GRADUATION PROJECT

Degree in Dentistry

Beyond oral candidiasis: the role of non-Candida fungi in oral health and disease

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ABSTRACT

English version:

Introduction: The oral cavity is one of the most biodiverse microbiomes of the body. While Candida species have been studied for years, the remainder of the non-Candida fungal community is less well characterized, even as studies of late indicate that such fungi play a role in oral ecological homeostasis, microbe-microbe interactions, and host immune response. **Objectives**: The purpose of this review was to compile recent information about non-Candida fungal diversity and ecological functions of the oral microbiome in different oral fungus diversity to assess applicability to a more informed understanding of oral health. **Material and Method**: A systematic review was conducted of the literature through PubMed, Medline, CINAHL, Scopus, and Google Scholar with specific search terms pertaining to the oral mycobiome. Articles published from 2010 to 2025 were chosen based on PRISMA criteria. This review also includes sequencing surveys, case reports, case series, and systematic reviews. **Results**: Fifteen studies were included. Results across studies showed a diverse non-Candida fungal microbiota, such as *Aspergillus spp.*, Penicillium, Cladosporium, Cryptococcus, Malassezia, and Geotrichum, all of which are significant contributors to ecological interactions with bacteria, implying immune homeostasis and, in some cases, opportunistic diseases. However, heterogeneity between studies is limited due to the significant differences between these varying studies. **Conclusion**: Non-Candida fungi appear to be relatively stable and potentially functional members of the oral microbiome. However, their ecological roles, clinical impact, and relationships with host immunity are largely unknown, indicating a need for standardized approaches and future studies.

Keywords :
Dentistry, oral microbiome, oral mycobiome, oral fungi, non-Candida fungi, fungal colonisation

Versión Española:

Introducción: La cavidad oral es uno de los microbiomas más biodiversos del cuerpo. Si bien las especies de *Candida* se han estudiado durante años, el resto de la comunidad fúngica no *Candida* está menos caracterizada, aun cuando estudios recientes indican que dichos hongos desempeñan un papel en la homeostasis ecológica oral, las interacciones entre microbios y la respuesta inmune del huésped. **Objetivos:** El propósito de esta revisión fue recopilar información reciente sobre la diversidad fúngica no Candida y las funciones ecológicas del microbioma oral en la diferente diversidad de hongos orales, para evaluar su aplicabilidad hacia una comprensión más informada de la salud oral. **Método:** Se realizó una revisión sistemática de la literatura a través de PubMed, Medline, CINAHL, Scopus y Google Scholar con términos de búsqueda específicos relacionados con el micobioma oral. Se seleccionaron artículos publicados entre 2010 y 2025 basándose en los criterios PRISMA. Esta revisión también incluye estudios de secuenciación, reportes de casos, series de casos y revisiones sistemáticas. **Resultados:** Se incluyeron quince estudios. Los resultados a través de los estudios mostraron una microbiota fúngica no *Candida* diversa, tal como *Aspergillus* spp., *Penicillium*, *Cladosporium*, *Cryptococcus*, *Malassezia* y *Geotrichum*, todos los cuales contribuyen significativamente a las interacciones ecológicas con bacterias, lo que implica homeostasis inmune y, en algunos casos, enfermedades oportunistas. Sin embargo, la comparabilidad entre los estudios es limitada debido a las diferencias significativas entre estos diversos trabajos. **Conclusión:** Los hongos no *Candida* parecen ser miembros relativamente estables y potencialmente funcionales del microbioma oral. Sin embargo, sus roles ecológicos, impacto clínico y relaciones con la inmunidad del huésped son en gran parte desconocidos, lo que indica la necesidad de enfoques estandarizados y estudios futuros.

Palabras clave:
Odontología, microbioma oral, micobioma oral, hongos orales, hongos no *Candida*, colonización fúngica

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1. INTRODUCTION

1.1 Background and Context

As the second most diverse site of the human microbiome, the oral cavity acts a surface organ in a microbial symbiotic relationship, transforming nutrients and acting as the human body's initial barrier against pathogen. (1) With a mix of viruses, bacteria, fungi, and protozoa, these organisms in the mouth significantly contribute to the health and function of body systems, making their study an important ongoing task (2). Most studies looking into this ecosystem continue to reveal mysteries, as new and improved technologies and theories have made new methods of scanning the state of these organisms. If the majority of the academic attention is still about bacteria in the visceral system; it's important to take a look of the microbiome as a whole, with their numerous and complex interactions. In this ecosystem, a fraction should play a role: the fungus (3).

For the most part, research into this field has focused mainly on *Candida albicans*, the most commonly found fungi in the mouth. The reason for its highlighted focus has to do with its commonality within numerous oral diagnoses, such as oral candidiasis, denture stomatitis, and a plethora of infections in individuals with compromised immune systems (4). However, the relatively recent discovery of other types of fungi has left a research gap where the knowledge and discussion of other types of fungi are severely limited compared to this species. This knowledge gap presents an opportunity for researchers to dig deeper into diverse fungi found in the mouth, as the sequencing technology available today is opening the doors to this undiscovered world (1).

