Journal of Current Research in Oral Surgery
2021, Volume 1, Page No: 47-56

Available online at: www.tsdp.net

ISSN: 3062-3480

Original Article

Phenotypic Presentation and Treatment Outcomes of Oral Candidiasis in Frail Older Patients: Focus on Antifungal Resistance and Non-albicans Species

Robert L. Peterson[1]*, Sofia L. Romano[1], James A. Wilson[1]

[1]Department of Oral and Maxillofacial Surgery, School of Dentistry, University of Washington, Seattle, United States.

***E-mail** ✉ robert.peterson@gmail.com

Received: 14 January 2021; **Revised:** 11 March 2021; **Accepted:** 11 March 2021

ABSTRACT

Oral candidiasis is a frequent fungal condition that disproportionately impacts older adults, individuals with weakened immunity, and patients undergoing oncology therapies. Although widespread, recognizing and managing this infection can be difficult because presentation varies widely and antifungal resistance may complicate care. This study sought to identify which clinical manifestations best indicate oral Candida infections, with particular attention to features linked to poor antifungal response. A secondary aim was to explore whether underlying health issues—such as frailty and coexisting medical conditions—affect vulnerability to infection or influence treatment outcomes. A sample of 57 adults aged ≥65 years (mean age 74) was recruited from oncology and hospitalist services in Northern Ontario. Most participants (65%) were receiving active cancer therapy. Each underwent an oral examination for candidiasis-related signs and symptoms, and fungal swabs were collected at baseline and again two weeks later. Species identification and therapeutic responses were documented. Most infections were due to *Candida albicans* and improved with standard antifungal therapy. In contrast, infections involving *Nakaseomyces glabratus* or *Pichia kudriavzevii* were more likely to continue, aligning with known resistance patterns. Clinically, pseudomembranous presentations—white plaques, tongue coating, taste changes—tended to resolve more readily, whereas erythematous findings, including oral redness and angular cheilitis, were often linked to persistent disease. Although 45% of participants met criteria for moderate to severe frailty, frailty did not demonstrate a significant relationship with persistent or resistant infection. The findings highlight the broad clinical variability of oral candidiasis and emphasize the need for rapid, point-of-care molecular diagnostics to distinguish species and guide timely management, particularly for older or medically complex individuals.

Keywords: Phenotypic, Oral candidiasis, Non-Albicans species, Frail older patients

How to Cite This Article: Peterson RL, Romano SL, Wilson JA, Carter WJ. Phenotypic Presentation and Treatment Outcomes of Oral Candidiasis in Frail Older Patients: Focus on Antifungal Resistance and Non-albicans Species. J Curr Res Oral Surg. 2021;1:47-56. https://doi.org/10.51847/knWA4toqf7

Introduction

Oral candidiasis is caused by excessive proliferation of *Candida* species within the oral cavity. It can lead to discomfort, localized soreness, increased oral dryness, impaired taste, and difficulty eating, and may progress to complications such as dehydration, poor nutrition, and reduced overall well-being [1, 2]. In more severe cases, the infection may extend into the bloodstream or internal organs—including the digestive tract—raising risks of sepsis and mortality [3-7].

Many *Candida* species reside harmlessly on mucosal surfaces [8]. Indeed, roughly half of adults in some populations harbor *Candida albicans* without symptoms [8, 9]. Maintaining proper dental hygiene and routine oral care helps prevent fungal proliferation and supports microbial balance [6, 10, 11]. This includes correct brushing habits and appropriate denture management, such as removing dentures during sleep [12].

Multiple factors can increase susceptibility to fungal overgrowth. Infants, older adults, and palliative care

patients are particularly vulnerable, as are individuals with xerostomia or immune-related and endocrine disorders, including HIV and cancer [2, 12–14]. Additional risks include polypharmacy, heavy alcohol use, smoking, poor denture cleaning, inadequate nutrition, and prolonged use of steroids, antibiotics, or antifungal agents [9, 12, 15]. The combined influence of these factors—and how they interact—remains insufficiently understood.

Common symptoms include dry mouth, altered taste, and burning sensations, while angular cheilitis, removable plaques, and mucosal redness are also characteristic. Presentation varies by location (localized vs. systemic) and form (pseudomembranous or erythematous) [9]. Pseudomembranous candidiasis, often called "oral thrush" in its acute form, appears as white, plaque-like lesions and may become chronic and hyperplastic if they cannot be wiped away [5]. Erythematous candidiasis manifests as red, inflamed tissue and burning sensations [16], while angular cheilitis produces similar symptoms at the mouth corners, sometimes with fissures [16]. Diagnosis requires careful evaluation of risk factors and symptom patterns by an experienced clinician [9]. However, laboratory confirmation—though costly and slow—is often needed to distinguish candidiasis from other conditions, complicating treatment decisions at the initial visit.

The central aim of this study was to identify which clinical indicators most reliably point to oral Candida infections, especially those unlikely to respond to antifungal therapy. A further goal was to examine how frailty and comorbid health conditions may influence both susceptibility to infection and treatment success.

