulmonary nocardiosis | | |
| Sputum | 37/71 | 52.1 |
| Bronchoalveolar lavage fluid | 33/71 | 46.5 |
| *N. farcinica* | 18/71 | 25.4 |
| *N. cyriacigeorgica* | 13/71 | 18.3 |
| *N. abscessus* | 8/71 | 11.3 |
| *N. amamiensis* | 8/71 | 11.3 |
| *N. beijingensis* | 5/71 | 7 |
| *N. otitidiscaviarum* | 5/71 | 7 |
| *N. wallacei* | 3/71 | 4.2 |
| *N. asiatica* | 3/71 | 4.2 |
| *N. flavorosea* | 2/71 | 2.8 |
| *N. africana* | 2/71 | 2.8 |
| *N. rhamnosiphila* | 1/71 | 1.4 |
| *N.pseudobrasiliensis* | 1/71 | 1.4 |
| *N. puris* | 1/71 | 1.4 |
| Skin and subcutaneous nocardiosis | | |
| Skin and soft tissue pus | 1/71 | 1.4 |
| *N. farcinica* | 1/71 | 1.4 |
| Smoking history | 17/71 | 23.9 |
| History of drinking | 9/71 | 12.7 |
| Diseases history | | |
| Yes/No | 64/7 | 90.1/8.9 |
| Underlying diseases | | |
| Bronchiectasis | 39/71 | 54.9 |
| Pulmonary tuberculosis | 16/71 | 22.5 |
| Type 2 diabetes mellitus | 12/71 | 16.9 |
| COPD | 8/71 | 11.3 |
| Hypertension | 8/71 | 11.3 |
| Anemia | 5/71 | 7 |
| Coronary heart disease | 3/71 | 4.2 |
| Sjogren's syndrome | 1/71 | 1.4 |

**Table 1** (continued)

| Characteristics | N | (%) |
|---|---|---|
| Chest radiograph | | |
| Nodular or consolidative opacities | 66/66 | 100 |
| Cavitary lesion | 16/66 | 24.2 |
| Pleural effusion | 21/66 | 31.8 |
| Laboratory data | | |
| WBC increased | 22/65 | 33.8 |
| Increased proportion of NEU(%) | 39/65 | 60 |
| C-reactive protein elevation | 29/42 | 69 |
| Increased ESR | 24/31 | 77.4 |
| Co-infection | | |
| Yes/No | 37/34 | 52.1/47.9 |
| MTB | 16/37 | 43.2 |
| Fungus (aspergillosis *spp*) | 5/37 | 13.5 |
| NTM | 2/37 | .5.4 |
| Other bacteria | 18/37 | 48.6 |
| Treatment Plan | | |
| TMP-SMX + One antibiotic | 10/61 | 16.4 |
| TMP-SMX + Two or more antibiotics | 22/61 | 36.1 |
| Amikacin + Other antibiotics | 20/61 | 32.8 |
| Linezolid + Other antibiotics | 20/61 | 32.8 |
| Quinolones + Other antibiotics | 24/61 | 39.3 |
| Other antibiotic treatments | 17/61 | 27.9 |
| Outcome | | |
| Unknow | 3/71 | 4.2 |
| Failer | 10/68 | 14.7 |
| Recovered | 58/68 | 85.3 |

*COPD* chronic obstructive pulmonary Disease

*WBC* white blood cell NEU,neutrophils

*ESR* erythrocyte sedimentation rate

*MTB* Mycobacterium tuberculosis

*NTM* nontuberculosis mycobacteria

*TMP-SMX* trimethoprim-sulfamethoxazol

pulmonary disease (COPD)(8), hypertension (8),anemia (5), coronary heart disease (3) and Sjogren's syndrome (1). During the diagnostic process for nocardiosis, 66 patients underwent complete imaging, where all CT scans revealed the presence of nodules or consolidative opacities. Lung cavity lesions were present in 24.2% of patients (16/66) and pleural effusions were observed in 31.8% of patients (21/66).Blood cell examinations were conducted on 65 patients. Among them, 33.8% (22/65) had elevated white blood cell counts, and 60% (39/65) had increased neutrophil proportions.CRP examinations were performed on 42 patients, and among them, 69% (29/42) showed elevated CRP levels. Additionally, among the 31 patients who underwent ESR examination, 24 had elevated ESR levels. Concurrent infections with other pathogens were present in 37 patients. These included 16 cases of *Mycobacterium tuberculosis*(MTB) infection, 5 cases of *Aspergillus.spp* infection, and 2 cases of non-tuberculous mycobacterium infection.Please refer to Table 1 for further details.

### Molecular identification and distribution of *Nocardia* species

We initially identified the *Nocardia* species using MALDI-TOF MS and confirmed it further through 16S rRNA sequencing. However, the results of MALDI-TOF MS identification for the rare *Nocardia* species (*N. africana, N.pseudobrasiliensis, N.flavorosea, N.amamiensis* and *N.rhamnosiphila*) were inadequate and inconsistent with the sequencing results. Conversely, the identification results for *N.cyriacigeorgica*,*N. farcinica*,*N. abscessus, N.beijingensis*,*N. otitidiscaviarum*,*N. asiatica*,*N. puris* and *N.wallacei* were generally consistent between the two methods.

In the Additional file 1, we provide details of annual *Nocardia* isolates.The detection rate of *Nocardia* has exhibited an upward trajectory, increasing from a single isolate in 2017 to 20 cases in 2022. Among the 71 collected *Nocardia* isolates, a total of 13 species were identified. The predominant *Nocardia* species comprised *N. farcinica*(26.8%,9),*N.cyriacigeorgica*(18.3%,13),*N.abscessus*(11.3%,8), *N.amamiensis* (11.3%,8), *N.otitidiscaviarum* (7.0%,5)and *N.beijingensis* (7.0%,5). In our study, *Nocardia* strains were obtained using both traditional culture methods (BAP) and the MGIT960 culture method. Notably, there were disparities in *Nocardia* species detection between these two methods, as visually represented in Fig. 2. *N. farcinica* was the most frequently detected species via MGIT960 culture, while *N. cyriacigeorgica* predominated in traditional BAP culture.

### Antibiotic sensitivity

Table 2 provides a summary of *Nocardia*'s sensitivity to 15 antibiotics, including the MIC inhibiting 50% (MIC50) and 90% (MIC90) of strains, along with the MIC range for all *Nocardia* isolates.It displays the sensitivity rate, intermediate rate, and resistance rate for each antibiotic. All *Nocardia* strains were 100% sensitive to TMP-SMX and linezolid. It is worth noting that different species of *Nocardia* demonstrate different antibiotic resistances, as shown in Table 2, *N. farcinica* has higher resistance rates to imipenem (47.4%), ceftriaxone (78.9%), tigecycline (78.9%) and clarithromycin (89.4%), while *N.cyriacigeorgica* has lower rates of resistance to imipenem(15.4%), ceftriaxone (15.4%), tigecycline (0%),and clarithromycin (23.1%) In addition, *N. farcinica* and *N. abscessus* exhibited different sensitivities to doxycycline and minocycline. One isolate of *N. pseudobrasiliensis* exhibited resistance to ceftriaxone, ciprofloxacin, doxycycline and minocycline, and intermediate susceptibility