The insights learned from these studies are key for dentists, because they will give the field a better idea of what these fungi do and how they contribute oral and bodily health.

This understanding can make the fields methods for keeping mouths healthy better because it reinforces the idea that a healthy mouth is one where different organisms are balanced to maintain stability, instead of thinking of the mouth as something that needs all micro-organisms removed, also, what insights could show the complicated connections between all the different organisms that live in a healthy mouth(1).

From this point of view, fungi are not simply seen as unwanted organisms that need elimination, but rather as positive guests that could help humans stay healthy.

1.2 Oral Fungi Microbiome Diversity Beyond Candida

These findings from numerous culture-independent investigations of heterogeneous, healthy human mouths are enough to spark interest in what and where these fungi are cultured. Ghannoum et al. investigated the mouth via oral rinse with many healthy participants, and found over 70 fungal genera, some more obscure than the commonly cultured and detected fungi in the oral cavity, and other tests (2). Among these more obscure cultures are *Aspergillus spp.*, *Cladosporium*, *Cryptococcus*, etc. The fact that other scholars compiling the same investigations in heterogeneous populations also found these genera implies that they are cultured in stable, necessary patterns within the human mouth, not a random occurrence in a geographical location or subpopulation (5).

The longer the research is performed and the more accurate the testing is done, the higher the inventory of known oral fungi will be made available. According to Defta et al., there are more than 85 species recognized so far, many of which are standard across assessed populations (4). In addition, the credibility of such information is confirmed by the results of Talaga-Cwiertnia et al., as they show that mouth fungal genera evenness is related to mouth health indicators (6). Thus, the presence of such variances and the results of such studies and findings create a symbiotic relationship with the other micro-organisms that exist in the mouth, regardless of population and health status.

Further studies have also revealed the contribution of external factors to the diversity of oral microbiomes. Factors such as environment (7), diet, hygiene habits, health conditions, salivary composition, and oral topography all play a role in determining patterns of fungi colonization in the mouth. (8) Other chemical-based factors can also determine the presence, or lack thereof, of specific fungal genera, as Candida seems to prefer acidic environments (9), whereas *Aspergillus spp.* tends to prefer neutral or slightly alkaline conditions, which can also explain their consistent presence in healthy mouths.

1.3 The Questioned Role of Fungi in Oral/Human Health

With their consistent presence confirmed across numerous populations and regions, we should understand their reason for being in the mouth. As the trend of the attendance of diverse microbiomes in the mouths of healthy individuals is strong, it suggests that their presence somewhat contributes to human health, or at the very least, they make it difficult for disease-causing organisms to thrive. The work of Diaz et al. offers evidence for the latter assumption, as their results suggest that the dynamic relationship between fungi and bacteria was both competitive and mutually beneficial as these species compete and exchange for

limited nutrients (10). The best example of such relationships is from Aspergillus, Penicillium, and Streptococcus (and other bacteria), as researchers believe the fungi produce metabolites that reduce bacteria (3). However, contrary results reveal that lactate, a metabolite of bacteria, increases fungal viability, suggesting that the two populations rely on each other. Such results support the hypothesis that fungi act as a mediating contributor to health in the oral cavity and beyond.

Additionally, the perpetual interaction between foreign organism and the immune system play a role in immunity, therefore in the human health. The fact that fungi are merely present may allow for the perpetually mediated tolerance and immune system activation, as tolerogenic epithelial cells sense them, resulting in a non-inflammatory, low-level activated immune system (10). In addition, fungal dysbiosis correlates positively with poor oral health, suggesting that it may either act as a homeostatic mediator of the microbiome or a victim of transorganismal interactions as health conditions shift. Either way, all findings strongly suggest that fungi are present in some collaborative fashion with other organisms in the mouth, which, on the contrary, makes it a potentially mediating factor of human/oral health.

1.4 Literature Gaps and Research Rationale

The presence of a high diversity of non-Candida fungi in the mouth is all but proven; there is still a significant knowledge gap pertaining to the different functions of these organisms. The majority of the studies revealing the presence of these fungi have relied on cross-sectional sequencing methods, which are great at detecting the presence of these micro-organisms but offer little insight into their function. Only a handful of studies have used techniques such as transcriptomic or metabolomic analysis to assess whether the presence of fungi contributes to metabolic reactions or is present as a consequence of inserted food and air in the mouth (4)

Additionally, the variances in the methods used by different researchers have made comparing their results and insights complicated. Other studies have collected their tested samples using different techniques across varying oral sites (e.g., tongue dorsum, plaque, saliva) and within different conditions, all of which may have significantly contributed to the noted diversity of the observed fungi (5) Additionally, as Diaz et al. suggests, the presence of these detected micro-organisms may be an indication of environmental contamination or sequencing artifacts as opposed to a confirmation of actual live orgasms in the mouth (11).

