



## Thrush Candidiasis: Classification, Chronic Hyperplastic Candidiasis, Systemic Immunocompromise, and Nutritional Deficiencies.

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### Abstract:

Thrush candidiasis, also known as oral candidiasis, is occurs in the mouth. This means that oral candidiasis is a mycosis (fungal/yeast infection) of the species of *Candida* on the mucous membranes of the mouth. Is an opportunistic infection of the oral cavity?

Aims of the study: - Studying candidia and its types, studying candidiasis, its types and divisions, and diagnosing a disease (candidiasis) in the mouth in children.

Methods: During the period between September 2021 and May 2022. In this study we have revised and reviewed most previous studies conducted on Candidiasis especially, Thrush and the method of isolation of candida species from oral cavity.

Result: According to statistics conducted by a number of researchers over the course of several years, and we studied them, we found several types of *Candida* that cause oral candida in children (*C. albicans*, *C. tropicalis*, *C. glabrata*, *C. krusei* .... etc). The rates of infection with *C. albicans* for 15 samples isolated from the mouth were (52%, 90%, 46%, 58.8%, 50%, 63%, 80%, 60.2%, 65%, 75%, 80. 7%, 69.35%, 61.5%, 43.7%) was the highest injury. While *C. pseudotropicalis* was found in two samples (1.8%, 4.6%) out of 15 samples, it can be considered the least infected.

**Keywords:** Chronic Hyperplastic Candidiasis, Nutritional Deficiencies, Thrush candidiasis, Systemic Immunocompromise



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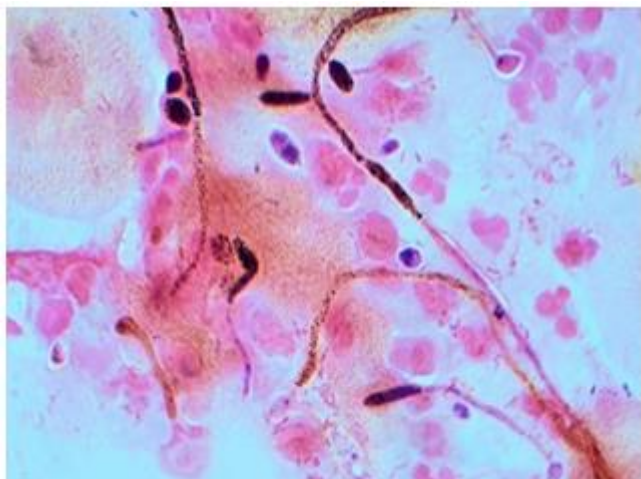
### Introduction:

Thrush candidiasis, also known as Oral candidiasis among other names (1), is candidiasis that occurs

in the mouth. That is, oral candidiasis is a mycosis (yeast/fungal infection) of *Candida* species on the

mucous membranes of the mouth. Oral candidiasis is an opportunistic infection of the oral cavity. It is common and underdiagnosed among the elderly, particularly in those who wear dentures and in many cases is avoidable with a good mouth care regimen. It can also be a mark of systemic disease, such as diabetes mellitus and is a common problem among the immunocompromised. Oral candidiasis is caused by an overgrowth or infection of the oral cavity by a yeast-like fungus, candida (2)(3) . The important ones are *C. albicans* (figure).

*C. tropicalis*, *C. glabrata*, *C. pseudotropicalis*, *C. guilliermondii*, *C. krusei*, *C. lusitaniae*, *C. parapsilosis*, and *C. stellatoidea*.



**Figure:1 Candida albicans as seen under light microscopy (courtesy of Dr Cunliffe, Consultant Microbiologist, Wirral NHS Trust).**

Oral candidiasis is the most common human fungal infection (4)(5) , especially in early and later life. In the general population, carriage rates have been reported to range from 20% to 75%4 without any symptoms.

The incidence of *C. albicans* isolated from the oral cavity has been reported to be 45% in neonates (6), 45%–65% of healthy children,7 30%–45% of healthy adults,8 9 50%–65% of people who wear removable dentures,9 65%–88% in those residing in acute and long term care facilities (6)(7) ,90% of patients with acute leukaemia undergoing chemotherapy (8) , and 95% of patients with HIV.

*C. albicans* is the most commonly implicated organism in this condition. *C. albicans* is carried in the mouths of about 50% of the world's population as a normal component of the oral microbiota. This candidal carriage state is not considered a disease, but when *Candida* species become pathogenic and invade host tissues, oral candidiasis can occur. This change usually constitutes an opportunistic infection by normally harmless micro-organisms because of local (i.e., mucosal) or systemic factors altering host immunity. In immunocompromised patients, infection can spread through the bloodstream or upper gastrointestinal tract leading to severe infection with significant morbidity and mortality. Systemic candidiasis carries a mortality rate of 71% to 79% (9) . It is important for all physicians looking after older patients to be aware of the risk factors, diagnosis, and treatment of oral candidiasis. In a recent study 30% of doctors said they would prescribe nystatin for oral candidiasis on the request of nursing staff without examination of the oral cavity (10). This is unfortunate as other pathology may be missed, the diagnosis may be incorrect, and failure to address risk factors may lead to recurrence of the candidiasis .

Notwithstanding, however, is the impressive repertoire of virulence factors that *C. albicans* possesses, enabling it to rapidly transition to a pathogen, the most notable of which are listed in Table 1 (11)( 12) .

