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### ORAL CANDIDIASIS - REVIEW

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#### ABSTRACT

Oral candidiasis is a common opportunistic infection of the oral cavity caused by an overgrowth of *Candida* species, the commonest being *Candida albicans*. The incidence varies depending on age and certain predisposing factors. *Candida* fungi are found almost everywhere in the environment. Some may live harmlessly along with the abundant "native" species of bacteria that normally colonize the mouth, gastrointestinal tract and vagina. Usually, *Candida* is kept under control by the body's immune defense. Candidiasis is classified using the Lehner system. Some of the subtypes almost always occur as acute and others chronic. Major signs and symptoms of oral candidiasis include White patches, or red lesions in oral cavity, pruritus, and vulval erythematous, curd-like discharge from vagina. Management involves taking a history, an examination, and appropriate antifungal treatment with a few requiring samples to be taken for laboratory analysis. In certain high risk groups antifungal prophylaxis reduces the incidence and severity of infections. The only prevention is Good Oral Hygiene.

#### KEY WORDS

Oral Cavity, Oral Candidiasis, *Candida albicans* and Oral Hygiene.

#### INTRODUCTION

Oral candidiasis is the one of the most common, opportunistic, treatable human fungal infection of the oral cavity seen in all stages of life<sup>1</sup>. Oral candidiasis is also known as oral candidosis, oral thrush, or oropharyngeal candidiasis, moniliasis, candidal stomatitis, muguet. It is common and under diagnosed among the elderly, particularly in those who wear dentures and in many cases is avoidable with a good mouth care regimen. It is an oral mucosal infection seen in persons with human immunodeficiency virus (HIV), infection or

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acquired immune deficiency syndrome (AIDS). It can also be a mark of systemic disease, such as diabetes mellitus and is a common problem among the immunocompromised<sup>2</sup>. Oral can be a frequent and significant source of oral discomfort, pain, loss of taste, and aversion to food. Oral candidiasis is caused by the overgrowth or infection of the oral cavity by a yeast-like fungus, *Candida*. *Candida* is commensal organism and part of the normal oral flora in about 30%-50% of the population, and is capable of producing opportunistic infections within the oral cavity when appropriate predisposing factors exist. More than 20 species of *Candida*, *Candida albicans* are the most common and important causative agent of oral candidiasis. Some other candidia species are *C tropicalis*, *C glabrata*, *Cpseudotropicalis*, *C guillierimondii*, *C krusei*, *C lusitaniae*, *C parapsilosis*, and *C stellatoidea*<sup>3</sup>.

#### **Candida albicans**

*C. albicans* is the most common fungal pathogen in humans, able to cause various Infections (Candidiasis) that may be severe enough to kill the host if the infection is systemic. Two important factors that affect the pathogenicity of *C. albicans* are the ability to switch between yeast growth and filamentous growth, i.e. the hyphal switch, and the ability to form biofilms which enables *C. albicans* to adhere to the surface of substrates. In biofilms cells show an increased resistance to the immune system and to antifungal drugs<sup>4</sup>.

#### **Causes**

The causative organism is *Candida* species usually *Candida albicans*, *C. albicans* accounts for about 50% of oral candidiasis and together, *C. albicans*, *C. tropicalis* and *C. glabrata* account for over 80% of cases. Candidiasis caused by non-*C. albicans* *Candida* species is associated more with immunodeficiency. Such as HIV/AIDS. Certain drugs can alter the natural organisms in the mouth, which can then promote the growth of *Candida*. These include the extended use of antibiotics, steroids and oral contraceptives with high estrogen content.

#### **Immunodeficiency/Immunocompromise**

Acute pseudo membranous candidiasis occurs in about 5% of newborn infants. *Candida* species are

acquired from the mother's vaginal canal during birth. At very young ages, the immune system is yet to develop fully and there is no individual immune response to candida species, infants antibodies to the bacteria are normally supplied by the mother's breast milk.

