Revista ARACÊ
ISSN: 2358-2472

THE ORAL FUNGAL MICROBIOTA AMONG PATIENTS WITH COVID-19

A MICROBIOTA FÚNGICA ORAL EM PACIENTES COM COVID-19

LA MICROBIOTA FÚNGICA ORAL EN PACIENTES CON COVID-19

https://doi.org/10.56238/arev7n6-081

Date of submission: 05/09/2025 **Date of publication:** 06/09/2025

Camila Vilela[1], Leonel Mendoza[2], Claudia Silami de Magualhães[3], Raquel Vilela[4], Rinosh Mani[5], Isadora França Vieira-Silva[6] and Amalia Moreno[7]

ABSTRACT

Objectives: Information regarding oral fungal microflora in patients with COVID-19 has yet to be evaluated. This study investigates the main fungal species (with focus on Candida species) present in the oral cavity of COVID-19 patients in intensive care units (ICU) and their health providers. Design: One hundred twenty-eight oral sawbs were collected and cultured on CHROMagar from COVID-19 patiens in the ICU, hospital personel, and individusals not in contact with hospital facilities. Following the CHROMagar manufacturer's instructions, an initial identification of the isolated fungal species was performed. The final identification of the species was carried out using Matrix-Assisted Laser Desorption Ionization-Time of Flight, Mass Spectrophotometry analysis (MALDI-TOF MS). Results: MALDI-TOF MS identified eight different Candida and Pichia species along with Ogataea polymorpha, Saccharomyces cerevisiae, and Trichosporum ashii. Conclussion: The study revealed the presence of several opportunistic fungal species among COVID-19 patients in an ICU facility without active disease. MALDI-TOF protein profile in cladistic analysis showed correlation between Candida species recovered from the investigated patients and health care personel.

Keywords: *Candida* species. COVID-19. MALDI-TOF.

---

[1] DDs, MSc
Department of Dental Clinic, Pathology and Surgery - Faculty of Dentistry, Federal University of Minas Gerais and Microbiology and Molecular Genetics, Michigan State University
Corresponding author
E-mail: camilavilela.odontoo@gmail.com
[2] PhD
Microbiology and Molecular Genetics, Biomedical Laboratory Diagnostics, , Michigan State University
[3] DDs, PhD
Department of Restorative Dentistry, Faculty of Dentistry, Federal University of Minas Gerais
[4] MD, PhD
Department of Clinical and Toxicological Analysis, Faculty of Pharmacy, Federal University of Minas Gerais and Microbiology and Molecular Genetics, Michigan State University
[5] DVM, PhD
Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University
[6] DDS, MSc
Department of Restorative Dentistry, Faculty of Dentistry, Federal University of Minas Gerais
[7] DDs, PhD
Department of Dental Clinic, Pathology and Surgery - Faculty of Dentistry, Federal University of Minas Gerais

RESUMO

Objetivos: As informações sobre a microflora fúngica oral em pacientes com COVID-19 ainda não foram avaliadas. Este estudo investiga as principais espécies fúngicas (com foco nas espécies Candida) presentes na cavidade oral de pacientes com COVID-19 em unidades de terapia intensiva (UTI) e seus profissionais de saúde. Desenho: Cento e vinte e oito swabs orais foram coletados e cultivados em CHROMagar de pacientes com COVID-19 na UTI, pessoal hospitalar e indivíduos que não tinham contato com instalações hospitalares. Seguindo as instruções do fabricante do CHROMagar, foi realizada uma identificação inicial das espécies fúngicas isoladas. A identificação final das espécies foi realizada usando a análise de ionização por desorção a laser assistida por matriz-tempo de voo, espectrofotometria de massa (MALDI-TOF MS). Resultados: O MALDI-TOF MS identificou oito espécies diferentes de Candida e Pichia, juntamente com Ogataea polymorpha, Saccharomyces cerevisiae e Trichosporum ashii. Conclusão: O estudo revelou a presença de várias espécies de fungos oportunistas entre pacientes com COVID-19 em uma unidade de terapia intensiva sem doença ativa. O perfil proteico MALDI-TOF na análise cladística mostrou correlação entre as espécies de Candida recuperadas dos pacientes investigados e dos profissionais de saúde.

Palavras-chave: Espécies de Candida. COVID-19. MALDI-TOF.

RESUMEN

Objetivos: La información relativa a la microflora fúngica oral en pacientes con COVID-19 aún no ha sido evaluada. Este estudio investiga las principales especies fúngicas (con especial atención a las especies de Candida) presentes en la cavidad oral de pacientes con COVID-19 ingresados en unidades de cuidados intensivos (UCI) y de sus profesionales sanitarios. Diseño: Se recogieron 128 muestras bucales y se cultivaron en CHROMagar de pacientes con COVID-19 en la UCI, personal hospitalario y personas que no estaban en contacto con las instalaciones hospitalarias. Siguiendo las instrucciones del fabricante de CHROMagar, se realizó una identificación inicial de las especies fúngicas aisladas. La identificación final de las especies se llevó a cabo mediante análisis de espectrofotometría de masas con ionización por desorción láser asistida por matriz y tiempo de vuelo (MALDI-TOF MS). Resultados: MALDI-TOF MS identificó ocho especies diferentes de Candida y Pichia, junto com Ogataea polymorpha, Saccharomyces cerevisiae y Trichosporum ashii. Conclusión: El estudio reveló la presencia de varias especies de hongos oportunistas entre pacientes con COVID-19 en una unidad de cuidados intensivos sin enfermedad activa. El perfil proteico MALDI-TOF en el análisis cladístico mostró una correlación entre las especies de Candida recuperadas de los pacientes investigados y el personal sanitario.

