

Epidemiology of oral candidiasis: a household-based population survey in a medium-sized city in Amazonas

Epidemiologia de candidíase oral: uma pesquisa de base populacional em um município de tamanho médio no Amazonas

Epidemiología de candidiasis oral: un estudio de base poblacional en un municipio mediano de Amazonas

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Abstract

There was an increase in the number of elderly people in Brazil and, along with this fact, there was an increase in the incidence of oral candidiasis in this population, so the early identification of the disease and the etiologic agent for effective intervention is essential. The study aimed to describe the prevalence of oral candidiasis and its clinical manifestations, identifying *Candida* yeast species and their prevalence in the palatine mucosa and dentures in the palatine mucosa and dentures, comparing these factors in rural and urban elderly people in this city. The study was conducted in the city of Tefé, Amazonas, with elderly people aged 65 to 74 years old registered in primary health care services in urban and rural areas, where through sample calculation we had a total sample of 484 elderly people after losses and refusals. These elderly people were randomly selected from within the entire public service network, which enabled the samples to be collected in all municipal Basic Health Units. Data collection included clinical oral examinations (use, duration, and need for dental prosthesis) and collection of biological material with swabs, which were stored in CHROMAgar™ *Candida* medium, during home visits to determine the prevalence of the species through staining and colony morphology. Statistical analysis was performed with Stata MP software, using relative and absolute frequencies. The prevalence of oral candidiasis was found in 20.7% of the elderly in the different areas of residence studied. A greater number of cases and clinical manifestations of the disease were found in elderly people living in urban areas ($p < 0.05$). The odds ratios for developing the disease were higher in women, edentulous elderly, and users of dental prostheses. *Candida albicans* species were prevalent in infection and colonization of prostheses, while oral colonization showed similar percentages among *Candida non-albicans* ($p = 0.657$). As for the prevalence of species about the studied area of residence, *Candida albicans* prevailed in the urban area and *Candida non-albicans* in the rural area ($p < 0.05$). In conclusion, this study identified a high prevalence of oral candidiasis in elderly participants in the research, who were mainly infected with *Candida albicans* species, but when comparing the living areas of the elderly, those living in the urban area had more prevalent colonization in the area. urban and *Candida*

non-*albicans* in the rural area, therefore, species differentiation was found regarding the place where the elderly person lives.

Keywords: *Candida albicans*; *Candida non-albicans*; Elderly; Oral candidiasis.

Resumo

Ocorreu um aumento do número de idosos no Brasil e juntamente com este fato houve um aumento da incidência da candidíase oral nesta população, por isto a identificação precoce da doença e do agente etiológico para uma intervenção eficaz é imprescindível. O objetivo do estudo foi descrever a prevalência de candidíase oral e suas manifestações clínicas, identificando as espécies de leveduras de *Candida* e sua prevalência na mucosa palatina e próteses dentária na mucosa palatina e próteses dentárias, comparando estes fatores em idosos rurais e urbanos deste município. O estudo foi realizado na cidade de Tefé, Amazonas, com idosos de 65 a 74 anos cadastrados em serviços de atenção primária à saúde da zona urbana e rural, onde através de cálculo amostral contamos com a amostra total de 484 idosos após perdas e recusas. Estes idosos foram selecionados aleatoriamente dentro de toda rede de serviço público, o qual possibilitou que as amostras fossem coletadas em todas as Unidades Básicas de Saúde municipais. A coleta de dados incluiu exames clínicos orais (uso, duração e necessidade de prótese dentária) e coleta de material biológico com *swabs*, os quais foram armazenados em meio CHROMATM *Candida*, durante visitas domiciliares para determinar a prevalência das espécies por meio de coloração e morfologia das colônias. A análise estatística foi realizada com o *software* Stata MP, por meio de frequências relativas e absolutas. A prevalência de candidíase oral foi encontrada em 20,7% dos idosos nas diferentes áreas de residências estudadas. Maior número de casos e manifestações clínicas da doença foi encontrado em idosos residentes em áreas urbanas ($p < 0,05$). As razões de chance para desenvolver a doença foram maiores em mulheres, idosos desdentados e usuários de próteses dentárias. As espécies de *Candida albicans* foram prevalentes na infecção e colonização de próteses, enquanto a colonização bucal apresentou percentuais semelhantes entre as *Candida não-albicans* ($p = 0,657$). Quanto à prevalência das espécies em relação à área de residência estudada, a *Candida albicans* prevaleceu na área urbana e *Candida não-albicans* na área rural ($p < 0,05$). Em conclusão, este estudo identificou alta prevalência de candidíase oral nos idosos participantes da pesquisa, que apresentaram possuir principalmente infecção por espécies de *Candida albicans*, porém ao comparar as zonas de moradia dos idosos, os que moravam na zona urbana possuíam colonização mais prevalente na zona urbana e *Candida não-albicans* na zona rural, portanto encontrada diferenciação de espécies quanto ao local que o idoso reside.

