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REVIEW ARTICLE

An Opportunistic Infection: Oral Candidiasis

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ABSTRACT

Oral candidiasis is a potentially malignant oral disorders caused typically by yeast like fungus candida albicans and also by some non-albicans candida. Normally, these are the commensal inhabitant and commonest isolated species of the oral cavity, vagina & gastrointestinal tract.But it can act as an opportunistic pathogens when immunological defences and host's physical are altered. Therefore, Oral candidiasis is associated up to 90% of patients suffering from Human immuno-deficiency virus (HIV) as their immune system is compromised. Pathogenesis of oral candidiasis involves yeast overgrowth and penetration in the oral epithelium followed by invasion in tissue by fungal hyphal supported by released of hydrolytic enzymes, formation and contact sensing. Clinically, there are multiple subtypes of candidiasis but commonly presented as white curd like removable plaque. Essential techniques that are employed for the diagnosis of candidal infections not only involves clinical examination but, also supplemented by smear, culture & immunological techniques. Although nystatin and amphotericin B were the most drugs used locally, whereas fluconazole for systemic treatment.

Keywords: Antifungal Drug, Calco-fluorescent-stain, Candida albicans, Immunosuppression, Sabouraud's agar.

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INTRODUCTION

The most frequent opportunistic infection found in the oral cavity due to impaired immunity and several predisposing factor is the oral candidiasis or thrust. It is a potentially malignant oral disorder(PMD) that demonstrated a higher risk of developing cancer.[1] The causative agent of these infectious condition is typically, Candida albicans and non-albicans Candida (C. tropicalis, C. glabrata, C. parapsilosis, C. dubliniensis) which is considered to be the most frequent commensal organism that are isolated from oral cavity.[2,3] But, the potential of Candida albicans to become a pathogenic organism from harmless organism occur when there is imbalance of the host immune system of individual and certain predisposing factors producing various forms of candidiasis.[4]**(Figure 1)** The group of diseases such as individuals with HIV/AIDS, consumption of immunosuppressive drugs, radiation, hyposalivation andchemotherapy for cancer treatment, diabetics and frequent use of antibiotics increases the risk.[5]**(Figure 2)** The most prevalent presented symptoms that have been seen may include pain, burning sensation, and dysphagia. Pathogenesis involves several specific adherence interactions between C. albicans and to complement receptors of oral epithelial surfaces along with colonization of Fungai.[6] Further penetration of fungal hyphe into the tissue by formation of different extracellular matrix proteins, hydrolytic enzymes and specific sugar residues displayed on host surface.[7]**(Figure 3)**

The present study highlights a literature review of the oral candidiasis providing various risk factors, pathogenesis, various clinical subtypes, therapeutic management and its objectives is to establish appropriate treatment without neglecting it.

Infection is caused
by Candida species, typically, Candida albicans. The candidiasis is seen orally in people with altered oral ecology (from dental
appliances, hyposalivation, or the use of immunosuppressants or antimicrobials) and/or impaired immunity (e.g., transplant
recipients, persons on immunosuppressive treatments, persons with HIV/AIDS, or other cellular immune defects)

Classification

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Proposed Revised Classification of Oral Candidiasis	
(A) Primary Oral Candidiasis (Group I)	
Acute	Pseudomembranous, Erythematous
Chronic	Hyperplastic, Erythematous, Pseudomembranous
Candida Associated Lesion	Denture stomatitis, Angular stomatitis, Median rhomboid glossitis
Keratinized Primary Lesion Super Infected With Candida	Leucoplakia, Lichen planus, Lupus erythematous
(B) Secondary candidiasis (Group II)	Manifestation of Systematic mucocutaneous candidiasis – Thymic aplasia and Candida Endocrinopathy Syndrome.

Figure 1: Classification of oral candidiasis. [8]

Risk Factors

Local host factors	Denture wearing, Steroid inhaler use, Reduced salivary flow, High sugar diet.
Systemic host factors	Extremes of age, Endocrine disorders (e.g. Diabetes), Immunosuppression, Receipt of broad spectrum antibiotics, Nutritional deficiencies.