#### **Denture Wearing**

Denture wearing and poor denture hygiene is another risk factor for both candidal carriage and oral candidiasis. Dentures provide a relative acidic, moist and anaerobic environment because the mucosa covered by the denture is sheltered from oxygen and saliva. Poorly fitting dentures may also cause minor trauma to the mucosa, which is increase the permeability of the mucosa and increase the ability of *C. albicans* to invade the tissues. These conditions all favor the growth of *C. albicans*.

#### **Dry Mouth**

Both the quality and quantity of saliva are important oral defenses against candida. Decreased salivary flow rate or a change in the composition of saliva, can cause the salivary hypo function or hypo salivation. It is an important predisposing factor for candidiasis.

#### **Diet**

Malnutrition, malabsorption or Poor diet, especially hematinic deficiencies (iron, vitamin B12, folic acid) can predispose to oral candidiasis, by causing diminished host defense and epithelial integrity.

#### **Smoking**

Heavy smoking is an important predisposing factor for candidiasis, but the relationships are unknown. One hypothesis is that cigarette smoke contains nutritional factors for *C. albicans*, or that local epithelial alterations occur that facilitate colonization of candida species.

#### **Antibiotics**

Broad-spectrum antibiotics eliminates the competing bacteria and disrupt the normally balanced ecology of oral micro-organisms. Acute oral candidiasis occurring due to medication with corticosteroids or broad-spectrum antibiotics (tetracycline).

### Other factors

Endocrine disorders, Presence of certain other mucosal lesions, Women undergoing hormonal changes, like pregnancy or those on birth control pills<sup>5</sup>.

### Classification

Oral candidiasis is classified using the Lehner system, originally described in the 1960s, into acute and chronic forms. Some of the subtypes almost always occur as acute (e.g., acute pseudo membranous candidiasis), and others chronic.

#### Primary oral candidosis

##### Acute form

Pseudo membranous

Erythematous

##### Chronic form

Erythematous

Pseudo membranous

Hyperplastic (Plaque like)

Nodular

##### Candida associated lesions

Denture stomatitis

Angular chealosis

Median rhomboid glossitis

Secondary oral candidosis

##### Oral manifestation of systemic mucocutaneous candidosis

Familial mucocutaneous candidiasis

Diffuse chronic mucocutaneous candidiasis

Familial mucocutaneous candidiasis

Chronic granulomatous disease

Candidosis endocrinopathy syndrome

Acquired immune deficiency syndrome (AIDS)

#### Pseudo membranous

Acute pseudo membranous candidiasis is a classic form of oral candidiasis; this is the most common type of oral candidiasis, accounting for about 35% of oral candidiasis cases. It is characterized by extensive white pseudo membranes consisting of desquamated epithelial cells, fibrin, and fungal hyphae these white patches occur on the surface of the labial and buccal mucosa, hard and soft palate, tongue, periodontal tissues, and or pharynx. The membrane can usually be scraped off with a swab to expose an underlying erythematous mucosa.

### Erythematous

Erythematous (atrophic) candidiasis is where the condition appears as a red, raw-looking lesion. Some sources consider denture-related stomatitis, angular stomatitis, median rhomboid glossitis, and antibiotic-induced stomatitis as subtypes of erythematous candidiasis, since these lesions are commonly erythematous/atrophic. It may precede the formation of a pseudo membrane, be left when the membrane is removed, or arise *de novo*. The erythematous candidiasis accounts for 60% of oral candidiasis cases. Where it is associated with inhalation steroids, erythematous candidiasis commonly appears on the palate or the dorsum of the tongue. On the tongue, there is loss of the lingual papillae (depapillation), leaving a smooth area on the tongue.

Acute erythematous candidiasis usually occurs on the dorsum of the tongue in persons taking long term corticosteroids or antibiotics, but occasionally it can occur after only a few days of using a topical antibiotic. This is usually termed antibiotic sore mouth “,” antibiotic sore tongue or "antibiotic induced stomatitis" because it is commonly painful as well as red.

Chronic erythematous candidiasis is more usually associated with denture wearing (see denture-related stomatitis).