### **Candida**

*Candida* is a genus of yeasts and is the most common cause of fungal infections worldwide (13) . Many species are harmless commensals or endosymbionts of hosts including humans; however, when mucosal barriers are disrupted or the immune system is compromised they can invade and cause disease, known as an opportunistic infection. *Candida* is located on most of mucosal surfaces and mainly the gastrointestinal tract, along with the skin (14) . *Candida albicans* is the most commonly isolated species and can cause infections (candidiasis or thrush) in humans and other animals. In winemaking, some species of *Candida* can potentially spoil wines (15) .

Many species are found in gut flora, including *C. albicans* in mammalian hosts, whereas others live as endosymbionts in insect hosts (16)(17)(18). Systemic infections of the bloodstream and major organs (candidemia or invasive candidiasis), particularly in patients with an impaired immune system (immunocompromised), affect over 90,000 people a year in the US (19).

### **Candida species**

Among *Candida* species,

*C. albicans*, which is a normal constituent of the human flora, a commensal of the skin and the gastrointestinal and genitourinary tracts (20) .

Yet, there is an increasing incidence of infections caused by *C. glabrata* and *C. rugosa* (21). Other medically important species include *C. parapsilosis*, *C. tropicalis*, *C. dubliniensis*(20).

And the more recent upcoming pathogen *C. auris* (22).

Other *Candida* species, such as *C. oleophila*, have been used as biological control agents in fruit.

### **Candidiasis**

Candidiasis or thrush is a fungal infection (presence of parasitic infection in or on any part of body i.e., mycosis) caused by any of the species from the genera *Candida*, amongst which *C. albicans* is the most common causative species. Systemic infections are commonly referred to as candidemia and are one of the prominent co-infections in immuno-compromised patients such as those suffering from cancer, HIV etc. as well as patients in non-trauma emergency surgery, with extensive use of powerful antibiotics and immune-suppressive therapies during organ transplant or anti-leukemia therapies (26)(27). A number of antifungal drugs are found to be efficient and are available for the treatment of candidiasis. Amphotericin B has served as a standard treatment for five decades but its usage is often limited due to toxic effects, fluconazole is as effective as amphotericin B with superior safety but certain non-*albicans* *Candida* species are less susceptible to fluconazole. New agents from echinocandins class, such as caspofungin, target the fungal cell wall and

retain the activity against isolates with resistance to azoles or polyenes (28).

### **Types of candidiasis**

There are several different types of it :

#### **Thrush (Oropharyngeal Candidiasis)**

When the *Candida* yeast spreads in the mouth and throat, it can cause an infection called thrush. It's most common in newborns, the elderly, and people with weakened immune systems(44) .

Also more likely to get it are adults who:

- Are being treated for cancer
- Take medications like corticosteroids and wide-spectrum antibiotics
- Have diabetes

The symptoms include:

- White or yellow patches on the tongue, lips, gums, roof of mouth, and inner cheeks
- Redness or soreness in the mouth and throat
- Pain when swallowing, if it spreads to the throat

#### **Genital Yeast Infection (Genital Candidiasis)**

Three out of four adult women will get at least one yeast infection during their lifetime. This happens when too much yeast grows in the vagina. (Men also can get a genital yeast infection, but it's much less common).

This can be caused by:

- Pregnancy
- Diabetes
- Some medicines, including antibiotics and birth control pills
- Use of some douches, vaginal sprays, lubricants, or spermicides
- A weakened immune system

The symptoms include:

- Extreme itchiness in the vagina
- Redness and swelling of the vagina and vulva (the outer part of the female genitals)
- Most times, an over-the-counter antifungal suppository, tablet, or cream will knock out the infection(45) .

## Diaper Rash From Yeast Infection

Though diaper rashes are usually caused by leaving a wet or soiled diaper on too long, once your baby's skin is irritated, infection is more likely. If their diaper rash isn't going away, check to see if their bottom is red and sensitive, and if there's a raised red border around the sores. If so, have your pediatrician check for candidiasis(46) .

## Invasive Candidiasis

If candida yeast enters the bloodstream (usually through medical equipment or devices), it can travel to the heart, brain, blood, eyes, and bones. This can cause a serious, life-threatening infection.

This happens most often to people who have recently been admitted to a hospital or live in a health care facility, such as a nursing home. Like other types of yeast infections, if you have diabetes, a weakened immune system, kidney failure, or are on antibiotics, your chances of getting it are greater(47) .

The symptoms include:

- fever
- chills (48) .

## Classification

There are a number of different types of oropharyngeal candidiasis including acute pseudomembranous, acute atrophic, chronic hyperplastic, chronic atrophic, median rhomboid glossitis, and angular cheilitis. The most discrete lesion represents conversion from benign colonisation to pathological overgrowth.

## Acute Pseudomembranous Candidiasis

Acute pseudomembranous candidiasis, often referred to as "thrush", usually presents as multifocal curdy yellow-white plaques throughout the oral mucosa .A diagnostic feature of this infection is that these plaques, consisting of desquamated epithelial and immune cells together with yeast and hyphae, can be removed by gentle scraping, leaving behind an underlying red erosive base (29)(30)(31).

The diagnosis of pseudomembranous candidiasis is essentially a clinical diagnosis based on the

presence of distinctive clinical features. Alternatively, a swab from the white patches can be sent for microscopic identification of *Candida* or for culture to identify the *Candida* species present .

## Angular Cheilitis

Angular cheilitis, as the term implies, affects the angles or commissures of the mouth and presents with erythema, maceration, fissuring, crusting, or a combination thereof . The presentation may be unilateral but is more often bilateral.

Angular cheilitis is commonly associated with DS or another pre-existing primary form of OC where the elevated numbers of *Candida* in the oral cavity result in direct spread and auto-inoculation of the angles of the mouth (30)(31) .

