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The Trio of Candida, Smoking and Oral cavity

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Abstract

Candida albicans is a yeast-like fungus. It is a very important cause of oral thrush. The probability of oral candidiasis increases in smokers. Conditions like HIV infection also enhance the chances of *Candida albicans* affecting the oral cavity and adjoining areas. This pathogen can be identified using conventional and newer methods. These have been detailed in a concise manner in this review article.

Keywords: Oral cavity, Smoking, Candida.

Introduction

Our oral cavity consists of many microorganisms including a number of bacterial species, along with fungi, protozoa and viruses. *Streptococcus sanguinis* and *S. salivarius* are most common microorganisms present. Among these microorganisms, *Candida albicans* is the most common yeast found in the oral cavity.

In a healthy person, *Candida albicans* is a normal, harmless commensal microorganism which colonizes the mucosal surfaces of the oral cavity. *C. albicans* is an opportunistic pathogen which exists in a balance with the host's immune system. Certain conditions, however, alter the immune system of the host or disbalance the oral ecosystem which can lead to an infection called oral Candididasis or oral thrush.

Common causes of Oral thrush: -

A. Medications

a. Antibiotics: -

Certain medications like broad spectrum antibiotics which kill the good bacteria and results in increase in the Candida counts.

b. Corticosteroids: -

Inhaled corticosteroids used for conditions like asthma and COPD can alter the microbial environment.

c. Immunosuppressant drugs: -

Medications like Methotrexate, cyclophosphamide and Azathioprine lower WBC count, creating a immunocompromised state that encourages *Candida* overgrowth.



B. Underlying health conditions: - They are also important. They are listed as follows: -

- (i) **Weakened immune system:** - Conditions like HIV, AIDS and some cancerous conditions makes hosts susceptible to oral thrush (1). The virus targets CD4+ and T-lymphocyte cells and destroy them, thus the body loses its ability to fight against Candida.
- (ii) **Diabetes:** - If diabetes is not controlled, high sugar level may cause immunosuppression. Studies show that high glucose levels make Candida more pathogenic. High blood sugar levels also impair function of WBCs (Neutrophils and Macrophages) which makes host harder to resist the attack of fungi.
- (iii) **Xerostomia (dry mouth):** - Decrease in salivary secretions leads to more growth of bacteria and fungi. Saliva contains natural antifungal agents like Histatins and beta-defensins which suppress fungal growth and adhesion.

Decreased salivary secretion provides a good environment for candida to grow.

Diminished Immunoglobulin A levels leads to increase in Candida growth.

Dryness reduces the pH and can thus cause microabrasions in the tissues, making *Candida* easier to transit from commensal to pathogenic state.

(i) Nutritional Deficiencies: -

Malnutrition or deficiency of nutrients like Iron, Folate or Vitamin B12 can lower defence systems of the body, which can result in *Candida* growth.

C. Lifestyle and Oral hygiene: -

1. **Dentures:** - Wearing ill-fitting dentures or failing to clear the dentures properly creates an ideal environment for yeasts to grow.
2. **Smoking:** - Excessive tobacco use can alter the oral environment and leads to increase in growth of *Candida albicans*. It is a major, independent risk factor for developing oral Candidiasis in adults.
Smoking in India is very common. About 14% of adults (about 100 million people) are tobacco smokers. In modern times nothing males and females smoke. About 1-4% people are female smokers. Nowadays smoking is of 3 types: - (i) Cigarette. (ii) Hookah. (iii) vapes or e-cigarettes.

- (i) Cigarettes mainly contain tobacco, paper, filter (made of mainly cellulose acetate), glues and inks. These, when

smoked, release chemicals like Formaldehyde, Arsenic, Benzene, Cadmium, Hydrogen cyanide etc.

- (ii) Moreover, e-cigarettes (vapes) are battery-operated devices that need a liquid and produce an aerosol. They typically contain Nicotine. It can also be used to deliver Cannabis and other drugs. It often comes in bright colours and flavours to attract people, like fruit, candy, menthol and mint.
- (iii) Hookah (sheeshe) contains mixture of shredded tobacco, sweetener, flavouring agent and glycerine.

