



Oral *Actinomycetes* from HIV-Infected Patients in Tehran, Iran

Aliakbar Bakhtiari¹, Ramin Mazaheri Nezhad Fard ^{2,*}, Seyed Reza Hosseini-doost¹, Golshid Javdani Shahedin³

¹ Department of Microbiology, Islamic Azad Tehran Medical Sciences University, Tehran, Iran

² Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

³ Department of Research and Production Complex, Pasteur Institute of Iran, Tehran, Iran

*Corresponding Author: Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Email: r-mazaherinf@sina.tums.ac.ir

Received: 8 November, 2025; Revised: 8 January, 2026; Accepted: 9 February, 2026

Abstract

Background: Human immunodeficiency virus (HIV) is a member of the retroviral family. The virus infects human white blood cells, including macrophages, dendritic cells, and CD4 lymphocytes, thereby weakening the immune system if patients are not appropriately treated with antiviral agents. Subsequently, the disease progresses to acquired immunodeficiency syndrome (AIDS), with clinical manifestations caused by opportunistic microorganisms, including filamentous bacteria and other bacterial and fungal agents. Filamentous bacteria, or actinomycetes, include important environmental and medically relevant species. These bacteria constitute a major component of the oral microbiota, including that of the oropharynx, particularly in periodontal pockets, gingival grooves, tonsil crypts, and dental plaques.

Objectives: The primary aim of this study was to isolate and phenotypically and genotypically characterize *Actinomycetes* from the oral cavity of HIV-infected participants.

Methods: In this retrospective cross-sectional study, conducted from March 2022 to August 2023, buccal samples were collected from 200 HIV-infected participants at a university clinic and transported under cold-chain conditions to the microbiology laboratory at Tehran University of Medical Sciences, Tehran, Iran. Samples were cultured on appropriate media, and bacterial isolates were identified using microscopic, biochemical, and molecular assays. The antimicrobial susceptibility of the *Actinomycetes* was assessed against selected antimicrobials. In addition, the phylogeny of the isolates was analyzed using sequencing and bioinformatics tools.

Results: Of 200 oral samples from HIV-infected patients, 19 *Actinomycetes* strains (9.5%) were isolated, including *Streptomyces* (n = 6), *Nocardia* (n = 6; all *N. farcinica*), Nocardiosis (n = 6; including two *N. alba*), and *Saccharopolyspora* (n = 1) species. Most isolates were multidrug resistant, exhibiting resistance to beta-lactams such as penicillin G and amoxicillin/clavulanic acid, as well as erythromycin, tetracycline, nalidixic acid, and clindamycin. However, the isolates were largely susceptible to other antimicrobials.

Conclusions: This study demonstrated a high prevalence of *Actinomycetes*, particularly *Nocardia* and *Streptomyces* spp., among HIV-infected patients. Accurate identification of *Actinomycetes* and determination of their antimicrobial susceptibility can effectively guide the treatment of oral ulcers, especially in patients infected with antimicrobial-resistant strains.

Keywords: Human Immunodeficiency Virus, *Actinomycetes*, HIV-associated Infections, Iran

1. Background

In Iran, approximately 46,000 people are living with human immunodeficiency virus (HIV), based on estimates from the Joint United Nations Programme on HIV/AIDS and the World Health Organization, as well as unofficial statistics (1-3). Among adults aged 15 years and

older, nearly 30,000 men and 15,000 women are living with HIV, indicating a predominance of male cases in the HIV epidemic. These patients are at a significantly higher risk of infection with various microorganisms, including filamentous bacteria.

Filamentous bacteria belong to the phylum Actinomycetota, formerly Actinobacteria, which

includes several families of medical and ecological importance. The most ecologically and medically important genera within these families are *Actinomyces*, *Bifidobacterium*, *Nocardia*, *Nocardiosis*, *Propionibacterium*, and *Streptomyces*. These gram-positive, anaerobic or microaerophilic, non-acid-fast, nonmotile, slow-growing bacteria are sometimes reported to cause opportunistic endogenous infections in humans and animals (4, 5). For example, *Actinomyces* spp. can cause actinomycosis, granulomatosis, multiple abscesses, and tissue fibrosis. Species such as *A. meyeri*, *A. naeslundii*, and *A. georgiae* are associated with periodontal diseases (5). Although *Streptomyces* produces a wide range of secondary metabolites, including nearly 70% of known antibiotics, it can also cause opportunistic infections (6). *Nocardia* is another genus within the *Actinomycetes* and can cause nocardiosis, pneumonia, encephalitis, cellulitis, and abscesses in various organs (7). Medically, people with dysfunctional immune systems, such as patients with cancer, transplant recipients, immunosuppressant drug users, and HIV-infected patients, are at higher risk of acquiring infections with *Nocardia* spp. than others (8).

The presence of *Actinomycetes* in the oral cavity of HIV-infected patients can directly or indirectly cause oral and dental infections (9). For example, these bacteria can facilitate the adhesion of anaerobic gram-negative bacteria, such as *Porphyromonas gingivalis*, to dental plaque (10). In HIV-infected patients, oral infections caused by *Actinomycetes* are routinely treated with beta-lactams, cyclines, macrolides, quinolones, and sulfonamides (11-15). The prevalence of *Actinomycetes* in healthy people and HIV-infected patients typically ranges from 1.5% to 3% and from 3% to 6%, respectively.

