



ORIGINAL ARTICLE



Epidemiological factors associated with *Candida albicans* in patients using complete denture: A scoping review

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ABSTRACT

Objective: This study undertakes a scoping review of research on epidemiological factors of *Candida albicans* in patients using complete denture (CD).

Methods: PubMed, LILACS, Embase, SciELO, Web of Science, and Scopus databases were used. Searches were conducted in December 2020. Keywords used in this search were *Candida albicans*, Complete Denture, Mouth, and Microbiology.

Results: Initially, 89 articles were identified; 19 of these comprised the final sample after applying the exclusion/inclusion criteria. There was a greater tendency for females to use CD. In addition, among all samples evaluating the incidence of the fungus (n = 2,724), approximately 44.7% (n = 1,218) had *C. albicans*-associated prosthetic stomatitis.

Conclusion: Prosthetic stomatitis is a condition that mainly affects women aged 50-70 years and has a multifactorial predisposition. Also, Newton's classification proposed in 1962 is the most used for the clinical diagnosis of oral candidiasis. The CD's hygiene status is a crucial factor for the progression of candidosis, in the same way that the *C. albicans* fungus plays an important role in the progression of this pathogenesis in the host.

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INTRODUCTION

According to data presented by the World Health Organization (WHO) in 2005, it is estimated that approximately 25% of the world population over sixty years of age have total edentulism¹. In this context, the rehabilitation treatment that presents a satisfactory performance, a pleasant aesthetic, low cost, and acceptable durability for the total edentulous patients is the complete denture (CD)^{2,3}. The use of CDs without the correct instructions on their use or hygiene can cause opportunistic diseases such as prosthetic stomatitis, which may significantly drop in the quality of life of patients when speaking or chewing^{4, 5}.

In this regard, several epidemiological investigations have shown that approximately two-thirds of patients using CDs may present prosthetic stomatitis^{2,6,7}. This type of lesion can be characterized by an intense inflammatory process in the supporting soft tissues, but it is clinically asymptomatic. However, some patients may present with symptomatic clinical conditions related to this condition, such as burning, itching, or pain⁸⁻¹⁰.

Clinical research has correlated the association between the colonization of *Candida* spp. in CD, since these microorganisms have high adherence abilities, which establishes a favorable environment for their growth, strict relationships with dimorphism between species, and secretion/production of enzymes such as phospholipase and proteinases. Those enzymes are important mediators of virulence to the host, thus contributing to the formation of a pathogenic biofilm that is firmly adhered between the acrylic resin surface and oral mucosa^{7,9,11-13}. Despite that, several researchers have linked its incidence to multifactorial conditions; therefore, it is necessary to understand its characteristics and ways to contribute to the onset of this comorbidity^{6,7,10}.

Thus, a scoping review was conducted to map the research done in this area and identify any existing gaps in knowledge about *Candida albicans* in patients using complete dentures. The following research question was formulated: What is known from the literature about epidemiological factors associated with *C. albicans* in patients using complete dentures? What are the literature articles in a twenty-year retrospective? Who evaluated the epidemiological profiles of *C. albicans* in patients using complete denture in several countries?

METHODS

This scoping review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).

Focused question

The focused question was proposed by following the PECO principles. The key established question was "What are the literature articles in a twenty-year retrospective who evaluated the epidemiological profiles of *C. albicans* in patients using complete denture in several countries?".

Search strategy

This research is a critical review of the literature, in which the following descriptors from the Medical Subject Headings (MeSH) and Descriptors in Health Sciences (DeCS) were used: "Candida albicans"[All Fields] AND "complete denture"[All Fields] AND "Mouth"[All Fields] AND "Microbiology"[All Fields]. The search was performed in PubMed, LILACS, SciELO, Web of Science, Embase, and Scopus databases until December 2020¹⁴.

Study selection and data extraction

Duplicates were removed using EndNote™ X7 software (Thomson Reuters, New York, NY, USA). This study included research conducted between 2000 and 2020, published in the English language, performed in humans, that assessed the incidence of *C. albicans* in total edentulous. Exclusion criteria were themes that addressed other types of rehabilitation; studies that associated only the treatment of oral candidosis without analyzing the epidemiological profile; literature reviews; and posters. The selection of articles was ordered in three important methodological steps:

- Article exclusion by title.
- Critical reading of the articles to perform a systematic investigation of the information.
- Selection and extraction of data by independent and calibrated researchers (FIDC and JAM). A third evaluator (MFH) was asked to perform the article's inclusion or exclusion in case of conflicting information.