Smoking, Candidiasis and Oral health: -

Smoking affects the pathogenicity of *Candida* spp., such as transition from yeast to hyphal form, virulence-related gene-expressions. Smoking is an excellent medium for all these processes.

Smoking induces the following: -

- (i) **Impaired immune response:** - It suppresses the immune defense of the oral cavity and hampers the inflammatory responses to suppress fungal infections. More care should be taken for immunocompromised patients.
- (ii) **Mucosal changes:** - Tobacco damages the delicate epithelial barrier of the mucosa and increases the thickness of the keratin layer, creating an ideal environment for the opportunistic fungal growth. E-cigarettes lead to death of oral epithelial keratocytes and periodontal fibroblasts. The cytotoxic effects of e-cigarette are caused by the generation of oxidative stress and increase in the release of proinflammatory cytokines.
- (iii) **Salivary changes:** - Immunoglobulins like IgA controls yeast growth. Smoking reduces the salivary flow, resulting in decreased production and protective qualities of the immunoglobulins. Chemical compounds found in tobacco dissolved in salivary, leading to disorders in its chemical composition.
- (iv) **Biofilm formation:** - Pure nicotine at minimum inhibitory concentration (4 mg per ml) prevents *C. albicans* growth but enhanced biofilm formation is seen at 0.1 mg per ml. Nicotine and smoke condensates directly increase *Candida* adhesion and biofilm formation, making treatment difficult as it is more resilient to treatment (2).

Clinical features: -

1. **White patches:** - Creamy, slightly raised spots resembling "cottage cheese" can be seen on buccal mucosa, tongue and palate in oral candidiasis (3).
2. **Redness/ soreness:** - Red, inflamed and painful areas under dentures and oral mucosa are seen.

3. Scraping test: - When scraped with swab, these white patches leave behind red, tender surfaces that may bleed easily.

Microscopic examination:-

- a. Staining: - Sample is stained and Periodic-acid Schiff (PAS) stain is done, which is visible under light or fluorescent microscope.
- b. KOH preparation: - Here the sample is placed on a slide with 10% KOH solution. This shows budding yeasts and root-like structures (hyphae and pseudohyphae).

Laboratory culture: -

Sabouraud's Dextrose agar (SDA) is the fungal growth medium that shows creamy white colonies of *Candida* spp.

Germ tube test: - This is the most ideal test to identify *Candida albicans*. It yields positive results (4).

Terminal chlamydospores are produced on corn meal agar with or without Tween-80 (Dalmau technique using slit inoculation) (5). Figure of terminal chlamydospore is shown below.

