Letter to Editor | Iran J Med Microbiol. 2025; 19(2): 147-149

Category: Medical Bacteriology | Peer Reviewed | Open Access

10.30699/ijmm.19.2.147

Iranian Journal of Medical Microbiology | ISSN:2345-4342

Identification of *Nocardia*: Current Challenges and Prospective

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Keywords: Nocardia, Identification, Molecular Methods, Antibiotic Suscebtibility

Received: 2025/02/24; **Accepted**: 2025/05/27; **Published Online:** 2025/06/06;

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Rezaei S, Mazaheri Nezhad Fard R. Identification of *Nocardia*: Current Challenges and Prospective. Iran J Med Microbiol. 2025;19(2):147-9.

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Dear Editor

Numerous challenges are often addressed during the practical phases of various studies, focusing on isolation and identification of filamentous bacteria such as *Nocardia* spp. as well as assessing their drug resistance patterns. *Based on practical experience the authors have observed*, this has greatly helped the authors in minimizing difficulties and tackling problems during research processes.

Nocardia spp. are filamentous bacteria with ecological importance and clinical implications that are characterized by their unique morphologies and pathogenic potentials. These bacteria are primarily recognized for their partially acid-fast characteristics due to the presence of mycolic acids (MA) in their cell wall (CW) **(1)**. Nocardiosis is a chronic infection caused by various species of *Nocardia*, which can manifest as pulmonary, cutaneous, cerebral and disseminated forms. These conditions primarily affect individuals with compromised immune systems **(2)**. As previously stated, identification of filamentous bacteria, particularly species such as *Nocardia*, presents several challenges in laboratory settings. These difficulties originate from distinctive characteristics of filamentous bacteria and their particular growth needs, broad-spectrum drug resistance patterns, slow growth rates, and oxygen requirements as well as limitations of the current assessment methods **(3)**.

High species diversity within various genera of filamentous bacteria such as *Nocardia* is difficult and traditionally biochemical methods for their identification are imprecise and time-consuming, leading to delays in their detection and treatment **(4)**. Another difficulty is associated with drug resistance variation of these bacteria. It is noteworthy that *Nocardia* spp. demonstrate various resistance patterns to various antimicrobials, affected by factors such as cell wall composition, environmental factors, and high diversity between the species, horizontal gene transfer, genetic mutation and production of numerous metabolites. This variability underscores the need for accurate susceptibility assessment to set the most effective treatments. In contrast, bacteria may demonstrate further well-defined resistance patterns, which facilitate detection and treatment schemes **(5)**. Therefore, use of colorimetric methods such as microplate Alamar blue assay as a reliable inexpensive method for assessing antimicrobial susceptibility patterns of various *Nocardia* isolates is recommended. The assay relies on the ability of living cells to reduce resazurin to resorufin. This reduction reveals cellular metabolic assay reliability and viability.

Alamar blue can continuously be monitored in cultures without interfering with cellular processes, making it an excellent tool for the real-time assessments **(6)**. This method is highly efficient due to its simplicity and reliability, particularly in laboratories with limited resources **(5, 7)**.

Since *Nocardia* colonies resemble fungi in culture media, sequencing is required for their definitive identification. However, due to variability of the conserved region in *Nocardia* genome, it is necessary to use more than one pair of primers, which presents challenges such as designing of specific primers **(8)**.

Advanced molecular methodologies such as multilocus sequence analysis (MLSA) and whole genome sequencing (WGS) have been shown to improve the species discrimination. These techniques analyze multiple genetic markers; thus, providing a further reliable framework for identifying *Nocardia* spp., compared to traditional techniques **(9)**. The Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) represents a significant advancement in identification of *Nocardia* spp., providing rapid reliable results that can enhance clinical decision-making. Integration of direct deposit techniques and updated databases likely improves its further uses, making it an essential tool in modern microbiology laboratories **(10)**. Additionally, bacteriophages serve as promising tools for the identification of *Nocardia* spp. due to their specificity, rapid functionality and ability to differentiate these bacteria from closely related genera. Generally, this method enhances diagnostic accuracy and can facilitate timely treatments for the infections caused by these pathogens **(11)**.