Palavras-chave: *Candida albicans*; *Candida não-albicans*; Idosos; Candidíase oral.

Resumen

Hubo un aumento en el número de ancianos en Brasil y, junto con este hecho, hubo un aumento en la incidencia de candidiasis oral en esta población, por lo que la identificación temprana de la enfermedad y el agente etiológico para una intervención eficaz es fundamental. El objetivo del estudio fue describir la prevalencia de candidiasis oral y sus manifestaciones clínicas, identificando especies de levadura *Candida* y su prevalencia en la mucosa palatina y prótesis dentales en la mucosa palatina y prótesis dentales, comparando estos factores en ancianos rurales y urbanos en esta ciudad. El estudio se realizó en la ciudad de Tefé, Amazonas, con ancianos de 65 a 74 años inscritos en servicios de atención primaria de salud en áreas urbanas y rurales, donde mediante cálculo muestral se tuvo una muestra total de 484 ancianos luego de pérdidas y rechazos. Estos ancianos fueron seleccionados aleatoriamente dentro de toda la red de servicios públicos, lo que permitió recolectar las muestras en todas las Unidades Básicas de Salud municipales. La recolección de datos incluyó exámenes clínicos orales (uso, duración y necesidad de prótesis dental) y recolección de material biológico con hisopos, que se almacenaron en medio CHROMATM *Candida*, durante las visitas domiciliarias para determinar la prevalencia de la especie mediante tinción y morfología de la colonia. El análisis estadístico se realizó con el *software* Stata MP, utilizando frecuencias relativas y absolutas. La prevalencia de candidiasis oral se encontró en el 20,7% de los ancianos en las diferentes áreas de residencia estudiadas. Se encontró un mayor número de casos y manifestaciones clínicas de la enfermedad en ancianos residentes en áreas urbanas ($p < 0,05$). Las razones de probabilidad para desarrollar la enfermedad fueron más altas en mujeres, ancianos edéntulos y usuarios de prótesis dentales. Las especies de *Candida albicans* fueron prevalentes en la infección y colonización de prótesis, mientras que la colonización oral mostró porcentajes similares entre *Candida no-albicans* ($p = 0,657$). En cuanto a la prevalencia de especies en relación al área de residencia estudiada, prevaleció *Candida albicans* en el área urbana y *Candida no-albicans* en el área rural ($p < 0,05$). En conclusión, este estudio identificó una alta prevalencia de candidiasis oral en los ancianos participantes de la investigación, quienes estaban principalmente infectados con especies de *Candida albicans*, pero al comparar las áreas de vivienda de los ancianos, los que viven en el área urbana tuvieron una colonización más prevalente en el área urbana y *Candida no-albicans* en el área rural, por lo que encontraron diferenciación de especies con respecto al lugar donde residen los ancianos.

Palabras clave: *Candida albicans*; *Candida no-albicans*; Ancianos; Candida oral.

1. Introduction

Candidiasis, caused by *Candida* yeast, a commensal fungus found in approximately 50% of the population, is a fungal infection that commonly affects individuals. It is usually asymptomatic, but it can cause infections depending on the host's immunological conditions. When the fungus multiplies, it penetrates the tissues, causes inflammation and becomes a pathogen. When infection is found in the oral mucosa region it is called Oral Candidiasis (Arendorg & Walker, 1980; Neville, Damm, Allen & Chi, 2015). This opportunistic fungus may cause several clinical manifestations in its pathogenic form, from mild and superficial to invasive infections, severe bloodstream infection, affect several organs, and life-threatening conditions in the most severe forms of infection (Taylor & Raja, 2021).