## Chronic Hyperplastic Candidiasis

Chronic hyperplastic candidiasis, also referred to as candidal leukoplakia, usually arises on the anterior buccal mucosa proximal to the anterior commissures (retrocommissural area) , but may also occur on the lateral tongue which is the second most common site of occurrence (Figure 4).Patients present with well-demarcated leukoplakias or raised fissured white plaques that cannot be removed by gentle scraping. The highest prevalence of this rare form of OC is in middle-aged male smokers. An important consideration of chronic hyperplastic candidiasis is its association with an increased risk of malignant transformation (up to10%) to oral squamous cell carcinoma, although the exact mechanism is currently unknown (32) .

## Predisposing Factors to Oral Candidiasis

The transition of *C. albicans* from a harmless commensal state to a pathogenic state is heavily reliant on many predisposing factors (33) .

## Local Factors

### Salivary Hypofunction

Saliva is enriched with antimicrobial proteins that aid in limiting *C.albicans* attachment to the oral epithelia, and this biofluid is largely responsible for the maintenance of *C. albicans* in its commensal state . The incidence of salivary hypofunction is



increasing due to the aging population and the increase in polypharmacy. Additionally, weakened immune states (e.g., HIV) and other iatrogenic therapies such as chemotherapy and head-and-neck radiation therapy result in profound insult to the salivary glands and contribute to the development of OC (34) (35)

### **Denture Wearing**

Prolonged denture wearing, poor denture hygiene, and mucosal trauma are important local factors that contribute to OC development, as a breach in the oral epithelium creates a portal of entry for Candida. An important contributing factor to the development of DS is the favorable environment for Candida growth that is created beneath the dentures. The micro-environment of the denture-bearing palatal mucosa is of low oxygen, largely devoid of saliva, and is of low acidic pH, which promotes SAP activity (37). In fact, it was reported that at least 40% of elderly denture wearers do not adequately disinfect or remove their dentures at night, and life-threatening pneumonia events are twice as likely to occur in these patients (36).

### **Smoking**

Tobacco cigarette users are known to have significantly higher oral candidal carriage levels and, therefore, are at an increased risk of developing OC (38).

### **Systemic Factors**

#### **Age-Related Immunosenesence**

Elderly patients were shown to have significantly lower activity levels of protective salivary innate defenses (34)(40).

#### **Broad-Spectrum Antibiotics**

Broad-spectrum antibiotics are responsible for the overwhelming majority of acute OC cases (41). Dysbiosis by bacterial depletion due to the use of broad-spectrum antibiotics can alter the local oral flora, creating a favorable environment for Candida to proliferate.

#### **HIV Infection and AIDS**

It is well established that HIV+ patients harbor increased levels of Candida colonizing the oral

cavity and are significantly predisposed to OC. Specifically, *C. dubliniensis* was recognized to have a strong proclivity for causing OC in HIV+ patients with the corollary that cluster of differentiation 4 (CD4) T-cell levels are directly proportional to the severity of OC in this patient population. Furthermore, HIV+ patients have significantly lower protective levels of antimicrobial peptides, namely, histatin-5 (Hst-5); thus, these patients are reported to have increased rates of OC compared to matched healthy controls (35).

### **Systemic Immunocompromise**

Aside from HIV disease, any systemic disease that results in systemic immunocompromise, whether the underlying etiology is developmental, iatrogenic, immune-mediated, autoimmune, endocrine, or associated with a malignancy state, may give rise to OC. A brief non-exhaustive list includes systemic immunocompromise as a result of thymic aplasia,

chronic mucocutaneous candidiasis syndromes, chemoradiation, cytotoxic therapies, immunomodulating agents and hypothyroidism (42).

### **Nutritional Deficiencies**

Malnutrition, malabsorption, and eating disorder states are reported to predispose to OC. Specifically, hematinic deficiencies and a high-carbohydrate diet are said to contribute to OC development. The following deficiencies were attributed to this increased risk: iron, zinc, magnesium, selenium, folic acid, and vitamins (A, B6, B12, and C) (39).

### **Diagnosis of oral candidiasis**

The diagnosis of any of the forms of oral candidiasis is essentially clinical and is based on recognition of the lesions, which can be confirmed by the microscopic identification of Candida in the oral samples and/or isolation in culture, among other diagnostic methods. In the case of Candida, detection of the fungus in the oral cavity is not indicative of infection, since it is a common commensal organism in this location. A definitive diagnosis of candidiasis requires the confirmation of tissue invasion by Candida. For this reason a

negative culture result is of greater use in discarding candidiasic infection than a positive culture result in confirming infection.

It may be stated that in the absence of clinical manifestations compatible with oral candidiasis, a positive culture result for *Candida* does not mean that the patient has oral candidiasis. The importance of the clinical diagnosis of the disease therefore must be underscored (43) .

## Methodologies

## Results:

**Table1. Summarized the findings of previous researches about isolation of *Candida* spp from oral infections.**

No. of specimens	Type of sample isolation method	<i>Candida</i> spp	Number of Isolate (%)	Researcher
75	The bronchoalveolar lavage fluid	<i>C. albicans</i> <i>C. tropicalis</i> <i>C. glabrata</i> <i>C. krusei</i> <i>C. parapsilosis</i> <i>C. kefyr</i> <i>C. guilliermondii</i>	52% 24% 14.7% 5.3% 1.3% 1.3% 1.3%	Zarrinfar et al., 2016
30	Tongue swabs	<i>C. albicans</i> <i>C. kefyr</i> <i>C. glabrata</i>	90% 7% 3%	Irena Glažaret et al., 2017
48	Sputum	<i>C. albicans</i> <i>C. krusei</i> <i>C. glabrata</i> <i>C. dublinensis</i> <i>C. tropicalis</i>	46% 23% 13% 10% 8%	Sujatha et al., 2015
116	Oral rinses and gingival bleeding index (GBI) before and after placement of the orthodontic conventional brackets for 12 weeks.	<i>C. albicans</i> <i>C. tropicalis</i> <i>C. glabrata</i> <i>C. parapsilosis</i> <i>C. krusei</i>	58.8% 21% 9.1% 6.1% 5%	Kinga Grzegocka et al., 2020
98	Swabs the oral mucosa	<i>C. albicans</i> <i>C. famata</i> <i>C. tropicalis</i>	50% 33% 17%	Simone et al., 2018
200	By rubbing sterile swabs on different mucosa areas in oral cavity.	<i>C. albicans</i> <i>C. tropicalis</i> <i>C. glabrata</i>	63% 21% 16%	A.Almansour et al., 2016