2. Objectives

Given the importance of oral infections in HIV-infected patients, the primary aims of the present study were to isolate *Actinomycetes* from the oral cavity of HIV-infected participants, characterize the isolates phenotypically and genotypically, and assess their antimicrobial susceptibility (AMS).

3. Methods

3.1. Ethical Considerations

The present study was conducted in full accordance with the Declaration of Helsinki. All participants were informed about the study objectives and benefits and subsequently provided written informed consent. All participants' personal information was archived as

strictly confidential. The study was approved by the Ethics Committee of Islamic Azad Medical Sciences University (IR.IAU.PS.REC.1402.385).

3.2. Sampling

This cross-sectional study was conducted from March 2022 to August 2024 and included 200 oral cavity samples from HIV-infected patients referred to the Southern Health Center of Tehran University of Medical Sciences, Tehran, Iran. Eligible participants were required to have no history of antimicrobial, antifungal, or mouthwash use during the two weeks before sampling and to have a CD4 count of 200 cells or more per microliter of blood. Participants were also required not to have severe infections or systemic diseases such as diabetes or cancer. Buccal swabs, including samples from periodontal and periapical lesions, were collected from participants into sterile tubes. The tubes were appropriately coded and sealed. Samples were transported under cold conditions to the Filamentous Bacteria Laboratory, Department of Pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

3.3. Materials

In the present study, all culture media and biochemicals were purchased from Merck, Germany, and were of analytical grade.

3.4. Culture

To facilitate bacterial growth, incubation was performed at 37°C for 7 days on blood agar (BA) (1, 16). In addition, BA and type-A gas packs were used for the growth of anaerobic bacteria. Differential culture media, including brain-heart infusion agar, were also used for bacterial cultivation. After primary isolation on BA, samples were subcultured on paraffin agar media and incubated for 14 days (17). Morphological characteristics of *Streptomyces* spp. included dry, powdery, and sometimes gray colonies, whereas *Nocardia* spp. formed wet colonies with prominent borders. For further phenotypic identification, samples were stained using a Gram stain (1).

3.5. Biochemical Assessment

To identify *Nocardia* spp., suspected colonies were cultured on agar media, and biochemical assays, including tyrosine degradation and casein, xanthine, and gelatin hydrolysis assays, were performed (17). *Actinomyces* spp. were identified using biochemical assays such as catalase, nitrate reduction, indole

production, and gelatin, urea, and cellobiose hydrolysis assays (2). For *Streptomyces* spp., identification was based on casein, xanthine, and urea hydrolysis assays, as well as various carbohydrate fermentation assays (18).

3.6. Scanning Electron Microscopy

To confirm the isolates and appropriately differentiate *Actinomycetes* from fungi, three isolates of each genus were examined using a scanning electron microscope (FEI Quanta 200 ESEM, USA) at 2500× magnification.

3.7. Antimicrobial Susceptibility Test

To investigate the AMS patterns of the isolates, antimicrobial susceptibility testing (AST) was performed using the Kirby-Bauer method, also known as the agar or disk diffusion method. The turbidity of the bacterial suspension was adjusted to the 0.5 McFarland standard using broth media or sterile normal saline (19). A sterile cotton swab dipped in the bacterial suspension was used to inoculate Mueller-Hinton agar plates by lawn culture, followed by incubation at 35°C for 18 - 24 hours. In general, AST of the isolates was performed against amikacin (30 µg), ciprofloxacin (50 µg), amoxicillin (25 µg), clavulanic acid (20 µg), linezolid (30 µg), penicillin G (10 µg), tetracycline (30 µg), clindamycin (30 µg), erythromycin (15 µg), nitrofurantoin (25 µg), rifampin (5 µg), nalidixic acid (30 µg), and gentamicin (10 µg) (Padtan Teb, Iran) (20, 21).

3.8. Genotypic Identification

To accurately confirm *Actinomycetes*, molecular methods, including polymerase chain reaction (PCR) and sequencing, were used. First, genomic DNA (gDNA) was extracted and used for PCR, and the PCR products were then sequenced. *Actinomycetes*-specific primers were used for molecular identification of the bacteria (16). In this study, the phenol-chloroform method and commercial extraction kits were used to extract gDNA from *Actinomycetes* isolates (SinaClon, Iran). The quality and concentration of the extracted gDNA samples were assessed using a NanoDrop spectrophotometer (Thermo Fisher Scientific, USA) by measuring absorbance at 260/280 nm. Universal primers for 16S rRNA loci were selected based on literature reviews, and PCR was performed using a thermal cycler (Bio-Rad, USA). The PCR cycling program included 35 cycles of denaturation at 94°C for 1 minute, annealing at 60°C for 1 minute, and elongation at 72°C for 1 minute. To analyze the PCR products, electrophoresis was performed on 1.5%

agarose gels with ethidium bromide staining, and the results were examined under ultraviolet light using a gel documentation apparatus (UV transilluminator). The PCR products were then sequenced using the Sanger sequencing method (SinaClon, Iran). After editing the raw data using BioEdit software, sequences were compared with those in the GenBank database (<https://www.ncbi.nlm.nih.gov/genbank>) for possible similarities.