Historically, greatest attention has been given to *Candida albicans* species (*C. albicans*) due to its prevalence in 60 to 90% of the isolates. However, other species may be present, although less frequently, called non-*Candida albicans*. Among them, the main isolates are *C. tropicalis*, *C. parapsilosis*, *C. Glabrata* and *C. krusei* (Mothibe & Patel, 2017; Cortegiani, Misseri & Chowdhary, 2019). The *Candida* genus is composed of more than 150 heterogeneous species, but just a few of them have been implicated in human candidiasis and oral candidiasis. Approximately 65% of *Candida* species are known to be unable to grow at a temperature of 37°C, which prevents them from being successful or becoming human commensal pathogens (Spampinato & Leonardi, 2013).

The prevalence of oral candidiasis has increased in recent decades. Studies of these infections mainly involve individuals with some type of immune deficiency, such as patients in Intensive Care Units (ICU) (Justiz Vaillant & Curie, 2020) or patients with human immunodeficiency virus / Acquired Immunodeficiency Syndrome (HIV/AIDS) (Shintani *et al.*, 2020). The incidence of oral candidiasis in the elderly has also increased (Sakaguchi, 2017). Given the importance of early identification of oral candidiasis and pathogen for effective drug therapy, surveillance and monitoring are essential for the development of oral health strategies and actions at individual and population levels.

In this context, knowing the importance of performing an analysis on the epidemiology of oral candidiasis in the elderly, we chose to achieve this through a household-based population survey, due to the need for these studies focusing on clinical and microbiological manifestations in municipalities in the interior of the Amazonas (AM), this study aimed to describe the prevalence of oral candidiasis and its clinical manifestations, identifying *Candida* yeast species and their prevalence in the palatine mucosa and dental prostheses, comparing these factors in rural and urban elderly people in the municipality of Tefé -Am.

2. Methodology

Population and study design

A household-based cross-sectional survey was conducted in the city of Tefé, Amazonas, from October 2018 to May 2019. This is a medium-sized city with low population density located in the center of Amazonas in the middle Solimões region, 522 km far from the state capital. The Family Health Strategy program offers 100% coverage in the city.

This municipality has 60,154 inhabitants, of which 1914 have the studied age group. Stratified random sampling was performed according to the geographic coverage of each healthcare team to obtain a representative sample for urban and rural areas

In this research, individuals aged 65 to 74 years were considered elderly, according to the cutoff criteria of the SB Brazil 2010 (BRASIL, 2012), in the 65 to 74 age group, the teams had 1914 elderly registered, of which 1660 (86.7%) urban and 254 (13.2%) dispersed in 164 locations in the rural zone.

The sample was obtained through the random stratified sampling technique and a sample was calculated for each study area, according to the territories covered by each team, to obtain a significant sample for the urban and rural areas. The sample size calculation considered a prevalence of 50% of outcomes, accuracy of 0.05, and 10% of dropouts or refusals, which was later adjusted for the finite population, resulting in a total of 511 elderly, after losses and refusals of 27 elderly people (5.3%), the final sample consisted of 484 elderly people, 325 of whom were residents of the urban area and 159 of the rural area, who were randomly chosen from the registration lists of their respective UBS's.

The elderly aged 65-74 years, who were randomly selected from the eligible population in the target population, were invited to participate in the study. After obtaining consent, biological material was collected, oral clinical examinations and interviews using closed questions were carried out during home visits by a single researcher (ERLB) accompanied by Community Health Agents (CHA) from each area.

Previously, a pilot study was carried out, aiming to standardize the measurement to ensure the reliability and reproducibility of the data, according to the predetermined criteria for diagnosis. In training, only the researcher herself was trained to perform the clinical examinations. This was carried out at the Open Foundation for the Third Age (FUNATI-Manaus, Amazonas, Brazil). Calibration was performed using a reduced questionnaire and an oral exam in 10% of the sample, totaling 51 elderly people. Participants were re-examined 30 days after the first exam. Data were tabulated in Excel for *Windows*, and the results showed that the reproducibility agreement measured by the intraclass coefficient was 0.998.

Elderly people whose health conditions made it impossible to perform the exam, those whose cognitive abilities were impaired or those who did not reach the minimum score on the mental state mini-examination (MMSE) (Brucki, Nitrini, Caramelli, Bertolucci, & Okamoto, 2003), with a cutoff point according to the years of education, were excluded from the study. The elderly who were hospitalized or who were not at home or refused to participate in the study were not included in the study.