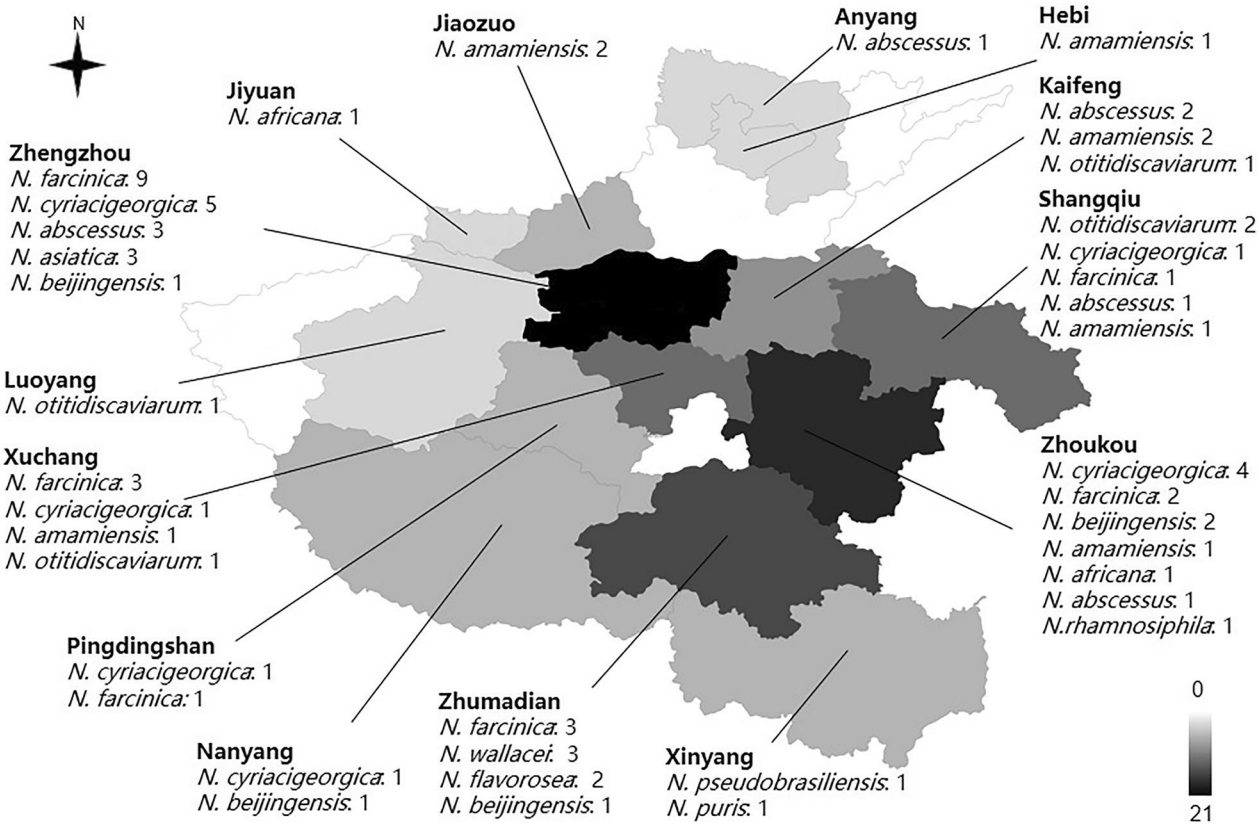


**Fig. 1** Geographical and spatial distribution of *Nocardia* isolates in Henan Province,China

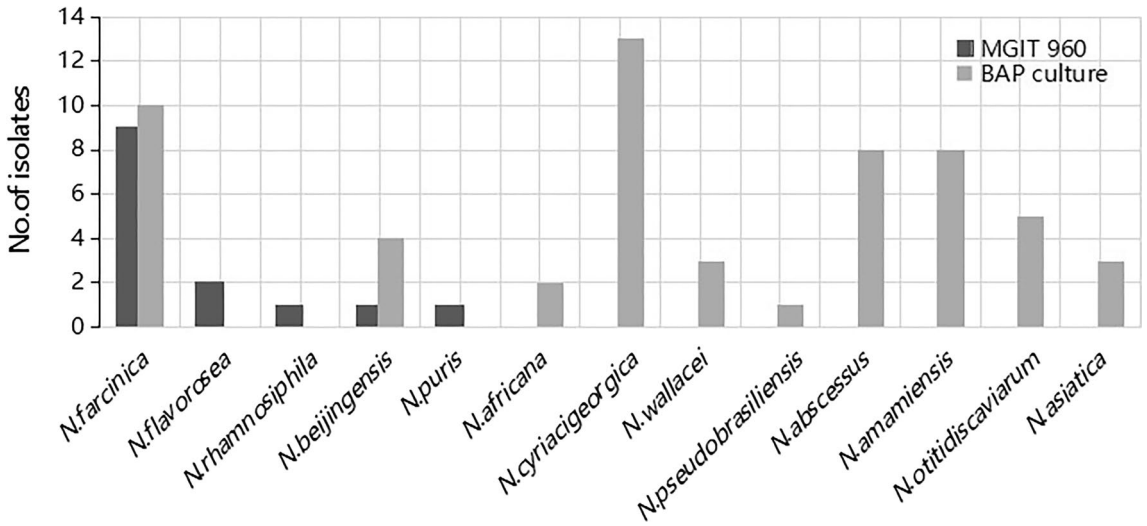


**Fig. 2** Distribution of *Nocardia* strains isolated by blood agar plate (BAP) culture and BACTEC MGIT 960 culture system (MGIT 960)

to imipenem, moxifloxacin, and amoxicillin-clavulanic acid.

The drug sensitivity results for each *Nocardia* species in this study were compared with the predicted antimicrobial drug sensitivity patterns provided by the CLSI standard M62 and larger-scale data studies. Table 3 showed a strong correlation between the drug pattern types and the identification of *Nocardia* species.

**Table 2** Antimicrobial susceptibility and MICs of 71 *Nocardia* isolates in clinical infections in Henan China from 2017 to 2023