Materials and Methods

Patients and setting

Participants were recruited through the North Eastern Cancer Center (NECC) Dental Clinic, the NECC Symptom Management Clinic, and the Health Sciences North (HSN) Hospitalist service in Sudbury, Ontario. Enrollment occurred between June 2019 and September 2021. Individuals were excluded if they had taken any antifungal medication within the two weeks preceding recruitment.

Inclusion criteria required that participants be 65 years of age or older, actively receiving care through one of the listed NECC or HSN clinics, capable of providing consent for two oral swabs (baseline and follow-up), eligible for fluconazole therapy, and presenting with at least one clinical sign or symptom of oral candidiasis at enrollment. Participants also needed to be able to return for a two-week follow-up visit and have sufficient cognitive capacity to complete study questionnaires.

Survey data captured demographic information, including age, sex, smoking behavior, comorbidity history (e.g., hypertension, cardiovascular disease, diabetes, cancer), and Clinical Frailty Scale (CFS) scores [17]. Frailty was grouped as: Fit/Low (CFS 1–4), Moderate (CFS 5–6), and Severe (CFS 7–9). Nutritional status was categorized as normal or compromised. Oral hygiene was classified as good, fair, or poor. Smoking history was listed as current, former, or never. Dentition categories included dentate, partially dentate, and edentulous.

Symptoms and fungal surveillance

Symptoms documented included dry mouth, altered taste, and burning sensations. Clinical signs assessed were angular cheilitis, tongue coating, mucosal redness, and removable plaques involving the oral cavity or oropharynx. Fluconazole was used as the primary therapy for most patients exhibiting at least one indicator of candidiasis. Depending on the presentation and severity, topical agents such as nystatin (polyene) or ketoconazole (Nizoral) were used instead.

A two-week follow-up evaluation determined whether the infection had cleared. When symptoms persisted, alternative antifungals—micafungin-S (echinocandin), miconazole, or clotrimazole—were prescribed. Swabs collected from the baseline visit (and from the follow-up when applicable) were processed in the HSN microbiology laboratory. Samples were taken from the bilateral buccal mucosa and the dorsal tongue.

For culture, swabs were plated on Sabouraud Dextrose Agar (SDA) and incubated at 35 °C for 48 h. Single colonies were selected for species-level identification using the VITEK® MS MALDI-TOF MS platform (bioMérieux, France). Colonies were applied to target plates, coated with α-cyano-4-hydroxycinnamic acid matrix, dried, and analyzed. Identifications were accepted when confidence scores were ≥95%. Glycerol stocks created from SDA plates were stored at −80 °C for future analyses.

Statistical analysis

Continuous variables were summarized using means and standard deviations; categorical variables were described with counts and percentages. Patient indication combinations were visualized using an upset plot generated with the "ComplexHeatmap" R package. Associations between baseline indications (dependent variable) and identified Candida species were analyzed via logistic regression, except for total indication count, which used ordered logistic

regression. Logistic regression was also used to estimate univariate associations between patient characteristics or indication patterns and infection persistence at follow-up. All analyses were completed using R v4.5.0.

Results and Discussion

Patients enrolled

Of the 65 individuals approached, 57 met the inclusion criteria and were enrolled **(Figure 1).** Ages ranged from 65 to 94 years, with 33 patients aged 65–74, 22 aged 75–84, and 2 aged 85 or older. The mean age was 74 years. Female and male representation was nearly even (47% and 53%, respectively) **(Table 1).**

Most participants (65%) were receiving active cancer treatment. Among the 37 patients in treatment, lung cancer was most frequent (n = 10), followed by tongue cancer (n = 4). Myeloma, tonsil, and prostate cancers each appeared in three cases. Two individuals each had cancers of the mouth, breast, or kidney. Single cases occurred for pelvic, bladder, skin, cheek, stomach, rectal, ear, and esophageal cancers. Cancer stage information was unavailable for 22 patients, while 11 were stage IV, 3 were stage II, and 1 was stage III.

Frailty distribution showed 53% with low/fit scores, 26% with moderate frailty, and 19% with severe frailty (1.8% missing). Regarding dentition, 36% were fully dentate, 19% were partially dentate, and 24% were edentulous (22.8% missing). A majority (60%) had compromised nutritional intake. Oral hygiene was mainly rated as fair (61.4%), with the remainder split evenly between poor (19.3%) and good (19.3%).

Twelve percent were current smokers, while 47% were former smokers. Medical histories varied widely, including cardiac, vascular, pulmonary, renal, neuromuscular, gastrointestinal, rheumatologic, and mental health conditions. The most prevalent comorbidities were hypertension (n = 31), diabetes (n = 17), cardiovascular disease (n = 13), and gastroesophageal reflux disease (GERD) (n = 13).