Methodological procedures

Questionnaires included demographic and socioeconomic data and general health conditions (diagnosis of chronic diseases and smoking). The clinical examination was performed at home and in accordance with the biosafety standards proposed by the World Health Organization (WHO). The clinical oral variables observed also followed the WHO recommendations (World Health Organization, 1997), regarding use, duration and need for dental prostheses. To measure the prevalence of oral candidiasis, the outcome was classified as "positive" or "negative" according to the presence or absence of one of the five following clinical manifestations: erythematous candidiasis, hyperplastic candidiasis, pseudomembranous candidiasis, median rhomboid glossitis and angular cheilitis (Neville *et al.* 2015).

Colony isolates and species identification

Sterile swabs were used to obtain the samples, performing friction movements for 30 seconds throughout the palatal mucosa area and dental prosthesis base, using one swab for each area, and stored in Cary-Blair medium (Starswab®) for transportation. Samples were plated on separate plates containing a selective medium for *Candida*, CHROMagar™ *Candida* (CHROMagar® Company, Paris, France) and identified according to the collection site. This procedure was performed by rotating the swab on the plate containing the culture medium using the depletion technique. The plates were incubated in a bacteriological oven at 37°C for 48 hours and the plates were read after this period. Yeast growth was observed in each plate and the samples were classified as "positive" or "negative", according to the presence or absence of the fungus, respectively. *Candida* isolates observed in CHROMagar™ *Candida* medium were identified at species level by colony morphology and

pigmentation according to the manufacturer's instructions and streaked and purified on Sabouraud-chloramphenicol agar (Difco DB Diagnostic Systems, Sparks, MD, USA).

Data analysis

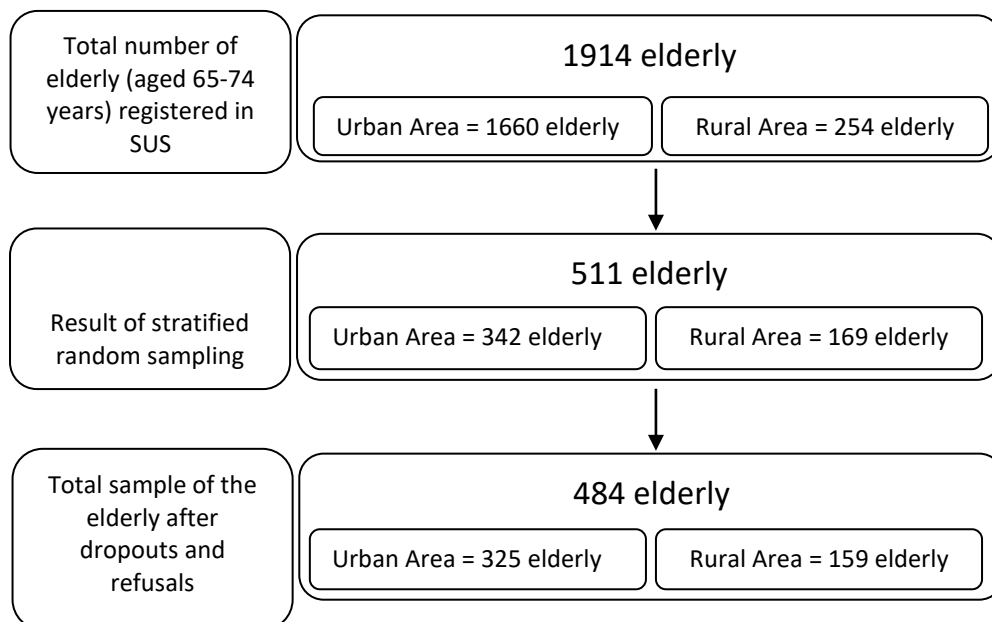
Data were tabulated using Microsoft Excel software and then exported to Stata MP software, version 14. For descriptive analysis, data were presented for the total sample and according to the area of residence using mean and standard deviation for the numerical variables and absolute and relative frequencies for categorical variables. The nonparametric Mann-Whitney and Kruskal Wallis tests were used to compare numerical variables between the groups. Fisher's chi-square and exact tests were used to compare the proportions. The presence of oral candidiasis was also assessed according to sex, use and need for dental prostheses, diagnosis of chronic disease and smoking, and the odds ratios (OR) and 95% confidence intervals (95% CI) were estimated using bivariate logistic regression and considering the *p*-value of 5%. Colonization by *Candida* spp. was also evaluated according to *C. albicans* and non-*C. albicans* species, both for the oral cavity and the dental prostheses.