The amplified gene fragments corresponded to the 16S rRNA gene. Raw nucleotide sequences were edited using bioinformatics software and subsequently used to construct phylogenetic trees. Homologous 16S rRNA gene sequences from closely related strains, including six *Nocardia* and five *Streptomyces* strains from other geographical regions, were retrieved using the BLAST online tool (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>). The genomic sequences of *Actinomycetes* were used for phylogenetic analysis using trial versions of Molecular Evolutionary Genetics Analysis (MEGA7) and CLC Genomics Workbench (Qiagen, Germany).

3.9. Statistical Analysis

Data were statistically analyzed using the Statistical Package for Social Sciences software for Windows (IBM, USA) and the chi-square test. P values of 0.05 or less were considered significant.

4. Results

In this study, phenotypic and genotypic methods were used to isolate and characterize *Actinomycetes* from buccal samples collected from 200 HIV-infected participants referred to the Southern Health Center of Tehran University of Medical Sciences, Tehran, Iran. Among the HIV-infected participants, most were male, and all were middle-aged. *Actinomycetes* were isolated more frequently from male participants. However, no statistically significant association was observed between bacterial isolation and the participants' sex ($P = 0.9772$) or age ($P = 0.6434$). The study cohort comprised 47.1% males, with a mean age of 45.2 years ($SD = 15.8$). The cohort predominantly consisted of individuals with low (40.6%) and middle-class (47.8%) incomes. Although bacterial isolation was most common in the middle-income group (52.1% of cases), the association between income level and bacterial isolation was not statistically significant ($P = 0.527$). All HIV-positive participants ($n = 18$) were receiving antiviral treatment. Most of these participants (83.3%) reported no significant side effects; however, this proportion was not statistically significant ($P = 0.344$).

An assessment of oral hygiene revealed that most participants had poor hygiene (78.4%), followed by fair (15.2%) and good (6.4%) hygiene. Although *Actinomyces* isolation occurred most commonly in the poor-hygiene group, this association was not statistically significant ($P = 0.071$). Similarly, there was no significant association with regular dental visits (regular visits: 34.1%; $P = 0.484$). Of 200 samples collected from HIV-infected participants, 19 *Actinomyces* strains were isolated (isolation rate: 9.5%). The taxonomic distribution was as follows: *Streptomyces* (six strains, 31.6%), *Nocardia* (six strains, 31.6%; all *N. farcinica*), *Nocardiosis* (six strains, 31.6%; including two *N. alba*), and *Saccharopolyspora* (one strain, 5.3%). All primary results were subsequently verified using phenotypic methods (scanning electron microscopy) and molecular methods (PCR and sequencing) (Figures 1 and 2). The nucleotide sequences were submitted to GenBank after primary editing (Table 1).

Table 1. GenBank Accession Numbers of the Isolated *Actinomyces* in the Current Study

Isolate	Accession No.
<i>Nocardiosis alba</i> strain 8a	PQ634397.1
<i>Nocardiosis flavescens</i>	PQ633385.1
<i>Nocardiosis</i> sp.	PQ634038.1
<i>Streptomyces</i> sp.	PQ634381.1
<i>Nocardiosis</i> sp.	PQ600881.1
<i>Nocardiosis</i> sp.	PQ600897.1
<i>Nocardiosis</i> sp.	PQ600898.1
<i>Saccharopolyspora</i> sp.	PQ600917.1
<i>Nocardiosis</i> sp.	PQ601059.1
<i>Nocardiosis alba</i>	PQ601058.1

AST results for *Actinomyces* isolated from HIV-infected participants showed that *Streptomyces* spp. and *N. farcinica* were multidrug-resistant (MDR) to penicillin G, amoxicillin and clavulanic acid, tetracycline, erythromycin, nalidixic acid, rifampin, and clindamycin, but were susceptible to other antimicrobials. Using the BLAST online tool, other filamentous bacterial species were identified with 99% similarity to the isolated bacteria (Figure 3). The isolates in this study were genetically similar to those from China, India, Indonesia, and the USA.

5. Discussion

In the present study, *Actinomyces* were isolated from 19 of 200 HIV-infected participants (9.5%). *Nocardia* and *Streptomyces* were the most common genera, with prevalence rates of 63.2% and 36.8%, respectively. Similarly, Steinbrink et al. showed that the frequency of

nocardiosis in HIV-infected patients was 1.85% (22). Fathi et al. reported that *Candida* spp. were isolated from 47.2% of HIV-infected patients (23). A study by Abbasian et al. highlighted that *N. farcinica* infections represented an important opportunistic infection in HIV-infected patients (24). Vujkovic-Cvijin et al. reported that Proteobacteria, particularly members of Enterobacteriaceae, were among the most common bacterial groups in infected patients (25).