After careful selection, the data obtained were ordered according to Table 1. Data obtained were analyzed using SPSS (SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Information obtained was evaluated by absolute (n) and relative (%) frequencies.

RESULTS

Initially, 89 original studies were selected. After removing all duplicates, 84 remained. Subsequently, the exclusion criteria were established, which allowed 19 unique studies to assess *C. albicans* incidence in patients using CD (Figure 1). Concerning the countries where most of the studies were conducted, 26.3% (n = 5) were in Turkey and 21% (n = 4) in Brazil. Almost half of the studies were done in these two countries (Table 2).

Table 3 shows the results regarding demographic evaluation and frequency of *C. albicans* contamination in patients using CD. Poland (37.6%; n = 1,025), Japan (19.2%; n = 524), and Turkey (14.3%; n = 388) showed the highest patient samples while Saudi Arabia (0.9%; n = 25) and United Kingdom (0.8%; n = 22), the lowest. There was also a greater trend in the use of CD in females compared to males. Poland (48.4%; n = 590), Brazil (12.5%; n = 153) and Turkey (11.4%; n = 139) presented the highest frequency of patients that correlated the contamination by *C. albicans* in CD. Countries such as Saudi Arabia (0.8%; n = 10) and United Kingdom (1.1%; n = 14) had the lowest recurrence rates. CD users presented prosthetic stomatitis associated with *C. albicans* microorganisms in approximately 1.218 (44.7%) of 2.724 cases studied.

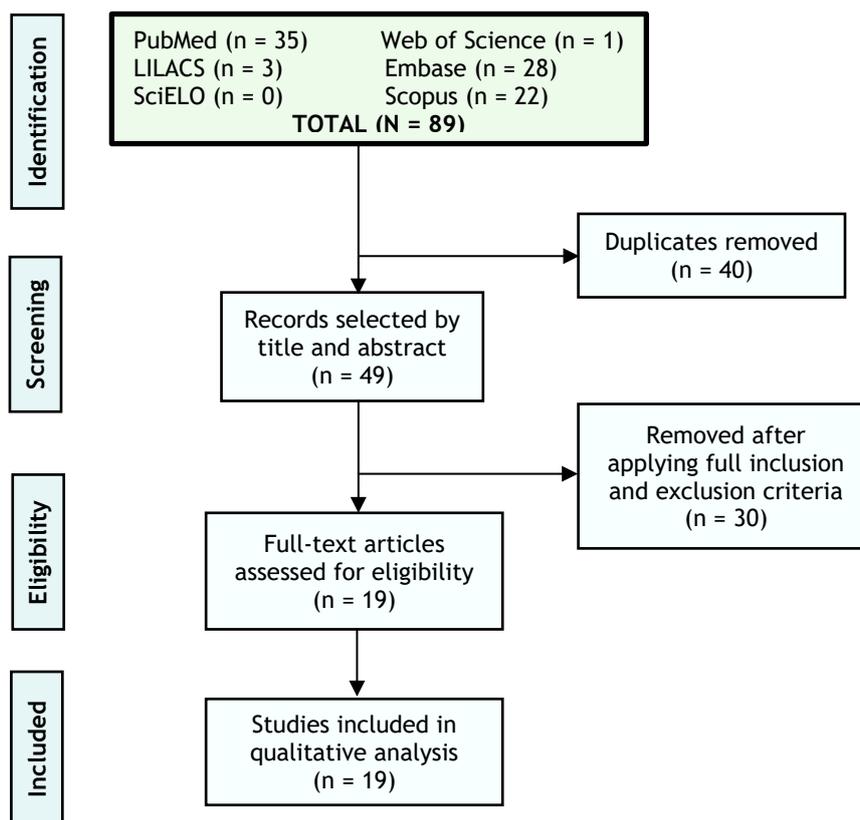


Figure 1 – Flow diagram of the identification, inclusion and exclusion process.

DISCUSSION

This review allowed us to trace the epidemiology of *C. albicans* in CD wearers, outlining its causes, the population most affected, thus giving some contribution in developing public health policies. With that in mind, the profile of patients who use CD, the most used classifications for diagnosing prosthetic stomatitis, hygiene factors of CD, systemic diseases associated with candidiasis, and *C. albicans* incidence in patients using CD will be discussed.