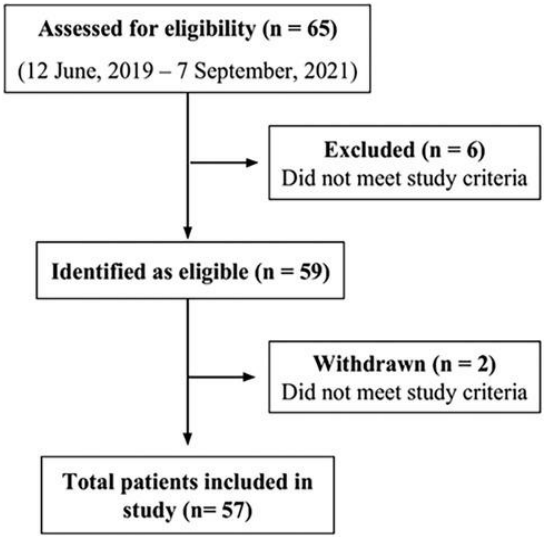

Figure 1. Flow diagram outlining participant recruitment.

Table 1. Baseline characteristics of enrolled individuals (n = 57). Continuous metrics are reported as mean (standard deviation), while categorical information is listed as count (percentage).

Variable	Values / Mean (SD) or n (%)
Age (years)	73.8 (6.63)
Sex	
Female	27 (47.4%)
Male	30 (52.6%)
Smoking status	
Never smoker	22 (38.6%)
Former smoker	27 (47.4%)
Current smoker	7 (12.3%)
Missing data	1 (1.8%)
Nutritional status	
Normal	23 (40.4%)
At risk / compromised	34 (59.6%)
Frailty Index	0.169 (0.102)
Missing	1 (1.8%)
Clinical Frailty Scale	
Fit / Low frailty	30 (52.6%)
Mild to moderate frailty	15 (26.3%)
Severe / very severe frailty	11 (19.3%)
Missing	1 (1.8%)
Currently receiving cancer treatment	
No	20 (35.1%)
Yes	37 (64.9%)
Oral hygiene status	
Poor	11 (19.3%)
Fair	35 (61.4%)
Good	11 (19.3%)
Dentition status	
Dentate (natural teeth present)	21 (36.8%)
Partially dentate	11 (19.3%)
Edentulous (no natural teeth)	12 (21.1%)

Missing data	13 (22.8%)

Baseline fungal screening and symptom presentation

Nearly all participants showed dry mouth (93.0%) (**Figure 2).** Roughly half reported taste alteration (50.9%), and around four in ten experienced burning sensations (42.1%), angular fissures (42.1%), mucosal erythema (43.9%) or detachable plaques (40.4%). Coated tongue was the least common finding (36.8%). Only one patient exhibited all six manifestations of oral candidiasis **(Figure 2).** The most common symptom cluster consisted of dry mouth, angular cheilitis, redness, and burning (n = 6). Logistic regression indicated that the likelihood of presenting with erythema [OR (95% CI) = 5.7 (1.57, 27.6)] or removable plaques [8.3 (2.0, 57.1)] was significantly elevated in the presence of any Candida infection **(Figure 3).** Total indication count was also associated with fungal presence, with odds increasing 3.9-fold (95% CI = 1.32, 11.8). Comparable trends were seen when Candida albicans alone was detected at baseline [erythema: 4.5 (1.44, 16.4); plaques: 5.3 (1.61, 21.5); total indications: 5.9 (1.98, 17.4)], along with greater odds of burning mouth [4.0 (1.28, 14.6)] **(Figure 3).** No meaningful relationships were observed for non–C. albicans species.

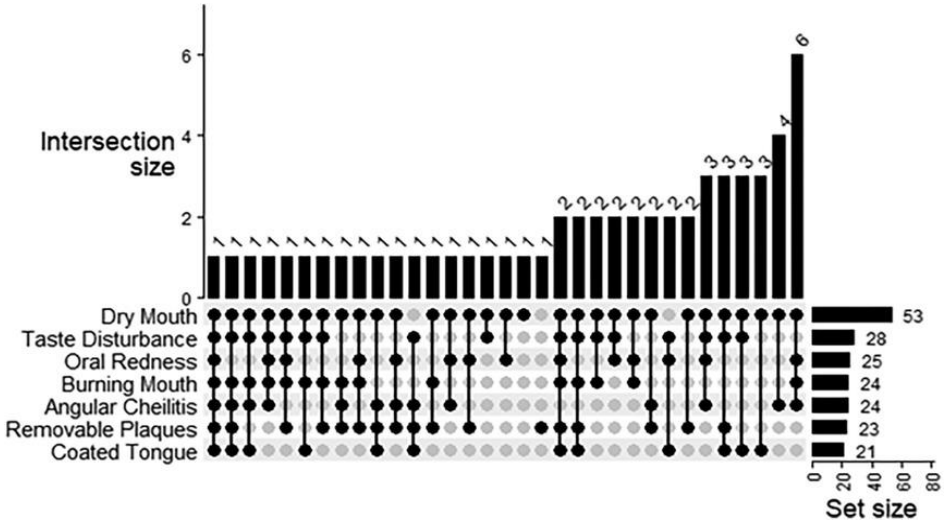

Figure 2. Symptom combinations recorded at enrollment.