1.5 Justification and Broader Implications

The term “microbiota” was popularized in late 20th century and it’s only in the beginning if the 21th century that the term “human microbiome” was truly conceptualized. Awareness of the importance of the microbiome, not only as a pathologic dysbiosis, but as a continuous general health contribution with impact in other system as important as the brain allowed to open a new field of research. (12)

Starting in 2007 with the Human Microbiome Project, the identification and characterisation of thousand of new species is very novel. Their complex interaction between them and the host, their role or their health consequences are a colossal ongoing task. Gap in research, unverified hypothesis or lack of quality studies are common and expected.

Make a review of our current knowledge of a specific less-studied population as non-candida oral fungi is a good marker of our current comprehension of this field: what we know, which direction studies should take, and see if even the forgotten studied micro-organisms have unexpected health impact.

2. OBJECTIVES

The **PICO** question guiding this investigation states:
In individuals with good oral health (**P**), how does the presence of non-Candida fungal genera (**I**), compared to individuals with less diverse or Candida-dominated oral microbiomes (**C**), contribute to health outcomes, oral microbe ecosystems, and immune systems (**O**)

Objective:

- Main: Assess the impact of non-Candida fungi in oral health by comparing population with high and low diversity of non-Candida fungi in the oral cavity.
- Secondary: Assess the dynamic relationships that non-Candida fungi share with other microbes in the mouth and the body's immune system.

3. METHODS AND MATERIALS

3.1 Study Design

This study will be a systematised literature review where studies evaluating the non-Candida fungi of the oral microbiome will be taken into consideration. This will be a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guided assessment,

which will ensure that only pertinent studies will be selected for this research process. Only peer-reviewed articles and high-quality reviews from trusted entities are used in this study.

3.2 Search Method

The primary method used to gather the studies reviewed for this investigation relied on using crafted search terms across reputable databases. The consulted databases include PubMed, Medline, CINAHL, and Scopus. When research into these databases proved inadequate, Google Scholar was consulted using the same search terms. The timeline limitation for these selected studies, which is between 2010 and 2025, is justified as this year marks a significant shift in the research methodologies of the field. New methods, such as molecular and high-throughput sequencing, which are better at detecting the DNA expression of fungal taxa compared to previous methods, gained significant popularity and use (Ghannoum et al., 2010).

The Boolean search phrases and keywords used to find the articles consulted within this literature review include:

- “Oral microbiome” OR “Oral Fungi” OR “Oral Cavity.”
- “Oral Fungi” OR “Oral Health” OR “Homeostasis.”
- “oral microbiome” OR “oral mycobiome.”
- “oral fungi” AND “non-Candida.”
- “oral fungi” AND “oral health.”
- “oral fungi” AND “microbiome diversity.”
- “fungal colonisation” AND “oral cavity.”
- Oral Microbiome

Keywords :
oral microbiome, oral mycobiome, oral fungi, non-Candida fungi, oral health, microbial diversity, fungal colonisation, oral ecology

Only studies written or translated into English were considered for the study. Additionally, when necessary, the reference lists of selected papers were also considered, ensuring that relevant studies that were not represented during the search were still included in the study.

3.3 Inclusion Criteria

The inclusion criteria for this study are:

- Peer-reviewed, relevant original research or review article published between 2010 and 2025.
- Studies solely focused on non-Candida fungal species that reside in the human mouth.
- Studies that report the connections between oral fungi, other oral bacteria, and human health outcomes.
- Studies employing techniques such as microscopy-based or sequencing-based detection methods.
- Reviews or case studies revealing insights into the nature and sources of non-Candida fungal species.

3.4 Exclusion Criteria

The exclusion criteria for this research effort included:

- Research articles focusing solely on the Candida fungus genus
- Articles with little relevance to the study's subject matter
- Articles whose publish date was earlier than 2010
- Articles focusing on non-human mouths
- Articles not written in English
- Papers that are not peer-reviewed
- Articles that are inaccessible due to paywalls or other factors

3.5 Data Extraction and Synthesis

The data extracted from the various selected articles were synthesized into a data table according to the following variables: author, year of publication, sample, identified fungal genera, and main findings. The evaluated studies were qualitatively analysed and categorized into one of three themes. These include:

- Fungal genera diversity and prevalence studies.
- Fungi function and ecosystem interactions.
- Clinical reports and connections to identified diagnoses.

Due to the vast differences in the methodologies and focus of these studies, it was impossible to conduct a reliable quantitative meta-analysis. Instead, the study had to adopt a narrative synthesis approach where qualitative patterns and converging evidence were noted and considered for analysis.

