

# Oral Candidiasis Prevalence in HIV Patients in the City of Nova Iguaçu, Province of Rio de Janeiro, Brazil.

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## ABSTRACT

**Background:** Human Immunodeficiency Virus (HIV) infection is a pandemic disease which causes a change in the immune system, mainly with a decrease in CD4 lymphocytes. This circumstance facilitates the appearance of opportunistic infections and the development of neoplastic processes that may lead the patient to a clinical state known as Acquired Immunodeficiency Syndrome (AIDS) and death. The objective of this research is to identify species of the genus *Candida* of patients with AIDS and affected by lesions in the oral cavity and hospitalized in the Nova Iguaçu General Hospital. **Methods:** 39 samples of oral lesions were collected and examined in the mycology laboratory of the Army Biology Institute (IBEx) through mycological procedures. All of the 39 samples were positive for species of the genus *Candida*. **Results:** *C. albicans* was the most frequent (74%), followed by *C. tropicalis* (15%), *C. glabrata* (8%) and *C. lambica* (3%). The most frequent clinical presentation was the pseudomembranous form, with 24 cases (61.54%), followed by erythematous (25.64%) and chronic multifocal form (12.82%). One of the patients presented the membranous clinical form with association of *C. albicans* and *Histoplasma capsulatum*. Oral candidiasis is one of the most serious health problems among immunocompromised people. **Conclusion:** Early diagnosis of the HIV infection and adequate treatment are essential to prevent opportunistic infections.

**Keywords:** Oral Candidiasis, *Candida* spp, HIV, Opportunistic Infections.

## INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a disease first diagnosed in 1981 in United States of America. This disease immediately had an explosive epidemic, which soon spread to other regions of the world, becoming one of the great problems of global public health.<sup>[1]</sup> Although primarily identified in America, it is believed that its origin is the African continent. AIDS is not considered to be an isolated disease, but the final stage of human immunodeficiency virus (HIV) infection, and is characterized as a fatal syndrome.<sup>[2,3]</sup>

In some infected people, the period between HIV infection and the development of the suggestive symptoms of the syndrome may be a few years, but

in other individuals this period may last ten years or more. Most HIV-infected individuals experience intermittent periods of the disease, whose severity increases as the virus advances promoting immune system depression. There are several pathogenic microorganisms which indicate the immune capacity at different stages of the disease. Health professionals who follow the patients can approximately calculate the state of the immune system by signals presented by HIV-infected patients. The number of CD4 cells per mm<sup>3</sup> of blood can also provide important data on patients' immunological status.<sup>[1,4,5]</sup>

Humans live in relative harmony with a large number of virus, bacteria and fungi that do not cause disease in healthy people, in whom immune defenses are intact, but these microorganisms can take advantage of a weakened immune system like those of HIV infected people and cause opportunistic infections, including candidiasis, which are fungal infections caused by species of the genus *Candida*. These fungi usually constitute part of the normal flora of the oral cavity of the healthy people, but become pathogens when there are appropriated conditions which favor their

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growth such as diabetes, pregnancy, carcinomas and immunodeficiencies, among other physiological changes, and may cause a superficial or deep infection.<sup>[1,6-8]</sup>

The term “candidiasis” comprises a group of physiological changes caused by yeast species belonging to the genus *Candida*. These changes acquire more clinical importance after the use of broad-spectrum bacterial antibiotics, immunosuppressive drugs and, more recently, with the growth of Acquired Immunodeficiency Syndrome (AIDS) epidemic.<sup>[9,10]</sup> Oral candidiasis is related to the infection restricted to buccal and peribuccal cavity tissues (primary oral candidiasis) and oral infection resulting from chronic mucocutaneous disease (secondary oral candidiasis). Primary candidiasis can be subdivided into: acute atrophic pseudomembranous, chronic multifocal, hyperplastic, angular and chronic atrophic cheilitis or stomatitis caused by dental prostheses. The first five variants are often observed in AIDS patients. The most frequent clinical form in these patients is the oropharyngeal candidiasis, which represents 32.6% of all clinical forms diagnosed in patients in the decade of 1980.<sup>[10,11]</sup>