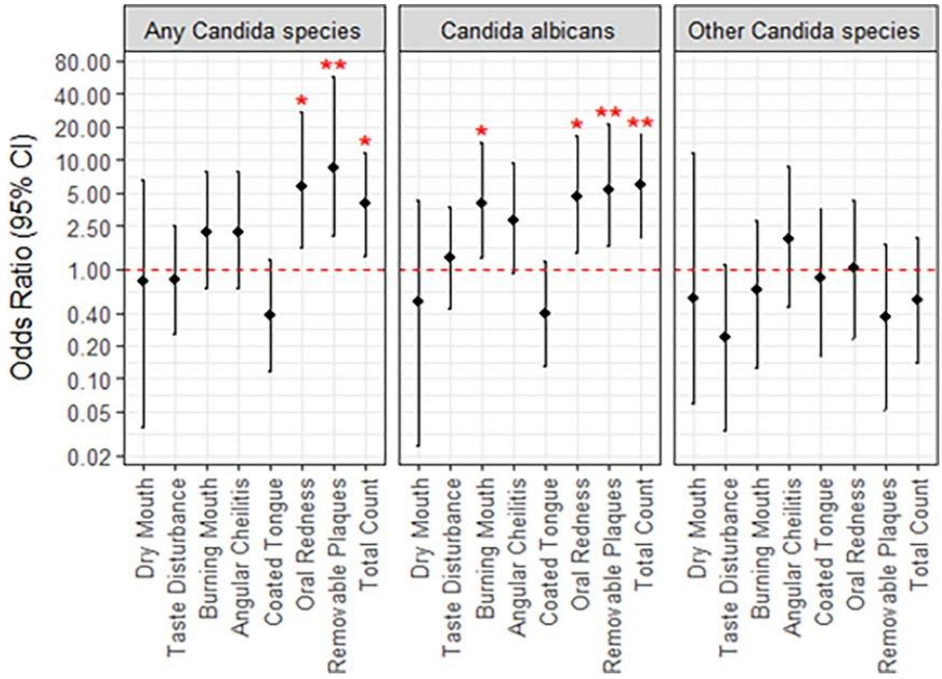

Figure 3. Univariate relationships between baseline Candida species and clinical features. Non-significant outcomes intersect the red dashed line; $p < 0.01$, $*p < 0.05$.

Most cases (57.6%) were managed with fluconazole as the primary therapy. Nystatin or Nizoral was used in 32.3% of patients, depending on presentation severity and lesion location. Approximately 65 isolates were obtained across initial (n = 48) and follow-up (n = 15) visits. At baseline, 17 samples (29.8%) were categorized as normal flora due to insufficient Candida load **(Table 2).** Among abnormal isolates, Candida albicans accounted for 61.0%. Nakaseomyces glabratus appeared next most frequently (n = 6), with smaller numbers of Pichia kudriavzevii (n = 1), Candida tropicalis (n = 2), and Candida lusitanae (n = 1) **(Table 2)**. Mixed-species infections were detected in eight baseline samples and four follow-ups **(Table 3).**

Table 2. Antifungal regimens and species distribution at baseline.

Variable	n (%)
Prescribed antifungal agent	
Fluconazole	34 (59.6%)
Nystatin	18 (31.6%)
Ketoconazole (Nizoral)	4 (7.0%)
Missing data	1 (1.8%)
Normal oral flora present	
No	40 (70.2%)
Yes	17 (29.8%)
Candida albicans isolated	
No	22 (38.6%)
Yes	35 (61.4%)
Nakaseomyces glabratus (formerly C. glabrata) isolated	
No	51 (89.5%)
Yes	6 (10.5%)
Pichia kudriavzevii (formerly C. krusei) isolated	
No	56 (98.2%)
Yes	1 (1.8%)
Clavispora lusitaniae (formerly C. lusitaniae) isolated	
No	56 (98.2%)
Yes	1 (1.8%)
Candida tropicalis isolated	
No	55 (96.5%)
Yes	2 (3.5%)

Table 3. Dual-species fungal detection in nine participants.

Species Combination	Initial Visit (n)	Follow-up Visit (n)
Candida albicans + Nakaseomyces glabratus	4	3
Candida albicans + Candida tropicalis	2	0
Candida albicans + Candida parapsilosis	0	1
Candida albicans + Rhodotorula mucilaginosa	1	0
Pichia kudriavzevii + Saccharomyces cerevisiae	1	0

Follow-up outcomes and regression results

After two weeks of therapy, many infections were fully cleared and did not require a second swab. Twelve participants died or were unavailable for reassessment. Ultimately, 15 individuals (26.3%) showed persistent infection at follow-up (5 C. albicans; 2 N. glabratus; 3 C. albicans + N. glabratus; 2 C. parapsilosis; 1 C. albicans + C. parapsilosis; 1 P. kudriavzevii; 1 C. tropicalis), while 18 (31.6%) demonstrated resolution. Patients initially presenting with erythema [OR (95% CI) = 4.68 (1.09, 22.9)] or angular cheilitis [6.50 (1.47, 34.3)] had significantly higher odds of unresolved infection **(Figure 4).** Conversely, coated tongue was linked to a lower likelihood of clearance [0.08 (0.01, 0.51)] **(Figure 4).** No significant associations were found between follow-up outcomes and baseline detection of C. albicans, N. glabratus, or other yeasts. However, those with N. glabratus at baseline had an elevated risk of persistence [OR = 9.4 (1.27, 196.2)], though estimates were imprecise. Among additional factors—age, smoking status, and antifungal type—only sex showed significance. Male participants were less likely to resolve infection compared with females [0.2 (0.04, 0.86)]. Adjusting for sex slightly reduced

effect sizes for erythema, angular cheilitis, and coated tongue, yet all remained notable at $p < 0.20$.