| Drugs Breakpoint | | Species/complex, no. of strains (%)[a] | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *N.farcinica,* 19(26.8) | *N.abscessus* complex,16 (22.5)[b] | *N. cyriacigeorgica,* 13,(18.3) | *N. amamiensis,* 8(11.3) | *N. otitidiscaviarum,* 5(7.0) | *N. wallacei,* 3(4.2) | *N. africana,* 2(2.8) | *N. flavorosea,* 2 (2.8) | *N.puris,* 1 (1.4) | *N.pseudobrasiliensis,* 1 (1.4) | *N. rhamnosiphila,* (1.4) |
| TMP-SMX (S ≤ 2/38, R ≥ 4/76) | $MIC_{50}$ | ≤ 0.25/4.75 | ≤ 0.25/4.75 | ≤ 0.25/4.75 | ≤ 0.25/4.75 | 0.5/9.5 | ≤ 0.25/4.75 | | | | | |
| | $MIC_{90}$ | 1/19 | 1/19 | 1/19 | 0.5/9.5 | 2/38 | 1/19 | | | | | |
| | S/R (%) | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 |
| Linezolid (S ≤ 8, ~) | $MIC_{50}$ | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | | | | | |
| | $MIC_{90}$ | 2 | ≤ 1 | ≤ 1 | ≤ 1 | 2 | ≤ 1 | | | | | |
| | S/NS (%) | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 | 100/0 |
| Ciprofloxacin (S ≤ 1, R ≥ 4) | $MIC_{50}$ | 1 | > 4 | > 4 | > 4 | 2 | 1 | | | | | |
| | $MIC_{90}$ | 4 | > 4 | > 4 | > 4 | 4 | 2 | | | | | |
| | S/I/R (%) | 78.9/10.5/10.5 | 18.8/18.8/62.5 | 0/0/100 | 0/0/100 | 20/40/40 | 66.7/33.3/0 | 0/50/50 | 100/0/0 | 0/0/100 | 0/0/100 | 100/0/0 |
| Imipenem (S ≤ 4, R ≥ 16) | $MIC_{50}$ | 8 | 4 | ≤ 2 | 4 | 64 | 8 | | | | | |
| | $MIC_{90}$ | 32 | 64 | 16 | 8 | > 64 | > 64 | | | | | |
| | S/I/R (%) | 26.3/26.3/47.4 | 50/0/50 | 61.5/23.1/15.4 | 75/25/0 | 0/0/100 | 33.3/33.3/33.3 | 0/0/100 | 100/0/0 | 100/0/0 | 0/100/0 | 100/0/0 |
| Moxifloxacin (S ≤ 1, R ≥ 4) | $MIC_{50}$ | 0.5 | 8 | 2 | 4 | 1 | ≤ 0.25 | | | | | |
| | $MIC_{90}$ | 2 | 16 | 4 | 8 | 2 | 1 | | | | | |
| | S/I/R (%) | 84.2/10.5/5.3 | 25/18.8/56.2 | 7.7/61.5/30.8 | 0/12.5/87.5 | 60/40/0 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 | 0/100/0 | 100/0/0 |
| Cefepime | $MIC_{50}$ | > 32 | 4 | 16 | 4 | > 32 | 4 | | | | | |
| | $MIC_{90}$ | > 32 | 16 | > 32 | > 32 | > 32 | 32 | | | | | |
| | Range | 16 to > 32 | ≤ 1 to 32 | 2 to > 32 | 2 to > 128 | ~ > 32 | 4 to 32 | | | | | |
| AUG (S ≤ 8/4, R ≥ 32/16) | $MIC_{50}$ | 8/4 | 16/8 | 16/8 | 16/8 | > 64/32 | 8/4 | | | | | |
| | $MIC_{90}$ | 16/8 | > 64/32 | 32/16 | 16/8 | > 64/32 | 16/8 | | | | | |
| | S/I/R (%) | 52.6/42.1/5.3 | 43.8/6.2/50 | 0/53.8/46.2 | 37.5/62.5/0 | 0/0/100 | 66.7/33.3/0 | 0/0/100 | 50/0/50 | 0/0/100 | 0/100/0 | 0/0/100 |
| Amikacin (S ≤ 8, R ≥ 16) | $MIC_{50}$ | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | 2 | | | | | |
| | $MIC_{90}$ | ≤ 1 | ≤ 1 | ≤ 1 | 2 | ≤ 1 | 16 | | | | | |
| | S/I/R (%) | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 | 66.7/0/33.3 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 |
| Ceftriaxone (S ≤ 8, R ≥ 64) | $MIC_{50}$ | 64 | 4 | ≤ 4 | ≤ 4 | > 64 | 8 | | | | | |

**Table 2** (continued)

| Drugs Breakpoint | | Species/complex, no. of strains (%)[a] | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *N.farcinica,* 19(26.8) | *N.abscessus* complex,16 (22.5)[b] | *N. cyriacigeorgica,* 13,(18.3) | *N. amamiensis,* 8(11.3) | *N. otitidiscaviarum,* 5(7.0) | *N. wallacei,* 3(4.2) | *N. africana,* 2(2.8) | *N. flavorosea,* 2 (2.8) | *N.puris,* 1 (1.4) | *N.pseudobrasiliensis,* 1 (1.4) | *N. rhamnosiphila,* (1.4) |
| | $MIC_{90}$ | > 64 | 8 | 64 | 64 | > 64 | 32 | | | | | |
| | S/I/R (%) | 5.3/15.8/78.9 | 93.8/6.2/0 | 76.9/7.7/15.4 | 87.5/0/12.5 | 0/20/80 | 66.7/33.3/0 | 0/0/100 | 50/50/0 | 100/0/0 | 0/0/100 | 100/0/0 |
| Doxycycline (S ≤ 1, R ≥ 8) | $MIC_{50}$ | 2 | 0.12 | 2 | ≤ 0.12 | 1 | 2 | | | | | |
| | $MIC_{90}$ | 4 | 0.5 | 2 | 2 | 2 | 2 | | | | | |
| | S/I/R (%) | 26.3/73.7/0 | 93.8/6.2/0 | 46.2/53.8/0 | 87.5/12.5/0 | 60/40/0 | 0/100/0 | 0/100/0 | 50/50/0 | 100/0/0 | 0/0/100 | 100/0/0 |
| Minocycline (S ≤ 1, R ≥ 8) | $MIC_{50}$ | 2 | ≤ 1 | ≤ 1 | ≤ 1 | ≤ 1 | 2 | | | | | |
| | $MIC_{90}$ | 2 | ≤ 1 | 2 | ≤ 1 | 2 | 2 | | | | | |
| | S/I/R (%) | 36.8/63.2/0 | 93.8/6.2/0 | 61.5/38.5/0 | 100/0/0 | 80/20/0 | 33.3/66.7/0 | 50/50/0 | 50/50/0 | 100/0/0 | 0/0/100 | 100/0/0 |
| Tobramycin (S ≤ 4, R ≥ 16) | $MIC_{50}$ | 16 | ≤ 1 | ≤ 1 | ≤ 1 | 2 | > 16 | | | | | |
| | $MIC_{90}$ | > 16 | ≤ 1 | ≤ 1 | 8 | 4 | > 16 | | | | | |
| | S/I/R (%) | 5.3/15.8/78.9 | 100/0/0 | 100/0/0 | 87.5/12.5/0 | 100/0/0 | 33.3/0/66.7 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 | 100/0/0 |
| Clarithromycin (S ≤ 2, R ≥ 8) | $MIC_{50}$ | > 16 | 1 | 2 | 0.06 | 16 | 0.5 | | | | | |
| | $MIC_{90}$ | > 16 | > 16 | > 16 | 4 | > 16 | 16 | | | | | |
| | S/I/R (%) | 5.3/5.3/89.4 | 56.2/6.2/37.5 | 69.2/7.7/23.1 | 87.5/12.5/0 | 20/20/60 | 66.7/0/33.3 | 0/0/100 | 50/50/0 | 0/0/100 | 100/0/0 | 100/0/0 |
| Cefoxitin | $MIC_{50}$ | 64 | 8 | 64 | 16 | > 128 | 64 | | | | | |
| | $MIC_{90}$ | > 128 | 16 | > 128 | > 128 | > 128 | 128 | | | | | |
| | Range | 32 to > 128 | ≤ 4 to 128 | 16 to > 128 | ≤ 4 to > 128 | 128 to > 128 | 64 to 128 | | | | | |
| Tigecycline | $MIC_{50}$ | 0.5 | 0.25 | 0.25 | 0.06 | 0.25 | 0.25 | | | | | |
| | $MIC_{90}$ | 2 | 0.5 | 1 | 0.25 | 0.5 | 0.5 | | | | | |
| | Range | 0.03 to 4 | ≤ 0.015 to 1 | 0.12 to 1 | 0.03 to 0.25 | 0.06 to 0.5 | 0.25 to 0.5 | | | | | |