Palabras clave: Especies de Candida. COVID-19. MALDI-TOF.

INTRODUCTION

The normal oral microflora in hospital patients has been related to morbidity and mortality[1-2]. Disruption of the oral micriobiota in these patients result in clinical manifestations involving the oral cavity capable of progresing into a systemic disease [3]. According to Terezakis et al [4] intubated patients with respiratory disorders, poor oral hygiene and other comorbidities (diabetes, use of drugs such as bisphosphonates – linked to osteonecrosis of the jaw - and AIDS and carriers of the Sars-CoV-2 virus), are associated to changes in the oral fungal microbiota, especially fungal species (*Candida*). In addition, immunosuppressed patients with indiscriminate iatrogenic use of antibiotics, corticosteroids, immunosuppressants, and/or in cases of systemic diseases, modulation in the oral microbiota may occur [5].

Candidiasis is the most frequently diagnosed fungal infection of oral cavity[6-7]. Oral infection involving *C. albicans* can result in acute or chronic maifestations, but the main presentation will depend on the host's immune status . Conversely, Ataídes et al [1] and Vallabhaneni et al [8], refer to the significant increase on hospitalized patients of other *Candida* species including *C. tropicalis*, *C. guilliermondii*, *C. parapsilosis*, and more recently *C. lusitaniae* and *C. auris*. These authors stated that *C. auris* is now considered one of the main risk factors of the oropharyngeal region due to its multidrug resistance.

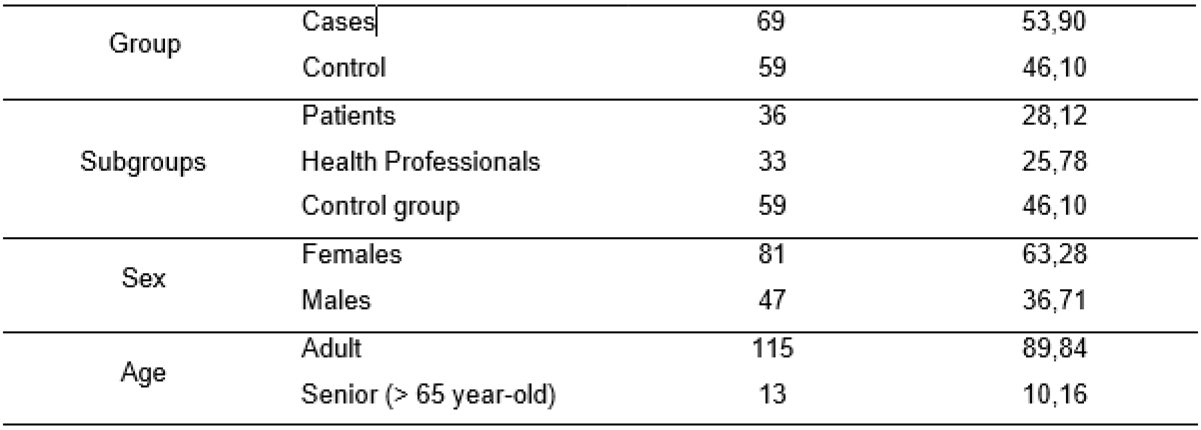
Considering the increased prevalence of these infections in the Intensive Care Unit (ICU), the exposure of health professionals and the possibility of horizontal transmission of these species is of concern [9]. The objectives of this study was to evaluate the fungal microbiota present in ICU patients with a PCR positive COVID-19 infection, and their health professionals who were in direct contact with these patients.

MATERIALS AND METHODS

STUDY DESIGN AND ETHICAL ASPECTS

This study investigate the presence of fungal species in the oropharyngeal cavity of the studied populations. The groups included 1) PCR positive COVID-19 ICU patients without antifungal therapy (n= 36 patients), 2) health professionals working in the ICU ward at the Hospital da Baleia, Belo Horizonte, Brazil (n= 33 individuals), and 3) a control group of healthy individuals not in contact with the hospital area (n= 59). Details of the investigated populations are found in Table 1. Every participant filled up a questionnaire indicating their consent to participate in the study following ethical protocols at the involved institutions (see below). The sample size calculation was that proposed by Fleiss [10], with reference to the value of "d" (size of the relative risk factor for comparison between groups) with a medium relative risk defined with the value of 0.05, suggested by Cohen[11]. Applying the Fleiss formula, considering the significance level values (respectively α= 5%) and the power of the test (respectively β= 80%). Descriptive analysis of categorical variables (qualitative variables) was carried out using absolute and relative frequencies. In describing the numerical variables (quantitative variables), measures of position, central tendency and dispersion were used. The results obtained for the case and control groups were compared using the Chi-Square Test [12]. The significance level adopted was p 0.05 using the software R v. 4.0.1.[13-14].