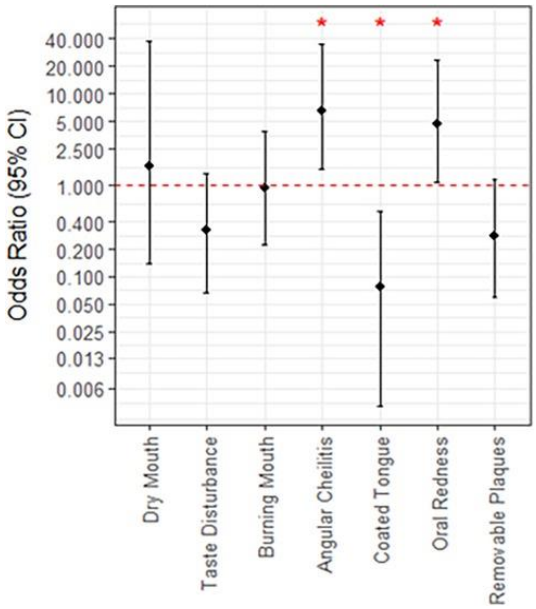

Figure 4. Relationships between baseline clinical features and the likelihood of ongoing Candida infection at follow-up. Non-significant effects intersect the red dashed reference line; *, $p < 0.05$.

This investigation sought to determine which clinical indicators and patient-related factors could help distinguish true Candida involvement and anticipate response to therapy. Numerous potential contributors were identified, but none showed a consistent individual association with infection status. In contrast, oral redness and detachable plaques clearly increased the probability of detecting Candida, with the likelihood rising further as the number of signs and symptoms accumulated. Comparable results were noted when focusing solely on Candida albicans, with burning sensations additionally elevating risk. After two weeks of treatment, patients who initially exhibited redness or angular cheilitis were more likely to remain infected, whereas coated tongue at baseline corresponded with greater odds of clinical resolution.

Signs and symptoms of oral candidiasis

The data show that Candida-related presentations vary widely, as reflected in the diverse symptom groupings. Although removable plaques are a well-recognized hallmark of infection, our findings underscore the need to evaluate the full range of features. Because almost all individuals reported dry mouth—and plaque development relies on adequate saliva—exclusive reliance on plaques may lead to missed diagnoses. The most common symptom combination (dry mouth, angular cheilitis, redness, and burning) did not contain plaques, yet these findings were strongly linked to Candida presence through associations with redness, plaques, and overall indication counts.

Dry mouth was nearly universal, affecting about 90% of participants. This limited variability likely explains its lack of statistical significance regarding infection detection. Even so, the absence of any candidiasis cases without xerostomia highlights its clinical importance. A study by Alt-Epping *et al*. (2012) reported similarly high rates of dry mouth (~90%) and a greater prevalence of taste disturbance (~80%) compared with the ~50% noted in our data [18]. Reduced salivary flow diminishes protective antifungal components such as histatins, defensins, and lysozymes [10], suggesting that management strategies aimed at improving salivary function may help prevent recurrence [18].

Factors associated with increased risk of oral candidiasis

In this cohort, the occurrence of oral Candida infections was comparable between males and females [9]. Other considerations—such as frailty category or oral hygiene status—were not significantly linked to ongoing infection, reinforcing that older adults prone to Candida overgrowth often present with multifaceted medical backgrounds requiring individualized assessment.

Frailty, an age-related state of increased vulnerability and considered one of the most challenging geriatric syndromes [19], has documented connections to microbiome imbalance, oral pathology, and infectious susceptibility [20, 21]. The relationship is reciprocal, as oral deterioration—including loss of natural dentition—can worsen frailty and contribute to poorer outcomes, including increased mortality [22]. In our sample, 45% were categorized as moderately or severely frail, yet no significant association with infection persistence or resistance was observed, potentially reflecting sample size limitations.

Diabetes is another condition frequently linked to candidiasis and symptoms like xerostomia [23]. Elevated salivary and blood glucose levels can promote the shift of Candida spp. into more invasive forms [24]. Prior work has shown that diabetes-associated Candida isolates may exhibit enhanced enzymatic behavior (hemolytic and phospholipase activity), enabling tissue invasion [24]. In our group, 18 of the 57 participants had diabetes, likely heightening their risk of chronic or invasive infection.

Follow-up outcomes

White plaques tended to resolve by the follow-up visit, indicating that pseudomembranous forms of oral candidiasis are generally more responsive to treatment.