Figure 2: Predisposing factors associated with OralCandidiasis. [9]

Pathogenesis

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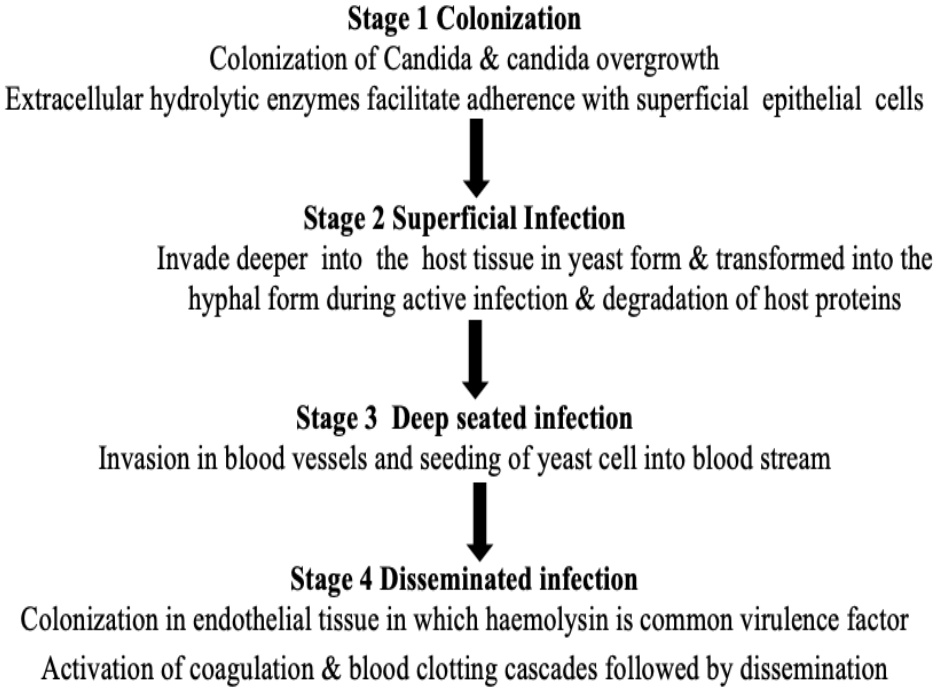

Figure 3: Pathogenesis of Candida

Forms of Oral Candidal Infection

(A) Primary Oral Candidiasis

I Pseudomembranous Candidiasis

This is the commonest subtype of candidiasis which is acute, typically frequent in immune-compromised individuals principally AIDS, diabetics, patients on immunosuppressive drugs & consumption of broad spectrum antibiotics.[10]

Mucosal surface lesions usually appear as whitish-yellow cream which is generally scrapable plaques similar to milk curd.[11] The components that form this superficial layer is desquamated epithelial cells, fibrin, fungal hyphal aggregates and various necrotic material. Removal of superficial pseudo-membrane with cotton gauze results in erythematous subsurface area.[12] The tongue, hard and soft palate, labial and buccal mucosa, and oropharynx are among the oral surfaces that are often affected.[13]**(Figure 4)**

II Erythematous Candidiasis

Erythematous candidiasis is also called as 'antibiotic sore mouth' because of the correlation to long-term usage of wide antibiotics and is sparsely seen. Clinically, the lesions often appear as de-papillated patches may be as bright red on the dorsum of the tongue similar to observed with low B12 serum. Interestingly, this is the only subtype of candidiasis which give the symptom of pain. Individuals with HIV frequently exhibit on dorsum of the tongue along with palate and rarely on buccal mucosa.[14]**(Figure 5)**

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III Hyperplastic Candidiasis