Table 1: Variables and characterization of the selected individuals in the study.



Variables	Individuals	Number	%
Group	Cases	69	53,90
	Control	59	46,10
Subgroups	Patients	36	28,12
	Health Professionals	33	25,78
	Control group	59	46,10
Sex	Females	81	63,28
	Males	47	36,71
Age	Adult	115	89,84
	Senior (> 65 year-old)	13	10,16

The protocols of the study were approved by the Research Ethics Committee of Hospital da Baleia (HB) (Belo Horizonte, Brazil; CAAE: 31806720.0.0000.5123). Subsequently, the research project was also approved by the Research Ethics Committee of the Federal University of Minas Gerais, Belo Horizonte, Brazil (UFMG CEP-UFMG; CAAE: 45240721.4.0000.5149). After signing the informed consent form for participation in the study, samples from the three groups were collected (PAS: PCR positive COVID-19 ICU patients; PUB: Health professionals working in the ICU; and ICH: Healthy individuals external to the hospital area).Sample collection and culture of clinical specimens

Specimen collectectors followed the Hospital regulations in place due to COVID-19 pandemic at all times. Glass tubes containing sterile swabs were used to collect the specimens. The swabs were positioned in the mouth against the buccal mucosa and the sample was collected with rapid rotational movements for 20 seconds. Tubes were identified, sealed and transported, on the same day of collection, to the HB Microbiology Laboratory. The swabs were removed from the tubes under class II biosafety cabinet, and CHROMOagar plates (CROMOagar, Pinhais, PR. Br) were aseptically inoculated. The swabs were gently inoculated on the CHROMOagar plates with rotating movements, distributed over the entire surface of the agar. The plates were inoculated at 37°C for seven days. Colored single colonies, indicating positive plates, were collected and subcultured on 2% Sabouraud Dextrose agar (SDA) for Matrix-Assisted Laser Desorption Ionization-Time of Flight, Mass Spectrophotometry (MALDI-TOF MS) analyses. Plates without mycological growth were discarded after 20 days of incubation and considered negative. Sub-cultured yeast colonies were kept on SDA slant tubes at 25°C until use. Fungal colonies on CHROMOagar plates were identify as *Candida* species following the company instructions (CROMOagar, Pinhais, PR. Br) .

IDENTIFICATION OF *CANDIDA* SPECIES BY MALDI-TOF

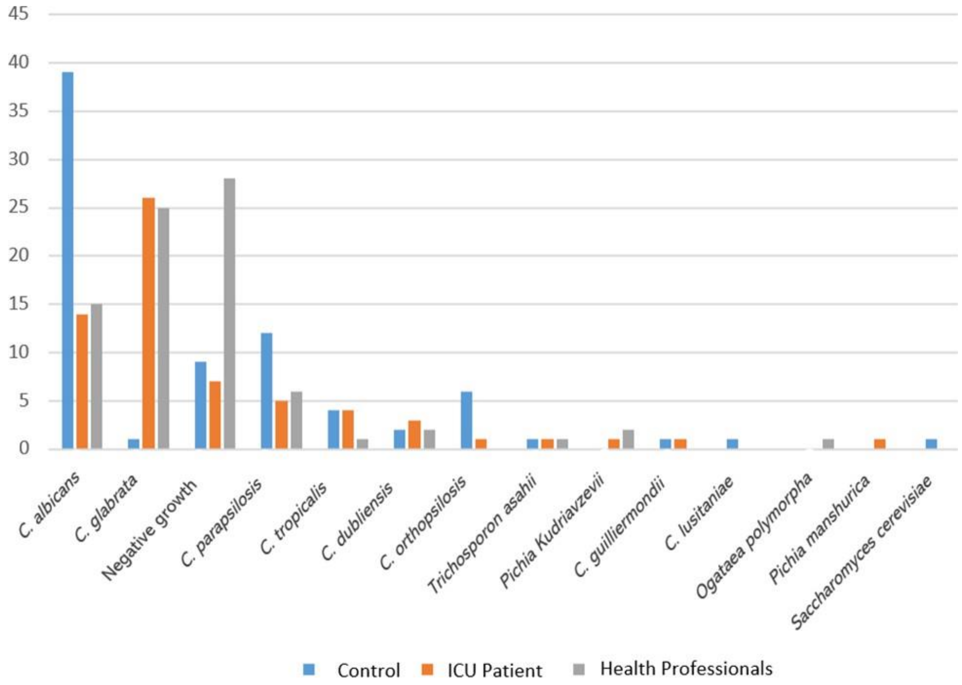
Colonies kept in slant 2% Sabouraud dextrose agar tubes were analyzed on a MicroFlex LT mass spectrophotometry platform (Bruker Daltonics Inc. Billerica, MA), available at Michigan State University. The fungal samples collected from the cultures were processed for mass spectrophotometry instrument according to the manufacturer's instructions (Bruker Daltonics Inc. Billerica, MA). Briefly, individual colonies were spotted on duplicate wells and 1.0 uL of freshly made 70% formic-acid was added on each spots. The fungal spots were allowed to dry and 1.0 uL of matrix (HCCA, Bruker Daltonics Inc. Billerica, MA), was added. Identification of the yeast was performed using MBT Compass Explorer 4.1 (Bruker Daltonics Inc. Billerica, MA), with Bruker reference library version 11.The MALDI-TOF scores range from 0.0 to 3.0 for proper species identification, and a score of 2.0 or greater than 2.0 is considered successful identification. Scores less than 1.7 were interpreted as an isolation of different yeast species (species other than the genus *Candida* sp.) according to the parameters provided by the manufacturer (Bruker Daltonics Inc. Billerica, MA). The data showed on the cladistic analyses were elaborated using MBT Compass Explorer 4.1 (Bruker Daltonics Inc. Billerica, MA).