Similarly, symptoms such as coated tongue and taste disturbance showed a tendency toward resolution, reflecting the typical clinical course of this infection type. Topical antifungal therapy appeared to be effective for these manifestations. The presence of a coated tongue at baseline was associated with a higher likelihood of infection clearance at follow-up, possibly because this sign can result from other conditions, including poor oral hygiene or xerostomia [25–27].

In contrast, erythematous forms of candidiasis, particularly when accompanied by angular cheilitis, were more persistent and often more challenging to treat [28]. The high odds of continued infection for patients presenting with redness and angular cheilitis are consistent with the characteristic inflammation and fissuring at the mouth corners. In such scenarios, topical agents may not fully eradicate the infection, and systemic antifungal therapy might be preferable for C. albicans infections. For infections involving inherently resistant species like N. glabratus or P. kudriavzevii, alternative treatments such as echinocandins may be required. Although N. glabratus and P. kudriavzevii have undergone taxonomic reclassification, they are included in this analysis alongside Candida species for consistency with prior literature, as both remain clinically significant oral pathogens.

No significant association was observed between the specific Candida species and infection resolution at the two-week follow-up. This aligns with the known susceptibility of most C. albicans strains to standard azole and polyene antifungals [2]. Among N. glabratus infections, 5 of 6 cases persisted at follow-up, likely reflecting its intrinsic azole resistance. Interestingly, Candida parapsilosis appeared in three follow-up infections despite being absent at baseline, suggesting a mycobiome shift during antifungal therapy that allowed colonization by this species. Emerging evidence indicates increasing fluconazole resistance in C. parapsilosis, which was previously typically susceptible to first-line treatment [29, 30].

One infection initially involving both C. albicans and N. glabratus resolved to reveal P. kudriavzevii, a fluconazole-resistant species, at follow-up. Some patients harbored multiple pathogenic Candida species simultaneously, underscoring the importance of rapid and sensitive point-of-care species identification to ensure antifungal therapy targets the full spectrum of infecting organisms.

Conclusion

This study's key strengths include its real-world clinical setting, longitudinal follow-up design, and detailed profiling of both patients and Candida isolates. The findings contribute valuable insights for cohorts in Northern Ontario, addressing knowledge gaps regarding oral candidiasis in this region. Limitations include the relatively small sample size and the wide variability in participants' medical histories, which complicated the identification of specific health factors as predictors for Candida infections. Future research with larger cohorts could allow stratification based on cancer type or other immunocompromising conditions. Geographic context also constrains the generalizability of these findings, as Candida species prevalence is known to vary regionally. In both Canada and the United States, C. albicans is generally reported as the most frequent pathogenic species, followed by Nakaseomyces glabratus [31–33]. Additionally, the limited number of persistent infections at follow-up reduced statistical power. A larger cohort could better clarify whether particular clinical signs and symptoms are associated with less common, antifungal-resistant species, which is increasingly important given the rising incidence of atypical Candida species and their contribution to higher mortality [34]. Notably, several patients displaying clinical features of candidiasis were found to have only normal oral flora. Conditions such as Sjögren's syndrome can mimic these symptoms without Candida overgrowth [35]. Future work should adopt a more comprehensive approach to studying the oral microbiome, which may identify other organisms involved in maintaining a healthy microbial balance.

Overall, the study highlights the variability in oral candidiasis presentation and underscores the need for molecular diagnostic tools to support accurate clinical assessment. Clinicians must consider multiple factors when managing patients with suspected infection to select appropriate antifungal therapy. Certain Candida species possess intrinsic resistance to first-line treatments, and others acquire resistance mutations that cannot be reliably identified without laboratory culture and molecular testing [2]. Current diagnostic procedures rely on skilled laboratory personnel to culture samples and use VITEK® mass spectrometry for species-level identification.

When C. albicans was the predominant pathogen, standard fluconazole therapy was typically effective. However, erythematous forms of candidiasis, including cases with angular cheilitis and oral redness, frequently persisted, particularly when treated topically with agents such as nystatin or Nizoral. Systemic fluconazole may have offered better efficacy. Species with innate resistance, such as Nakaseomyces glabratus (previously C. glabrata), responded poorly to fluconazole, with 5 of 6 infections (83%) remaining at follow-up and requiring alternative antifungal therapy.

Clinical symptoms alone do not differentiate these species, emphasizing the need for molecular characterization to detect antifungal-resistant pathogens.

The development of point-of-care species identification could allow clinicians to tailor antifungal therapy more precisely. Other fluconazole-resistant species include Pichia kudriavzevii (formerly C. krusei) and the emergent multi-drug resistant Candida auris. Over 95% of P. kudriavzevii isolates, and approximately 90% of C. auris strains are resistant to fluconazole [36, 37]. While C. auris has not yet been reported in the human oral cavity, it has been isolated from a canine oral sample in Kansas [38]. Rapid identification of these species, alongside typical Candida pathogens, could enhance monitoring of emerging transmission patterns [39].

Few studies integrate clinical signs, patient health data, and microbiological testing comprehensively. Future investigations should include antifungal susceptibility testing and molecular gene expression analyses, particularly focusing on resistant strains. Combining these approaches will deepen understanding of the pathophysiology of oral candidiasis in vulnerable populations, including older adults and immunocompromised patients.