This is the chronic subtype of oral candidiasis which is often appearing bilaterally commissural region on the buccal mucosa & the lateral boundaries of the tongue. Clinically, it is recognised as speckled or homogenous white lesions therefore sometime it is also called as candidal leukoplakia.[15] This form of candida infection is strongly associated with smoking with capacity to transform into dysplasia or malignancy. Therefore, such lesion might be mistaken for squamous cell cancer, pemphigoid/pemphigus and lichen planus. Contrasting to the pseudomembranous subtype, this form of lesions cannot be scraped off.[16] **(Figure 6)**

IV Denture Stomatitis

This subtype is also called as chronic atrophic candidiasis where lesion is generally limited to the denture bearing area that causes mucosal inflammation.[17] The associated lesion is chronic, frequently associated with hard palate and mandibular area. Poor dental hygiene habits, poorly fitting prosthetics and decreased salivary flow are some factor responsible for such condition.[18]**(Figure 7)**

V Angular Cheilitis

Typically, this subtype of candidiasis presented as an erythematous fissuring bilaterally at corners of the mouth. Also, staphylococci and streptococci are other reservoir microbes that have been identified.[19] The predisposing factor for such infectious condition include especially older individual and resorption of ridges due to long term use of denture.[20]**(Figure 8)**

VI Median Rhomboid Glossitis

Median rhomboid glossitis is a chronic subtype which is closely correlated to smoking and the use of inhaled steroids. It is widely situated at the dorsum of the tongue's midline anterior portion of circumvallate papillae as well demarcated depapillated area. In most the instances the area is asymptomatic whereas some individuals may report discomfort and irritation.[21]**(Figure 9)**

(B) Secondary Oral Candidiasis

This infectious condition is a chronic form manifested by candida infections of the oral mucosa reported in about 90% of the cases including cutaneous, nail beds and vulvo-vaginal Candidiasis. It is related to a variety of immunodeficiency illnesses, including Addison's disease, Di George syndrome, hypoparathyroidism and SCID syndrome etc.[22]

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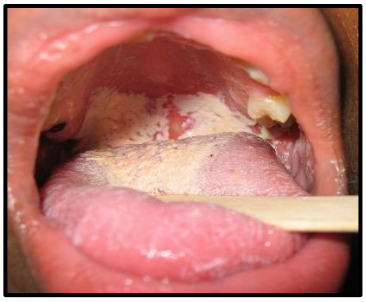

Figure4: Pseudomembranous candidiasis.

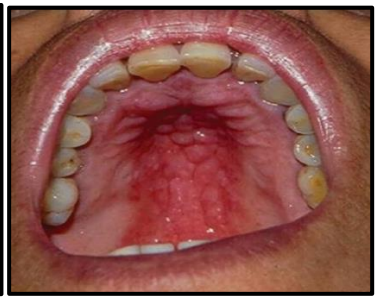

Figure 5: Erythematous candidiasis.

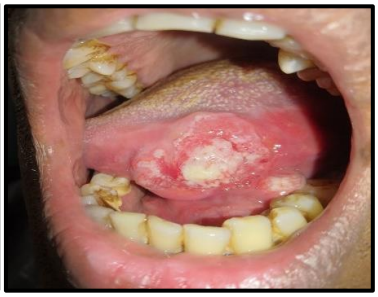

Figure 6: Hyperplastic candidiasis.

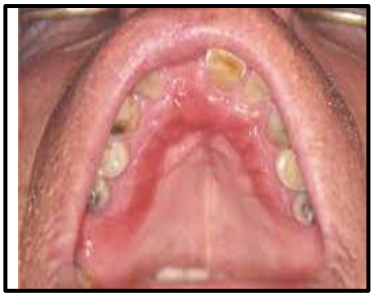

Figure 7: Denture stomatitis.

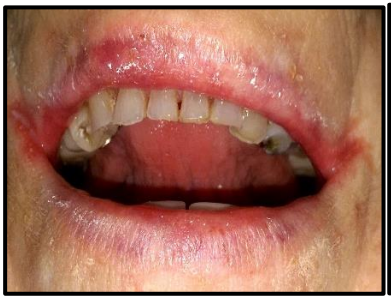

Figure 8: Angularcheilitis.