The pathogenicity or the virulence of a microorganism is defined by its ability to cause diseases, mediated by several factors. Among them, we can mention as virulence factors: adhesion, germ tube production, dimorphism, phenotype variation, genotype variation, biofilm formation, toxin production, and exoenzyme production (proteinase and phospholipase).<sup>[12,13]</sup> The high production of proteinase by species of the genus *Candida* determines a strongly proteolytic activity, which facilitates a greater adhesion to the cells of the buccal epithelium and leading to tissue destruction. Proteinases are usually involved in a number of processes, including pseudomycelium formation, adhesion, and “switching” phenomena, which further contribute to the pathogenicity of yeast. Phospholipases are hydrolytic enzymes that degrade phospholipids, which is the largest constituent of the biological membrane of animals, plants and bacteria. The presence of this enzyme on the surface of the yeast propitiates the tissue injury by damaging the lipid constituents of the host cell membrane. For this reason, yeast strains that have high amounts of phospholipases present a greater capacity of adhesion and invasion.<sup>[13,14]</sup>

Oral candidiasis has been described as a disease associated with the first cases described in the AIDS literature, being the most frequent fungal infection in HIV-positive patients. It is estimated that up to 90% of HIV-infected people will experience at least one episode of oropharyngeal candidiasis.<sup>[15]</sup>

Considering these aspects of the mentioned diseases, the present research has the objective of

study the prevalence and the etiology of buccal lesions caused by *Candida* species among HIV patients interned in the Infectious Diseases outpatient clinic of the Nova Iguaçu General Hospital, Province of Rio de Janeiro, Brazil.

## MATERIALS AND METHODS

This research has an observational, analytic and transversal design. The total sample was constituted by 39 patients with positive diagnostic to HIV with severe oral cavity lesions hospitalized at the Infectious Diseases outpatient clinic of the Nova Iguaçu General Hospital, Province of Rio de Janeiro, Brazil. The research protocol complied with the standards of the Hospital's Ethics and Clinical Studies Committee. All the patients were informed about the purpose of the research and gave their consent. For the mycological analyzes, samples of the lesions of the buccal cavity were collected with sterile swabs, which were preserved in Stuart transport medium and sent to the Laboratory of Mycology of the Brazilian Army Biology Institute (IBEx), where the material analyzes were performed. The material was seeded in Petri dishes containing the Sabouraud-dextrose-agar and Mycosel media, incubated at 37°C for 48 hours. Samples of the colonies were stained by the Gram method. Those with yeast cells were considered positive. The test for the formation of the germinative tube was performed in order to characterize the species. Sampled colonies were seeded in sterile tubes containing 0.5mL of human serum and incubated at 37°C for three hours. A drop of each suspension was then deposited on slides that were covered with coverslips and observed under a 40X objective optical microscope. The presence of filaments from the yeasts allowed the presumptive identification of *Candida albicans*, and the yeast samples without germ tubes were identified as non-*albicans*. For the final identification of the species, all the samples were submitted to biochemical tests by the BioMérieux-Vitek system.

## RESULTS

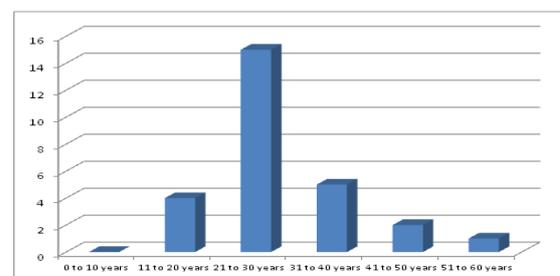


Figure 1: Distribution of 27 male AIDS patients by age classes.

The 39 examined patients were aged between 21 and 66 years old, with 27 male patients, predominantly those aged 30 to 39 years (55.56%). About the female patients, there were 12 cases of AIDS, predominantly in the age group between 40 and 49 years (41.67%) [Figure 2].

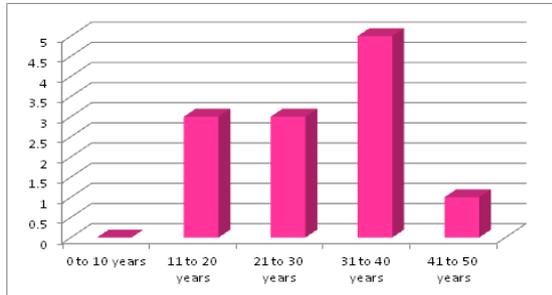


Figure 2: Distribution of 12 female AIDS patients by age classes. Graph 2 – Distribution of 12 female AIDS patients by age classes.