3. Results and Discussion

The final sample consisted of 484 elderly, 325 residents in the urban area and 159 residents in the rural area of the city. The percentage of dropouts and refusals in the study was 5.4% (Figure 1).

The mean age was 69.5 years old (\pm SD = 3.4), most of them were female (54.3%), illiterate (46.3%) and with low average education (2.1 years of schooling, \pm SD = 2.8). Family income averaged R\$2,106.00 (\pm SD = 927.00), ranging from R\$300,00 to R\$ 6,000.00. There was no difference for these variables between rural and urban areas. The elderly of the city declared themselves as predominantly brown (51.5%). There was a difference in skin color between the populations ($p < 0.001$) and the largest number of white individuals resided in the urban area.

Figure 1. Sample selection flowchart in the study population.



Source: Authors.

Smoking prevalence was 12.4% with a higher frequency identified in rural residents. The prevalence of diabetes mellitus was higher in urban areas, but the difference was not significant for systemic arterial hypertension. As for dental

prostheses, more than half (63.4%) the elderly wore them with a higher prevalence in the urban area. Duration of prosthesis use was also higher in the rural area, which implied a greater need for dental prosthesis in the rural area, both due to the need for replacement and new dental prostheses. The distribution of participants related to smoking, diagnosis of chronic diseases and characteristics related to the use and need for dental prostheses is shown in Table 1.

Table 1. Smoking, chronic diseases, use and need for dental prostheses in the elderly according to area of residence.

| Variable | Total n=484 | Urban Area n=325 | Rural Area n=159 | P value |
|---|-------------------|---------------------|---------------------|---------|
| Smoking, n (%) | | | | 0.007** |
| Never | 87 (18.0%) | 69 (21.2%) | 18 (11.3%) | |
| Smoker | 60 (12.4%) | 33 (10.2%) | 27 (17.0%) | |
| Former-smoker | 337 (69.6%) | 223 (68.6%) | 114 (71.7%) | |
| Diabetes, n (%) | | | | 0.041* |
| Yes | 82 (16.9%) | 63 (19.4%) | 19 (12.0%) | |
| No | 402 (83.1%) | 262 (80.6%) | 140 (88.0%) | |
| Hypertension, n (%) | | | | 0.051 |
| Yes | 268 (55.4%) | 190 (58.5%) | 78 (49,1%) | |
| No | 216 (44.6%) | 135 (41.5%) | 81 (50,9%) | |
| Prosthesis use, n (%) | | | | 0.034* |
| Yes | 307 (63.4%) | 219 (67.4%) | 88 (55.4%) | |
| No | 176 (36.6%) | 106 (32.6%) | 71 (44.6%) | |
| Time of use, n (%) | | | | 0.019* |
| < 2 years | 55 (11.4%) | 41 (12.6%) | 14 (8.8%) | |
| 2 - 4 years | 253 (52.3%) | 119 (55.1%) | 74 (46.5%) | |
| > 4 years | 176 (36.3%) | 165 (32.3%) | 71 (44.7%) | |
| Time of use > 4 years, mean (\pm SD) | 13.6 (\pm 9.0) | 12.9 (\pm 9.2) | 15.1 (\pm 8.0) | 0.021* |
| Need for dental prosthesis, n (%) | | | | 0.001** |
| Yes | 396 (81.8%) | 263 (80.9%) | 133 (83.7%) | |
| No | 88 (18.2%) | 62 (19.1%) | 26 (16.3%) | |

* p<0.05 ** p<0.01. Source: Authors.

The prevalence of oral candidiasis was found in 20.7% of the elderly examined, with higher percentages in the urban area, showing a difference in the distribution of the pathology in relation to the area of residence. The same was observed regarding the number of clinical manifestations of the disease, which was higher in residents in the urban area. The differences identified, however, regarding the type of clinical manifestation, were not significant. These clinical manifestations ranged from 1 to 5 per elderly, but most presented only one type (Table 2).