*Nocardia* species/complex responsible for clinical infections in Henan China from 2017 to 2023. TMP-SMX, trimethoprim-sulfamethoxazole. AUG, Amoxicillin-clavulanic acid

S, susceptible; I, intermediate; R, resistant; NS, nonsusceptible; MIC50 and MIC90,MICs at which 50% and 90% of the strains were inhibited, respectively

The table shows the antimicrobial susceptibilities profifiles and MIC values (in *m*g/mL) (as determined by the broth microdilution method) to 15 antibiotics of the major

[a] Percentage with respect to the total number of identifified *Nocardia* strains (n = 71)

[b] *N. abscessus complex* (16) includes *N. abscessus* (8), *N. asiatica* (3), and *N. beijingensis* (5)

**Table 3** Main results of antibiotic susceptibility testing of clinical *Nocardia* isolates, derived from large-scale studies published beteen 2014 and 2023

| % of susceptible isolates | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **First author, year** | **AST method** | **Break-points** | **N of isolates** | **Amikacin** | **AUG** | **Ceftriaxone** | **Ciprofloxacin** | **Imipenem** | **Linezolid** | **Minocycline** | **Moxifloxacin** | **TMP-SMX** | **Tobramycin** |
| All *Nocardia* isolates | | | | | | | | | | | | | |
| This study | BMD | CLSI | 71 | 98.6 | 32.4 | 53.5 | 33.8 | 45.1 | 100 | 66.2 | 46.5 | 100 | 70.4 |
| Hao Wang, 2022 [7] | BMD | CLSI | 441 | 99.3 | 39.5 | 40.6 | 33.6 | 43.3 | 100 | 43.5 | 57.1 | 99.1 | 56.5 |
| Hamdi, 2020 [8] | BMD | CLSI | 2091 | 94 | 44 | 36 | 16 | 73 | 100 | 30 | 30 | 98 | 52 |
| Schlaberg, 2014 [9] | BMD | CLSI | 1299[b] | 95 | 37 | 56 | 17 | 49 | 100 | 22 | 40(n = 642) | 98 | 55 |
| Jing Yang, 2023 [10] | BMD | CLSI | 130 | 100 | 35.4 | 48.5 | 17.7 | 43.9 | 100 | 63.9 | 48.5 | 97.7 | 74.6 |
| *N.farcinica* (N.farcinica[a]) | | | | S | S | R | S | V | S | V | N/A | S | R |
| This study | BMD | CLSI | 19 | 100 | 52.6 | 5.3 | 78.9 | 26.3 | 100 | 36.8 | 84.2 | 100 | 5.3 |
| Hao Wang, 2022 [7] | BMD | CLSI | 176 | 100 | 61.9 | 8.5 | 68.8 | 39.8 | 100 | 26.1 | 90.3 | 97.7 | 14.2 |
| Hamdi, 2020 [8] | BMD | CLSI | 319 | 100 | 96 | 3 | 49 | 83 | 100 | 7 | 76 | 99 | 1 |
| Schlaberg, 2014 [9] | BMD | CLSI | 204[b] | 100 | 76 | 3 | 43 | 33 | 100 | 5 | 79(n = 99) | 99 | 0 |
| Jing Yang, 2023 [10] | BMD | CLSI | 27 | 100 | 66.7 | 7.4 | 59.3 | 29.7 | 100 | 29.6 | 92.6 | 92.6 | 14.8 |
| *N.abscessus* (*N.abscessus* complex[a]) | | | | S | S | S | R | V | S | V | N/A | S | V |
| This study | BMD | CLSI | 16 | 100 | 43.8 | 93.8 | 18.8 | 50 | 100 | 93.8 | 25 | 100 | 100 |
| Hao Wang,2022 [7] | BMD | CLSI | 54 | 100 | 48.1 | 90.7 | 18.5 | 46.3 | 100 | 79.6 | 29.6 | 100 | 87 |
| Hamdi, 2020 [8] | BMD | CLSI | 205 | 100 | 61 | 93 | 3 | 64 | 100 | 93 | 13 | 100 | 100 |
| Schlaberg, 2014 [9] | BMD | CLSI | 110[b] | 100 | 78 | 98 | 0 | 31 | 100 | 85 | 8(n = 39) | 100 | 100 |
| Jing Yang, 2023 [10] | BMD | CLSI | 20 | 100 | 55 | 95 | 10 | 55 | 100 | 85 | 10 | 100 | 90 |
| *N.cyriacigeorgica* (*N.cyriacigeorgica*[a]) | | | | S | R | S | R | S | S | V | N/A | S | S |
| This study | BMD | CLSI | 13 | 100 | 0 | 76.9 | 0 | 61.5 | 100 | 61.5 | 7.7 | 100 | 100 |
| Hao Wang, 2022 [7] | BMD | CLSI | 126 | 100 | 6.3 | 66.7 | 2.4 | 58.7 | 100 | 42.9 | 18.3 | 100 | 96 |
| Hamdi, 2020 [8] | BMD | CLSI | 352 | 99 | 8 | 64 | 0 | 99 | 100 | 14 | 1 | 100 | 99 |
| Schlaberg, 2014 [9] | BMD | CLSI | 264[b] | 100 | 3 | 88 | 0 | 43 | 100 | 6 | 4(n = 128) | 100 | 99 |
| Jing Yang, 2023 [10] | BMD | CLSI | 49 | 100 | 6.1 | 67.3 | 0 | 61.2 | 100 | 63.3 | 22.4 | 100 | 100 |
| *N.otitidiscaviarum* (*N.otitidiscaviarum*[a]) | | | | S | R | R | S | R | S | V | N/A | S | V |
| This study | BMD | CLSI | 5 | 100 | 0 | 0 | 20 | 0 | 100 | 80 | 60 | 100 | 100 |
| Hao Wang, 2022 [7] | BMD | CLSI | 26 | 100 | 11.5 | 3.8 | 7.7 | 3.8 | 100 | 61.5 | 46.2 | 100 | 57.7 |
| Hamdi, 2020 [8] | BMD | CLSI | 30 | 100 | 0 | 0 | 0 | 3 | 100 | 60 | 23 | 87 | 53 |
| Schlaberg, 2014 [9] | BMD | CLSI | 29[b] | 100 | 0 | 0 | 7 | 7 | 100 | 45 | 35 (n = 17) | 100 | 62 |
| Jing Yang, 2023 [10] | BMD | CLSI | 14 | 100 | 7.1 | 7.1 | 7.2 | 0 | 100 | 61.5 | 57.1 | 100 | 78.6 |
| *N.wallacei* (*N.transvalensis* complex[a]) | | | | R | V | S | S | V | S | V | N/A | S | R |
| This study | BMD | CLSI | 3 | 100 | 66.7 | 66.7 | 66.7 | 33.3 | 100 | 33.3 | 100 | 100 | 33.3 |
| Hao Wang, 2022 [7] | BMD | CLSI | 11 | 72.7 | 63.6 | 63.6 | 72.7 | 36.4 | 100 | 27.3 | 90.9 | 100 | 9.1 |