Profile of patients using Complete Dentures

Clinical studies analyzing the use of CD and prosthetic stomatitis association showed a higher prevalence of females in Turkey^{7,8}, Brazil, Japan, Iran, and Poland^{3,5,10,15,16}. Mesas et al.¹⁷ evaluated an incidence of chronic infection in patients with CD in Brazil, showing that 59.9% of their sample was also composed of women. Other authors have confirmed these findings in different Brazilian cities^{3,18}.

Also, in Poland, it was observed an association between age and gender with the incidence of oral candidiasis in a sample of 920 CD users¹⁰. A total of 613 female patients aged 50-70 years were studied, and 58% had their prosthesis contaminated by *C. albicans*. In the same direction, Azevedo et al. assessed the use and need for dental prostheses in elderly patients in Brazil, observing that 62.2% were composed of women aged 65-74 years old¹⁹.

It can be recognized that women are

predominant, aged 50-70 years, when the profiles of patients using CD are tracked. This is justified because women have a higher perception of the impact of rehabilitation on the quality-of-life indexes, are more concerned with oral health and are more often looking for dental care for function rehabilitation and aesthetics²⁰⁻²². Age should be highlighted as a crucial factor for edentulism since progressive and cumulative diseases, such as caries and periodontal disease, play an essential role in the gradual loss of dentition in this population^{19,22}.

Diagnosis of prosthetic stomatitis

Several classifications were developed to diagnose prosthetic stomatitis, such as the proposed by Newton and Ambjornsen²³. It was observed in this scoping review that the most used classification divided prosthetic stomatitis into three types: Type I (presence of small points of inflammation), Type II (presence of erythematous areas covered by a white exudate), and Type III (characterized by a hyperplastic or nodular reaction)^{24,25}.

In this context, a study conducted in Turkey demonstrated a correlation between inflammation points in the oral mucosa and a slight formation of yeasts of *C. albicans* in CDs, classified as prosthetic stomatitis type II (n = 18; 83.3%)²⁶. However, another study in Turkey stated that Type III clinical intensity was the one with the highest colony forming units per milliliter (mean = $3.6 \times 10^6 \pm 3.8 \times 10^6$ cfu/mL) due to the clinical characteristics of an intense inflammatory process and

Table 1 – Characteristics of the studies and sample included in the scoping review.

Author, year Country	Full sample	Sample distribution		Clinical features and prevalence of patients with <i>C. albicans</i> using CD			Characteristics of published studies		
		Male	Female	Clinical criteria used for the diagnosis	Prevalence n (%)	Follow-up	Objectives of the study	Original title	Journal of publication
Abaci et al., 2010 ⁷ Turkey	110	47	63	Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton. *	14 (12.72)	12 months	The aim of this study was to determine <i>Candida spp.</i> incidence in the oral cavity of denture wearers and characterize predisposing factors in denture-related stomatitis.	Determining <i>Candida spp.</i> Incidence in denture wearers.	Mycopathologia.
Aleva et al., 2007 ⁴ Brazil	51	DNI	DNI	DNI	30 (58.82)	DNI	This investigation was designed to evaluate the frequency of erythematous candidosis and <i>Candida</i> species, proteinase and phospholipase exoenzyme production, and to compare clinical features in patients with complete dentures and HIV+/Acquired Immunodeficiency Disease Syndrome.	Erythematous candidosis in patients with complete dentures and HIV+/AIDS.	Mycoses
Bilhan et al., 2009 ⁶ Turkey	91	DNI	DNI	Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton. *	58 (54.94)	24 months	The aim of this study was to investigate the relationship of DRS with the presence of <i>Candida albicans</i> hyphae and <i>Lactobacillus</i> .	The role of <i>Candida albicans</i> hyphae and <i>Lactobacillus</i> in denture-related stomatitis.	Clinical Oral Investigation
Cross et al., 2004 ¹¹ United Kingdom	22	5	12	Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton. *	11 (50)	36 months	The aim of the study was to determine the recurrence rate of denture stomatitis and persistence of <i>Candida</i> in 22 patients over a 3-year period.	Evaluation of the recurrence of denture stomatitis and <i>Candida</i> colonization in a small group of patients who received itraconazole.	Oral Surgery Oral Medicine Oral Pathology

Table 1 – Characteristics of the studies and sample included in the scoping review (cont.)