RESULTS

FUNGAL SPECIES RECOVERED IN CULTURE

Using MALDI-TOF analyses thirteen different fungal species were identified in the three investigated populations (Table 2). This included *Candida albicans*, *C. dubliensis*, *C. glabrata*, *C. guillermondii*, *C. orthopsilosis*, *C. parapsilosis*, *C. tropicalis*, *C. lusitaniae*, *Ogataea polymorpha*, *Pichia kudriavzevii*, *P. manshurica*, *Saccharomyces cerevisiae*, and *Trichosporon asahii*. In the examined culture specimens 19.7% of them showed negative growth (Fig. 1). None of the isolates recovered during this study were linked to disease on the investigated populations including COVID-19 patients.In COVID-19 ICU patients the most prevalent species were *Candida albicans* (12.7 %) followed by *C. glabrata* (23.6%), *C. parapsilosis* (4.5%), *C. tropicalis* (3.6%), *C. orthopsilosis* (0.9%) and *C. dubliensis* (2.7% each), *Pichia kudriavzevii*, *Pichia manshurica, Trichosporon asahii* , and *C. guiliermondii* (0.9% each), (0.9%), respectively (Table 3). Similar results were also found in health care workers (Table 3).

FIGURE 1. The chart shows the number of fungal species recovered during the study and their correlation with their health professional involvement, including culture positive and negative individuals (ICU= Intensive Care Unit).



When the number of isolates recovered from health care individuals within hospital environments and those from the control group were compared, *C. albicans* was the most prevalent species (Table 2) (Fig. 1). Relevant to the study was the high number of *C.*

albicans isolates recovered from individuals in the control group (Fig. 1). In contrast, *C. glabrata* was significantly more prevalent among patients and hospital workers (46.4%) than the control group (1.4%) (Table 2). *Candida parapsilosis* was isolated in 10% of hospital individuals and 17.4% in the control group, whereas *C. tropicalis* showed a similar percentage in both groups (4.5% hospital versus 5.8% control group). (Table2) *Candida dubliensis* was more prevalent in hospital individuals (4.5%) than those in the control group (2.9%) (Table 2). The opposite occurred with *C. orthopsilosis* with 0.9% recovered in hospital personnel and 8.7% in the control group (Fig. 1) (Table 2). Interestingly, *Pichia kudriavzevii*, was isolated only in individuals related to the hospital environment (2.7%) but not in the control group (Table 2) (Fig. 1). Similar results were observed also in *Ogataea polymorpha* and *Pichia manshurica* both with 0.9% of frequency (Table 2). The percentage of *Trichosporon asahii* recovered in both groups were in some way similar (1.8% and 1.4% respectively) (Table 2). Comparable results were obtained in *C. guiliermondii* in both groups (0.9% - Hospital versus 1.4% - grupo control respectively) (Table 2). *Candida lusitaniae* (1.4%) and *Saccharomyces cerevisiae* (1.4%) were recovered in culture only from individuals in the control group (Table 2) (Fig. 1). Negative cultures were found among hospital workers (n= 28) followed by the control group (n= 9) and ICU patients (n= 7) (Fig. 1).

Table 2. Cross comparison between isolates recovered from hospital individuals versus control group.

Species	Hospital (%)	Control (%)	Total (%)
Candida albicans	29 (26,4%)	39 (56,5%)	68 (38,0%)
C. dubliensis	5 (4,5%)	2 (2,9%)	7 (3,9%)
C. glabrata	51 (46,4%)	1 (1,4%)	52 (29,1%)
C. guilliermondii	1 (0,9%)	1 (1,4%)	2 (1,1%)
C. lusitaniae	0 (0,0%)	1 (1,4%)	1 (0,6%)
C. orthopsilosis	1 (0,9%)	6 (8,7%)	7 (3,9%)
C. parapsilosis	11 (10,0%)	12 (17,4%)	23 (12,8%)
C. tropicalis	5 (4,5%)	4 (5,8%)	9 (5,0%)
Pichia kudriavzevii	3 (2,7%)	0 (0,0%)	3 (1,7%)
Pichia manshurica	1 (0,9%)	0 (0,0%)	1 (0,6%)
Ogataea polymorpha	1 (0,9%)	0 (0,0%)	1 (0,6%)
Saccharomyces cerevisiae	0 (0,0%)	1 (1,4%)	1 (0,6%)
Trichosporon asahii	2 (1,8%)	1 (1,4%)	3 (1,7%)
Total	110 (100,0%)	68 (100,0%)	178 (100,0%)