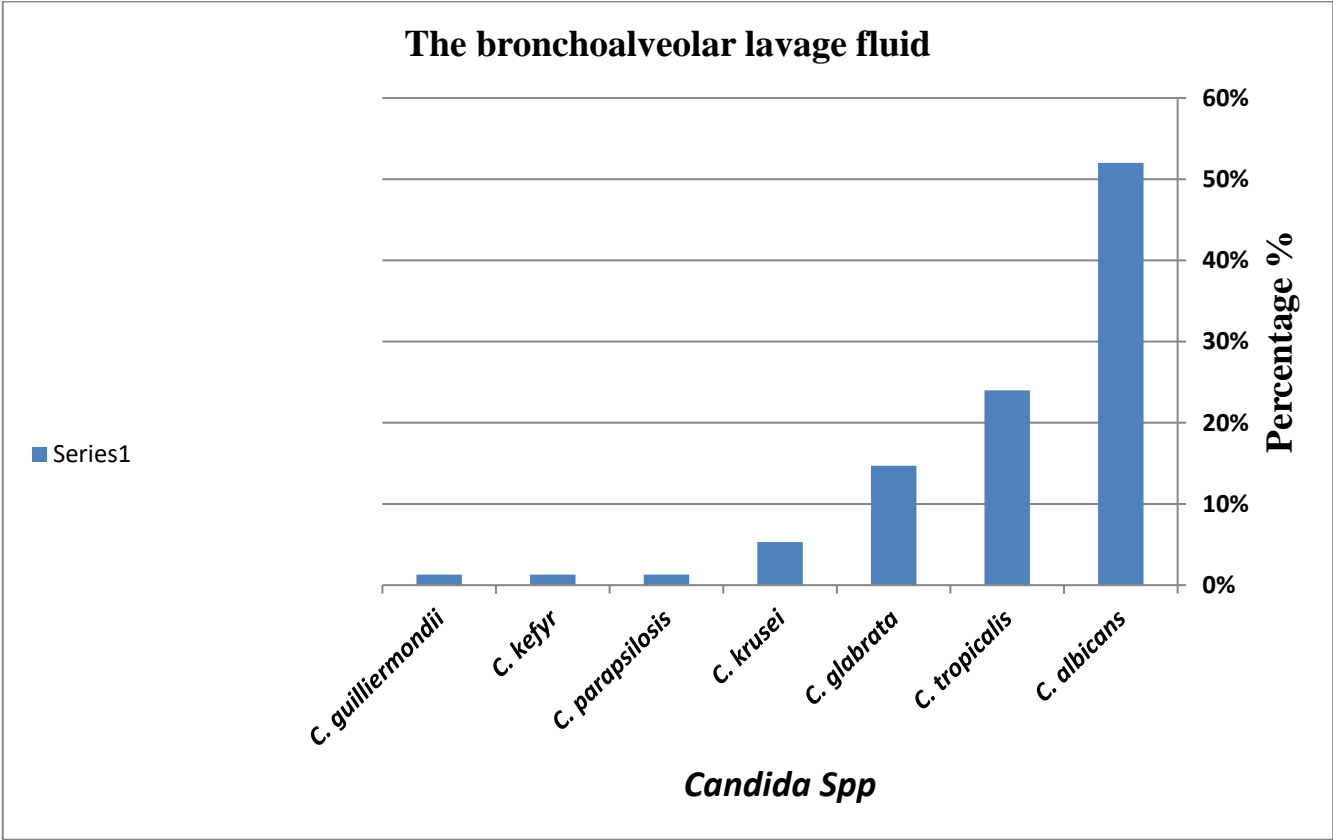
During the period between September 2021 and May 2022. In this study we have revised and reviewed most previous studies conducted on Candidiasis especially, Thrush and the method of isolation of *Candida* species from oral cavity. Also, we have calculated the data of isolations of *Candida* spp. All data of each researcher was calculated by plotting the figures of the *Candida* spp. (No) vs percentages (%) in Microsoft Excel programmed.