In a study by Larijanian et al., two cases of *A. naeslundii*, one case of *A. israelii*, one case of *A. viscosus*, three cases of *N. asteroides*, and one case of *N. brasiliensis* were reported (4). In a 6-month study by Eshraghi et al. in 2003 on 100 patients with periodontal infections, three positive samples of *A. viscosus* and two samples of *A. naeslundii*, with symptoms of gingivitis and periodontitis, were reported (26). In a study by Borsen et al., *A. naeslundii* and *A. israelii* were isolated from 72 abscess samples collected from the roots of oral canals (27). Another study by Khatibi et al. in 2019 on the pathogenicity of *Actinomyces*, which caused stomatitis in 24% - 60% of denture wearers, showed that the causative agents included *C. albicans* and filamentous bacteria such as *Actinomyces* spp. The results showed that *Actinomyces* were isolated from five of the 15 control samples and 11 of the 15 patient samples (28). In a study by Abtahi et al. in 2003 in Arak City, Iran, on the prevalence of nocardiosis in patients with pulmonary infections, nocardiosis was diagnosed in 4.32% of patients (29). In a study by Hashemzadeh et al., PCR and sequencing results showed that 27 samples were positive for nocardiosis, including isolates of *N. nova*, *N. farcinica*, *N. cyriacigeorgica*, and *N. asteroides* (30). A study by Fatahi Bafghi indicated that the epidemiology of the disease was rapidly expanding globally (31). Findings showed that most oral microflora in these patients consisted of filamentous bacteria, causing destruction of gum tissue integrity and pathological changes. In a study by Kenga et al. on 808 HIV-infected children, infections with *Staphylococcus aureus*, *Salmonella* spp., *Escherichia coli*, and *Klebsiella* spp. were reported (32).

In the present study, AST was performed on 19 *Actinomyces* isolates, including *Nocardia* and *Streptomyces* spp., against 13 antimicrobial agents using the Kirby-Bauer method. The isolates generally showed resistance to penicillin G, amoxicillin and clavulanic acid, erythromycin, tetracycline, rifampin, nalidixic acid, and clindamycin, but were susceptible to gentamicin, ciprofloxacin, amikacin, linezolid, trimethoprim-sulfamethoxazole, and nitrofurantoin. A comparison with the findings of a study by Abbasian et al. revealed consistent susceptibility to trimethoprim-

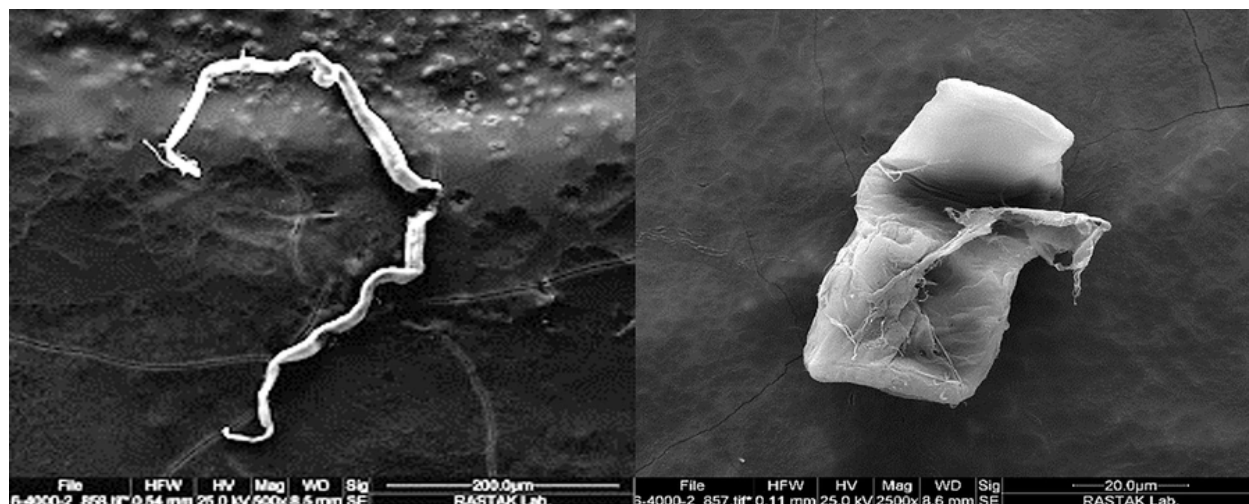


Figure 1. Phenotypes of *Actinomycetes* from HIV-infected participants using scanning electron microscopy at 2500×. Left, *Streptomyces* sp.; right, *Nocardia* sp.



Figure 2. Electrophoresis of bacterial gDNA on 1.5% agarose gels using ethidium bromide staining. Right) C-, negative control; C+, positive control; lanes 1 - 9, 1500-bp 16S rRNA gene PCR products; 100-bp DNA ladder; and left) C-, negative control; lanes 1 - 6, 1500-bp 16S rRNA gene PCR products; M, 1-kb DNA ladder.

sulfamethoxazole and amikacin in the two studies (24). In a study by Osamu et al. on clinical samples, *A. israelii* was resistant to ofloxacin and sodium fluoride compared with other *Actinomyces* strains. Naturally, *Actinomyces* spp. are susceptible to penicillin, cephalosporins, clindamycin, carbapenem, and tetracycline; however, they are exceptionally resistant to penicillin (33). Salehipour et al. reported that, among 31 isolates of *N. asteroides*, all were fully susceptible to trimethoprim-sulfamethoxazole and linezolid and

moderately susceptible to amoxicillin and clavulanic acid, cefepime, ceftriaxone, ciprofloxacin, imipenem, moxifloxacin, and tobramycin (34). A summary of other similar studies is provided in Table 2 (35-39).