Table 2. Prevalence of oral candidiasis, number and type of clinical manifestations in the elderly according to area of residence.

| Variable | Total | Urban Area | Rural Area | P value |
|---|--------------------|--------------------|--------------------|---------|
| Prevalence of Oral Candidiasis, mean (\pm SD) | 0.20 (\pm 0.40) | 0.23 (\pm 0.42) | 0.14 (\pm 0.35) | 0.018* |
| Prevalence of Oral Candidiasis, n (%) (n=484) | | | | 0.023* |
| Yes | 100 (20.7%) | 77 (23.7%) | 23 (14.5%) | |
| No | 383 (79.3%) | 248 (76.3%) | 136 (85.5%) | |
| Number of clinical Manifestations, mean \pm SD (n=100) | 0.29 \pm 0.66 | 0.33 \pm 0.69 | 0.22 \pm 0.59 | 0.024* |
| Number of clinical Manifestations per person, n (%) (n=100) | | (n=65) | (n=35) | 0.039* |
| 1 | 65 (65%) | 52 (80%) | 25 (71%) | |
| 2 – 5 | 35 (35%) | 13 (20%) | 10 (29%) | |
| Type of clinical manifestation, n (%) (n=144) | | (n=109) | (n=35) | 0.271 |
| Erythematous candidiasis | 74 (51.4%) | 56 (51.4%) | 18 (51.5%) | |
| Hyperplastic candidiasis | 17 (11.8%) | 15 (13.8%) | 2 (5.7%) | |
| Pseudomembranous candidiasis | 24 (16.7%) | 20 (18.3%) | 4 (11.4%) | |
| Atrophic glossitis | 11 (7.6%) | 7 (6.4%) | 4 (11.4%) | |
| Angular cheilitis | 18 (12.5%) | 11 (10.1%) | 7 (20.0%) | |

* p<0.05. Source: Authors.

Table 3 shows the results of bivariate regression analyses. The unadjusted chance of presenting oral candidiasis was higher in the female elderly, those with teeth, wearers of dental prostheses with some chronic diseases and smokers, as shown in Table 3.

Table 3. Unadjusted odds ratios for oral candidiasis in the elderly according to area of residence.

| Variable | N | Urban Area OR (95% IC) | Rural Area OR (95% IC) |
|---------------------|-----|---------------------------|---------------------------|
| Sex | | | |
| Woman | 262 | 4.6(2.4-8.4)*** | 1.0 (0.4-2.5) |
| Man | 222 | ref. | ref. |
| Presence of teeth | | | |
| Edentulous | 181 | 2.7 (1.6-4.6)*** | 1.6 (0.7-4.1) |
| Dentulous | 303 | ref. | ref. |
| Prosthesis use | | | |
| Yes | 309 | 7.9 (3.3-19.1)*** | 6.4 (1.8-22.1)** |
| No | 175 | ref. | ref. |
| Need for prosthesis | | | |
| Yes | 396 | 0.6 (0.3-1.2) | 0.6 (0.2-2.0) |
| No | 88 | ref. | ref. |
| Chronic diseases | | | |
| Yes | 287 | 1.3 (0.8-2.4) | 2.1 (0.8-5.6) |
| No | 197 | ref. | ref. |
| Smoking | | | |
| Yes | 60 | 0.6 (0.3-1.5) | 5.2 (0.7-0.4) |
| No | 424 | ref. | ref. |

** p<0.01; *** p<0.001. Source: Authors.

Of the 100 elderly who presented oral candidiasis, the prevalence of *Candida* species involved in the infection was analyzed. *Candida albicans* was responsible for most infections, especially in urban areas. Despite the predominance of *Candida albicans* in rural areas, infections specifically caused by non-*albicans* *Candida* accounted for twice the proportion when compared to the urban area. *Candida spp.* colonization, both in the mouth and dental prostheses (n=278) was similar in

both regions. There was, however, a significant difference in colonization when the mouth and dentures were evaluated together. Despite the higher frequency of non-*albicans Candida* colonization in the rural region, the difference was not significant when colonization was compared between groups (Table 4).

Table 4. Prevalence and characterization of species involved in infection, colonization in the mouth and dental prostheses of the elderly according to area of residence.