3.6 Study Selection Method

The selected studies had to go through a number of filters to reach the final 15 studies, which the investigation considers. The first search results produced 240 studies, which were later cut down to 156 after duplicate studies were eliminated across selected databases. From this list of selected studies, 36 qualified for the next round of filtration due to the availability of their full text and increased relevance to the primary focus of the study. After a complete text analysis of these articles, the final 15 studies were selected as viable sources for the paper's discussion due to the strength of their methodologies and the converging evidence they presented. These studies also offer a holistic view of the subject at hand by providing both molecular and clinical perspectives on the role and function of identified non-Candida fungi.

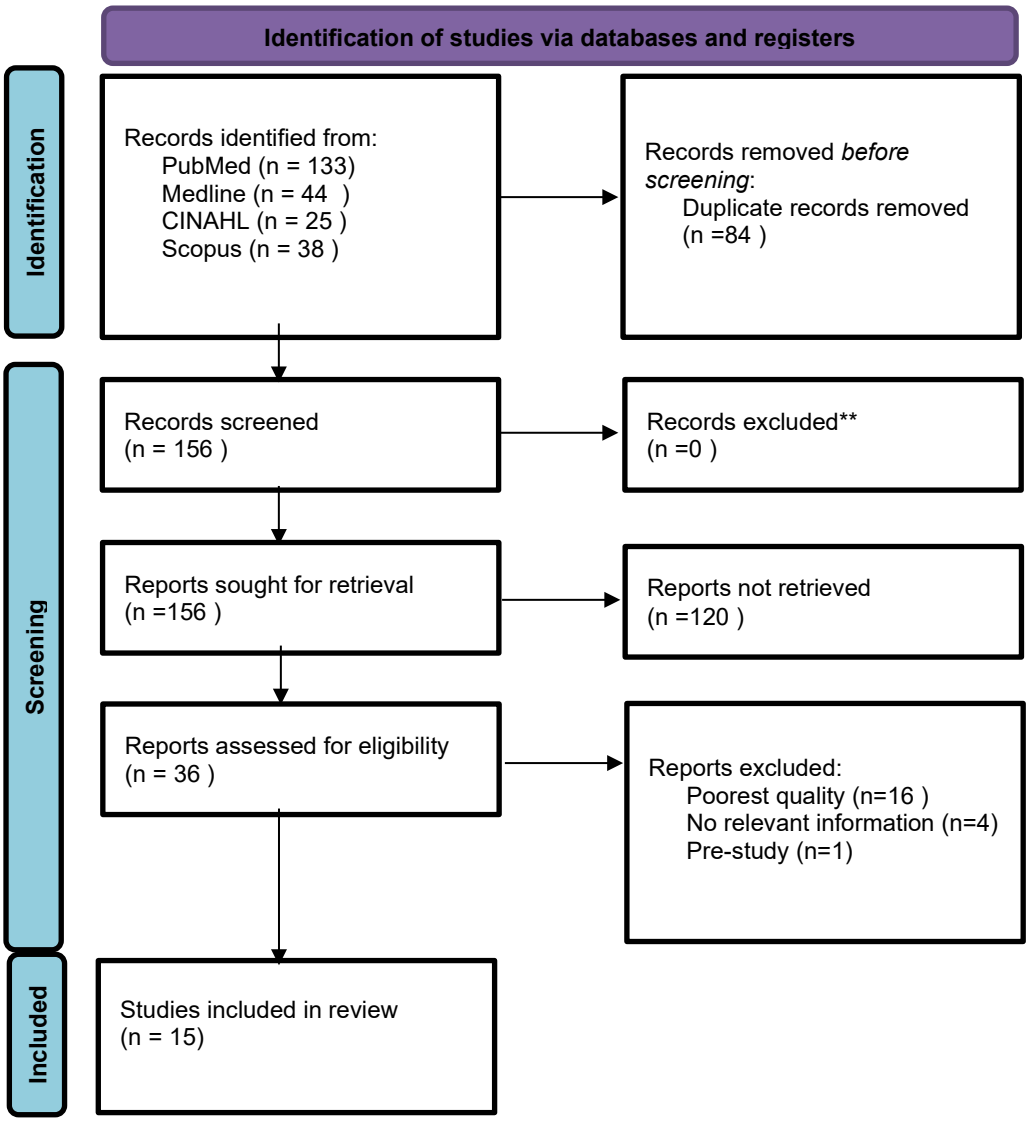


Figure 1 *PRISMA flow diagram*

4. RESULTS

Table 1 *Included articles for the study (4 pages)*

Author(s) and Year	Study Design	Sample/Population	Primary non-Candida fungi Species	Methodology	Key Findings
Ghannoum et al., 2010 (2)	Cross-Sectional Sequencing	20 orally healthy adults	Aspergillus, Cladosporium, Aureobasidium, Cryptococcus, Fasarium, Saccharomycetales	ITS pyrosequencing	Established the first oral mycrobiome map consisting of over 80 fungal genera. Aspergillus and Cladosporium are positively correlated with healthy individuals.
Peters et al., 2017 (5)	Case studies	15 healthy adults and 15 adults diagnosed with periodontitis	Aspergillus, Penicillium, Rhodotorula, Gibberella, Schizophyllum	ITS sequencing	Some genera, such as Aspergillus and Penicillium, are ubiquitous. These fungi play a commensal role.
Bandara et al., 2019 (3)	Narrative Review	General Population	Multiple Non-Candida Fungi	Literature Synthesis	Authors propose that fungi play a vital role in oral microbiome ecosystems. They also encouraged more research in the field.