In a study by Ezeonwumelu et al. in England, bacteria were isolated from the oral cavities of HIV-infected patients. Their results indicated that trimethoprim-sulfamethoxazole had the weakest inhibitory effect against *S. aureus* and the strongest inhibitory effect

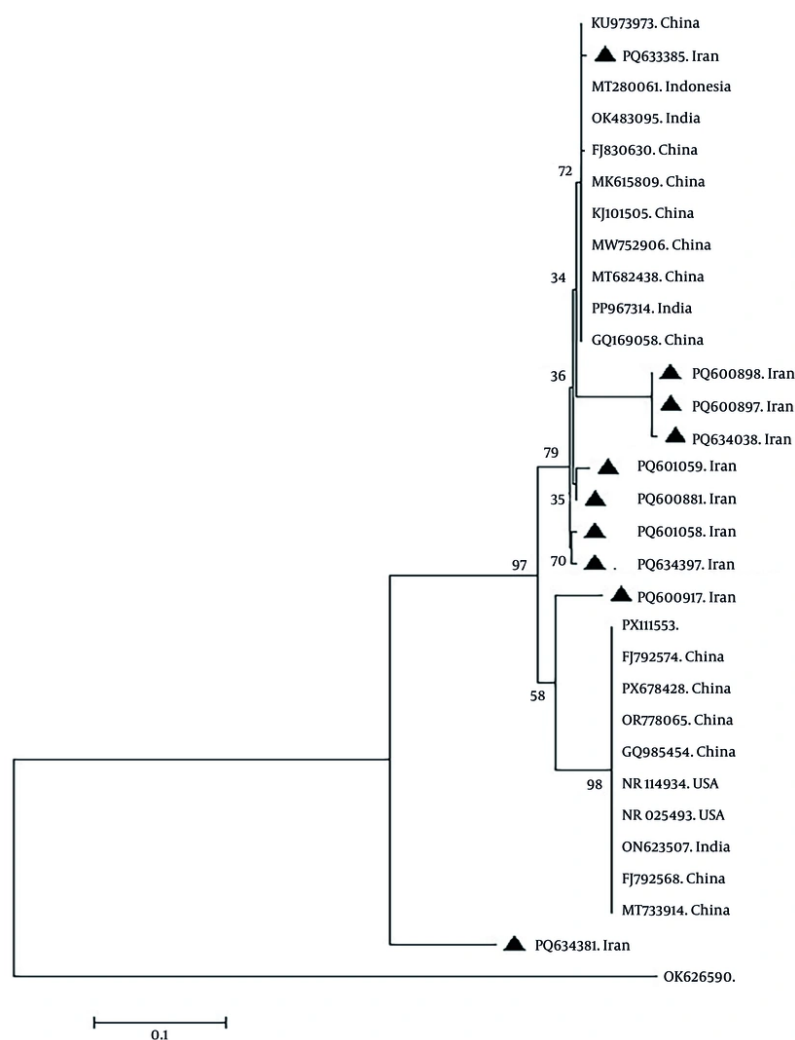


Figure 3. Phylogenetic tree of the *Streptomyces* and *Nocardia* species isolated in the current study using the neighbor-joining method and bootstrap replicates of 1000.

against *E. coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 (40).

In the present study, PCR amplification of the 16S rRNA gene enabled accurate species identification of the *Actinomycetes*. Nucleotide sequences showed 99% similarity with reference sequences in GenBank for *Streptomyces* and *Nocardia* isolates, indicating close phylogenetic relationships. Phylogenetic analysis of the isolates, including *N. farcinica* and *Streptomyces* sp., revealed close relationships with strains from neighboring and distant countries. The rooted phylogenetic tree illustrated evolutionary relationships

among various *Streptomyces* and *N. farcinica* strains, allowing inference of their divergence from a common ancestor. The *N. flavescens* (PQ633385.1) identified in the present study clustered closely with strains isolated from China, India, and Indonesia. *Saccharopolyspora* sp. (PQ600917.1) was genetically close to bacteria isolated from China, the United States, and India. Seven bacterial strains, including *Nocardiopsis* sp. (PQ600898.1), *Nocardiopsis* sp. (PQ600897.1), *Nocardiopsis* sp. (PQ634038.1), *Nocardiopsis* sp. (PQ601059.1), *Nocardiopsis* sp. (PQ600881.1), *Nocardiopsis* sp. (PQ634397.1), and *N. alba* (PQ601058.1), isolated in this study were less similar to filamentous bacteria isolated

Table 2. Summary of *Actinomyces* Isolation and Antibiotic Resistance Profiles in HIV-Infected Patients from Other Studies

Study (y)	Study Subject	Organism	Antimicrobial	Major Finding
Wolff et al. (2022) (35)	Oral clinical isolates	<i>Actinomyces</i> spp. (n = 100)	Penicillin, ampicillin-sulbactam, meropenem, clindamycin, moxifloxacin, linezolid, tigecycline	Low resistance to β -lactams; high resistance to moxifloxacin and daptomycin; good susceptibility to linezolid
Smith et al. (2005) (36)	Clinical isolates	<i>Actinomyces</i> spp. (n = 87)	Penicillin, amoxicillin, ceftriaxone, tetracycline, clindamycin, ciprofloxacin	High susceptibility to β -lactams; resistance to ciprofloxacin and macrolides
Steininger and Willinger (2016) (37)	Retrospective clinical isolates	Pathogenic <i>Actinomyces</i> spp. (n = 392)	β -lactams, carbapenems, tetracyclines, metronidazole	Susceptible to β -lactams and carbapenems; intrinsic resistance to metronidazole
Brooks et al. (2022) (38)	Systematic review of oral microbiome studies	Oral microbiota (ARGs)	Multiple antibiotic classes	Widespread antibiotic resistance genes detected in the oral cavity
Dollas et al. (2025) (39)	Saliva samples from adults	Oral bacterial flora	Multiple antibiotic classes	High prevalence of antimicrobial resistance in salivary isolates

from China, India, and Indonesia. Furthermore, a bacterial strain of *Streptomyces* sp. (PQ634381.1) isolated in this study showed no similarity to filamentous bacteria isolated from other countries.