150	swab oral cavity	<i>C. albicans</i> <i>C. dubliniensis</i> <i>C. glabrata</i> <i>C. krusei</i> <i>C. tropical</i>	80% 3% 1% 12% 4%	Castellote <i>et al.</i> , 2013
378	Mouth swabs	<i>C. albicans</i> <i>C. glabrata</i> <i>C. krusei</i> <i>C. tropicalis</i> <i>C. parapsilosis</i> <i>C. pseudotropicalis</i>	60.2% 16.9% 12.3% 6.4% 2.3% 1.8%	Ambe <i>et al.</i> , 2020
151	Oral swabs	<i>C. albicans</i> <i>C. parapsilosis</i> <i>C. guilliermondii</i> <i>C. glabrata</i> <i>C. krusei</i> <i>C. dubliniensis</i> <i>C. tropicalis</i> <i>C. famata</i> <i>C. kefir</i> <i>C. pelliculosa</i> <i>C. pulcherrima</i> <i>C. rugosa</i>	60.2 % 10.2 % 9.3 % 6.5 % 3.7 % 2.8% 2.8% 0.9 % 0.9% 0.9% 0.9% 0.9%	Sahand <i>et al.</i> , 2009
130	Oral swabs	<i>C. albicans</i> <i>C. glabrata</i> <i>C. famata</i> <i>C. krusei</i> <i>C. sphaerica</i> <i>C. tropicalis</i>	65% 13% 13% 3.6% 3.6% 1.8%	Ali <i>et al.</i> , 2020
9,769	Saliva samples	<i>C. albicans</i> <i>C. tropicalis</i> <i>C. krusei</i> <i>C. glabrata</i>	75.37% 6.06% 2.79% 2.02%	Hong <i>et al.</i> , 2019
482	Swabs from tongue surfaces	<i>C. albicans</i> <i>C. dublinensis</i> <i>C. guilliermondii</i> <i>C. parapsilosis</i> Other sp	80.7% 5.7% 6.8% 3.4% 3.4%	Toshiro Majima <i>et al.</i> , 2014
62	The samples were taken by scaling the lesions with a sterile wooden spatula.	<i>C. albicans</i> <i>C. parapsilosis</i> <i>C. tropicalis</i> <i>C. krusei</i> <i>C. glabrata</i>	69.35% 14.89% 12.77% 4.26% 2.13%	Robertis <i>et al.</i> , 2007

		<i>C. lusitaniae</i>	2.13 %	
65	Specimens were collected by rubbing the sterile swab sticks on the surface of the tongue.	<i>C. albicans</i> <i>C. krusei</i> <i>C. guilliermondii</i> <i>C. parapsilosis</i> <i>C. tropicalis</i> <i>C. stellatoidea</i> <i>C. pseudotropicalis</i>	61.5% 9.2% 7.7% 6.2% 6.2% 4.6%	Aniebo <i>et al.</i> , 2012
59	Sterile swabs	<i>C. albicans</i> <i>C. glabrata</i> <i>C. tropicalis</i>	43.7 % 31.2% 25.1%	Nascimento <i>et al.</i> , 2016

The data obtained from current study showed that there are several studies confirmed isolation of candida spp from oral cavity of pediatric, for example study by (Hussein Zarrinfar et al., 2016) found that the Candida spp were isolated samples

from bronchoalveolar lavage fluid including *C. albicans*, *C. tropicalis*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. kefyr*, *C. guilliermondii* and the optimum app was *C. albicans* followed by *C. tropicalis* (Figure1).

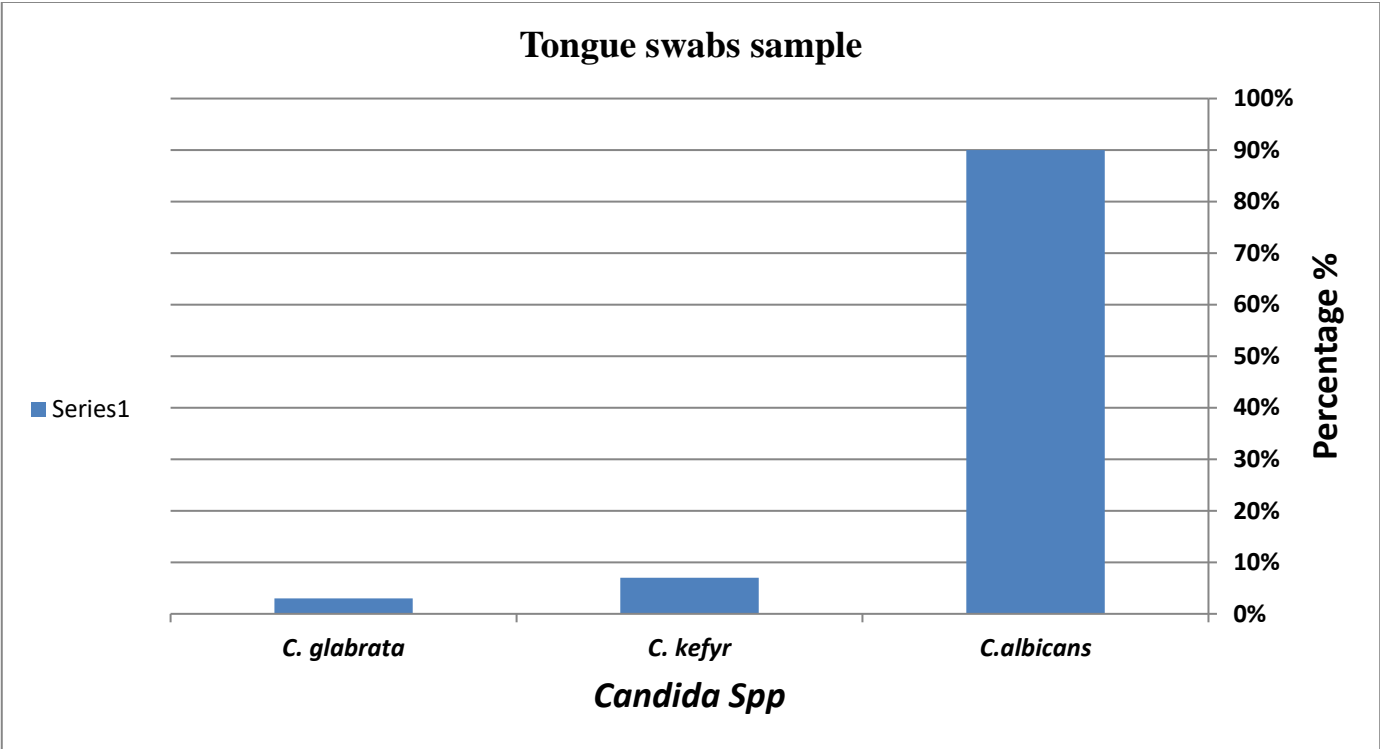


**Figure1:** Showed the percentage of isolations of Candida Spp isolated from bronchoalveolar lavage fluid.

Irena Glažaret et al. (2017) found that the Candida spp were isolated samples from the tongue swabs including *C.albicans*, *C. kefyr*, *C. glabrata* and the