MALDI-TOF CLADISTIC ANALYSIS

Using *Candida* species spectra in MALDI-TOF cladistic analysis they grouped in diferent clusters according to their protein profile. For instance, dendograms using *C. albicans* (n= 29) (Fig. 2) and *C. glabrata* (n= 50) (Fig. 3) protein spectra in MALDI-TOF cladistic analysis showed *C. albicans* and *C. glabrata* distributed in independent clusters according to their spectra. These analyses placed the isolates recovered from some COVID-19 ICU patients (orange) in the same clusters with that of their health professionals (green) suggesting a common origin (Figs. 2, 3).

According to statistical data, the fungal species found in Health Professionals and the group of ICU patients did not differ significantly, maintaining equivalent proportions in both groups. For example, the proportion of *C. glabrata* found in healthcare professionals is similar to the ratio found in ICU patients (Table 3). This trend was also observed in *C. albicans* as well as in other yeast species (Table 3).

DISCUSSION

The alarming number of individuals with COVID-19 infection during the pandemic, introduced immediate and important impacts in the health care system worldwide**[15]**. Patients infected with the SARS-CoV-2 virus often developed moderate to advanced disease and thus, the use of corticosteroids to control the exacerbated inflammation, was a common practice **[15]**. Patients under this regime are in bed for prolonged periods usually developing problems related to the immune system. In turn, this condition favors the appearance of secondary infections, one of them being oral and systemic candidiasis, causing serious secondary side effects impairing the recovery of patients after contracting the virus **[15]**.

In this study, the three investigated groups harbored several *Candida* species, with *C. albicans* and *C. glabrata* being the most frequent isolates . Studies such as those by Ataídes et al **[1]** and Vallabhaneni et al **[8]**, refer to the significant increase in *Candida* spp species in hospitalized patients, with special relevance to *C. tropicalis*, *C. guilliermondii*, *C. parapsilosis* and more recently *C. glabrata* and *C. auris*. Our data showed that *C. glabrata* has a prevalence of 46.4% in ICU patients and their health professionals (26 patients and 25 health professionals) (Tables 2, 3). Subsequently, *C. albicans* was in second place with 26.4%, from which 14 were ICU patient and 15 health professional (Tables 2, 3). In third place, *C. parapsilosis* has a prevalence of 10% of the total sample, with five ICU patients and six health professionals (Tables 2, 3). In fourth place *Candida tropicalis* and *C. dubliensis* (4.5%), followed by *Pichia kudriavzevii* (2.7%), *Trichosporon asahii* (1.8%), and in the last place *C. orthopsilosis*, *C. guilliermondii*, *Pichia manshurica*, and *Ogataea polymorpha* (0.9%) (Tables 2, 3). In the control group *C. albicans*, showed a prevalence of 56.5%, followed by *C. parapsilosis* with 17.4%, *C. orthopsilosis* with 8.7%, *C. tropicalis* is present with 5.8%, and *C. dubliensis* with 2.9%. *C. glabrata*, *C. guilliermondii*, *C. lusitaniae*, *Trichosporon asahii*, and *Saccharomyces cerevisiae* displayed the lowest porcentage (1.4%) in this group (Table 2) . *Candida auris* was detected in this study.

Table 3. The use of Chi-square test to investigate differences between Subgroups.

Species	Patient ICU	Health Care workers	Total
Candida glabrata	26(23,6%)a	25(22,7%)a	51(46,4%)
C. albicans	14(12,7%)a	15(13,6%)a	29 (16,5%)
C. parapsilosis	5(4,5%)a	6(5,5%) a	11(10,0%)
C. tropicalis	4(3,6%)a	1(0,9%) a	5(4,5%)
C. dubliensis	3 (2,7%)a	2 (1,8%)a	5 (4,5%)
Pichia kudriavzevii	1(0,9%)a	2(1,8%) a	3(2,7%)
Trichosporon asahii	1(0,9%)a	1(0,9%) a	2(1,8%)
C. guilliermondii	1(0,9%)a	0(0,0%)a	1(0,9%)
Ogataea polymorpha	0(0,0%)a	1(0,9%)a	1(0,9%)
C. orthopsilosis	1(0,9%)a	0(0,0%)a	1(0,9%)
Pichia manshurica	1(0,9%)a	0(0,0%) a	1(0,9%)
Total	57(51,8%)	53(48,2%)	110(100,0%)

[a] Do not differ significantly from each other at the 0.05 level by the chi-square test.