Author, year Country	Full sample	Sample distribution		Clinical features and prevalence of patients with <i>C. albicans</i> using CD			Characteristics of published studies		
		Male	Female	Clinical criteria used for the diagnosis	Prevalence n (%)	Follow- up	Objectives of the study	Original title	Journal of publication
Daniluk et al., 2006 ³⁴ Poland	95	42	53	Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton. *	38 (40)	DNI	The aim was to determine the fungi occurrence rate in the oral cavity of denture wearer patients in comparison to those without dentures.	Occurrence rate of oral <i>Candida albicans</i> in denture wearer patients.	Advances in Medical Sciences
Gumru et al., 2006 ²⁶ Turkey	75	24	51	Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton. *	31 (33.33)	DNI	The aim of this study was to evaluate the correlation between frequency and phospholipase activity of <i>Candida</i> species and denture stomatitis according to Newton's classification.	Distribution and phospholipase activity of <i>Candida</i> species in different denture stomatitis types.	Mycopathologia
Iinuma et al., 2015 ⁵ Japan	524	228	296	Denture plaque was assessed using a modification of the Ambjornsen Denture Plaque Index. †	108 (20.61)	36 months	"To identify modifiable oral health-related risk factors, we prospectively investigated associations between a constellation of oral health behaviors and incident pneumonia in the community-living very elderly (i.e., 85 years of age or older)."	Denture wearing during sleep doubles the risk of pneumonia in the very elderly.	Clinical Research Supplement
Jafari et al., 2013 ³⁶ Iran	28	18	10	DNI	16 (52)	3 months	Determine the distribution profile of <i>Candida</i> species isolated from cheek angles of patients with old denture before and after replacing with new ones.	Distribution profile of <i>Candida</i> species involved in angular cheilitis lesions before and after denture replacement.	Jundishapur Journal of Microbiology

Table 1 – Characteristics of the studies and sample included in the scoping review (cont.)

Author, year	Full sample	Sample distribution		Clinical features and prevalence of patients with <i>C. albicans</i> using CD			Characteristics of published studies		
		Male	Female	Clinical criteria used for the diagnosis	Prevalence n (%)	Follow-up	Objectives of the study	Original title	Journal of publication
Vanden Abbeele et al., 2008 ¹³	87	26	61	Inclusion criterion was wearing a maxillary removable acrylic prosthesis and exclusion criteria were the presence of stomatitis, acute illness, chronic infection and the use of oral hygiene care products with antimicrobials or antifungals	53 (60.91)	6 months	The aim of this study was to investigate yeast carriage in healthy denture wearers by swabbing and to evaluate the effect of denture hygiene habits.	Denture contamination by yeasts in the elderly	Gerodontology
Zomorodian et al., 2011 ¹⁶	114	35	79	DNI	61 (53.50)	DNI	“In this study, we investigated risk factors associated with progression to <i>Candida</i> -related denture stomatitis in patients using complete dentures, and we genetically identified <i>Candida</i> isolates associated with disease and colonization.”	Assessment of <i>Candida</i> species colonization and denture-related stomatitis in complete denture wearers	Medical Mycology

DNI: did not inform; CD: complete denture.

*Clinical examination was performed by the clinicians, who classified according to the criteria proposed by Newton: Type I denture-related stomatitis showed localized inflammation or pinpoint hyperemia, Type II showed a generalized erythema and Type III showed papillary hyperplasia of the palate.

†Denture plaque was assessed using a modification of the Ambjornsen Denture Plaque Index: 1) the incisive papilla, 2) the most caudal areas of both maxillary tuberosities, and 3) two areas 1 cm lateral to the midline of the palate at the bisecting point between the impression of the superior labial frenum and the most posterior point on the median line of the maxillary denture.

‡The degree of palatal erythema was scored by using the following clinical index: 0: No inflammation, 1: Slight inflammation (Localized slight hyperaemia), 2: Moderate inflammation (Diffuse hyperaemia), 3: Severe inflammation (Diffuse and papillary hyperplasia).

the presence of hyperplasia⁶. Another study conducted in Brazil reported Type I as the most recurrent clinical condition (n = 21; 27.2%), and it was considered a positive factor related to the other classifications¹⁵. Thus, the definitive diagnosis of prosthetic stomatitis should be based on the clinical characteristics, such as tissue color, tissue weight, and symptom assessment. Also, the importance of the differential diagnosis and complementary exams for this condition must be emphasized (Figure 2)^{27,28}.

Table 2 – Countries where studies were developed.

Countries	n (%)
Turkey	5 (26.3)
Brazil	4 (21.0)
Iran	2 (10.5)
Poland	2 (10.5)
Belgium	1 (5.3)
India	1 (5.3)
Japan	1 (5.3)
Norway	1 (5.3)
Saudi Arabia	1 (5.3)
United Kingdom	1 (5.3)

Table 3 – Demographic evaluation and frequency of *C. albicans* contamination in patients using Complete Denture.