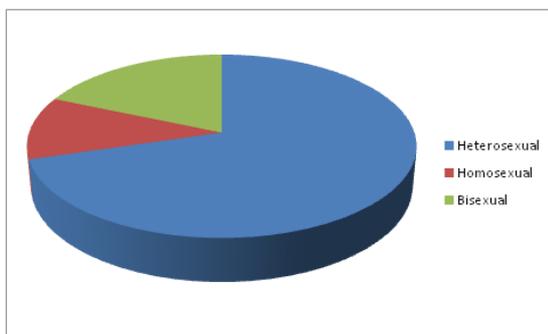


Figure 3: Distribution of the 27 AIDS patients according to sexual tendency.

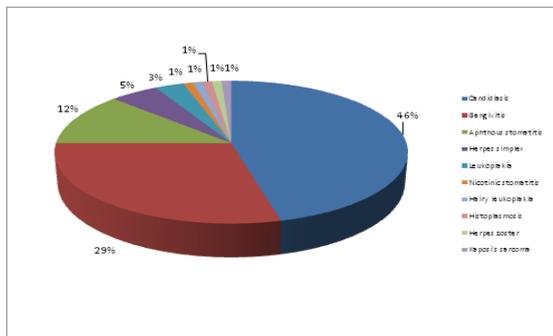


Figure 4: Oral pathologies in the 39 AIDS patients.

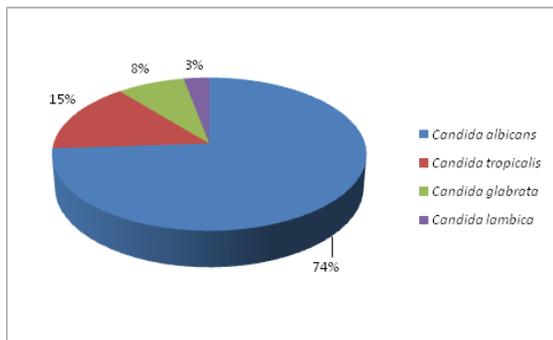


Figure 5: Candida species among the 39 AIDS patients.

Regarding smoking and illicit drug use among male patients, 7 patients were smokers and drug users, 2 were drug users but not smokers, 11 were smokers but not drug users, 7 were non-smokers and non-drug users. As for the female gender, five were smokers but did not use drugs, three did not smoke and also did not use drugs, and four patients refused to provide this information.

## DISCUSSION

According to Sharma et al,<sup>[8]</sup> candidiasis is the most common oral fungal infection in man, and may present several clinical forms. This fact, in some cases, makes difficult the diagnosis. Many patients may manifest a single clinical form, although some patients develop more than one clinical form. This fact was also verified in our research, where 18 patients presented more than one clinical form.

Species of the Candida genus may be normal components of the oral flora in 30% to 50% of the population with no evidence of infection. In the past, candidiasis was considered by researchers as an opportunistic infection that affected people debilitated by other diseases. Certainly such patients constitute a significant percentage of those infected with Candida spp. but today it's largely known that oral candidiasis can develop in healthy people. According to López and Marín,<sup>1</sup> pseudomembranous candidiasis begins when exposing the patient to broad spectrum antibiotics or reducing the immunity of the patient. Exposure to antibiotics is responsible for an evolution of fungal disease that produces the chronic form of long-term pseudomembranous candidiasis as these antibiotics changes the microflora dynamics. In the diagnosis of clinical forms of candidiasis in our research, the pseudomembranous clinical form was the most frequent.

Clinical evidence of infection depends on three general factors: host immune status, nasal mucosal environment, and resistance of the Candida species to antifungal agents.<sup>[16]</sup> In the analysis of our results, not all patients presented an evaluation regarding the degree of immunodepression at the time when the material was collected for laboratory analysis, however, they were also affected by other pathologies caused by another microbial agents, being the C. albicans (74%) the most featured. The prevalence of C. albicans is a fact confirmed unanimously by other researchers.