Author(s) and Year	Study Design	Sample/Population	Primary non-Candida fungi Species	Methodology	Key Findings
Diaz & Dongari-Bagtzoglou, 2020 (11)	Critical Review	N/A	Malassezia, Low Abundance Molds	ITS Data Review	The fungi genera that are consistent across many mouth mycrobiomes are Candida and Malassezia. The authors suggest that other fungi are transient.
Diaz et al., 2021 (10)	Review/Methodology	N/A	Malassezia, Aspergillus, Cladosporium	Culture compared to sequencing data	Emphasized the need for more research to reveal the metabolic activity of non-Candida fungi
Bonifaz et al., 2010 (19)	Case Series	12 patients demonstrating different health statuses	Geotrichum Candidium, Geotrichum Capitatum	Culture and microscopy	Conditions like diabetes and immunocompromise provide rare opportunities for geotrichosis fungi to develop.
Abed et al., 2023 (20)	Case Report	15-year-old immunocompromised teen	Geotrichum Silvicola, Geotrichum Candidium	Culture and Molecular ID	Authors identified the first dual Geotrichum

Author(s) and Year	Study Design	Sample/Population	Primary non-Candida fungi Species	Methodology	Key Findings
					infections, which proper hygiene practices eliminated.
Folk & Nelson, 2017 (16)	Clinical Case	44-year-old	Histoplasma Capsulatum	Biopsy and histopathology	Oral histoplasmosis mimics ulcers, reinforcing differential diagnosis
Mora-Martinez et al., 2023 (17)	Systematic Review	74 cases from 20 studies	Mucorales	Systematic Review	A post-COVID-19 patient experienced increased ulcer and bone erosion due to oral mucormycosis.
Pondé de Sena et al, 2024 (15)	Clinical Case and Literature Review	57-year-old transplant patient	Cryptococcus Neoformans	Histopathology, PCR, and literature review	From the 26 reviewed cases of oral cryptococcosis, the palate and tongue were the most affected.
Chen et al., 2023 (18)	Population-Based Case Study	476 cases and 537 controls	Saccharomyces Cerevisiae, Lodderomyces, Elongisporus, Fasarium poae	ITS-2 Sequencing	The use of antibiotics reduced fungal diversity and

Author(s) and Year	Study Design	Sample/Population	Primary non-Candida fungi Species	Methodology	Key Findings
Talaga-Ćwiertnia et al., 2025 (6)	Cross Sectional	COVID-19 convalescents and controls	Malassezia, Aspergillus, Penicillium	ITS-1 NGS Sequencing	
Ayers et al., 2025 (14)	Pilot Observational	12 adults demonstrating varying health statuses	Aspergillus, Penicillium	ITS and 16S Sequencing	There was covariation between fungal and bacterial diversity. Aspergillus was correlated with positive oral health.
Defta et al., 2024 (4)	Narrative Review	General population	Over 85 genera of core taxa	Literature Review	The authors defined the core oral microbiome and urged further research.
O'Connell et al., 2020 (13)	Cross Sectional	33 children with varying carrier or health statuses	Nigrospora Oryzae, Microdochium, Aspergillus	ITS-1 amplicon sequencing	Healthy plaque harbours diverse populations of non-Candida fungi. Lost diversity tends to shift to yeast, signalling the need for a balanced fungi population for optimal oral health.

The data above synthesizes the insights collected for the research efforts. The collected studies consist of several types of research, including sequencing surveys, culture-based clinical reports, individualized case studies, and integrated interviews, providing a multi-perspective analysis on the roles and functions of non-Candida fungi. The insights provided by the efforts of these researchers challenge the previous notions of oral fungi colonies as an unwanted presence within healthy individuals.

Some of the most recognized fungal genera, through sequencing efforts among healthy mouths, were Aspergillus, Penicillium, Cladosporium, Cryptococcus, and Malassezia (2,4). These consistent results across different contexts and in both healthy and non-healthy mouths suggest that these taxa are familiar oral microbiome ecosystem participants and an indicator of optimal oral health (5,12). The plethora of non-Candida fungal genera found in the mouth, with some studies identifying over 80 genera, also suggests that there is a core consortium of diverse fungi within oral cavities, whose role needs further investigation.