| Variable | Total | Urban Area | Rural Area | P value |
|---|-------------|-------------|------------|----------|
| Type of <i>Candida</i> spp. infection per person (n=100) | | | | 0.003* |
| Specifically <i>Candida albicans</i> | 57 (60%) | 45 (61.7%) | 12 (54.6%) | |
| Specifically non- <i>albicans Candida</i> | 19 (20.0%) | 12 (16.4%) | 7 (31.8%) | |
| Both species | 19 (20.0%) | 16 (21.9%) | 3 (13.6%) | |
| Prevalence of <i>Candida</i> spp. colonization in mouth per person (n=484) | 191 (39.5%) | 137 (42.2%) | 54 (34.0%) | 0.083 |
| Colonization type of <i>Candida</i> spp. in the mouth (n=191) | | | | 0.657 |
| Specifically <i>Candida albicans</i> | 100 (52.4%) | 72 (52.6%) | 28 (51.8%) | |
| Specifically non- <i>albicans Candida</i> | 60 (31.4%) | 41 (29.9%) | 19 (35.2%) | |
| Both species | 31 (16.2%) | 24 (17.5%) | 7 (13.0%) | |
| Prevalence of <i>Candida</i> spp. colonization in dental prostheses (users, n=278) | 180 (64.7%) | 129 (64.5%) | 51 (65.4%) | 0.890 |
| Colonization type of <i>Candida</i> spp. in dental prostheses (n=180) | | | | 0.164 |
| Specifically <i>Candida albicans</i> | 110 (61.1%) | 81 (60.9%) | 29 (61.7%) | |
| Specifically non- <i>albicans Candida</i> | 37 (20.6%) | 24 (18.1%) | 13 (27.7%) | |
| Both species | 33 (18.3%) | 28 (21.0%) | 5 (10.6%) | |
| Prevalence of mutual colonization of <i>Candida</i> spp. in the mouth and dental prostheses (n=118) | 118 (100%) | 91 (77,1%) | 27 (22.9%) | 0.000*** |

* p<0.05; *** p<0.001; Source: Authors.

The species involved in mouth colonization resulted in a total of 228 *Candida* spp. isolates. Although there were no significant differences between rural and urban areas, a higher prevalence of *Candida albicans* was found than non-*albicans Candida*. In the rural area, *Candida tropicalis* was more frequent, while *Candida krusei* was detected exclusively in the urban area (Table 5).

Table 5. Percentages of species involved in colonization in the mouth of the elderly according to area of residence.

| Species involved in mouth colonization | Total n=228 | Urban Area n=164 | Rural Area n=64 | P value |
|--|-------------|------------------|-----------------|---------|
| <i>Candida albicans</i> | 125 (54.8%) | 90 (54.8%) | 35 (54.7%) | 0.979 |
| Non- <i>albicans Candida</i> | 103 (45.2%) | 74 (45.2%) | 29 (45.3%) | |
| <i>Candida</i> spp. | 79 (34.7%) | 58 (35.4%) | 21 (32.8%) | 0.143 |
| <i>Candida tropicalis</i> | 19 (8.3%) | 11 (6.7%) | 8 (12.5%) | |
| <i>Candida krusei</i> | 5 (2.2%) | 5 (3.1%) | 0 (0%) | |

Source: Authors.

The elderly population from a medium-sized city in Amazonas presented a high prevalence of oral candidiasis with differences regarding the area of residence of the elderly. The residents in the urban area presented the highest prevalence of

the disease. *Candida* species also showed a heterogeneous distribution, which was observed in colonization and infection in which the *Candida albicans* species were the main etiological agents, especially in the urban area, and non-*albicans Candida* species were more frequent in infections in rural areas. The use of dental prostheses proved to be a determining factor for the development of the disease in these individuals.

Conducting population-based surveys in the Amazon has unique peculiarities when considering demographics, culture and geography. Conducting epidemiological surveys mainly at home among the elderly becomes a challenge especially when it involves the rural and riverside population (Ribeiro dos Santos, Huang, Menezes & Sczufca, 2016), since they are individuals with limited access to oral health services and reside in difficult areas for situational diagnosis due to the distance from the main cities, as well as to the state capital, which provides more complex health services. This study consisted of a representative sample of the population of a city in the interior of the Amazon with the purpose of evaluating a highly prevalent pathology since few studies have investigated this population.

The main oral health epidemiological studies conducted in Brazil focus on tooth-related diseases, but developed and high-income countries have investigated these variables together with other diseases affecting the stomatognathic system. In their methodologies, in addition to using the parameters proposed by the WHO, they include biological factors, such as the prevalence of oral microorganisms and serum cytokines (Myazaki, Jones & Beltran-Aguillar, 2017). There are many reasons for conducting epidemiological studies to determine the prevalence of oral candidiasis, particularly because of its possible correlation with potentially malignant mucosal disorders as there is a positive association between *Candida spp.* and epithelial dysplasia (Chung, Liang, Lin, Sun & Kao, 2017).