**Table 3** (continued)

| % of susceptible isolates | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **First author, year** | **AST method** | **Break-points** | **N of isolates** | **Amikacin** | **AUG** | **Ceftriaxone** | **Ciprofloxacin** | **Imipenem** | **Linezolid** | **Minocycline** | **Moxifloxacin** | **TMP-SMX** | **Tobramycin** |
| Hamdi, 2020 [8] | BMD | CLSI | 121 | 26 | 89 | 64 | 49 | 9 | 100 | 31 | 72 | 88 | 0 |
| Schlaberg, 2014 [9] | BMD | CLSI | 83 | 28 | 47 | 63 | 84 | 6 | 100 | 15 | 100 | 81 | 4 |
| Jing Yang, 2023 [10] | BMD | CLSI | 3 | 100 | N/A | N/A | N/A | N/A | 100 | N/A | N/A | N/A | N/A |

*AST* antimicrobial susceptibility testing, *BMD* broth microdilution, *CLSI* Clinical and Laboratory Standards Institute, *N* number, *N/A* not available

[a] Expected antimicrobial susceptibility patterns of the most com monly isolated *Nocardia* species or species complexes provided by CLSI standard M62 [11]; the expected pattern "R/S/V" represents resistant/susceptible/variable

[b] Except for moxifloxacin

Nonetheless, some differences were observed.For example, although only 52.6% of the cutaneous *Nocardia* isolates were sensitive to amoxicillin-clavulanate, the drug pattern indicated sensitivity according to the CLSI M62.The sensitivity rate of amoxicillin-clavulanate in *N.abscessus* complex isolates was only 43.8%, despite the drug pattern indicating sensitivity.The sensitivity rate of ciprofloxacin in *N.otitidiscaviarum* isolates was 20%, with the drug sensitivity pattern also indicating sensitivity.Furthermore, despite the sensitivity rate of 100% for amikacin in *N.wallacei* isolates, the drug sensitivity pattern indicated resistance.

### Comparison between pulmonary nocardiosis complicated with bronchiectasis group and non-bronchiectasis group

Bronchiectasis was found to be the predominant underlying disease among the patients based on the data presented in Table 1. The collected cases of nocardiosis were classified into two groups: the bronchiectasis group (39) and the non-bronchiectasis group(29), based on the patients' radiological examination results. We conducted a comprehensive comparison of the clinical characteristics, distribution of bacterial species, and drug sensitivity results between these two groups.Further detailed comparisons are provided in Tables 4 and 5.

It can be concluded from Table 4 that there was no statistically significant difference in the distribution of age groups between the two groups ($p > 0.05$), but in terms of gender composition, the bronchiectasis group was predominantly female, whereas the non-bronchiectasis group was predominantly male. There was a statistical difference between the two groups in terms of smoking history, with patients with a history of smoking in the non-bronchodilated group being more susceptible to

**Table 4** Characteristics of patients with nocardiosis

| Characteristics | Bronchiectasis (n = 39)[a] | Non bronchiectasis (n = 29)[a] | P value* |
|---|---|---|---|
| Patient demographics | | | |
| Male/female | 18/21 | 8/21/2023 | **0.030** |
| < 40 years | 8 (20.5%) | 5 (17.2%) | 0.734 |
| 40–60 years | 13 (33.3%) | 14 (48.3%) | 0.213 |
| ≥ 60 years | 18 (46.2%) | 10 (34.5%) | 0.333 |
| Smoking history | 6 (15.4%) | 11 (37.9%) | **0.034** |
| History of Drinking | 3 (7.7%) | 6 (20.7%) | 0.156 |
| Underlying diseases | | | |
| Healthy | 6 (15.4%) | 1 (3.4%) | 0.225 |
| COPD | 5 (12.8%) | 3 (10.3%) | 1.000 |
| Diabetes | 3 (7.7%) | 9 (31.0%) | **0.013** |
| Hypertension | 2 (5.1%) | 6 (20.7%) | 0.065 |
| Pulmonary tuberculosis | 6 (15.4%) | 10 (34.5%) | 0.066 |
| Coronary heart disease | 0 (0%) | 3 (10.3%) | 0.073 |
| Anemia | 2 (5.1%) | 3 (10.3%) | 0.644 |
| Chest radiograph | | | |
| Nodular or consolidative opacities | 38 (97.4%) | 28 (96.5%) | 1.000 |
| Cavitary lesion | 6 (15.4%) | 10 (34.5%) | 0.066 |
| Pleural effusion | 8 (20.5%) | 13 (44.8%) | **0.032** |
| Co-infection | | | |
| MTB | 4 (10.3%) | 10 (34.5%) | **0.015** |
| NTM | 1 (2.6%) | 1 (3.4%) | 1.000 |
| Fungus (*aspergillosis spp.*) | 1 (2.6%) | 4 (13.8%) | 0.155 |
| Other bacteria | 11 (28.2%) | 7 (24.1%) | 0.707 |
| Outcome | | | |
| Failer | 1 (2.6%) | 9 (31.0%) | **0.001** |
| Cure | 38 (97.4%) | 20 (69.0%) | **0.001** |

*Due to total number < 40 and some of the expected number < 5, Fisher exact test's result was used

[a] Three patients were lost to follow-up (including two pulmonary and one cutaneous), whose presence or absence of bronchiectasis was unknown due to incomplete case data

**Table 5** *Nocardia* species identification and antibiotic risistance

| Characteristics | Bronchiectasis (n = 39)[a] | Non bronchiectasis (n = 29)[a] | P value* |
|---|---|---|---|
| *Nocardia* species identififfication | | | |
| *N.cyriacigeorgica* | 9 (23.1%) | 3 (10.3%) | 0.173 |
| *N.abscessus* | 8 (20.5%) | 0 (0%) | **0.017** |
| *N.farcinica* | 6 (15.4%) | 12 (41.4%) | **0.016** |
| *N.amamiensis* | 6 (15.4%) | 2 (6.9%) | 0.451 |
| *N.otitidiscaviarum* | 4 (10.3%) | 1 (3.4%) | 0.384 |
| *N.beijingensis* | 2 (5.1%) | 3 (10.3%) | 0.644 |
| *N.asiatica* | 1 (2.6%) | 2 (6.9%) | 0.571 |
| *N.puris* | 1 (2.6%) | 0 (0%) | 1.000 |
| *N. wallacei* | 1 (2.6%) | 2 (6.9%) | 0.571 |
| *N. pseudobrasiliensis* | 1 (2.6%) | 0 (0%) | 1.000 |
| *N.flavorosea* | 0 (0%) | 1 (3.4%) | 0.426 |
| *N.rhamnosiphila* | 0 (0%) | 1 (3.4%) | 0.426 |
| *N.africana* | 0 (0%) | 2 (6.9%) | 0.178 |
| Antibiotic resistance profiffiles | | | |
| AUG | 14 (35.9%) | 10 (34.5%) | 0.904 |
| Ceftriaxone | 9 (23.1%) | 15 (51.7%) | **0.014** |
| Imipenem | 14 (35.9%) | 12(41.4%) | 0.645 |
| Tobramycin | 3 (7.7%) | 13 (44.8%) | **0.000** |
| Ciprofloxacin | 25 (64.1%) | 12 (41.4%) | 0.063 |
| Moxifloxacin | 11 (28.2%) | 10 (34.5%) | 0.799 |
| Amikacin | 0 (0%) | 1 (3.4%) | 0.426 |
| Linezolid | 0 (0%) | 0 (0%) | > 1.000 |
| TMP-SMX | 0 (0%) | 0 (0%) | > 1.000 |
| Clarithromycin | 16 (41%) | 15 (51.7%) | 0.381 |
| Doxycycline | 1(2.6%) | 0 (0%) | 1.000 |
| Minocycline | 1 (2.6%) | 0 (0%) | 1.000 |