Overall, the reported similarities may be attributable to developed transportation networks and frequent travel between geographical regions for vocational, educational, occupational, official, and commercial purposes. However, infections transmitted through food, devices, and especially prosthetics cannot be dismissed. This molecular identification approach was consistent with modern standards, as highlighted by Kim et al., who described molecular methods as the gold standard for bacterial identification (41).

5.1. Study Limitations

This study had a few limitations that should be addressed. First, some potentially important confounding variables were not investigated. Factors such as individual oral hygiene practices and smoking status may affect the oral microbial composition and antimicrobial resistance patterns observed in HIV-positive patients. Second, the prices of laboratory materials increased dramatically during the study. Third, variability in personal oral health behaviors and access to dental care among HIV-positive participants might have contributed to inter-individual differences that were not fully assessed in the analysis. Fourth, citations were limited because of the limited number of studies on oral AMS schemes among HIV-positive patients in Iran and other regional countries.

5.2. Conclusions

This study revealed that *Actinomyces*, primarily *Nocardia* and *Streptomyces* spp., were highly prevalent in Iranian HIV-infected patients. The current findings also revealed that most of these isolates were MDR isolates.

Accurate molecular characterization of *Actinomyces* and assessment of their AMS profiles can significantly improve the targeted treatment of Actinomycete-associated oral infections.

Acknowledgements

The authors sincerely thank Dr. Ashrafi and Ms. Faridfar for their technical advice.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: All authors confirm that they made substantial contributions to the conception and design of the study, execution of the work, data analysis and interpretation, and preparation of the final manuscript. All authors have read and approved the final version of the manuscript and agree to be accountable for the accuracy, integrity, and scientific content of the work.

Conflict of Interests Statement: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Data Availability: The data that support the findings of this study are available from the corresponding author upon reasonable request. Due to privacy and ethical restrictions related to HIV-positive participants, the data are not publicly available.

Ethical Approval: This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. All participants were informed about the study objectives and provided written

informed consent, and their personal information was kept strictly confidential. The study was approved by the Ethics Committee of Islamic Azad Medical Sciences University (approval no. IR.IAU.PS.REC.1402.385; 28 August 2023).

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Trial Registration: Approval no. IR.IAU.PS.REC.1402.385, issued 28 August 2023.