Hospital environment harbor a wide variety of microorganisms facilitating transmission between individuals [16]. It is important to mention that in immunosuppressed patients and those with prolonged use of antibiotics, corticosteroids, immunosuppressant, which is the case in COVID-19 patients, the modulation in the oral microbiota may occur by species selection, or by nosocomial colonization [17]. According to Silva et al. [18] these type of patients can be colonized by yeast species some of them multiresistan to antifungals drugs. One example is *C. glabrata* that posseses intrinsic resistance to Fluconazole, Itraconazole and Amphotericin B [18]. Our data showed *C. glabrata* is present in both ICU patients and health professionals taking care of those patients, a data consistent to that in other studies [19]. The number of health professionals with *C. glabrata* increase the likelihood of horizontal transmission of this species to ICU patients (Fig. 1). Doi et al. [9] described the transmision of *C. glabrata* between health professionals and ICU patients. The same situation was reported with other yeast isolates [9]. For instance, in this study it was observed possible transmission of *P. kudriavzevii* between , one ICU patient and two health professionals (2.7%) (Fig. 1, Table 3). According to Xi et al. [20] *P. kudriavzevii*, is the sexual stage of *C. krusei*, and previously reported *Candida* sexual reproduction gives the ability of transmission between hosts.

Figure 2. Dendogram based on protein spectra profile (MALDI-TOF) of *Candida albicans* showing several clusters comprising intensive care unit patients (orange) and health professionals (green). The subdivisions within the clusters represents isolates with similar spectra profile, suggesting a commum origin.

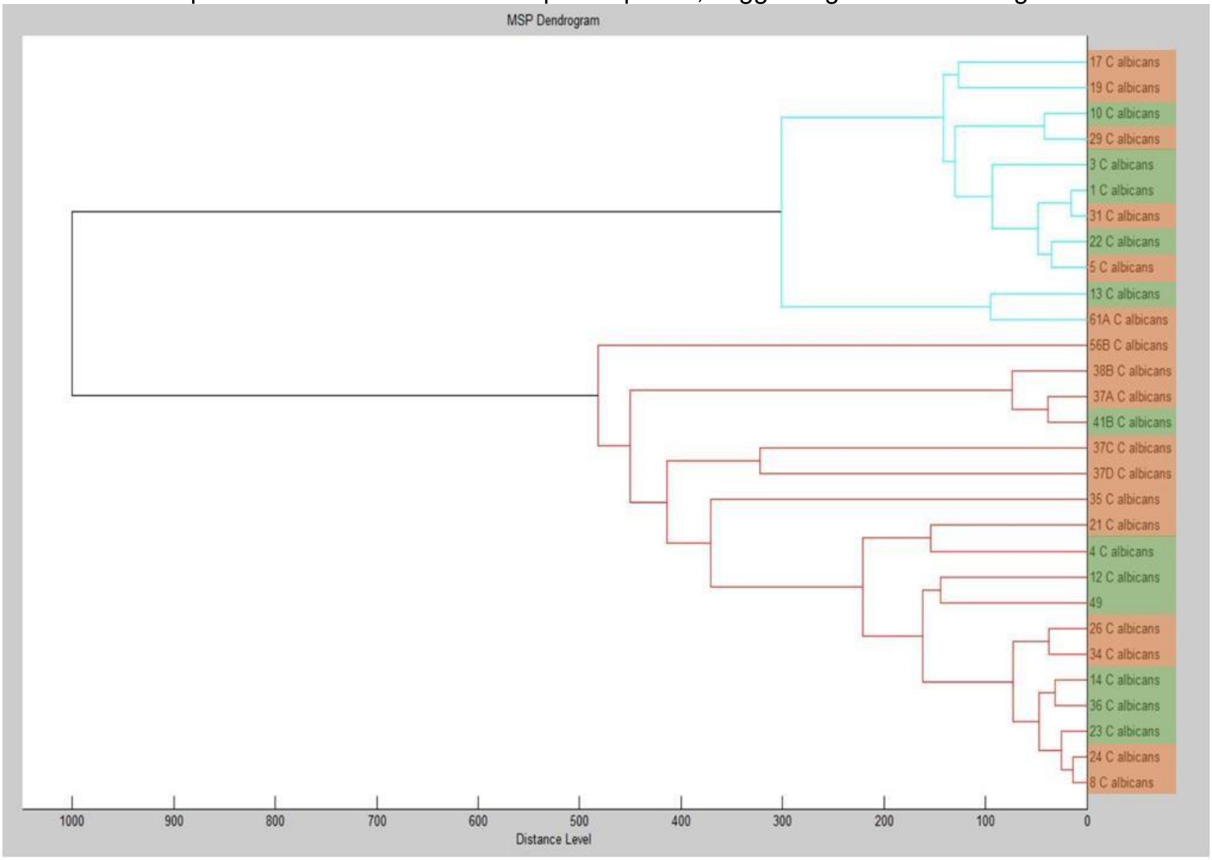
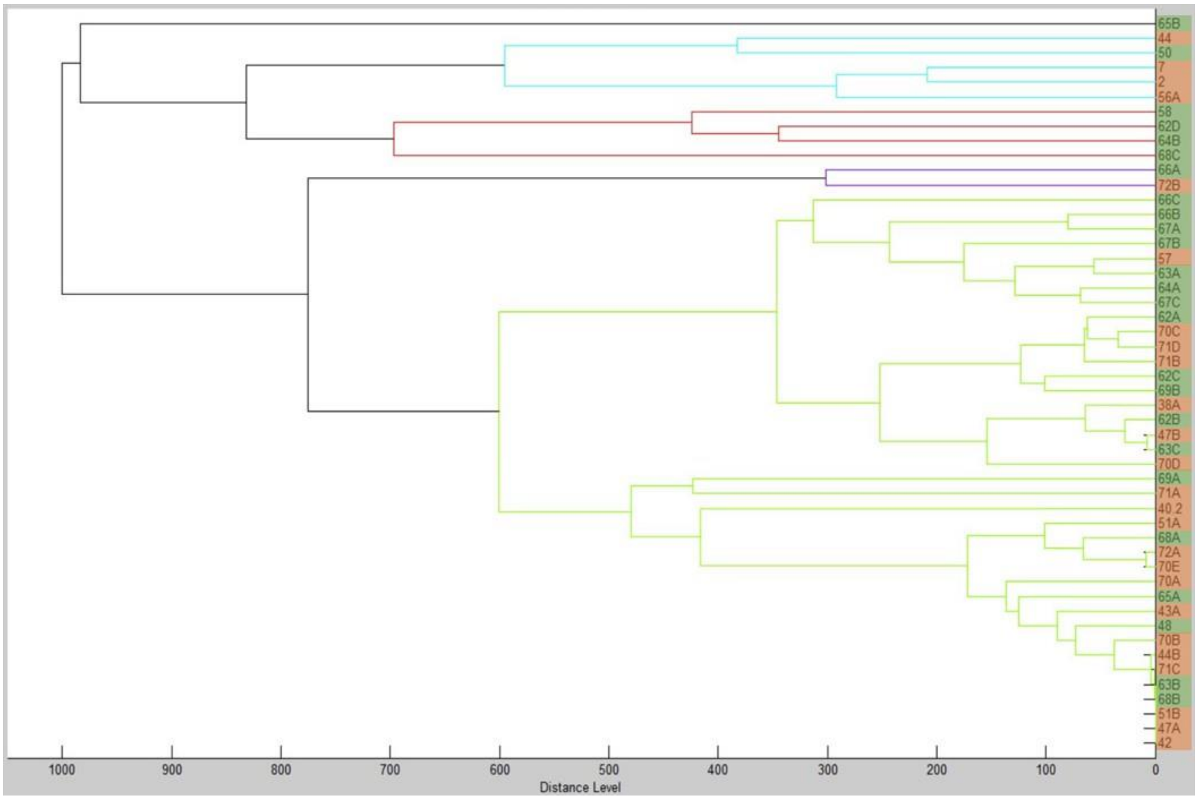