Acknowledgments: C.P.V is supported as the HSN Foundation Research Chair in Healthy Aging. We thank Logan Bach for screening and recruiting patients, obtaining samples, filling out the questionnaires with the participants and collecting chart data. We also thank Jacob Bennett, Emelie Cote, Massimo Marrone and Michael Reich for their contributions in assisting with data collection and medical chart extraction, and ethics administration.

Conflict of Interest: None

Financial Support: The author(s) declare that financial support was received for the research and/or publication of this article. This research was funded by the following agencies and grants: 1. the Northern Ontario Academic Medicine Association (NOAMA) AFP Innovation Fund (A-22-14), 2. the Northern Ontario School of Medicine University (NOSM U) Faculty Association Research Development Award, 3. the Northern Ontario Heritage Fund Corporation (NOHFC) Internship Fund (7400852), 4. the Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant (RGPIN-2022-03159) and 5. the Northern Cancer Foundation.

Ethics Statement: The studies involving humans were approved by Health Sciences North Research Ethics Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

References

1. Bensadoun RJ, Patton LL, Lalla RV, Epstein JB. Oropharyngeal candidiasis in head and neck cancer patients treated with radiation: update 2011. Support Care Cancer. 2011;19:737–44. doi:10.1007/s00520-011-1154-4
2. Czajka KM, Venkataraman K, Brabant-Kirwan D, Santi SA, Verschoor C, Appanna VD, et al. Molecular mechanisms associated with antifungal resistance in pathogenic Candida species. Cells. 2023;12:2655. doi:10.3390/cells12222655
3. Lichtenstern C, Herold C, Mieth M, Brenner T, Decker S, Busch CJ, et al. Relevance of Candida and other mycoses for morbidity and mortality in severe sepsis and septic shock due to peritonitis. Mycoses. 2015;58(7):399–407. doi:10.1111/myc.12331
4. Yamaguchi M, Katsuno T, Iwagaitsu S, Nobata H, Kinashi H, Banno S, et al. Oral candidiasis is a significant predictor of subsequent severe infections during immunosuppressive therapy in anti-neutrophil cytoplasmic antibody-associated vasculitis. BMC Infect Dis. 2019;19(1):664. doi:10.1186/s12879-019-4300-0
5. Dangi YS, Soni ML, Namdeo KP. Oral candidiasis: a review. Int J Pharm Pharm Sci. 2010;2:36–41.
6. Patel M. Oral cavity and Candida albicans: colonisation to the development of infection. Pathogens. 2022;11:335. doi:10.3390/pathogens11030335
7. Ferreira DT, da Silva PV, de Oliveira Junior HCC, Rocha KAP, da Silva DR, de Souza Pitangui N, et al. Can there be a relationship between oral candidiasis and candidemia in ICU patients? Curr Fungal Infect Rep. 2023;17:195–201. doi:10.1007/s12281-023-00470-4
8. Samaranayake L. Commensal oral Candida in Asian cohorts. Int J Oral Sci. 2009;1:2–5. doi:10.4248/ijos.08006
9. Taylor MT, Brizuela M, Raja A. Oral candidiasis. In: Raja A, Brizuela M, editors. StatPearls. Treasure Island, FL: StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK54528