4.1 Oral Fungi Diversity and Prevalence

Supporting differences studies found non-Candida fungi in varying biofilm environments as well. In the healthy population, filamentous mould was 60% of fungal reads, with Aspergillus and Penicillium most common in temperate populations, while Malassezia and Cladosporium were most common in tropical populations (3). However, O'Connell et al.'s findings in children seek to further healthy plaque assessment to include non-Candida species such as Nigrospora and Microdochium (12). Thus, findings suggest that equilibrium and diversity of non-Candida species occur in the oral microbiome throughout the lifespan.

4.2 Site-Specific Colonisations and Environmental Influences

Results from studies of a few of those analysed suggest that particular genera have preferred placement in various regions of the mouth. For instance, according to Bandara et al., the greatest occurrence of genera took place on the tongue dorsum and buccal mucosa, the areas most exposed to food and air, and with the least friction (3). Despite the in-situ stabilization of genera such as Aspergillus and Cladosporium even without populations from this experimentalized oral setting, it's clear that these types of fungi are naturally dispersed, and in many circumstances (2). The state of oral saliva, e.g., pH levels and known flow patterns, also influenced the site presence and diversity of fungal microbiomes as acidic conditions favour yeast-like fungi and neutral or slightly alkaline conditions favour mould-like fungi (6). Dietary conditions, such as high fibre and vegetable intake, influenced fungi diversity evenness, whereas the ingestion of immune system-enhancing

medication, e.g., antibiotics, reduced fungi diversity (6). Oddly, healthy oral hygiene habits, e.g., regular teeth brushing, were associated with broader mycobiome diversity.

4.3 Functional Interactions within the Oral Microbiome

Relative studies within the realm of fungi and other oral micro-organisms validate codependent/dynamic interactions in the oral microbiome. Research by Ayers et al. assessed that non-Candida fungal involvement and diversity in the mouth positively correlates with the non-pathogenic oral microbes Streptococcus mitis and Veillonella dispar, a clear indicator of metabolic, mutually beneficial interaction (13). In addition, research by Bandara et al. and Diaz et al. validates the idea of cohabitative interaction in the oral microbiome as they determine that secondary polyketides, the byproduct of fungi's work, help maintain bacterial frequencies and operation (3)(8). They also determined that the presence of certain bacteria might help in the adhesion of fungi on oral surfaces to help form biofilms. Finally, O'Connell et al.'s findings also investigate the role of protective elements in human health, as they noted that the reduction of diversity and frequency of non-Candida fungi positively correlates with an increase in detrimental bacteria (12).

4.4 Non-Candida Fungi and Body Systems

Some of the studies included in this review show a connection between non-Candida fungi and the systems of the body. For example, Diaz et al. found that fungal beta-glucans can induce non-inflammatory responses from antimicrobial elements of the immune system. In addition, Ayers et al. had some new findings about how the non-Candida fungi interact with the systems of the body, as they found that increased salivary cytokine levels negatively correlated with increased fungal genus diversity (17). De Sena et al. also revealed insight suggesting a cooperative or neutral relationship between diverse fungi populations and body systems, as the presence of Cryptococcus Neoformans within healthy oral environments did not cause any health issues (18). In contrast, Bonifaz et al. (2010) and Ayers et al. found that monocultures of Geotrichum can cause localized lesions when they encounter stress from antibiotic agents, suggesting an optimal balance needed to maintain homeostasis (17). Overall, these results indicate that in a state of immune system homeostasis, a fungal genus diversity is complemented as opposed to eliminated.

4.5 Clinical and Pathological Observations

Yet while these results are a bit counterintuitive to anticipated findings from other studies that consider non-Candida fungi to be less than welcomed oral guests, Folk, Nelson, and Mora Martinez et al. (2023) discover that rare occurrences of Histoplasma Capsulatum and Mucorales

contribute to systemic mycosis where the immunocompromised population is concerned (15,17). But even in these findings, a majority was strongly noted to be previously identified non-Candida fungi with a secondary occurrence of malign fungi, indicating strong measures to be taken by these fungi to find a permanent home. In addition, Chen et al. observed that a lower mouth fungal diversity was linked to a higher risk of nasopharyngeal carcinoma, meaning that there is a direct correlation between oral health and diversity of fungi in the oral microbiome (18).

4.6 Synthesis of Findings

From a holistic perspective, such results suggest that the presence of non-Candida fungi in the oral microbiome is not an opportunistic situation, but rather, a natural facet of oral symbiosis, where they act as first responders to bacterial overgrowth, warrant immune mediator suppression, and become reliable indicators of phenomena elsewhere in the body or dysfunctional immune response. These results take non-Candida fungi into account as an underappreciated feature of mouth microbiomes and oral balance.