*Due to total number < 40 and some of the expected number < 5, Fisher exact test's result was used

[a] Three patients were lost to follow-up (including two pulmonary and one cutaneous), whose presence or absence of bronchiectasis was unknown due to incomplete case data

nocardiosis than those with a history of smoking in the bronchodilated group. In terms of comorbidities between the two groups, we learnt that patients with diabetes mellitus in the non-bronchiectasis group were more likely to develop nocardiosis. Other differences are detailed in Table 4.

In Table 5, our study found that there was a statistical difference between the two groups in terms of species distribution of *Nocardia* isolates, in both *N.abscessus* ($p < 0.05$) and *N.farcinica* ($p < 0.05$) detection rates, with patients with bronchodilatation being more likely to be detected with *N. abscessus* than those with non-bronchodilatation. In antibiotic susceptibility testing, there was a statistical difference between the two groups in ceftriaxone and tobramycin ($p < 0.05$) antimicrobial drugs.

### Treatment and outcome

Out of the 71 cases of nocardiosis that were collected, treatment details were available for 61 patients, while the treatment plans for 10 patients were missing.Based on the data presented in Table 1, out of the 61 patients with treatment plans, 32 patients (52.5%) received combination therapy comprising of TMP-SMX. Among these patients, 10 received TMP-SMX combined with a single drug, while 22 patients received TMP-SMX combined with two or more antibiotics as part of a multidrug treatment plan.Moreover, 20 patients (32.8%) received a multidrug regimen containing amikacin and other antibiotics, while 20 patients (32.8%) received a regimen consisting of linezolid combined with other antibiotics. Furthermore, 24 patients (39.3%) were treated with a combination of quinolone antibiotics and other antibiotics, and 17 patients were prescribed alternative antibiotic regimens during the treatment. Out of the 71 patients' treatment outcomes, 3 patients were lost to follow-up with unknown treatment results, 58 patients (85.3%) achieved a cure or improvement in clinical symptoms, and 10 patients (14.7%) were discharged without being cured.

## Discussion

*Nocardia*, an important group of actinomycetes in the environment, can lead to human infections through traumatic inoculation or inhalation [1]. The latest taxonomic study of *Nocardia* reveals the existence of 119 species, with 54 of them being associated with human infections [12, 13]. Some medically relevant bacterial species include *N. asterosa*, *N.brasiliensis*, *N.farcinica a*nd *N.abscessus*. Over the past decade, China has witnessed an increasing trend in *Nocardia* infections [7, 10, 14, 15]. However, there is a scarcity of reports on *Nocardia* in Henan. Given the variation in *Nocardia* distribution across different geographical regions, it is essential to investigate the epidemiology, clinical characteristics, and antibiotic resistance of *Nocardia* in various areas.

The incidence of nocardiosis is influenced by age. Our data showed that the majority of patients were older with a slight male predominance, which is consistent with previous literature [7, 10]. Occupational classification was dominated by farmers, who may be more susceptible to environmental *Nocardia* infections due to their greater outdoor exposure to contaminated soil.In our study, the diagnostic methods for *Nocardia* infection include BAP culture and MGIT960 culture. As shown in Fig. 2, *N.farcinica* was most frequently detected through the MGIT 960 culture method (n = 9, 60%), which is consistent with the literature [16, 17]. A study by Hu et al. [16] found that the high recovery rate of *N.farcinica* in MGIT 960 and the growth of other *Nocardia* species are due to their resistance to

trimethoprim-sulfamethoxazole. The main species of *Nocardia* varies from region to region, in Australia [18] and USA [9], the most common is *N. nova* complex. in Iran [19], France [20] and Japan [21], the most prevalent species are *N.asteroides, N.farcinica* and *N.cyriacigeorgica*. Even in China, the distribution characteristics of *Nocardia* vary from region to region. In Taiwan, China [22] and Hebei province, China [10], the most frequently occurring species are *N.brasiliensis* and *N.cyriacigeorgica*.

*Nocardia* is mainly transmitted by inhalation and pulmonary nocardiosis usually affects frail patients, especially immunocompromised patients due to organ transplantation and/or treatment with corticosteroids and COPD patients, and forms infected lesions in the lungs [23, 24]. Bronchiectasis was the most common (54.9%) among the patients with pulmonary nocardiosis combined with the underlying disease in our study. In a study by Huang et al. [25]. bronchiectasis was most common (30.4%) among the underlying diseases.In a study by Yang et al. bronchiectasis was comorbid in 6 out of 12 (50%) patients diagnosed with nocardiosis [26]. A study in Taiwan reported that the most common comorbidities were diabetes mellitus (30%) and COPD (26.7%) [27], which is similar to our report. Data show that an increasing number of patients with bronchiectasis are being diagnosed with pulmonary nocardiosis, but the reasons for this are not fully understood and may be due to environmental exposures, microbiological surveillance, and other factors [5].Woodworth et al. concluded that *N.nova c*omplex was more likely to be detected in patients with bronchiectasis than in other patients [5], but in our study data (Table 5) *N.abscessus* was more likely to be detected in patients with bronchiectasis, which is clearly inconsistent.

In this study, the clinical symptoms and CT manifestations of patients with pulmonary nocardiosis lacked specificity, making it difficult to distinguish them from other diseases such as filamentous fungi (e.g., Aspergillus and trichothecenes) or mycobacterial infections [28]. Pulmonary nocardiosis may be mistaken for tuberculosis, and tuberculosis and HIV are common co-infections [29]. Of 10 patients diagnosed with nocardiosis after death, 40% were misdiagnosed with TB before death [30]. A study evaluating patients with suspected tuberculosis in Ghana found that 16.7% were co-infected with HIV and *Nocardia spp*. [31] The antibiotic regimen for nocardiosis and other diseases varies considerably, making accurate diagnosis critical to treatment.

To this day, that TMP-SMX is the main drug used for the treatment of nocardiosis, however, some studies have raised concerns about the increased resistance of *Nocardia* isolates in particular to TMP-SMX.In the study of Lebeaux et al. [20], 5.4% of isolates were insusceptible to TMP-SMX; in the study of Uhde et al., the rate of resistance to TMP-SMX was 42% [32]; these discrepancies may be caused by inter-labortory differences or differences in species distribution in different geographical regions. A multicentre study of 441 *Nocardia* strains in China showed a resistance rate to TMP-SMX of only 0.9% [7], which is more consistent with the results of this study. In Table 3 the main results of studies reported from antibiotic sensitivity testing of large-scale clinical *Nocardia* isolates published between 2014 and 2023 show a strong correlation between the type of drug pattern and the identification of *Nocardia spp*. species, with some differences between different strains and the corresponding drug susceptibility patterns; Therefore, for the optimal treatment of nocardiosis, the *Nocardia spp.* species should be identified as accurately as possible and antimicrobial drug susceptibility testing should be performed.