Figure 3. Dendogram based on protein spectra profile (MALDI-TOF) of *Candida glabrata* showing several clusters comprising intensive care unit (ICU) patients (orange) and health professionals (green). The subdivisions within the clusters represents isolates with similar spectra profile, suggesting a commum origin.



One of the main features of *Candida* species is their ability to adhere abiotic surfaces developing biofilms, and to decrease basal cell production to survive outside the host **[16-21-22]**. Our study found some health professionals (green) with direct contact with COVID-19 patients (orange) displayed the same *Candida* according to their MALDI-TOF protein profile (Figs. 2, 3). These observations agree with several authors investigating horizontal transmission between hospital individuals **[16-21-22]**. Interestingly, none of the *Candida* species recovered form COVID-19 ICU patients developed active disease, even in cases of severe COVID-19 infection.

CONCLUSION

The study detected a variety of opportunistic fungal species in COVID-19 patients admitted to the ICU, underscoring that colonization can occur even in the absence of active fungal disease. This finding highlights the importance of routine mycological surveillance in critical-care settings, particularly during viral outbreaks that may predispose patients to secondary infections.

Moreover, cladistic analysis of MALDI-TOF protein profiles revealed a notable correlation between the Candida strains isolated from these patients and those obtained from healthcare personnel. This overlap suggests possible microbial exchange within the clinical environment and reinforces the need for stringent infection-control measures to prevent cross-transmission in intensive-care units.

ACKNOWLEDGEMENTS

The authors thanks the Department of Microbiology and Molecular Genetics, Michigan State University for their funding support to this study.

CONFLICT OF INTEREST

The authors declared no conflict interest.

AUTHORS CONTRIBUTION

Camila Vilela: Data curation; Performed analyses; Methodology; Writing the manuscript. **Leonel Mendoza**: Data curation; Original design; Writing the original draft; Investigation; Funding acquisition; Editing. **Claudia Silami de Magualhães**: Data curation; Writing the original draft. **Raquel Vilela**: Data curation; Conceptualization; Original design; Writing the first draft; Editing. **Rinosh Mani**: MALDI-TOF analysis; Writing review; editing. **Isadora França Vieira-Silva:** Writing-review & editing. **Amalia Moreno**: Conceptualization; Funding acquisition; Methodology; Writing-review & editing.