5. DISCUSSION

5.1 Diversity and Symbiosis in Oral Fungi

The results from these fifteen studies suggest that the human oral mycobiome is diverse and stable and that there are many other fungal genera beyond Candida. The presence of Aspergillus, Penicillium, Cladosporium, Cryptococcus, and Malassezia in various studied populations and sampling methods of the studies renders them commensal or conditionally symbiotic fungi (2,4). Moreover, the stability of these fungi regardless of continent, diet, and time in life suggests that these are the best-suited fungi for the oral microecosystem. While oral fungi were previously considered opportunistic pathogens, the culture-independent identification of stable, low-biomass communities of moulds and basidiomycetous yeasts in otherwise healthy individuals makes this symbiotic idea more complex (5,3). The ability to find such genera in the absence of disease implies a mutualistic relationship where certain fungi reside in their niche without more pathogenic elements taking advantage. O'Connell et al. extended these insights to children, suggesting that the role of these microbes extended throughout life (12). Sick children had significantly reduced non-Candida moulds and overrepresented acid-tolerant yeasts. These results reinforce the idea that microbial heterogeneity is a positive factor within oral microbiomes, and fungal dysbiosis represents the opposite. The more stable the various fungi populations, the less likely they are to experience adverse health outcomes.

5.2 Ecological Interactions and Functional Roles

One of the most impactful contributions made from the literature was the findings associated with interkingdom cooperation within oral microbiomes. Fungi comprise the biofilm, and since bacteria release lactate, a sugar which they metabolize, this helps fungi stick to the biofilm (11,3). Such mutually interdependent feedback loops foster microbial stability. According to Ayers et al., Aspergillus and Streptococcus mitis and Veillonella (bacterial keystones) have similar metabolic cycles that are symbiogenetically pH regulated to avoid excess acid (13). Yet where one would suspect mould decrease after antibiotics with a shift toward bacterial dominance, Talaga-Ćwiertnia et al. note an increase of Candida and a reduced bacterial diversity (6). Thus, it seems that only the Candida fungi operate as destabilizers, whereas the rest of the non-Candida fungi are more like ecological stabilizers that balance out bacterial fluctuations and community-level metabolism.

Additional data strengthen the idea of fungal activity/diversity as chemical regulators and stabilizers. Fungal secondary metabolites, polyketides, peptides, and volatile organic compounds reduce cariogenic bacteria and mediate quorum sensing (3,11). These suggest that these could act as probiotics and provide selective pressure against human health-adverse bacteria and in favour of commensal microbiota settlement

5.3 Host Immunity and Homeostasis

The immune system appears to maintain a precarious homeostatic balance with these fungi, as they not only allow for foreign introductions but also maintain a system in preparation for anything fungal that may get out of hand. Pattern-recognition receptors such as Dectin-1 and Toll-like receptors detect β-glucans and mannans on fungi, which facilitate low-level stimulation of innate defences but not so much that the inflammatory response is detrimental (10). In other words, this helps the immune system reinforce what the mucosa has established. For instance, Ayers et al. found that a greater diversity of fungi was associated with lower salivary cytokine production and that a neutrally mediated mycobiome represents an anti-inflammatory status quo (13). In addition, C. neoformans was established in non-inflamed histopathological changes to the tissue, meaning that these fungi are harmless, non-pathogenic, and that the immune system was tolerogenic to them.

Dysbiosis of the oral microbiome, exacerbated by dietary differences and antibiotic exposure, constitutes a health concern. Bonifaz et al. and Abed et al. (2023) report Geotrichum infection after systemic administration of drugs, showing that it is not the Geotrichum alone that is pathogenic but the systemic host-fungal interactions manipulated by drug use that cause pathogenesis (19,20). Ultimately, the conclusions drawn in this review corroborate an immuno-

ecological model of oral health wherein diversity fosters tolerance and dysbiosis fosters inflammation, or at least, indicates negative health outcomes.

5.4 Clinical and Preventive Implications

Recognizing that other types of fungi besides Candida can affect the well-being of the mouth's collection of microbes also changes how dentists think about finding and fixing oral problems. Instead of just checking for Candida to find a fungal issue, using sequencing shows that fungal genera types such as Aspergillus and Geotrichum can be common or scarce when someone is sick, or even helpful (5,13). If diagnostic tests also looked at these other fungi to determine a diagnosis, they could prescribe fewer general antifungal drugs and use medicines that target specific kinds of fungi, which would help keep the good fungi around while getting rid of the health-diminishing ones.

From a preventative standpoint, this information suggests that the best means of remaining healthy is through purposeful maintenance of microbiome diversity with food and oral hygiene and careful antibiotic use. According to Talaga-Ćwiertnia et al., less fungal diversity comes from greater exposure to antibiotics, which means that for the best oral health, antibiotics should be used sparingly (6). Furthermore, O'Connell et al.'s results support the idea that mycobiome disruption occurs alongside early childhood caries, meaning that in the very beginning, a diverse genus of fungi is protective and beneficial for the future (12).

Fungal probiotic or prebiotic approaches are an emerging field of study that is yet to bear more beneficial results. Although bacterial probiotics are a well-established field with lots of supporting evidence encouraging their use, fungal probiotics have yet to experience the same focus. In the future, researchers should look to non-pathogenic fungi that create antimicrobial metabolites to engineer medical solutions that help stabilize fungi populations and encourage ecological balance.