#### Hyperplastic

This variant is also sometimes termed "plaque-like candidiasis" or "nodular candidiasis". The most common appearance of hyperplastic candidiasis is a persistent white plaque that does not rub off. The lesion may be rough or nodular in texture. Hyperplastic candidiasis is uncommon, accounting for about 5% of oral candidiasis cases and is usually chronic and found in adults. The most common site of involvement is the commissural region of the buccal mucosa, usually on both sides of the mouth.

Another term for hyperplastic candidiasis is "candidal leukoplakia". This term is a largely historical synonym for this subtype of candidiasis, rather than a true leukoplakia. It can be clinically indistinguishable from true leukoplakia, but tissue

biopsy shows candidal hyphae invading the epithelium. Some sources use this term to describe leukoplakia lesions that become colonized secondarily by *Candida* species, thereby distinguishing it from hyperplastic candidiasis. It is known that *Candida* resides more readily in mucosa that is altered, such as may occur with dysplasia and hyperkeratosis in an area of leukoplakia.

#### **Associated lesions**

*Candida*-associated lesions are primary oral candidiasis (confined to the mouth), where the causes are thought to be multiple. For example, bacteria as well as *Candida* species may be involved in these lesions. Frequently, antifungal therapy alone does not permanently resolve these lesions, but rather the underlying predisposing factors must be addressed, in addition to treating the candidiasis.

#### **Angular cheilitis**

Angular cheilitis is inflammation at the corners (angles) of the mouth, very commonly involving *Candida* species, when sometimes the terms "*Candida*-associated angular cheilitis", or less commonly, "monilialperlèche" are used. *Candida* organisms alone responsible for about 20% of cases, and a mixed infection of *C. albicans* and *Staphylococcus aureus* for about 60% of cases. Signs and symptoms include soreness, erythema (redness), and fissuring of one, or more commonly both the angles of the mouth, with edema seen intraorally on the commissures. Angular cheilitis is generally occurs in elderly people and is associated with denture related stomatitis.

#### **Denture related stomatitis**

This term refers to a mild inflammation and erythema of the mucosa beneath a denture, usually an upper denture in elderly edentulous individuals (with no natural teeth remaining). Some report that up to 65% of denture wearers have this condition to some degree. About 90% of cases are associated with candida species, where sometimes the terms "*candida*-associated denture stomatitis, "or" *Candida*-associated denture induced stomatitis" (CADIS), are used. Some sources state that this is by far the most common form of oral candidiasis.

Although this condition is also known as "denture sore mouth", there is rarely any pain. *Candida* is associated with about 90% of cases of denture related stomatitis.

#### **Median rhomboid glossitis**

This is an elliptical or rhomboid lesion in the center of the dorsal tongue, just anterior (in front) of the circumvallate papillae. The area is depapillated, reddened (or red and white) and rarely painful. There is frequently *Candida* species in the lesion, sometimes mixed with bacteria.

#### **Linear gingival erythema**

This is a localized or generalized, linear band of erythematous gingivitis (inflammation of the gums). It was first observed in HIV infected individuals and termed "HIV-gingivitis", but the condition is not confined to this group. *Candida* species are involved, and in some cases the lesion responds to antifungal therapy, but it is thought that other factors exist, such as oral hygiene and human herpes viruses. This condition can develop into necrotizing ulcerative periodontitis.

#### **Chronic multifocal oral candidiasis**

This is an uncommon form of chronic (more than one month in duration) candidal infection involving multiple areas in the mouth, without signs of candidiasis on other mucosal or cutaneous sites. The lesions are variably red and/or white. Unusually for candidal infections, there is an absence of predisposing factors such as immune suppression, and it occurs in apparently healthy individuals, normally elderly males. Smoking is a known risk factor.