2/

10. Vila T, Rizk AM, Sultan AS, Jabra-Rizk MA. The power of saliva: antimicrobial and beyond. PLoS Pathog. 2019;15(11):e1008058. doi:10.1371/journal.ppat.1008058
11. Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral candidiasis: a disease of opportunity. J Fungi. 2020;6:15. doi:10.3390/jof6010015
12. Garcia-Cuesta C, Sarrion-Pérez MG, Bagán JV. Current treatment of oral candidiasis: a literature review. J Clin Exp Dent. 2014;6(5):e576. doi:10.4317/jced.51798
13. Taverne-Ghadwal L, Kuhns M, Buhl T, Schulze MH, Mbaitolum WJ, Kersch L, et al. Epidemiology and prevalence of oral candidiasis in HIV patients from Chad in the post-HAART era. Front Microbiol. 2022;13:844069. doi:10.3389/fmicb.2022. 844069
14. Noël de Tilly A, Tharmalingam S. Review of treatments for oropharyngeal fungal infections in HIV/AIDS patients. Microbiol Res (Pavia). 2022;13(2):219–34. doi:10.3390/microbiolres13020019
15. Hellstein JW, Marek CL. Candidiasis: red and white manifestations in the oral cavity. Head Neck Pathol. 2019;13:25–32. doi:10.1007/s12105-019-01004-6
16. Patil S, Rao RS, Majumdar B, Anil S. Clinical appearance of oral Candida infection and therapeutic strategies. Front Microbiol. 2015;6:1391. doi:10.3389/ fmicb.2015.01391
17. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ Can Med Assoc J. 2005;173(5):489–95. doi:10.1503/cmaj.050051
18. Alt-Epping B, Nejad RK, Jung K, Groß U, Nauck F. Symptoms of the oral cavity and their association with local microbiological and clinical findings-a prospective survey in palliative care. Support Care Cancer. 2012;20:531–7. doi:10.1007/ s00520-011-1114-z
19. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752–62. doi:10.1016/S0140-6736(12)62167-9
20. Oh J, Robison J, Kuchel GA. Frailty-associated dysbiosis of human microbiotas in older adults in nursing homes. Nat Aging. 2022;2:876. doi:10.1038/s43587-022- 00289-7
21. Zakaria MN, Furuta M, Takeshita T, Shibata Y, Sundari R, Eshima N, et al. Oral mycobiome in community-dwelling elderly and its relation to oral and general health conditions. Oral Dis. 2017;23(7):973–82. doi:10.1111/odi.12682
22. Yang M, Liu Y, Watanabe Miura K, Matsumoto M, Jiao D, Zhu Z, et al. Frailty risk patterns and mortality prediction in community-dwelling older adults: a 3-year longitudinal study. J Am Med Dir Assoc. 2025;26(1):105359. doi:10.1016/j.jamda. 2024.105359
23. Mohammed L, Jha G, Malasevskaia I, Goud HK, Hassan A. The Interplay Between Sugar and Yeast Infections: Do Diabetics Have a Greater Predisposition to Develop Oral and Vulvovaginal Candidiasis? Cureus. 2021;13(2):e13407.
24. Nouraei H, Jahromi MG, Jahromi LR, Zomorodian K, Pakshir K. Potential pathogenicity of Candida species isolated from oral cavity of patients with diabetes mellitus. Biomed Res Int. 2021;2021(1):9982744. doi:10.1155/2021/ 9982744
25. Martins M de L da C, Barros Cd. (No) oral health in palliative care patients: predisposing factors and treatment. J Palliat Care. 2023;40:113–9. doi:10.1177/ 08258597231212305
26. Van Tornout M, Dadamio J, Coucke W, Quirynen M. Tongue coating: related factors. J Clin Periodontol. 2013;40(2):180–5. doi:10.1111/jcpe.12031
27. Buranarom N, Komin O, Matangkasombut O. Hyposalivation, oral health, and Candida colonization in independent dentate elders. PLoS One. 2020;15(11 November):e0242832. doi:10.1371/journal.pone.0242832
28. Williams D, Lewis M. Pathogenesis and treatment of oral candidosis. J Oral Microbiol. 2011;3:5771. doi:10.3402/jom.v3i0.5771
29. Escribano P, Guinea J. Fluconazole-resistant Candida parapsilosis: a new emerging threat in the fungi arena. Front Fungal Biol. 2022;3:1010782. doi:10.3389/ffunb.2022.1010782
30. Daneshnia F, de Almeida Júnior JN, Ilkit M, Lombardi L, Perry AM, Gao M, et al. Worldwide emergence of fluconazole-resistant Candida parapsilosis: current framework and future research roadmap. Lancet Microbe. 2023;4:e470–80. doi:10.1016/S2666-5247(23)00067-8
31. McTaggart LR, Cabrera A, Cronin K, Kus JV. Antifungal susceptibility of clinical yeast isolates from a large Canadian reference

laboratory and application of whole-genome sequence analysis to elucidate mechanisms of acquired resistance. Antimicrob Agents Chemother. 2020;64(9):e00402-20. doi:10.1128/AAC.00402-20

32. Fuller J, Dingle TC, Bull A, Shokoples S, Laverdière M, Baxter MR, et al. Species distribution and antifungal susceptibility of invasive Candida isolates from Canadian hospitals: results of the CANWARD 2011–16 study. J Antimicrob Chemother. 2019;74:iv48–54. doi:10.1093/jac/dkz287
33. dc.gov. Data and Statistics on Candidemia; 2024.
34. Pinho S, Miranda IM, Costa-de-Oliveira S. Global epidemiology of invasive infections by uncommon Candida species: a systematic review. J Fungi. 2024;10:558. doi:10.3390/jof10080558
35. Ergun S, Çekici A, Topcuoglu N, Migliari DA, Külekçi G, Tanyeri H, et al. Oral status and Candida colonization in patients with Sjögren's syndrome. Med Oral Patol Oral Cir Bucal. 2010;15(2):310–5. doi:10.4317/medoral.15.e310
36. Whaley SG, Berkow EL, Rybak JM, Nishimoto AT, Barker KS, Rogers PD. Azole antifungal resistance in Candida albicans and emerging non- albicans Candida species. Front Microbiol. 2017;7:2173. doi:10.3389/fmicb.2016.02173
37. Public Health Ontario. King's Printer for Ontario. Focus on: Candida Auris. 2023.
38. White TC, Esquivel BD, Rouse Salcido EM, Schweiker AM, dos Santos AR, Gade L, et al. Candida auris detected in the oral cavity of a dog in Kansas. mBio. 2024;15(2):e0308023. doi:10.1128/mbio.03080-23
39. Alfaifi A, Brooks JK, Jabra-Rizk MA, Meiller TF, Sultan AS. Does Candida auris colonize the oral cavity? A retrospective institutional experience. Oral Dis. 2024;30(4):2716. doi:10.1111/odi.14720