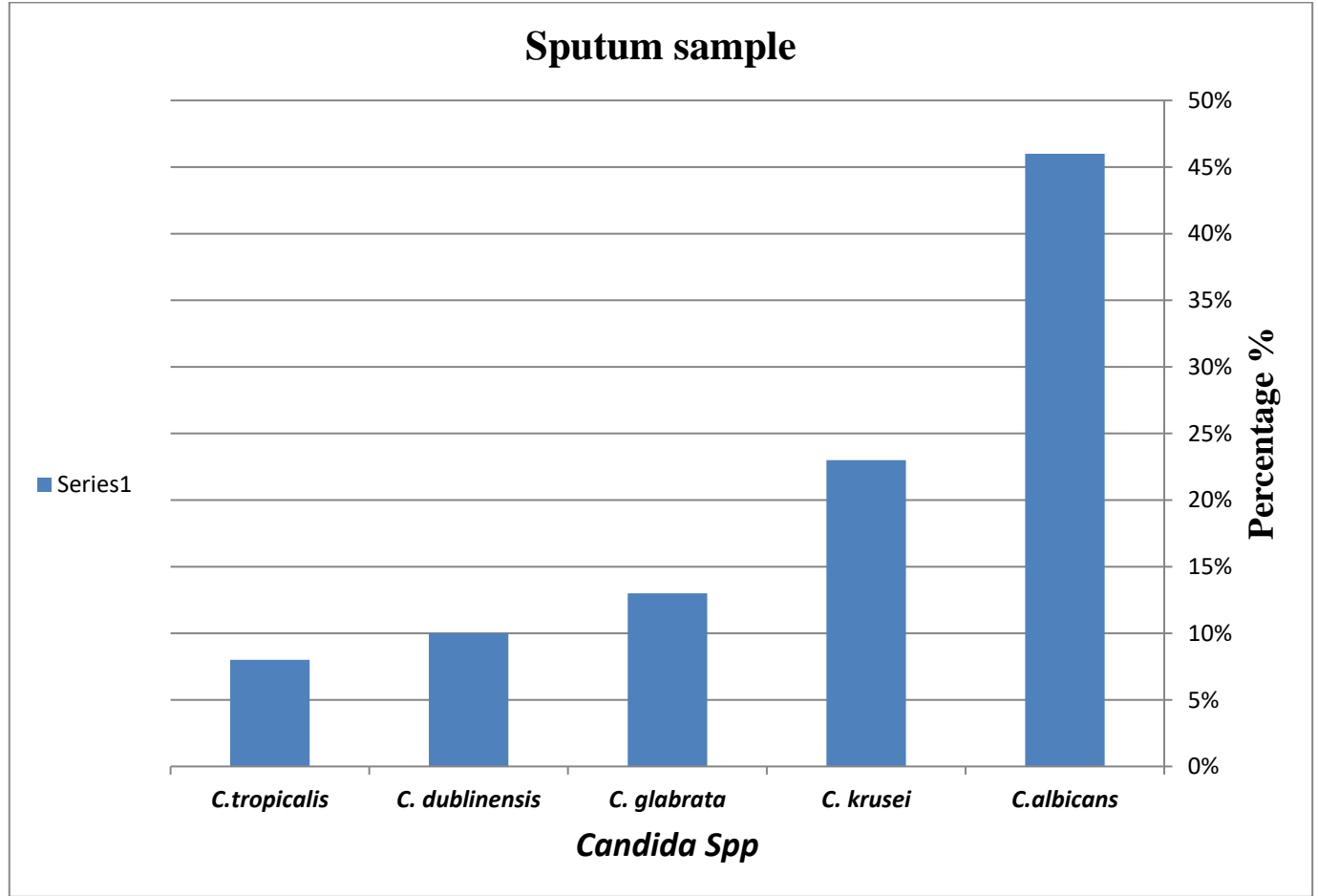
optimum species was *C. albicans* followed by *C. kefyr* (Figure2.)





**Figure2:** Showed the percentage of isolations of Candida Spp isolated from Tongue swabs sample patients.

Findings obtained by Sujatha et al. (2015) found that the Candida spp were isolated samples from the sputum including *C. albicans*, *C. krusei*, *C. glabrata*, *C. dublinensis*, *C.tropicalis* and the optimum spp. was *C. albicans* followed by *C. krusei* (Figure3) .



**Figure3:** Showed the percentage of isolations of Candida Spp isolated from sputum sample patients.

## Conclusion:

At the end of our research, we dealt with the candida thrush known as oral candidiasis. The infection is technically referred to as candidiasis, moniliasis as well as onychomycosis, which is also called yeast infection. Several articles were studied about *Candida* spp from 2012 to 2020.

After extensive study of 15 samples taken from different places of the oral cavity for example (tongue swabs, oral swabs, swabs from tongue surfaces, saliva samples, sputum, by rubbing smears Sterile was applied to different areas of the mucous membranes in the oral cavity ... etc.) Important results were reached, which is that the highest infection rate was with *Candida albicans*, followed by *Candida glabrata*.