#### **Chronic mucocutaneous candidiasis**

This refers to a group of rare syndromes characterized by chronic candidal lesions on the skin, in the mouth and on other mucous membranes (i.e., a secondary oral candidiasis). These include Localized chronic mucocutaneous candidiasis, diffuse mucocutaneous candidiasis (*Candida granuloma*), candidiasis-endocrinopathy syndrome and candidiasis thymoma syndrome. About 90% of people with chronic mucocutaneous candidiasis have candidiasis in the mouth<sup>6</sup>.

## SIGNS AND SYMPTOMS

Signs and symptoms are dependent upon the type of oral candidiasis. Often, apart from the appearance of the lesions, there are usually no other signs or symptoms. Most types of oral candidiasis are painless, but a burning sensation may occur in some cases. Candidiasis can therefore sometimes be misdiagnosed as burning mouth syndrome. A burning sensation is more likely with erythematous (atrophic) candidiasis, while hyperplastic candidiasis is normally entirely asymptomatic. Acute atrophic candidiasis may feel like the mouth has been scalded with a hot liquid. Another potential symptom is a metallic, acidic, salty or bitter taste in the mouth. The pseudo membranous type rarely causes any symptoms apart from possibly some discomfort or bad taste due to the presence of the membranes. Sometimes the patient describes the raised pseudo membranes as "blisters". Occasionally there can be dysphagia (difficulty swallowing), which indicates that the candidiasis involves the oropharynx or the esophagus, as well as the mouth. The trachea and the larynx may also be involved where there is oral candidiasis, and this may cause hoarseness of the voice<sup>7</sup>.

## DIAGNOSIS

The diagnosis of *Candida* overgrowth is often made on the basis of clinical suspicion of the somewhat typical white, red, and white-red mucosal changes. Associated angular cheilitis substantially enhances the probability of candidiasis. These findings are almost always associated with some degree of discomfort or pain. The diagnosis can be confirmed by scrapings that are processed by potassium hydroxide or Gram-stained before microscopic examination or by cultures with the cultures, quantitation and qualification can be performed by candidal counts and speciation. Quantitation is done by plating *Candida* brom cresol green (BCG) agar, incubating, and counting colony-forming units. Qualitation is accomplished by using germ tube growth (for *albicans*) and carbohydrate assimilations (for other species). Biopsy specimens can be stained with the periodic acid-Schiff (PAS)

stain, which effectively reveals pseudomycelia and hyphae when present. Angular cheilitis, with or without oral signs and symptoms, should always raise the possibility or probability of candidiasis. In establishing the diagnosis, etiologic factors must be taken into consideration. Bacterial and viral infections as well as immune pathologic diseases must also be considered, particularly if there is no response to antifungal treatment. Epithelial dysplasia often manifests as white, red, and white-red lesions and must be ruled out<sup>8</sup>.

## TREATMENTS

Priority in the treatment of oral candidosis is the alleviation of any identifiable predisposing factor. Acquiring a thorough medical history is, therefore, an essential Component in the management process. The regular and frequent use of a denture cleanser with anti-candidal properties such as 1% sodium hypochlorite preparations, together with the removal of dentures overnight. Chlorhexidine (0.2%) should be used if the denture has metal components since hypochlorite will otherwise cause discolouration. Certain predisposing factors are; however, more difficult if not impossible to eradicate such as where there is an underlying disease (e.g. leukaemia or AIDS). In these cases, targeted antifungal therapy plays an important role in the management strategy. Both the physical and chemical reduction of *Candida* load in the oral cavity can be achieved by good oral hygiene practices including tooth brushing and the use of antimicrobial mouthwashes. Several mouthwashes exhibit anti-candidal activity including triclosan, chlorhexidinegluconate, and essential oil formulations. The latter tend to contain natural plant extracts such as thymol, eucalyptol, and bioflavonoid and these can have a direct anti-candidal activity in vitro through cell membrane disruption and enzyme inhibition. When compared with antibacterial agents, the availability of antifungal agent is significantly lower. There as on for this relates to the relatively recent recognition of the significance of human fungal infections and also the fact that fungal organisms are eukaryotic and share many features with mammalian cells making

selection of suitable targets for antifungal agents' problematic<sup>9</sup>.