In conclusion, laboratory diagnosis of *Nocardia* spp. is a complex challenge due to the bacterial non-specific clinical characteristics, limitation of traditional culture methods and needs for advanced laboratory diagnostic techniques that may not readily be available. Therefore, further studies are necessary to better understand the antibiotic resistance nature of these bacteria. Studies should include assessment of drug resistance and its effects on conventional treatments, increasing the current knowledge of researchers and medical specialists as early detection of nocardiosis can help decrease complications associated with this severe chronic disease. Additionally, there is an urgent need for developing novel identification methods for these bacteria. This may include various comprehensive Omics knowledge-based studies; thereby, offering a further reliable identification framework, compared to traditional ones.

1. Declarations

1.1 Acknowledgment

None.

1.2 Ethical Considerations

No ethical consideration was needed.

1.3 Authors' Contributions

Ramin Mazaheri Nezhad Fard conceptualized the idea and edited the manuscript; Shabnam Rezaei drafted the preliminary version of the manuscript.

1.4 Conflict of Interests

The authors declare no conflict of interest.

1.5 Financial Support and Sponsorship

The manuscript did not receive funds or grants from institutions or grant bodies.

1.6 Using Artificial Intelligence Tools (AI Tools)

Not applicable.

References

1. McHugh KE, Sturgis CD, Procop GW, Rhoads DD. The cytopathology of Actinomyces, Nocardia, and their mimickers. Diagn Cytopathol. 2017; 45(12):1105-15. [DOI:10.1002/dc.23816] [PMID]
2. Besteiro B, Coutinho D, Fragoso J, Figueiredo C, Nunes S, Azevedo C, et al. Nocardiosis: a single-center experience and literature review. Braz J Infect Dis. 2023;27(5):102806. [PMCID] [DOI:10.1016/j.bjid.2023.102806] [PMID]
3. Joseph J, Sharma S, Dave VP. Filamentous gram-negative bacteria masquerading as actinomycetes in infectious endophthalmitis: a review of three cases. J Ophthalmic Inflamm Infect. 2018;8(1):15. [PMID] [PMCID] [DOI:10.1186/s12348-018-0157-4]
4. Lu SH, Qian ZW, Mou PP, Xie L. Clinical Nocardia species: identification, clinical characteristics, and antimicrobial susceptibility in Shandong,

China. Bosn J Basic Med Sci. 2020;20(4):531-8. [DOI:10.17305/bjbms.2020.4764]

5. Zhao P, Zhang X, Du P, Li G, Li L, Li Z. Susceptibility profiles of Nocardia spp. to antimicrobial and antituberculotic agents detected by a microplate Alamar Blue assay. Sci Rep. 2017;7(1):43660. [DOI:10.1038/srep43660] [PMID] [PMCID]
6. Dinh MN, Hitomi M, Al-Turaihi ZA, Scott JG. Alamar Blue assay optimization to minimize drug interference and inter assay viability. MethodsX. 2024;13:103024. [PMID] [PMCID] [DOI:10.1016/j.mex.2024.103024]
7. Hershko Y, Levytskyi K, Rannon E, Assous MV, Ken-Dror S, Amit S, et al. Phenotypic and genotypic analysis of antimicrobial resistance in Nocardia species. J Antimicrob Chemother. 2023; 78(9):2306-14. [DOI:10.1093/jac/dkad236] [PMID]
8. Conville PS, Brown-Elliott BA, Smith T, Zelazny AM. The complexities of Nocardia taxonomy and identification. J Clin Microbiol. 2017;56(1): e01419-17. [DOI:10.1128/JCM.01419-17] [PMID] [PMCID]
9. Traxler RM, Bell ME, Lasker B, Headd B, Shieh WJ, McQuiston JR. Updated review on Nocardia species: 2006-2021. Clin Microbiol Rev. 2022; 35(4):e00027-21. [DOI:10.1128/cmr.00027-21] [PMID] [PMCID]
10. Hodille E, Prudhomme C, Dumitrescu O, Benito Y, Dauwalder O, Lina G. Rapid, easy, and reliable identification of Nocardia sp. by MALDI-TOF Mass Spectrometry, VITEK®-MS IVD V3. 2 database, using direct deposit. Int J Mol Sci. 2023;24(6):5469. [DOI:10.3390/ijms24065469] [PMID] [PMCID]
11. Acosta F, Vega B, Monzón-Atienza L, Superio J, Torrecillas S, Gómez-Mercader A, et al. Phylogenetic reconstruction, histopathological characterization, and virulence determination of a novel fish pathogen, Nocardia brasiliensis. Aquaculture. 2024;581:740458. [DOI:10.1016/j.aquaculture.2023.740458]