Study location	Full sample investigated by the study n (%)	Males (n)	Females (n)	Sample prevalence of <i>C. albicans</i> n (%)
Poland	1025 (37.6)	349	666	590 (48.4)
Brazil	370 (13.6)	63*	157*	153 (12.5)
Turkey	388 (14.3)	100*	127*	139 (11.4)
Japan	524 (19.2)	228	296	108 (8.9)
Iran	142 (5.2)	54	89	77 (6.3)
India	100 (3.7)	50	50	57 (4.7)
Belgium	87 (3.2)	26	61	53 (4.3)
Norway	41 (1.5)	22	19	20 (1.6)
United Kingdom	22 (0.8)	5	12	14 (1.1)
Saudi Arabia	25 (0.9)	25	0	10 (0.8)

* Studies that did not report sample data but were counted as zero; CD: Complete Denture.

Hygiene of the Complete Denture

There are several reports associating hygiene and CD contamination by *C. albicans*, considering it critical for developing prosthetic stomatitis in the host^{2,8,29}. Factors such as brushing, motor debility, poor hygiene and usage instructions given by the dental surgeon, products with low antimicrobial efficiency, and inadequate anatomical morphologies of the prosthesis may result in poor hygiene of CDs^{9,16}. Other factors such as old age, systemic debility, poor hygiene, and wear of the CD end up contributing to the proliferation of a pathogenic biofilm that is firmly adhered between the acrylic resin and the patient's oral mucosa, which would suddenly cause a decline in the state of oral health and the quality of life due to the interference in talking and chewing^{2,8}.

A study conducted in Singapore confirmed that 69.3% (n = 52) of patients removed organic matter by daily brushing, and 38.6% (n = 29) had poor hygiene status (n = 29; 38.6%)²⁹. Furthermore, these values can be observed in a Turkish study that associated oral candidiasis and the hygiene status and cleanliness state of the CD in an elderly population. Their results showed that 78.6% of patients (n = 33) only brushed the CD to remove the biofilm, and 28.5% (n = 12) showed poor hygiene status².

Systemic diseases and association with oral candidiasis

It has been shown that oral candidiasis may be associated with the progression of some systemic diseases such as HIV, pneumonia, progressive

malignancies, and severe malnutrition^{4,5,28,30,31}. The correlation between erythematous candidiasis in HIV-positive patients and CD users has been reported. Results showed that 15 patients in the examined sample (71.4%) had their prostheses contaminated by *C. albicans*. Furthermore, these results were observed in other systemic diseases, such as pneumonia, in which 19.9% of the elders in Japan (n = 108) presented their prostheses contaminated by *C. albicans* with a mild association in the patient's oral and systemic health status.

Sample of *C. Albicans* in patients using Complete Dentures

Oral candidiasis is a condition predominantly found in patients using CD, and it is considered a critical public health problem worldwide²⁴⁻²⁶. This disease can be characterized by the growth of the *C. albicans* fungus and the supporting action of other species such as *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata*^{3,6,16,26,32-36}.

The growth of *C. albicans* (n = 31; 41.3%) and the secondary participation of other yeasts such as *C. krusei* (n = 6; 8%), *C. glabrata* (n = 3; 4%), *C. tropicalis* (n = 3; 4%), *C. kefyr* (n = 1; 1.3%) and *C. guilliermondii* (n = 1; 1.3%) has been reported previously in Tukey²⁶. These results were similar to Norwegian findings in which *C. albicans* (n = 20; 90.9%) was highlighted as the main microorganism in the prosthetic stomatitis pathogenesis³². Similar results were found in an elderly Iranian population, in which the same growth pattern of these fungi was observed: *C. albicans* (41.5%), *C. glabrata* (18.4%), *C. Tropicalis* (12.9%), *C. dubliniensis*