### CONVENTIONAL THERAPY

The antifungal agent is based on the target of activity. The treatment for 2 weeks after resolution of the lesions. When the topical therapy fails then one has to start systemic therapy because failure of drug response is the initial sign of underlying systemic disease. Follow-up appointment after 3 to 7 days is important to check the effect of drugs. Main Goals of treatment are,

#### To identify and eliminate possible contributory factors:

- To prevent systemic dissemination
- To eliminate any associated discomfort
- To reduce load of candida

#### For infants and nursing mothers

If you're breast-feeding an infant, you and your baby will do best if you're both treated. Otherwise, you're likely to pass the infection back and forth.

- A mild antifungal medication for your baby and an antifungal cream for your breasts.
- If baby is using a pacifier or feeds from a bottle, rinse nipples and pacifiers in a solution of equal parts water and vinegar daily and allow them to air dry to prevent fungus growth.
- If you use a breast pump, rinse any of the detachable parts that come in contact with your milk in a vinegar and water solution<sup>10</sup>.

#### For adults with weakened immune systems

##### Antifungal medication

Treatment options are mainly categorized in to two lines, primary and secondary line of treatment. This comes in several forms, including lozenges, tablets or a liquid that you swish in your mouth and then swallow.

##### Primary line of treatment

Nystatin is the drug of choice as a primary line of treatment. Usually for the mild and localized candidiasis this primary line of treatment is used other drugs includes Clotrimazole which can be taken as is Lozenges and Amphotercin B as oral suspension.

##### Nystatin

It is a drug which can be used as a primary line of treatment. It is available as cream, oral suspensions, liquid and pastille (lozenge) form. The liquid dose is 5 milliliters four times a day for one or two weeks; it should be swished around the mouth slowly, for as long as possible (i.e., a few minutes) and then swallowed. One or two pastilles are taken four or five times a day for 7 to 14 days they should be dissolved in the mouth slowly and should not be chewed or swallowed whole. There is no significant drug interaction or side effects.

##### Amphotercin B

This drug is available as Lozenge (Fungilin 10mg) and oral suspension 100mg/ml which is to be applied 3 to 4 times daily. Amphotericin-B inhibits the adhesion of *Candida* to epithelial cells. The side effect of the drug is nephrotoxicity

##### Clotrimazole

This drug decreases fungal growth by inhibiting the synthesis of ergo sterol. It is not indicated for systemic infection. This drug is available in Creams and Lozenge 10mg. Main side effects of this drug is unpleasant mouth sensation, increases liver enzyme levels, nausea and vomiting.

##### Second line of treatment:

The second lines of treatment are used for severe, localized, immune suppressed patients and patients who respond poorly to primary line of treatment. Drugs mainly used in second line of treatment are,

Ketoconazole

Fluconazole

Itraconazole

##### Ketoconazole

It blocks ergosterol synthesis in fungal cell membrane and is absorbed from the gastro intestinal tract and metabolized in the liver. The dosage is 200-400 mg tablets once or twice daily for 2 weeks. Side effects are nausea, vomiting, liver damage and also it interacts with anticoagulants. Ketoconazole (as tablets) due to its potential liver toxicity is not introduced as initial therapy.

##### Fluconazole

This drug inhibits fungal cytochrome P450 sterol C-14 alpha demethylation. It is used in oropharyngeal candidosis and dosage is 50-100mg capsule once a

day for 2-3 weeks. Main side effects are nausea, vomiting and headache. It interacts with anticoagulants and this drug is contraindicated in pregnancy, liver and renal disease

#### **Itraconazole**

It is one of the broad spectrum antifungal agents and contraindicated in pregnancy and liver disease. The dosage of the drug is 100 mg capsule once a day for 2 weeks. The main side effects are nausea, neuropathy and rashes.

#### **Treatment for pregnant women**

Because many of the drugs used to treat fungal infections can be toxic to the developing fetus, only topical treatments-such as creams - are used when ever possible<sup>11,12</sup>.