According to Patton et al. and Miziara et al,<sup>[17,18]</sup> lesions that occur in the oral cavity such as oral candidiasis and hairy leukoplakia are considered important prognostic indicators of progression of HIV infection. The presence of these lesions not only suggests HIV infection, but may be one of the first signs of evolution of the HIV-infected patient to the development of Acquired Immunodeficiency Syndrome (AIDS). We agree with the indication of

the cited authors as the suggested clinical signs of HIV infection advance are also considered as markers in outpatient clinics evaluated in the Nova Iguaçú General Hospital.

Favalessa et al.<sup>[19]</sup> studied the mycological aspects and in vitro susceptibilities of Candida yeasts in 102 HIV patients in the Province of Mato Grosso, Brazil, and found 100% positivity for Candida species. Among these patients, 82 (78.1%) were diagnosed for Candida albicans, 8 (7.6%) for C. parapsilosis, 8 (7.6%) C. tropicalis, 4 (3.8%) C. krusei and 2 (1.97%) C. glabrata. These results present small differences when compared to our results, but the highest incidence in that group was also due to C. albicans.

Oral candidiasis among HIV-positive patients was researched by Santa Anna et al.<sup>[5]</sup> at the Institute of Tropical Medicine of Puebla, Mexico. They conducted a prospective research to understand the clinical and mycological aspects in a population of 97 adult HIV-infected patients. The average age of the participants was 34.97 years, distributed in 76 male and 21 female patients. The predominant sexual tendency was heterosexual, with 56.7%, followed by homosexual, with 24.7%, and bisexual, 8.5%. Candida albicans was the most frequent species in 92%, followed by Candida non-albicans, with 8%. The percentage of C. albicans was also the most frequent in our research.

According to Ellepola and Samaranayake and Huang et al.<sup>[21,21]</sup> researches with HIV-positive patients reveals that among Candida species, C. albicans is the most frequent etiological agent in oral cavity candidiasis associated to HIV infections and AIDS cases. We agree with the citation of these authors when we found positivity for C. albicans of 74% among patients attended in the city of Nova Iguaçú.

A research about oral candidiasis in patients HIV-infected with AIDS was released by Machín et al.<sup>[22]</sup> This research was performed with 25 patients hospitalized at Pedro Kouri Tropical Medicine Hospital in the city of Havana, Cuba. The four main clinical forms of oral candidiasis were found in HIV-positive patients with AIDS, being the pseudomembranous form caused by C. albicans the most common, identified in 17 of the 25 sampled patients (68%). Erythematous candidiasis caused by C. tropicalis was diagnosed in 8 patients (32%). Similar results were recorded among patients in our research.

References to clinical forms of oral candidiasis in HIV/AIDS patients differ about their predominant form and presentation. The researchers Machín et al. and Feigal et al.<sup>[22,23]</sup> reported the prevalence of pseudomembranous lesions, fact also observed in our research, where this clinical form was observed in 24 patients (74%) among the 39 examined. The erythematous clinical form was the most frequent among the patients investigated by McCarthy et

al.<sup>[24]</sup> in our research, this clinical form occurred in 10 patients among the 39 examined.

## CONCLUSION

This was the first study on Candida species involving HIV/AIDS patients in the city of Nova Iguaçú. The results obtained in this research confirm a high prevalence of oral lesions caused by species of the Candida genus and show the need to appreciate the oral cavity examination as a sign of possible immunodeficiency. Tests should be performed periodically on all HIV-positive or suspected patients, and this is considered a useful clinical finding. Candidiasis of the oral cavity may reveal a reduction in immunity and a warning of the evolution of AIDS, showing the need of special cares in the prevention of opportunistic diseases.