REFERENCES

1. Ataídes FS, Abrao F, Costa C, Silva M, Pimenta F, Palos M, et al. Identificação de espécies de *Candida* em saliva de profissionais da saúde. Rev Eletr Enf, Goiânia., 2010; 12:498-501. https://doi.org/10.5216/ree.v12i3.6472

2. Avila M, Ojcius D M, Yilmaz O. The Oral Microbiota: Living with a Permanent Guest. J DNA Cell Biol. 2009; 28:405-411. https://doi.org/10.1089/dna.2009.0874

3. Wade W. The oral microbiome in health and disease. J Pharmacological Res. 2013;69:137-143. https://doi.org/10.1016/j.phrs.2012.11.006

4. Terezakis E, Needleman I, Kumar N, Moles D, Agudo E. The impact of hospitalization on oral health: a systematic review. J Clin Periodontol. 2011;38;628–636. https://doi.org/10.1111/j.1600-051x.2011.01727.x

5. He J, Li Y, Cao Y, Xue J, Zhou X. The oral microbiome diversity and its relation to human diseases. J Folia Microbiol. 2015;60:69-80. https://doi.org/10.1007/s12223-014-0342-2

6. Spolidorio LC, Martins V, Nogueira R, Spolidorio D. The frequency of *Candida* sp. In Biopsies of oral mucosal lesions. Pesqui Odontol Bras 2003;17:89-93. https://doi.org/10.1590/s1517-74912003000100017

7. Neto M, Danesi C, Unfer D. Candidíase Bucal revisão da literatura. RevSaúde, RS, 2005; 31:16-26. https://doi.org/10.5902/223658346404

8. Vallabhaneni S, Jackson B, Chiller T. *Candida auris*: An Emerging Antimicrobial Resistance Threat. Ann Internal Med. 2019;171:432-433. https://doi.org/10.7326/m19-2205

9. Doi AM, Pignatari A, Edmond M, Marra A, Camargo L, Siqueira R et al. Epidemiology and microbiologic characterization of nosocomial candidemia from a Brazilian national surveillance program. PloS One 2016;11:e1. https://doi.org/10.1371/journal.pone.0146909

10. Fleiss JL. The design and analysis of clinical experiments. New York: John Wiley & Sons. 1989. https://doi.org/10.1002/bimj.4710300308

11. Cohen J. Statistical power analysis for the behavioral sciences. 1988. https://doi.org/10.4324/9780203771587

12. Agresti, A., Kateri, M. Categorical Data Analysis. Gainesville, Florida: John Wiley., 2011;45.

13. Mckight PE, Najab J. Kruskal-wallis test. The corsini encyclopedia of psychology 2010;1-1. https://doi.org/10.1002/9780470479216.corpsy0491

14. Katz BM, Mcsweeney M. A multivariate Kruskal-Wallis test with post hoc procedures.

Multivariate Behavioral Research 1980;15:281-297. https://doi.org/10.1207/s15327906mbr1503_4

15. Mattos-Silva P, Felix NS, Silva Pl, Robba C, Battaglini D, Pelosi P, et al. Pros and cons of corticosteroid therapy for COVID-19 patients. Respir Physiol Neurobiol. 2020;280:103492. https://doi.org/10.1016/j.resp.2020.103492

16. Facciolá A, Pellicanò G, Visalli G, Paolucci I, Venanzi Rullo E, Ceccarelli M et al. The role of the hospital environment in the healthcare-associated infections: a general review of the literature. Eur Ver Med Pharmacol. Sci. 2019;23:1266-1278. https://doi.org/10.26355/eurrev_201902_17020

17. Ghannoum MA, Jurevic R, Mukherjee P, Cui F, Sikarrodi M, Naqvi A, et al. Characterization of the oral fugal microbiome (mycobiome) in healthy individuals. J PLoS Pathog 2010;6:e1. https://doi.org/10.1371/journal.ppat.1000713

18. Silva S, Negri M, Henriques M, Oliveira R, Williams DW, Azeredo J. *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis*: biology, epidemiology, pathogenicity and antifungal resistance. FEMS Microbiology Reviews 2012;36:288–305.
https://doi.org/10.1111/j.1574- 6976.2011.00278.x

19. Mushi MF, Gross U, Mshana S E, Bader O. High diversity of *Candida glabrata* in a tertiary hospital—Mwanza, Tanzania Med Mycol 2019;57:914-917.https://doi.org/10.1093/mmy/myy036

20. Xi Y, Zhan T, Xu H, Chen J, Bi C, Fan F, et al. Microbial Biotechnology published by Society for Applied Microbiology and John Wiley & Sons Ltd, Microbial Biotechnology 2021;14:1130–1147. https://doi.org/10.1111/1751-7915.13781

21. Mayer FL, Wilson D, Hube B. *Candida albicans* pathogenicity mechanisms. Virulence 2013;4:119–128. https://doi.org/10.4161%2Fviru.22913

22. De Groot P, Bader O, Boer A, Weig M, Chauhan N. Adhesins in human fungal pathogens: Glue with plenty of stick. Eukaryotic Cell 2013;12:470–481. https://doi.org/10.1128/EC.00364-12