Most studies on oral candidiasis are conducted at hospitals and outpatient clinics (Hertel, Schmidh-Westhausen & Strietzel, 2016; Kawashita *et al.* 2018). However, identifying the prevalence of this disease in different areas of the same city gives us a better understanding of the distribution of the disease, as well as showing that it does not affect only bedridden and hospitalized elderly. When comparing the prevalence of other oral candidiasis non-population-based studies of the elderly, the percentages found in this study were higher (Glažar *et al.* 2016; Sakaguchi, 2017; Martori, Ayuso-Montero, Martinez-Gomis, Viñas & Peraire, 2014), differing only from studies with hospitalized elderly with brain injury or patients with HIV/AIDS, that found 32% and 31% of individuals affected by the disease, respectively (Odgaard & Kothari, 2018; Shintani *et al.* 2020).

Differences in oral clinical conditions among individuals living in rural and urban areas have been reported (Bilings *et al.* 2017). Oral candidiasis is a disease that is triggered when there are immunological changes, which may or may not be combined with microenvironmental variations. Despite evidence on the distinct distribution of the disease worldwide, this relation has not yet been fully elucidated (Sakaguchi, 2017) and that is why the factors need to be analyzed individually, such as the risks faced by the population. The possible explanations so far for the differences in geographic areas for the prevalence of the disease and *Candida* yeast species are based on environmental impacts, use of therapeutic protocols (antifungal use) and oral hygiene. In the present study, the elderly residents in the urban area presented more clinical manifestations of oral candidiasis. This may be explained by the higher prevalence of chronic diseases, use of dental prostheses and different psychosocial conditions, since behavioral characteristics and stress may also predispose the development of the pathology. The elderly who wear dental prostheses are more susceptible to *Candida albicans* infections and colonization, which would explain the higher prevalence in the elderly in the urban area (Kassebaum *et al.* 2017).

Studies have shown that the prevalence of *Candida spp.* species is heterogeneous (Guinea, 2014). Historically, *Candida albicans* has always been the most frequently reported species and to date there are still studies reporting infections caused by this species (Hertel *et al.* 2016; Zakaria *et al.* 2017). However, non-*albicans Candida* species have gained significance in the world and become the most prevalent in some countries. Some studies have reported that non-*albicans Candida* species have a similar prevalence to *Candida albicans* and others have reported a higher prevalence (Taj-Aldeen *et al.*

2014; Sato *et al.* 2017). By analyzing the biology, epidemiology, pathogenicity and antifungal resistance of *C. glabrata*, *C. parapsilosis* and *C. tropicalis* species, the results indicate that there has been an increased incidence and antifungal resistance of non-*albicans* *Candida* species (Silva *et al.* 2012), which are species with high pathogenic potential. Thus, diagnosis and identification of the species and appropriate therapy against these emerging pathogens are imperative.

In addition to the etiological aspects, it is important to identify the species involved in both colonization and infection for the recommendation of appropriate therapeutic protocols. This condition is widely treated in primary health care, but primary and secondary drug therapy is not effective against some non-*albicans* *Candida* species because antifungals have been developed to treat the most prevalent *Candida albicans* species (Brazil, 2012; Singh, Kumari, Kaur, Sethi & Chakrabarti, 2018). Therefore, clinical diagnosis together with a greater understanding of the species may play an important role in the management of oral candidiasis at this level of care.

The main limitations of this study were its performance, as, as with all research in rural areas in the Amazon region, we have difficulties with moving and accessing the homes of the elderly, where we often had the need to carry out home visits through river transport. Another limitation was the need to transport the biological material to the state capital so that the analysis could be carried out, causing pauses in data collection, as the analysis was carried out jointly, as the biological material is stored for a long time sensitive.

4. Conclusion

In conclusion, this study, analyzing the prevalence of oral candidiasis in the elderly, found a high prevalence of the disease in the population studied, both in rural and urban elderly. When comparing the species identified in the surveyed regions, the findings pointed to a higher prevalence of infection by *Candida albicans* species in both areas of residence, but when making a comparison, it was found that those living in urban areas had more prevalent colonization in the urban area and *Candida non-albicans* in the rural area, therefore, species differentiation was found regarding the place where the elderly person lives. This study is of great importance to understand the epidemiology of oral candidiasis in this location and how the species can differ depending on the area of residence.

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