TMP-SMX is typically used as the drug of choice for the treatment of nocardiosis, either alone or in combination with other drugs such as amikacin, imipenem, or third-generation cephalosporins. Amikacin can be used in combination with TMP-SMX or other drugs for the treatment of critical nocardiosis [33]. Imipenem is more active than meropenem or ertapenem against most *Nocardia* [34], and the combination of amikacin and imipenem is more effective in treating cerebral and pulmonary nocardiosis than TMP-SMX alone in a mouse model [35, 36]. The combination of imipenem and cefotaxime, amikacin and TMP-SMX, imipenem and TMP-SMX, amikacin and cefotaxime, or amikacin and imipenem provided enhanced activity [37]. For most forms of nocardiosis, initial combination drug therapy is recommended [28]. Among our 61 patients with a treatment plan for pulmonary nocardiosis, TMP-SMX in combination with amikacin and linezolid was the more common regimen. Although TMP-SMX is a common treatment option for nocardiosis, some patients in our study cases opted for other effective antimicrobials due to allergy to oral sulfonamides. Linezolid has shown good clinical efficacy in *Nocardia* infections and can be recommended as an alternative therapy to TMP-SMX due to its oral availability and activity against most *Nocardia* species [38]. In our patients with nocardiosis, after aggressive clinical treatment, 14.7% of them still failed, and the failure may be due to the severity and complexity of the patient's own underlying disease.

The study has several limitations.Firstly, being a retrospective study, it carries inherent limitations of this study design,especially in terms of data loss, such as missed patient cases and loss to follow-up. Secondly, the study's small scale may introduce biases in epidemiology and prognosis.The data may not be representative, indicating the need for further research with a larger sample size.

In summary,This is the first study on the epidemiological and clinical characteristics of nocardiosis on a larger scale in Henan, China, and describes the distribution, clinical characteristics and antibiotic drug sensitivity of the identified *Nocardia* species. Drug susceptibility varies among different *Nocardia* species, and accurate species identification and confirmation of antimicrobial susceptibility patterns are necessary in diagnosis and selection of antibiotic therapy. Pulmonary nocardiosis is prone to comorbidities with other underlying diseases such as bronchiectasis, tuberculosis, diabetes mellitus and COPD. nocardia infections are susceptible to concurrent comorbidities with a variety of pathogens such as *Mycobacterium* and *Aspergillus*. Our study also showed that bronchiectasis occurs more frequently with *Nocardia* infections, and the data from the bronchiectasis and non-bronchiectasis groups showed statistical differences in clinical characteristics and drug sensitivity. Our study adds new value to the characterisation of nocardiosis in China, and a better understanding of the characteristics of *Nocardia* infections will help physicians make better decisions in the diagnosis and treatment of nocardiosis.

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12941-024-00677-4.

**Additional file 1.** Distribution of *Nocardia* species detected in each year (No. of isolates).

**Acknowledgements**
Thank the microbiology staff of the Key Laboratory of medical laboratory in Henan Provincial chest hospital for the experimental tests, and thank the staff of the clinical laboratory for their contributions and dedication to the work. We are very grateful for the platform support provided by the Central Laboratory of Henan Provincial Infectious Disease (TB) Clinical Medical Research Center and the Henan International Joint Laboratory of Tuberculosis. Finally, we sincerely thank all the research participants.

**Author contributions**
Conceptualization,YH, WW; Methodology, YH; Software, YH, ZL; Validation, YH, MC, YW; Analysis, YH, HC; Resources, YH, YZ, SX, WH; Writing-Original Draft Preparation, YH; Writing-Review & Editing, ZL; Visualization, YH; Supervision, YH; Project Administration, MC; Funding Acquisition, YH, All authors reviewed the manuscript.

**Funding**
This study was supported by the Medical Science and Technology Project of Henan Province, with the grant number: LHGJ20190759.

**Data availability**
The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

## Declarations

**Ethics approval and consent to participate**
The interests and privacy of the patients involved were not affected, and informed consent was waived.

**Consent for publication**
All authors approved the final manuscript and the submission to this journal.

**Competing of interests**
The authors declare that they have no conflict of interest.

Received: 18 November 2023 Accepted: 6 February 2024
Published online: 06 March 2024

**References**

1. Brown-Elliott BA, Brown JM, Conville PS, et al. Clinical and laboratory features of the *Nocardia spp.* based on current molecular taxonomy. Clin Microbiol Rev. 2006;19(2):259–82. https://doi.org/10.1128/CMR.19.2.259-282.2006.
2. Traxler RM, Bell ME, Lasker B, et al. Updated review on *Nocardia* Species: 2006–2021. Clin Microbiol Rev. 2022;35(4): e0002721. https://doi.org/10.1128/cmr.00027-21.
3. Fatahi-Bafghi M. Nocardiosis from 1888 to 2017. Microb Pathogenesis. 2017;114:369–84. https://doi.org/10.1016/j.micpath.2017.11.012.
4. Maggiorelli C, Di Pierro I, Manta C, et al. *Nocardia* and lungs in COPD: beyond immuno-deficiencies. COPD. 2014;12(3):315–9. https://doi.org/10.3109/15412555.2014.933951.
5. Woodworth MH, Saullo JL, Lantos PM, et al. Increasing *Nocardia* incidence associated with bronchiectasis at a tertiary care center. Ann Am Thorac Soc. 2017;14(3):347–54. https://doi.org/10.1513/AnnalsATS.201611-907OC.
6. Wei M, Wang P, Yang C, et al. Molecular identification and phylogenetic relationships of clinical *Nocardia* isolates. Anton Leeuw Int J G. 2019;112(12):1755–66. https://doi.org/10.1007/s10482-019-01296-2.
7. Wang H, Zhu Y, Cui Q, et al. Epidemiology and antimicrobial resistance profiles of the *nocardia* species in China, 2009 to 2021. Microbiol Spectr. 2022;10(2): e0156021. https://doi.org/10.1128/spectrum.01560-21.
8. Hamdi, AM, Fida, M, Deml, SM, et al. Retrospective analysis of antimicrobial susceptibility profiles of *nocardia* species from a tertiary hospital and reference laboratory, 2011 to 2017. Antimicrob Agents Ch. 2020; https://doi.org/10.1128/AAC.01868-19
9. Schlaberg R, Fisher MA, Hanson KE. Susceptibility profiles of *Nocardia* isolates based on current taxonomy. Antimicrob Agents Ch. 2013;58(2):795–800. https://doi.org/10.1128/AAC.01531-13.
10. Yang J, Ren HT, Wang J, et al. Clinical characteristics, susceptibility profiles, and treatment of nocardiosis: a multicenter retrospective study in 2015–2021. Int J Infect Dis. 2023;130:136–43. https://doi.org/10.1016/j.ijid.2023.02.023.
11. Clinical and Laboratory Standards Institute. 2018. Performance standards for susceptibility testing of mycobacteria, *Nocardia spp*., and other erobic actinomycetes, 1st ed. Approved standard M62. Clinical and Laboratory Standards Institute, Wayne, PA.
12. Martínez-Barricarte R. Isolated nocardiosis, an unrecognized primary immunodeficiency? Front Immunol. 2020;11:590239. https://doi.org/10.3389/fimmu.2020.590239.
13. Mehta HH, Shamoo Y. Pathogenic *Nocardia:* a diverse genus of emerging pathogens or just poorly recognized? Plos Pathog. 2020;16(3): e1008280. https://doi.org/10.1371/journal.ppat.1008280.
14. Lu SH, Qian ZW, Mou PP, et al. Clinical *Nocardia* species: Identification, clinical characteristics, and antimicrobial susceptibility in Shandong, China. Bosnian J Basic Med. 2020;20(4):531–8. https://doi.org/10.17305/bjbms.2020.4764.
15. Huang L, Chen X, Xu H, et al. Clinical features, identification, antimicrobial resistance patterns of *Nocardia* species in China: 2009–2017. Diagn Micr Infec Dis. 2018;94(2):165–72. https://doi.org/10.1016/j.diagmicrobio.2018.12.007.
16. Hu Y, Zhu Y, Li C, et al. Evaluation of BACTEC MGIT 960 system for recovery of *Nocardia* from clinical specimens. Diagn Micr Infec Dis. 2023;106(4):115989. https://doi.org/10.1016/j.diagmicrobio.2023.115989.
17. Xiao-ping Z, Song-lin Y, Pei-lei H, Xiao T, Jing-wei G, Zhong-nan C, et al. Detection of nine *Nocardia* farcinica strains with BACT MGIT 960 system and their drug resistance. J Tuber Lung Health. 2017;6(2):118–22.