References

- UNAIDS. Geneva: UNAIDS; 2023.
- Dehghan P, Mohammadi F, Javaheri MR, Nekoeian S. Identification of *Candida* species in the oral cavity of diabetic patients. *Current Medical Mycology*. 2016;**2**(2):1-0. [PubMed ID: 28681013]. [PubMed Central ID: PMC5490298]. <https://doi.org/10.18869/acadpub.cmm.2.2.4>.
- Heidarian A, Dehghan P, Chadeganipour M, Tayeri K. Frequency of *Candida* species isolated from the Oral Cavity of HIV-Infected Patients referring to Behavioral disease Counseling Center of Isfahan in 2017 - 2018. *Scientific Journal of Kurdistan University of Medical Sciences*. 2019;**24**(5):30-41. <https://doi.org/10.29252/sjku.24.5.30>.
- Larijanian L, Hashemi J, Siadat D. Identification of Etiologic Agents of Actinomycetal Infections among Patients Referred to the Health Faculty of Tehran University of Medical Sciences. *Iranian Journal of Medical Microbiology*. 2018;**11**:203-9.
- Könönen E, Wade WG. Actinomyces and related organisms in human infections. *Clinical microbiology reviews*. 2015;**28**(2):419-42. [PubMed ID: 25788515]. [PubMed Central ID: PMC4402957]. <https://doi.org/10.1128/CMR.00100-14>.
- Genilloud O. Actinomycetes: still a source of novel antibiotics. *Natural product reports*. 2017;**34**(10):1203-32. [PubMed ID: 28820533]. <https://doi.org/10.1039/C7NP00026J>.
- Saubolle MA, Sussland D. Nocardiosis: review of clinical and laboratory experience. *Journal of clinical microbiology*. 2003;**41**(10):4497-501. [PubMed ID: 14532173]. [PubMed Central ID: PMC254378]. <https://doi.org/10.1128/JCM.41.10.4497-4501.2003>.
- Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. *Clinical microbiology reviews*. 2006;**19**(2):259-82. [PubMed ID: 16614249]. [PubMed Central ID: PMC1471991]. <https://doi.org/10.1128/CMR.19.2.259-282.2006>.
- Li J, Li Y, Zhou Y, Wang C, Wu B, Wan J. Actinomyces and alimentary tract diseases: a review of its biological functions and pathology. *BioMed research international*. 2018;**2018**(1):3820215-8. [PubMed ID: 30225251]. [PubMed Central ID: PMC6129341]. <https://doi.org/10.1155/2018/3820215>.
- Abdulkareem AA, Al-Taweel FB, Al-Sharqi Ajb, Gul SS, Sha A, Chapple ILC. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. *Journal of Oral Microbiology*. 2023;**15**(1):2197779. [PubMed ID: 37025387]. [PubMed Central ID: PMC10071981]. <https://doi.org/10.1080/200002297.2023.2197779>.
- Ganesan A, Mesner O, Okulicz JF, O'Bryan T, Deiss RG, Lalani T, et al. A single dose of benzathine penicillin G is as effective as multiple doses of benzathine penicillin G for the treatment of HIV-infected persons with early syphilis. *Clinical Infectious Diseases*. 2015;**60**(4):653-60. [PubMed ID: 25389249]. [PubMed Central ID: PMC6477935]. <https://doi.org/10.1093/cid/ciu888>.
- Seddon J, Bhagani S. Antimicrobial therapy for the treatment of opportunistic infections in HIV/AIDS patients: a critical appraisal. *HIV/AIDS-Research and Palliative Care*. 2011;19. [PubMed ID: 22096404]. [PubMed Central ID: PMC3218711]. <https://doi.org/10.2147/HIV.S9274>.
- Faiela C, Sevene E. Antibiotic prescription for HIV-positive patients in primary health care in Mozambique: a cross-sectional study. *Southern African Journal of Infectious Diseases*. 2022;**37**(1):340. [PubMed ID: 35284563]. [PubMed Central ID: PMC8905412]. <https://doi.org/10.4102/sajid.v37i1.340>.
- Dube PS, Legoabe LJ, Beteck RM. Quinolone: a versatile therapeutic compound class. *Molecular Diversity*. 2023;**27**(3):1501-26. [PubMed ID: 36527518]. [PubMed Central ID: PMC9758687]. <https://doi.org/10.1007/s11030-022-10581-8>.
- Staehelin C, Elzi L, Weber R, Furrer H. Treatment and prevention of opportunistic infections. *Ther Umsch*. 2014;**71**(8):475-82. [PubMed ID: 25093312]. <https://doi.org/10.1024/0040-5930/a000540>.
- Najafi Mosleh M, Salari MH, Yousefi Mashoof R, Yousefi Mashoof K. The prevalence of obligatory anaerobic bacteria in oral cavity infections. *Iranian Journal of Otorhinolaryngology*. 2008;**19**(50):199-205.
- Abdi Soofiani S, Dehnad AR, Nahaei MR, Parsa Yegane L, Barzegari A, Maleki Kakolr H. Molecular Identification of *Streptomyces* Spp. with Antibacterial Activity Isolated from East Azerbaijan Soils. *Medical Journal of Tabriz University of Medical Sciences Health Services*. 2011;**33**(2):49-56.
- Zaini F, Mahboub SA, Emami M. *Medical Mycology*. Tehran: Tehran University Press; 2004.
- Blouiri M, Sadiki M, Ibnouda SK. Methods for in vitro evaluating antimicrobial activity: A review. *Journal of pharmaceutical analysis*. 2016;**6**(2):71-9. [PubMed ID: 29403965]. [PubMed Central ID: PMC5762448]. <https://doi.org/10.1016/j.jpha.2015.11.005>.
- Preston BD, Poesz BJ, Loeb LA. Fidelity of HIV-1 reverse transcriptase. *Science*. 1988;**242**(4882):1168-71. [PubMed ID: 2460924]. <https://doi.org/10.1126/science.2460924>.
- AIDSinfo; AIDSinfo. *AIDSinfo*. 2016, [cited 2025 Oct 8]. Drug name abbreviations. Available from: <https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/drug-name-abbreviations>.
- Steinbrink J, Leavens J, Kauffman CA, Miceli MH. Manifestations and outcomes of nocardia infections: comparison of immunocompromised and nonimmunocompromised adult patients. *Medicine*. 2018;**97**(40):e12436. [PubMed ID: 30290600]. [PubMed Central ID: PMC6200467]. <https://doi.org/10.1097/MD.00000000000012436>.
- Fathi F, Mahmoudabadi AZ, Fatahinia M. A comparative study on the production of extracellular hydrolytic enzymes of *C. albicans* and non-albicans *Candida* species isolated from HIV+/AIDS patients and healthy individuals. *Current Medical Mycology*. 2022;**8**(2):32. [PubMed ID: 36654790]. [PubMed Central ID: PMC9825789]. <https://doi.org/10.18502/cmm.8.2.10330>.
- Abbasian L, Dehghan Manshadi SA, Hassan Nezhad M, Masoumzadeh N, Ghaderkhani S, Keyvanfar A, et al. A Case Report of Disseminated Nocardiosis in a Patient with HIV Infection: Concurrent Liver, Pulmonary, and Brain Involvements. *Archives of Clinical Infectious Diseases*. 2024;**19**(2):e140527. <https://doi.org/10.5812/archcid-140527>.
- Vujkovic-Cvijin I, Somsouk M. HIV and the gut microbiota: composition, consequences, and avenues for amelioration. *Current HIV/AIDS Reports*. 2019;**16**(3):204-13. [PubMed ID: 31037552]. [PubMed Central ID: PMC6579656]. <https://doi.org/10.1007/s11904-019-00441-w>.
- Eshraghi SS, Zomorodian K, Kordbacheh P, Gerami Shoar M, Saber S. Nocardiosis in Pulmonary Patients. *Journal of Guilan University of*