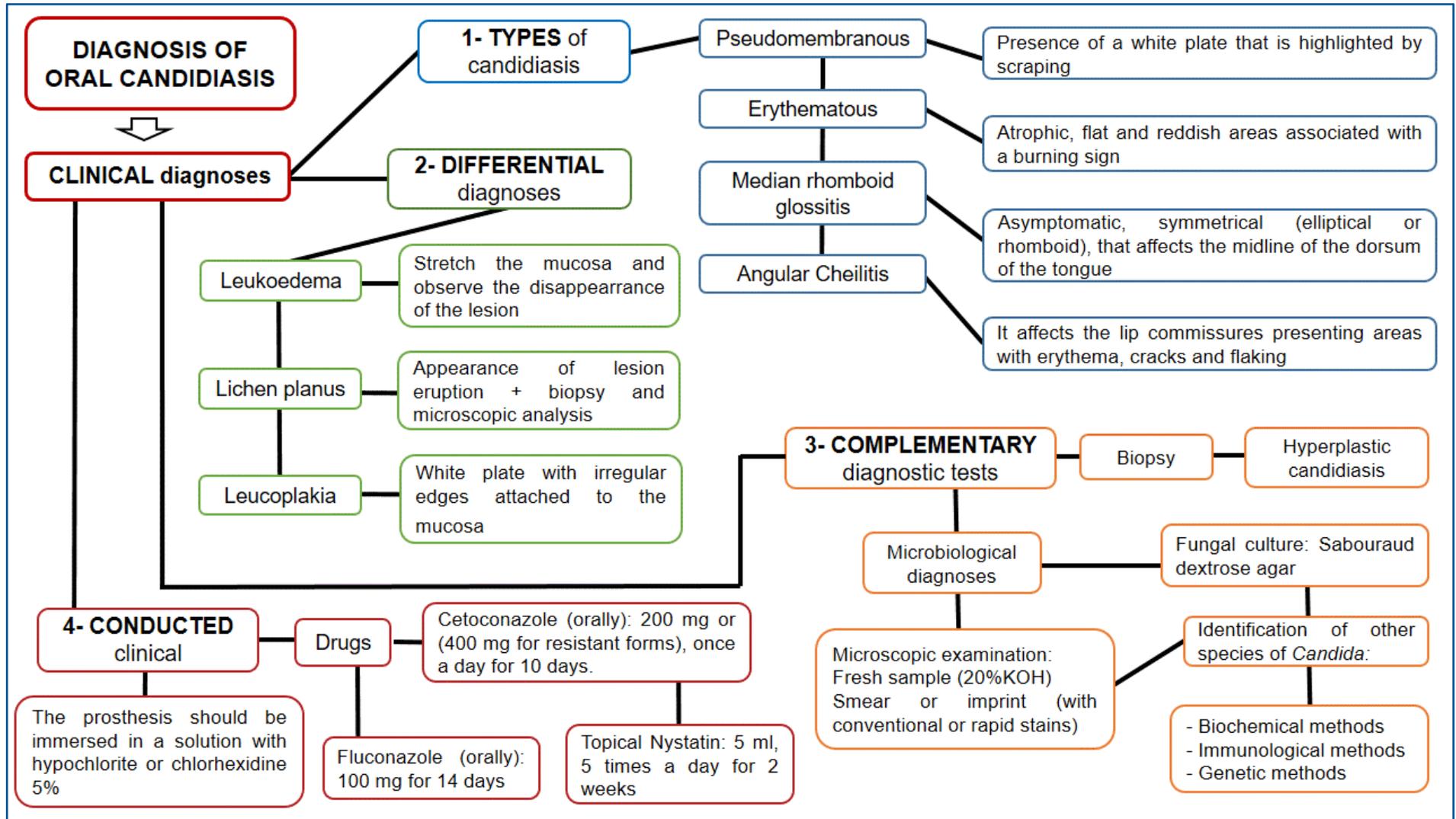


Figure 2 – Differential diagnostic flowchart, types of candidiasis, clinical conduct and complementary diagnostic tests. Information taken from Dorko et al., 2001²⁷ and Neville et al., 2016²⁸.

(10.9%), and *C. parapsilosis* (6.1%)¹⁶. In this study, approximately 44.7% of CD users presented prosthetic stomatitis associated with *C. albicans* (total n = 2,724).

Limitations of the review process and the extent of information uncovered

This review has some limitations. To make this review more feasible, we opted to conduct an integrative, not a systematic review. So, the quality of the included studies was not an analyzed criterion. Also, there was a limitation in the database selection, and the gray literature was not searched. It is also possible to mention as a limitation the period of analysis of the literature since studies published more than 20 years ago were excluded.

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CONCLUSION

Prosthetic stomatitis is a condition that mostly affects women aged 50-70 years and has a multifactorial predisposition. Furthermore, the classification proposed by Newton in 1962 is the most used for the clinical diagnosis of oral candidiasis. Still, the state of hygiene of CD is a crucial factor for the progression of candidosis, in the same way that *C. albicans* plays an essential role in the progression of this pathogenesis in the host.

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