18. Tan YE, Chen SC, Halliday CL. Antimicrobial susceptibility profiles and species distribution of medically relevant *Nocardia* species: results from a large tertiary laboratory in Australia. J Glob Antimicrob Re. 2019;20:110–7. https://doi.org/10.1016/j.jgar.2019.06.018.
19. Hashemi-Shahraki A, Heidarieh P, Bostanabad SZ, et al. Genetic diversity and antimicrobial susceptibility of *Nocardia* species among patients with nocardiosis. Sci Rep. 2015;5:17862. https://doi.org/10.1038/srep17862.
20. Lebeaux D, Bergeron E, Berthet J, et al. Antibiotic susceptibility testing and species identification of *Nocardia* isolates: a retrospective analysis of data from a French expert laboratory, 2010–2015. Clin Microbiol Infec. 2018;25(4):489–95. https://doi.org/10.1016/j.cmi.2018.06.013.
21. Toyokawa M, Ohana N, Ueda A, et al. Identification and antimicrobial susceptibility profiles of *Nocardia* species clinically isolated in Japan. Sci Rep. 2021;11(1):16742. https://doi.org/10.1038/s41598-021-95870-2.
22. Liu WL, Lai CC, Ko WC, et al. Clinical and microbiological characteristics of infections caused by various *Nocardia* species in Taiwan: a multicenter study from 1998 to 2010. Eur J Clin Microbiol. 2011;30(11):1341–7. https://doi.org/10.1007/s10096-011-1227-9.
23. Jorgensen JH, Pfaller MA. Manual of clinical microbiology[M]. Translated by Wang H, Ma YL, Qian Y, et al. Beijing:Chinese Medical Multimedia Press, 2017:641–642
24. Ercibengoa M, Càmara J, Tubau F, et al. A multicentre analysis of Nocardia pneumonia in Spain: 2010–2016. Int J Infect Dis. 2019;90:161–6. https://doi.org/10.1016/j.ijid.2019.10.032.
25. Huang L, Sun L, Yan Y. Characteristics of nocardiosis patients with different immune status from a Chinese tertiary general hospital during 8-year period: a STROBE-compliment observational study. Medicine. 2019;98(45): e17913. https://doi.org/10.1097/MD.0000000000017913.
26. Yang HQ, Shi HZ, Tong ZH. Retrospective analysis of 13 cases of nocardiosis. Zhonghua Jie He He Hu Xi Za Zhi. 2017;40:588–91. https://doi.org/10.3760/cma.j.issn.1001-0939.2017.08.009.
27. Yang CH, Kuo SF, Chen FJ, et al. Clinical manifestations and outcome of nocardiosis and antimicrobial susceptibility of *Nocardia* species in southern Taiwan, 2011–2021. J Microbiol Immunol. 2022;56(2):382–91. https://doi.org/10.1016/j.jmii.2022.11.002.
28. Wilson JW. Nocardiosis: updates and clinical overview. Mayo Clin Proc. 2012;87(4):403–7. https://doi.org/10.1016/j.mayocp.2011.11.016.
29. Méndez-Samperio P. Diagnosis of tuberculosis in HIV co-infected individuals: current status, challenges and opportunities for the future. Scand J Immunol. 2017;86(2):76–82. https://doi.org/10.1111/sji.12567.
30. Lucas SB, Hounnou A, Peacock C, et al. Nocardiosis in HIV-positive patients: an autopsy study in West Africa. Tubercle Lung Dis. 1994;75(4):301–7. https://doi.org/10.1016/0962-8479(94)90137-6.
31. Sakyi SA, Danquah KO, Ephraim RD, et al. Evaluating the contribution of *Nocardia spp.* and *Mycobacterium tuberculosis* to pulmonary infections among HIV and Non-HIV patients at the Komfo Anokye Teaching Hospital. Ghana Can J Infect Dis Med. 2018;2018:2910198. https://doi.org/10.1155/2018/2910198.
32. Uhde KB, Pathak S, McCullum I, et al. Antimicrobial-resistant *Nocardia* isolates, United States, 1995–2004. Clin Infect Dis. 2010;51(12):1445–8. https://doi.org/10.1086/657399.
33. Ott SR, Meier N, Kolditz M, et al. Pulmonary nocardiosis in Western Europe-Clinical evaluation of 43 patients and population-based estimates of hospitalization rates. Int J Infect Dis. 2019;81:140–8. https://doi.org/10.1016/j.ijid.2018.12.010.
34. Cercenado E, Marín M, Sánchez-Martínez M, et al. In vitro activities of tigecycline and eight other antimicrobials against different *Nocardia* species identified by molecular methods. Antimicrob Agents Ch. 2006;51(3):1102–4. https://doi.org/10.1128/AAC.01102-06.
35. Gombert ME, Aulicino TM, duBouchet L, et al. Therapy of experimental cerebral nocardiosis with imipenem, amikacin, trimethoprim-sulfamethoxazole, and minocycline. Antimicrob Agents Ch. 1986;30(2):270–3. https://doi.org/10.1128/AAC.30.2.270.
36. Gombert ME, Berkowitz LB, Aulicino TM, et al. Therapy of pulmonary nocardiosis in immunocompromised mice. Antimicrob Agents Ch. 1990;34(9):1766–8. https://doi.org/10.1128/AAC.34.9.1766.
37. Gombert M, Aulicino T. Synergism of imipenem and amikacin in combination with other antibiotics against *Nocardia* asteroides. Antimicrob Agents Ch. 1984;25(2):299–299. https://doi.org/10.1128/aac.25.2.299-b.
38. Margalit I, Lebeaux D, Tishler O, et al. How do I manage nocardiosis? Clin Microbiol Infec. 2021;27(4):550–8. https://doi.org/10.1016/j.cmi.2020.12.019.


## Publisher's Note