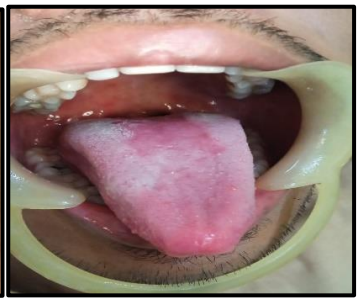

Figure 9: Median rhomboid glossitis.

Laboratory Diagnosis

(A) Physiological Tests

The capacity of a Candida species to assimilate and ferment various carbon and nitrogen sources, as well as the production of a germ tube in the presence of human serum or egg white, are required for confirmation diagnosis.[23]

(B) Culture

When collected swabs are seeded on Sabouraud's dextrose agar with antibioticswhich is regularly used culture medium at 25°C for 3-4 daysand on blood agar at 37°C they enable distinction of yeasts which is visualised as cream colonies.[24]

(C) Direct Microscopy

Identification of Candida speciestypicallyinvolvespreparationof smear from the lesions localized to the oral cavity after treating with 10% potassium hydroxide (KOH) and KOH-Calco-fluorescent-stain. In 10% KOH the epithelial components dissolve so that remaining candida can be visualised as septate hyphae or yeast cells with dichotomous branching whereas KOH-Calco-fluorescent-stain method fluoresce fungal elements.[25] The prepared smear stained either by the gram stain or by the periodic acid Schiff technique or Gridley-Gomori-methenamine silver in which candidal hyphae and yeasts impart either dark blue or red/purple or black colour respectively.[26]

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(D) Biopsy

When chronic hyperplastic candidiasis is suspected then additional biopsy for microscopical examination is indeed the diagnostic tool to observe dysplastic features. Based on the clinical form of candidiasis, histopathologic appearance might change.[27] The characteristic feature is hyperplastic epithelium with a superficial parakeratotic desquamating layer with penetration of hyphae, or pseudo-hyphae to the depth of the stratum spinosum Along with this, inflammatory cell infiltration chiefly polymorphonuclear cells is appreciated in the epithelium and lamina propria.[28]

(E) **Immunological and Genetic Method**

Specific diagnosis of invasive candidiasis may be obtained by immunologic (ELISA) and genetic techniques(Hybridization based detection method).[29] So,the correct diagnosis of pathogenic organisms may be collected in a few minutes with the useof specific antibodies and by Candida antigens to test delayed skin hypersensitivity.[30]

Treatment

The prognosis of these infectious condition is almost always good which require prevention or suitable treatment. The most important factor in the management of candida infection that plays a crucial role is appropriate assessment of predisposing factors.[31] These can be acquired through proper detailed medical history and its evaluation. This are usually corrected as soon as possible by maintenance of oral hygiene by use of antimicrobial mouthwashes, adequate denture cleansing, scaling & tooth brushing along with cessation of smoking and stoppage of corticosteroid or antibiotic use.[32]

Mostly the infection which are uncomplicated can be managed with topical antifungal therapy, such as nystatin, miconazole, Gentian violet or amphotericin B as a first line treatment. However, the principle means of administration in oral infection include topical application in the form of lozenges and oral suspensions. Moreover, in some instances the topical agents may not be effective such as in chronic mucocutaneous candidiasis & patients intolerant in which systemic administration of medications (fluconazole) may be beneficial feasible option. Other possible recommended strategies include surgical excision of lesions if they do not respond to antifungal agents.[33]

CONCLUSION

C. albicans is a typical commensal found in the oral mucosa which is the third most frequent cause of nosocomial bloodstream infection but its virulence factors play a significant role in morbidity and death dueto candidal infection. As these infectious condition most often appear due to predisposing factors it is important to resolve it before it become complicated. So, depending on the severity of the infection, either topical or systemic anti-fungals are used for suitable treatment.

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