- Medical Sciences*. 2003;**11**(44):28-33.
27. Borssén E, Sundqvist G. Actinomyces of infected dental root canals. *Oral Surgery, Oral Medicine, Oral Pathology*. 1981;**51**(6):643-8. [PubMed ID: 6942364]. [https://doi.org/10.1016/S0030-4220\(81\)80016-3](https://doi.org/10.1016/S0030-4220(81)80016-3).
 28. Khatibi M, Zaker Bostanabad S, Rahimi MK, Semsar Asl Y. The relation between Actinomyces and denture stomatitis. *Journal of Research in Dental Sciences*. 2019;**16**(2):102-9. <https://doi.org/10.29252/jrds.16.2.102>.
 29. Abtahi H, Saffari M, Jourabchi A, Rafiei M. Pulmonary nocardiosis and its related factors in patients with pulmonary infection in Arak. *Feyz Journal of Kashan University of Medical Sciences*. 2003;**7**(3):87-91.
 30. Hashemzadeh M, Asareh Zadegan Dezfouli A, Afzal Zadeh S. Isolation and identification of Nocardia species from bronchial and sputum samples of patients suspected of Nocardiosis using molecular PCR method in Khuzestan Province. *New Cellular and Molecular Biotechnology Journal*. 2021;**11**(42):9-17.
 31. Fatahi-Bafghi M. Nocardiosis from 1888 to 2017. *Microbial Pathogenesis*. 2018;**114**:369-384. [PubMed ID: 29146497]. <https://doi.org/10.1016/j.micpath.2017.11.012>.
 32. Kenga DB, Gebretsadik T, Simbine S, Maússe FE, Charles P, Zaqueu E, et al. Community-acquired bacteremia among HIV-infected and HIV-exposed uninfected children hospitalized with fever in Mozambique. *International Journal of Infectious Diseases*. 2021;**109**:99-107. [PubMed ID: 34174435]. [PubMed Central ID: PMC8437032]. <https://doi.org/10.1016/j.ijid.2021.06.047>.
 33. Tsuzukibashi O, Fukatsu A, Fuchigami M, Uchibori S, Komine C, Umezawa K, et al. Isolation and identification methods for Actinomyces israelii involved in actinomycosis. *Open Journal of Stomatology*. 2022;**12**(4):108-18. <https://doi.org/10.4236/ojst.2022.124011>.
 34. Salehipour M, Zaker Bostanabad S, Rezaee S, Hashemi-Shahraki A. Antimicrobial susceptibility of clinical isolates of Nocardia in Iran. *New Cellular and Molecular Biotechnology Journal*. 2016;**6**(21):99-106.
 35. Wolff A, Rodloff AC, Vielkind P, Borgmann T, Stingu CS. Antimicrobial susceptibility of clinical oral isolates of Actinomyces spp. *Microorganisms*. 2022;**10**(1):125. [PubMed ID: 35056574]. [PubMed Central ID: PMC8779083]. <https://doi.org/10.3390/microorganisms10010125>.
 36. Smith AJ, Hall V, Thakker B, Gemmell CG. Antimicrobial susceptibility testing of Actinomyces species with 12 antimicrobial agents. *Journal of Antimicrobial Chemotherapy*. 2005;**56**(2):407-9. [PubMed ID: 15972310]. <https://doi.org/10.1093/jac/dki206>.
 37. Steininger C, Willinger B. Resistance patterns in clinical isolates of pathogenic Actinomyces species. *Journal of Antimicrobial Chemotherapy*. 2016;**71**(2):422-7. [PubMed ID: 26538502]. <https://doi.org/10.1093/jac/dkv347>.
 38. Brooks L, Narvekar U, McDonald A, Mullany P. Prevalence of antibiotic resistance genes in the oral cavity and mobile genetic elements that disseminate antimicrobial resistance: A systematic review. *Molecular Oral Microbiology*. 2022;**37**(4):133-53. [PubMed ID: 35674142]. <https://doi.org/10.1111/omi.12375>.
 39. Dollas MN, Nilsson M, Larsen T, Nygaard N, Moser C, Belstrøm D. High prevalence of antibiotic resistance of Streptococcus species in saliva from non-hospitalized adults-a pilot study. *Journal of Oral Microbiology*. 2025;**17**(1). 2486647. [PubMed ID: 40182115]. [PubMed Central ID: PMC11966976]. <https://doi.org/10.1080/200002297.2025.2486647>.
 40. Ezeonwumelu J, Ntale M, Kasozi K, Ogbonnia S, Tanayen J, Agwu E, et al. Resistance, Minimum Inhibitory and Bactericidal Concentration Profiles of Oral Bacteria from HIV/AIDS Patients in South Western Uganda. *Journal of Advances in Medicine and Medical Research*. 2016;**18**(11):1-4. [PubMed ID: 27338010]. [PubMed Central ID: PMC4919687]. <https://doi.org/10.9734/BJMMR/2016/28491>.
 41. Kim G, Ahn D, Kang M, Park J, Ryu D, Jo Y, et al. Rapid species identification of pathogenic bacteria from a minute quantity exploiting three-dimensional quantitative phase imaging and artificial neural network. *Light: Science & Applications*. 2022;**11**(1). 190. [PubMed ID: 35739098]. [PubMed Central ID: PMC9226356]. <https://doi.org/10.1038/s41377-022-00881-x>.