## REFERENCES

1. López EM, Marín AF. La candidíasis como manifestación bucal en el SIDA. Rev Cubana Estomatol 2001; 38(1): 25-32.
2. Aguirre JM. Candidíases orales. Rev Ibero Am Micol 2002; 19: 17-21.
3. Veronesi R, Focaccia R. Tratado de Infectologia. Atheneu, São Paulo, 2015.
4. Coura JR. Dinâmica das Doenças Infecciosas e Parasitárias. Guanabara Koogan, Rio de Janeiro, 2013.
5. Santa Anna LMP, Zaragoza MTI, Rodallegas EGR, Herrero BL, Sanchez NM, Francisco NC et al. Candidíasis oral en pacientes soropositivos al HIV y casos SIDA. Aspectos clínicos, micológicos y terapéuticos. Rev Cubana Med Trop 2006; 58(3): 173-180
6. Fuentes FWR. Candidíasis oral: su relevancia actual. Rev Odontostomato 1992; 4(4): 4-9.
7. López J. Actualización de candidíasis oral. Rev Archivos Odontostomato 1997; 13(5): 259-272.
8. Sharma G, Oberoi SS, Vohra P, Nagpal A. Oral manifestations of HIV/AIDS in Asia: systematic review and future research guidelines. J Clin Exp Dent 2005; 7(3): 19-27.
9. Lima MCBF, Silva-Jr A, Torres SR. Prevalence of oral manifestations in HIV-infected children: a literature review. Rev Bras Odontol 2017; 74(3): 240-243.
10. Matsuka LK. Análise de alguns aspectos clínicos e epidemiológicos da Síndrome da Imunodeficiência Adquirida. Arq Med ABC 1986; 9(2): 10-15.
11. Pindborg JJ. Classification of oral lesions associated HIV infection. Oral Surg Med Oral Pathol 1989; 67: 292-295.
12. Álvares CA, Svirzinski TIE, Consolaro MEL. Candidíase vulvovaginal: fatores predisponentes do hospedeiro e virulência das leveduras. J Bras Patol Med Lab 2007; 435: 319-327.
13. Hartman A, Missio R, Hammad MP, Alves IA. Incidência de Candida spp. na mucosa oral de pacientes infectados pelo Vírus da Imunodeficiência Humana (HIV) no município de Santo Ângelo – RS. Rev Epidemiol Control Infec 2016; 6(3): 125-130.
14. Costa CR. Fatores de virulência de isolados de Candida de pacientes imunocomprometidos: caracterização molecular de Candida albicans suscetíveis e resistentes ao fluconazol. Universidade Federal de Goiás, UFG, 2009.
15. Barbedo LS, Sgargi DBG. Candidose. J Bras Doenças Sexualm Transm 2010; 4(22): 1.

16. Armstrong-James D, Meintjes G, Braun GD. A neglected epidemic: fungal infections in HIV/AIDS. *Trends Microbiol* 2014; 22(3): 120-127.
17. Patton LL, McKaig RG, Rogers D, Strauss RP, Eron JJ. The role oral manifestations of HIV and body signs in suspicion of possible HIV infection. *Oral Surg Oral Med Oral Radiol* 1998; 85(4): 416.
18. Miziara ID, Lima AS, Cortina RAC. Candidíase oral e leucoplasia pilosa como marcadores de progressão da infecção pelo HIV em pacientes brasileiros. *Rev Bras Otorrinolaringol* 2004; 70(3): 310-314.
19. Favalessa OC, Martins MA, Hahn RC. Aspectos micológicos e suscetibilidade in vitro de leveduras do gênero *Candida* em pacientes HIV positivos provenientes do estado de Mato Grosso. *Rev Soc Bras Med Trop* 2010; 43(6): 673-677.
20. Ellepola ANB, Samaranyake LP. Oral candidal infections and antimycotics. *Crit Rev Oral Biol Med* 2000; 11: 173-198.
21. Huang CC, Yang YL, Lauderdale TL, McDonald J, Hsiao CF, Cheng HH. Colonization of Human Immunodeficiency Virus infected outpatients in Taiwan with *Candida* species. *J Clin Microbiol* 2005; 43: 1600-1603.
22. Machín GM, Lancha MP, Corvagal JM, Andreu CMF, Tirado FB. Aislamiento, identificación y tipificación de levaduras en pacientes HIV positivos con candidíasis oral. *Rev Cubana Med Trop* 1997; 48(3): 1-8.
23. Feigal DW, Katz MH, Greenspan D, Westenhous J, Winkelstein W, Lang W et al. The prevalence of oral lesions in HIV infected homosexual and bisexual men three. *San Francisco Epidemiological Cohorts. AIDS* 1991; 5(5): 519-525.
24. McCarthy GM, Mackie ID, Koval J, Sandhu HS, Daley TD. Factors associated with increased frequency of HIV-related oral candidiasis. *J Oral Pathol Med* 1991; 20(7): 332-336.

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