### **LIFESTYLE AND HOME REMEDIES<sup>13</sup>**

To ease the pain, discomforts, and inconvenience of oral thrush, consider the following home remedies:

#### **Practice Good Oral Habits**

Brushing 22 at least twice a day and flossing at least once can cut down on the amount of time you have to suffer an oral thrush infection. Make sure to frequently replace your toothbrush until the infection is gone<sup>14</sup>.

#### **Natural Home Remedies for Oral Thrush**

Mix equal parts of a tincture consisting of liquorice, myrrh, and Echinacea. Use one teaspoon of this remedy as a mouthwash that is taken with water every three to four hours.

#### **Saltwater Rinses**

Add ½ teaspoon of salt into one cup of warm water. After the salt has dissolved, swish the rinse in your mouth and then spit out.

#### **Anti-Fungal Home Mouthwashes**

Blend warm water, cider vinegar and a pinch of salt to create a home remedy that fights fungus. Swish the wash around the mouth, making sure to reach all corners. Use it as a gargle for the throat.

#### **Garlic and Onions**

Tap into the antifungal power of onions and garlic, which can help kill candida in the mouth. Increase the amount of garlic used in your diet to eliminate yeast infection. Onions also help heal the white patches (lesions) found in the mouth.

#### **Yogurt**

Incorporate yogurt with live-acting cultures into your diet to boost the level of healthy bacteria in your mouth. Swish the yogurt about your mouth and then refrain from eating or drinking anything shortly afterwards.

#### **Thorough Cleaning**

If you wear dentures 23 and have thrush, cleaning your mouth and dentures each night is a must. Make sure to soak your dentures in a cleaner overnight. Rinse them well after removing from the solution<sup>24</sup>and before placing back into your mouth<sup>15</sup>.

### **PREVENTION**

The risk of getting oral thrush can be reduced by following the advice outlined below.

#### **Oral hygiene**

- Your chances of getting oral thrush are reduced if you keep your mouth clean and healthy. You can do this by,
- Rinsing your mouth after meals
- Visiting your dentist regularly for check-ups
- Eating a healthy balanced diet
- Keeping your dentures clean
- Brushing your teeth twice a day with a toothpaste that contains fluoride
- Flossing regularly
- Using a mouthwash as part of your routine.

#### **Denture hygiene**

If you wear dentures clean them every night before you go to bed. They can be done by brushing them with warm, soapy water and scrubbed with a nailbrush on the non-polished side of the dentures. Dentures can then be soaked in any liquid that can be used to sterilize babies' bottles. However, products containing bleach should not be used on dentures that contain metal. You should visit your dentist to correct dentures that do not fit properly. This can also reduce the risk of oral thrush and soreness underneath the dentures.

#### **Smoking**

Smoking encourages yeast in your mouth to grow and increases your chance of getting oral thrush.

### Topical or systemic corticosteroid or immunosuppressive treatment HIV infected/AIDS patients

Patients with CD4+ T lymphocyte counts below 200 cells/ $\mu$ L, who are not receiving a successful antiretroviral therapy. These patients are also at increased risk for oral candidosis, with potential regional extension and systemic dissemination. Antifungal prophylaxis may be needed to prevent candidosis in these patients.

### Asthma patients

Use inhaled corticosteroids as part of your asthma treatment; you can help prevent oral thrush by:

Rinsing your mouth with water after using your inhaler

Developing a good technique when you inhale corticosteroids by using a spacer<sup>16</sup>.

### CONCLUSION

Candida species are frequent members of the commensal oral micro flora of humans, they are opportunistic Pathogens can cause a spectrum of oral infection. C. albicans is the species most frequently implicated in oral candidosis, although other species are increasingly being encountered. The prevention of oral candidiasis will be less costly than the treatment of the oral and systemic diseases that occur as a consequence of poor oral health. The provision of effective oral care can make a huge difference to people's health, comfort, wellbeing and quality of life. In most of the cases, oral candidiasis is a cause of superficial infection which can easily be resolved with antifungal therapy.

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### CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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