5.5 Broader Systemic Connections

Many studies note a correlation between the oral fungal mycobiome and systemic disease. Chen et al. explore how low oral fungal diversity represents a nasopharyngeal carcinoma risk factor, implying that either a biased mycobiome reflects systemic inflammation, metabolic dysregulation, or the opposite (14). Likewise, rare Histoplasma and Mucorales infections implicate the oral soft tissues as sentinel locations of systemic, disseminated, fungal disease (15,17). These findings support the idea that the mouth acts as a signifier for systemic health. Localized changes to the ecology might be a precursor to or a consequence of whole-body immunological dysbiosis. Hence, mycobiome

mapping should be evaluated in the mouth for precision dentistry and enhanced preventive dentistry.

5.6 Methodological Limitations

Despite these cohesive, trusted results throughout the studies, they are not without caveats. The sequencing studies rely on varying collection efforts, sites of collection, and interpretation methods. Such differences significantly influence what can be determined at the taxonomic level (4). In addition, low-abundance reads may be sequenced byproducts or environmental contamination rather than true residents, as stated by Diaz & Dongari-Bagtzoglou (11). In addition, many of the identifications are unculturable taxa, which creates additional complications, as metabolic function has yet to be confirmed.

Another potential limitation is the cross-sectional nature of many investigations. The main issue with these studies is their inability to establish authentic causal relationships. While the implications of these studies are substantial, more research is needed to confirm these assertions concerning the contribution of non-Candida fungi in oral health and ecological homeostasis. Ultimately, a metatranscriptomic and metabolomic assessment would reveal the upregulated genes and metabolites in an unstressed condition.

With most studies featuring population bias, it is hard to establish whether these results are generalizable, as many of these identified research studies include adult populations of developed countries. Due to this bias, it may be incorrect to assume these results are generalizable enough to paediatric, geriatric, and more diverse populations, which are bound by different environmental and diet factors. To avoid this outcome, it is important to use uniform DNA extraction methods and feature more diverse populations.

5.7 Future Directions

Future oral mycobiome research should focus less on taxonomic characterization and more on functional ecology. Future perspectives include:

1. Standardization of sampling and sequencing strategies for a more global comparison.

2. Omics approaches (metatranscriptomics, metabolomics) to determine whether fungi are metabolically active in the oral microbiome.

3. Co-culture and imaging approaches to determine fungal-bacterial syntrophy and positioning within the biofilms.

4. Longitudinal studies of antifungal or antibiotic treatment to show variability of mycobiome resilience and immunity over time.

5. Therapeutic capacities of commensal fungi

Such recommendations will dictate whether a stable fungal community is an evaluable index of oral health relative to bacterial diversity of the gut microbiome.

6. CONCLUSION

- Non-*Candida* fungi (such as *Aspergillus spp.*, *Penicillium*, and *Malassezia*) are not passive contaminants but essential, active residents that contribute to the balance and stability of the oral microbiome. Disruptions caused by antibiotic use, poor diet, or hygiene issues reduce beneficial diversity, creating an environment where opportunistic strains can cause dysbiosis and diseases.

- There is a correlation between diversity and health. High fungal diversity is linked to homeostasis, reduced inflammation, and better bacterial balance. These fungi assist in biofilm stability, pH regulation, and interkingdom signaling. Non-*Candida* fungi produce metabolites that can inhibit caries-inducing bacteria and help regulate immune responses (tolerogenic effects), challenging the previous view that the mycobiome is either non-relevant or pathogenic.

- Future studies are needed with advanced research methods, such as metatranscriptomics, metabolomics, and immunological studies, whose are required to move from theoretical ecology to pragmatic clinical applications.

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7. SUSTAINABILITY

Increased awareness of non-Candida fungi in the oral microbiome supports longitudinal viability of clinical and research efforts. (9th goal of the U.N. sustainable development: “Industry and innovation”) (21)

By learning about previously unknown genera and their ecological contributions, dental professionals might spare patients from unnecessary widespread antifungal application, which alters levels, fosters AMR, and negatively impacts oral and systemic health. (3th goal: “Good health and well-being”)

Additionally, recognizing fungal diversity could result in more preventative approaches that keep the microbiome in homeostasis instead of more interventionist treatment. These findings apply to the economic, environmental, and socio-cultural sustainability of oral health, as well. Natural oral microbiomes reduce the need for increased pharmaceuticals and treatments, which, socio-culturally speaking, decrease medical expenses in well-resourced and poorly-resourced environments. For an environmentally safest approach, excess antifungals and antibiotics prevent pharmaceutical runoff into water sources and extended microbiomes and natural ecosystems. (12th goal: “Responsible consumption and production”)

In the end, more longitudinal and standardized investigations into the oral mycobiome will allow for diagnostic accuracy and clinical deduction like never before for more efficient, ethically managed, and sustained oral care.

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