Recommend, improving diagnostic methods that help diagnose candida infection early, which means that the patient will receive the correct and timely treatment, and this will stop the transmission of infection from one person to another.

Finally, the initial collaboration between institutions and the lack of knowledge regarding the physiology and mechanisms of drug resistance in *C. albicans* requires more and stronger collaboration networks to deal with this global health problem and to improve diagnostic and identification methodologies, as well as to ensure the development and use of new antifungal antibiotics in treatment. and controlling disease outbreaks.

## References:

- James, William D.; Berger, Timothy G.; et al. (2006). *Andrews' Diseases of the Skin: Clinical Dermatology*. Philadelphia: Saunders Elsevier. p. 308. ISBN 978-0-7216-2921-6. OCLC 62736861.
- Epstein JB. Antifungal therapy in oropharyngeal mycotic infections. *Oral Surg Oral Med Oral Pathol* 1990;69:32–41.
- Guida RA. Candidiasis of the oropharynx and oesophagus. *Ear NoseThroat J* 1988;67:832–40.
- Ghannoum MA, Radwan SS. *Candida* adherence to epithelial cells. Boca Raton, FL: CRC Press, 1990.
- Abu-Elteen KH, Abu-Alteen RM. The prevalence of *Candida albicans* populations in the mouths of complete denture wearers. *New Microbiol* 1998;21:41–8.
- Arendorf TM, Walker DM. The prevalence and intra-oral distribution of *Candida albicans* in man. *Arch Oral Biol* 1980;25:1–10.
- Holbrook WP, Hjorleifsdottir DV. Occurrence of oral *Candida albicans* and other yeast-like fungi in edentulous patients in geriatric units in Iceland. *Gerodontology* 1986;2:153–6.
- Rodu B, Carpenter JT, Jones MR. The pathogenesis and clinical significance of cytologically detectable oral candida in acute leukaemia. *Cancer* 1988;62:2042–6.
- Höfs, S.; Mogavero, S.; Hube, B. Interaction of *Candida albicans* with host cells: Virulence factors, host defense, escape strategies and the microbiota. *J. Microbiol.* 2016, 53, 149–169. [CrossRef]
- Mayer, F.L.; Wilson, D.; Hube, B. *Candida albicans* pathogenicity mechanisms. *Virulence* 2013, 4, 119–128. [CrossRef]
- Williams, D.; Lewis, M. Pathogenesis and treatment of oral candidosis. *J. Oral Microbiol.* 2011, 3. [CrossRef][PubMed]
- Naglik, J.R.; Moyes, D.L.; Waächtler, B.; Hube, B. *Candida albicans* interactions with epithelial cells and mucosal immunity. *Microbes Infect.* 2011, 13, 963–976. [CrossRef][PubMed]
- Manolakaki, D.; Velmahos, G.; Kourkoumpetis, T.; Chang, Y.; Alam, H. B.; De Moya, M. M.; Mylonakis, E. (2010). "Candida infection and colonization among trauma patients". *Virulence*. 1 (5): 367–75. doi:10.4161/viru.1.5.12796. PMID 21178472.
- Kourkoumpetis TK, Velmahos GC, Ziakas PD, Tampakakis E, Manolakaki D, Coleman JJ, Mylonakis E (2011). "The effect of cumulative length of