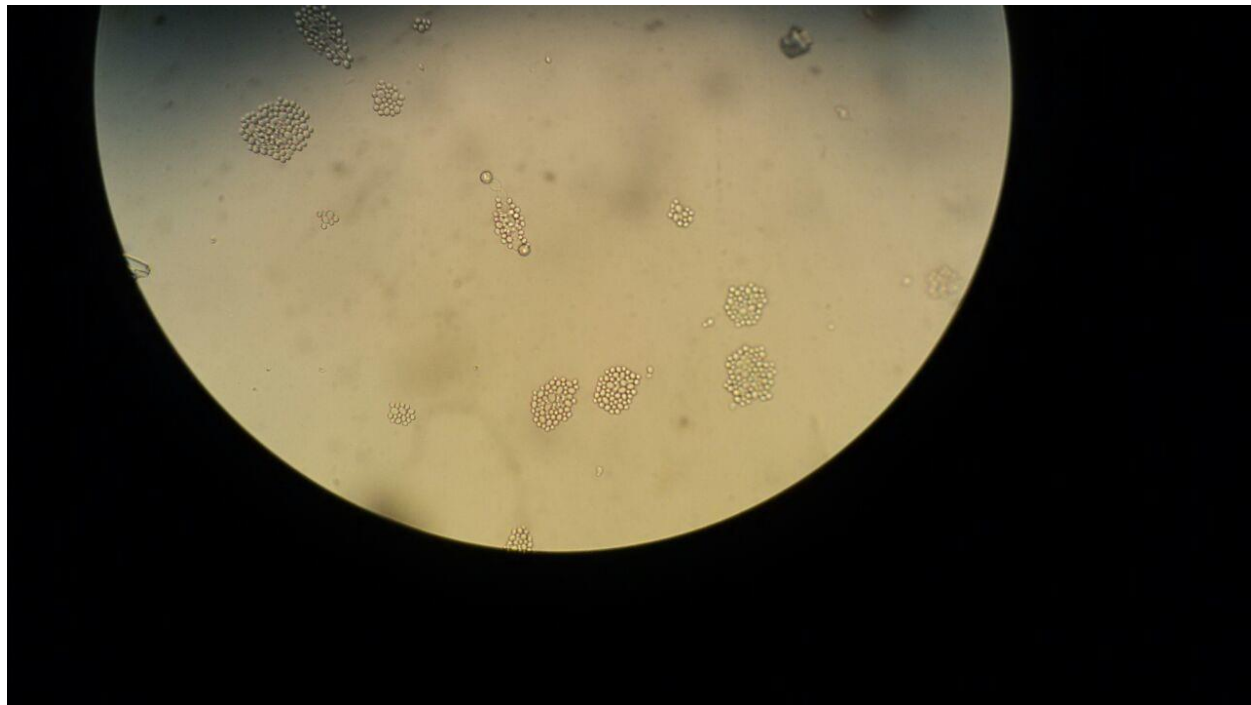


Fig. 1: - Terminal chlamydospores of *Candida albicans* in

Dalmau technique (image: -author)

The figures below show oral lesions and vaping devices.



Fig. 2. Oral candidiasis. (Source: - Internet)



Fig. 3: - electronic smoking devices (vaping devices). Source: - Internet



Advanced Molecular techniques

1. Polymerase chain reaction: - PCR (Polymerase chain reaction) is used to amplify genes and makes many copies of a specific targeted segment of DNA.
2. MALDI-TOF (Matrix Assisted Laser Desorption Ionization-Time of Flight) Mass spectrometry: - This is used to rapidly identify and characterize biomolecules like proteins, peptides, lipids and microorganisms, by measuring their mass-to charge ratio, from isolated colonies (6).

Prevention

1. Quitting or lowering the frequency of smoking.
2. Maintaining good oral hygiene, like brushing twice daily, toothbrush, using mouthwashes (as advised by dentist), cleaning dentures regularly.
3. Maintaining hydration.
4. Probiotics can help inhibit the infection-causing yeasts.
5. Regular check-ups every 6 months can help prevent Candidiasis (oral thrush) (7).

Treatment of oral Candidiasis

- A. Antifungal mouth washes like Nystatin and Nystatin oral suspension may be used (8). Lozenges like Clotrimazole also work well.
- B. If topical treatment does not respond, Fluconazole or Itraconazole can be given.
- C. Supportive home care like salt in warm water can be given as mouth rinse (9).
- D. Dietary support like Vitamin C (to boost immune system) and probiotics can be contemplated (10).
- E. Eradicating any underlying causes like taking excessive broad-spectrum antibiotics and ill-fitting dentures should be accorded due importance.

Cigarette smoke exerts marked effects on saliva, oral commensal bacteria as well as fungi (11). Cigarettes smoking also suppresses the protective immune response to *C. albicans* in rats occurring via the NLRP3 (NOD-like receptor family pyrin domain containing 3) inflammasome (12). Smoking is known to induce oxidative stress and redox dysfunction in the milieu of the oral mucosa (13). Thus, a complex interplay of many factors determines the effect of Cigarette smoking on oral mucosa and the future development of oral Candidiasis.

Conclusion

The fungus *Candida albicans* causes oral thrush, plaque-like oral lesions and even premalignant lesions like chronic mucocutaneous Candidiasis. Smoking plays a very important role in the pathogenesis of *Candida* spp., by enhancing its adhesion to the oral cavity. Diagnosis relies upon various old

and new methods. Awareness and prompt management are important for control.

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