- hospital stay on the antifungal resistance of *Candida* strains isolated from critically ill surgical patients". *Mycopathologia*. 171 (2): 85–91. doi:10.1007/s11046-010-9369-3. PMC 4093797. PMID 20927595.
15. Fugelsang, K.; Edwards, C. (2010). *Wine Microbiology* (2nd ed.). Springer. pp. 3–28. ISBN 978-0387333496.
16. Spanakis EK, Kourkoumpetis TK, Livanis G, Peleg AY, Mylonakis E (2010). "Statin therapy and decreased incidence of positive *Candida* cultures among patients with type 2 diabetes mellitus undergoing gastrointestinal surgery". *Mayo Clin. Proc.* 85 (12): 1073–9. doi:10.4065/mcp.2010.0447. PMC 2996154. PMID 21123633.
17. Nguyen NH, Suh SO, Blackwell M (2007). "Five novel *Candida* species in insect-associated yeast clades isolated from Neuroptera and other insects". *Mycologia*. 99 (6): 842–858. doi:10.3852/mycologia.99.6.842. PMID 18333508.
18. Suh SO, Nguyen NH, Blackwell M (2008). "Yeasts isolated from plant-associated beetles and other insects: seven novel *Candida* species near *Candida albicans*". *FEMS Yeast Res.* 8 (1): 88–102. doi:10.1111/j.1567-1364.2007.00320.x. PMID 17986254.
19. Steckelberg, James M. (2012-09-18). "Male yeast infection: Can I get it from my girlfriend?". *Mayo Clinic*. Retrieved 2014-03-23.
20. Gow, Neil A. R.; Yadav, Bhawna (2017). "Microbe Profile: *Candida albicans*: a shape-changing, opportunistic pathogenic fungus of humans". *Microbiology*. 163 (8): 1145–1147. doi:10.1099/mic.0.000499. PMID 28809155.
21. Pfaller, M. A.; Diekema, D. J.; Colombo, A. L.; Kibbler, C.; Ng, K. P.; Gibbs, D. L.; Newell, V. A. (2006). "*Candida rugosa*, an emerging fungal pathogen with resistance to azoles: geographic and temporal trends from the ARTEMIS DISK antifungal surveillance program". *J. Clin. Microbiol.* 44 (10): 3578–82. doi:10.1128/JCM.00863-06. PMC 1594768. PMID 17021085.
22. Spivak, Emily S.; Hanson, Kimberly E. (2017). "*Candida auris*: an Emerging Fungal Pathogen". *Journal of Clinical Microbiology*. 56 (2). doi:10.1128/JCM.01588-17. PMC 5786713. PMID 29167291.
23. Antifungal chemotherapy in patients with acquired immuno deficiency syndrome. British Society for Antimicrobial Chemotherapy Working Party. *Lancet*, 1992, 340(8820), 648–51.
24. Greenspan, D.; John, S.G. HIV-related oral disease. *Lancet*, 1996, 348, 729–734.
25. Smeekens, S.P.; Ng, A.; Kumar, V.; Johnson, M.D.; Plantinga, T.S.; van Diemen, C.; Arts, P.; Verwiel, E.T.; Gresnigt, M.S.; Fransen, K.; van Sommeren, S.; Oosting, M.; Cheng, S.C.; Joosten, L.A.; Hoischen, A.; Kullberg, B.J.; Scott, W.K.; Perfect, J.R.; van der Meer, J.W.; Wijmenga, C.; Netea, M.G.; Xavier, R.J.
26. Functional genomics identifies type-I interferon pathway as central for host defense against *C. albicans*. *Nat. Commun.*, 2013, 4, 1342.
27. Millsop, J.W.; Faze, L.N. Oral candidiasis. *Clin. Dermatol.* 2016, 34, 487–494. [CrossRef] [PubMed]
28. Hellstein, J.W.; Marek, C.L. Candidiasis: Red and white manifestations in the oral cavity. *Head Neck Pathol.* 2019, 13, 25–32.
29. Lewis, M.A.O.; Williams, D.W. Diagnosis and management of oral candidosis. *Br. Dent. J.* 2017, 223, 675–681.
30. Bakri, M.M.; Hussaini, M.H.; Holmes, R.A.; Cannon, D.R.; Rich, M.A. Revisiting the association between candidal infection and carcinoma, particularly oral squamous cell carcinoma. *J. Oral Microbiol.* 2010, 2.
31. Williams, D.; Lewis, M. Pathogenesis and treatment of oral candidosis. *J. Oral Microbiol.* 2011, 3.
32. Sroussi, H.Y.; Epstein, J.B.; Bensadoun, R.J.; Saunders, D.P.; Lalla, R.V.; Migliorati, C.A.; Heavilin, N.; Zumsteg, Z.S. Common oral complications of head and neck cancer

- radiation therapy: Mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med.* 2017, 6, 2918–2931.
35. Khan, S.A.; Fidel, P., Jr.; Al Thunayyan, A.; Meiller, T.; Jabra-Rizk, M.A. Impaired histatin-5 level and salivary antimicrobial activity against *C. albicans* in HIV-infected individuals. *J. AIDS Clin. Res.* 2013, 4, 1000193.
36. Iinuma, T.; Arai, Y.; Abe, Y.; Takayama, M.; Fukumoto, M.; Fukui, Y.; Iwase, T.; Takebayashi, T.; Hirose, N.; Gionhaku, N.; et al. Denture wearing during sleep doubles the risk of pneumonia in the very elderly. *J. Dent. Res.* 2015, 94, 28S–36S.
37. Schaller, M.; Borelli, C.; Korting, H.C.; Hube, B. Hydrolytic enzymes as virulence factors of *Candida albicans*. *Mycoses* 2005, 48, 365–377.
38. Mun, M.; Yap, T.; Alnuaimi, A.D.; Adams, G.G.; McCullough, M.J. Oral candidal carriage in asymptomatic patients. *Aust. Dent. J.* 2016, 61, 190–195.
39. Manfredi, M.P.L.; Giovati, L.; Alnuaimi, A.; McCullough, M.J. Oral and Maxillofacial Fungal Infections. In *Contemporary Oral Medicine*; Farah, C., Balasubramaniam, R., McCullough, M., Eds.; Springer: Berlin/Heidelberg, Germany, 2018.
40. Johnson, D.; Yeh, C.K.; Dodds, M.W. Effect of donor age on the concentrations of histatins in human parotid and submandibular/sublingual saliva. *Arch. Oral Biol.* 2000, 45, 731–740.
41. Farah, C.S.; Lynch, N.; McCullough, M.J. Oral fungal infections: An update for the general practitioner. *Aust. Dent. J.* 2010, 5, 48–54.
42. Samaranayake, L.P.; Keung Leung, W.; Jin, L. Oral mucosal fungal infections. *Periodontology* 2000 2009, 49, 39–59.
43. Moulias R. Clinical manifestations of candidosis in the older adult. *Revue de Geriatrie.* 2002;49:1741-2
44. CDC: “Candidiasis,” “Oropharyngeal/Esophageal Candidiasis,” “Genital/vulvovaginal candidiasis (VVC),” “Invasive Candidiasis.”
45. HealthyChildren.org: “Thrush and Other Candida Infections, “Diaper Rash”<https://www.webmd.com/skin-problems-and-treatments/guide/what-is-candidiasis-yeast-infection>.”
46. American Congress of Obstetricians and Gynecologists: “Vaginitis.” <https://www.webmd.com/skin-problems-and-treatments/guide/what-is-candidiasis-yeast-infection> .
47. WomensHealth.gov: “Vaginal Yeast Infection.” <https://www.webmd.com/skin-problems-and-treatments/guide/what-is-candidiasis-yeast-infection> .
48. National Health Service (U.K.): “Oral Thrush in Adults.” <https://www.webmd.com/skin-problems-and-treatments/guide/what-is-candidiasis-yeast-infection> .