JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

ORAL CANDIDIASIS – A REVIEW

[1]Dr. Desika Palanimuthu, [2]Dr. Mathumala Subramanian, [3]Dr. G. Keerthana,

[4]Dr. P. Karthika, [5]Dr. M. Sathish kumar

[1]CRI, [2,3]Post graduate, [4]Professor, [5]Head of the department

Department of Oral and Maxillofacial Pathology

Karpaga Vinayaga Institute of Dental Sciences

Chengalpet ,India

ABSTRACT

Oral candidiasis, commonly known as thrush, is a prevalent opportunistic fungal infection of the oral cavity primarily caused by an overgrowth of Candida species, especially Candida albicans. This condition manifests in various forms, including acute pseudomembranous, erythematous (atrophic), and hyperplastic types, each presenting distinct clinical features. Predisposing factors encompass extremes of age, immunosuppression, prolonged antibiotic or corticosteroid use, denture wearing, and systemic conditions like diabetes. Diagnosis typically involves clinical examination and may be confirmed through microbiological tests. Management strategies include addressing underlying predisposing factors and administering antifungal therapies, with the choice of treatment tailored to the specific clinical presentation and patient needs.

Key words: Candida albicans, steroids, fungal infections.

INTRODUCTION

Research indicates that oral candidiasis, first reported by Veilleux in 1838, is precipitated by Candida albicans overgrowth in immunocomprmised individuals, highlighting the interplay between host immunity and fungal pathogenesis.

Oral candidiasis, also referred to as oral thrush, is a fungal infection of the oral mucosa caused predominantly by Candida albicans. As an opportunistic pathogen, Candida species are commensal organisms in the human microbiome, but they can become pathogenic under certain conditions. This infection commonly affects individuals with compromised immune systems, such as those with HIV/AIDS, cancer patients undergoing chemotherapy, or individuals on long-term antibiotic or corticosteroid therapy. Other predisposing factors include diabetes, malnutrition, and denture use[1].

Oral candidiasis presents in diverse clinical forms, such as pseudomembranous, erythematous, and hyperplastic variants, each characterized by unique symptoms and visual manifestations. While the infection is typically mild, untreated cases can lead to discomfort and complications, particularly in immunocompromised individuals. Diagnosis involves clinical assessment and laboratory confirmation through fungal cultures or microscopy. [2]

Oral candidiasis is commonly linked to local immunosuppression, particularly from inhaled corticosteroids used to manage asthma and chronic obstructive pulmonary disease (COPD), which can suppress oral cavity immunity and increase susceptibility to infections. Acute pseudomembranous candidiasis, or thrush, is the most prevalent form, characterized by white plaques that can be wiped away to reveal an inflamed, red surface.[3]

Other forms of oral candidiasis present as white lesions, such as chronic hyperplastic candidiasis, or red lesions, including acute and chronic erythematous candidiasis, angular cheilitis, median rhomboid glossitis, and linear gingival erythema. While rarer types like cheilocandidiasis, chronic mucocutaneous candidiasis, and chronic multifocal candidiasis exist, they are beyond the scope of this discussion. Accurate diagnosis and effective management are essential, especially for individuals on inhaled corticosteroids or other immunosuppressive therapies[4].

Candida albicans is a normal commensal organism in the mouth and typically does not cause issues in healthy individuals. However, overgrowth can result in local symptoms such as discomfort, altered taste, and dysphagia due to esophageal involvement, which may lead to poor nutrition, delayed recovery, and prolonged hospital stays. [5]

ETIOLOGY

Candida species, predominantly Candida albicans, are the primary causative agents of oral candidiasis, accounting for over 80% of lesions. Candida albicans exhibits polymorphism, existing as both hyphal and yeast forms in response to environmental cues.

Besides Candida albicans, other Candida species implicated in oral candidiasis include Candida glabrata, Candida tropicalis, and others. Notably, non-albicans Candida species exhibit a higher colonization frequency in patients aged 80 and above compared to younger individuals.

Candida species are a natural component of the oral microbiome in immunocompetent individuals. Prevalence studies indicate that a significant proportion of adults (30-60%) and infants (45-65%) harbor Candida species in their oral cavities, primarily as commensal organisms.[6]

Pathologic colonization of Candida is facilitated by various risk factors, including malnourishment, age extremes (pediatric and geriatric populations), metabolic disorders, immunocompromising conditions, concurrent infections, radiation therapy, organ transplantation, prolonged corticosteroid use, antibiotic treatment, and salivary gland hypofunction.[7]

RISK FACTORS

PATHOGEN

Candida, a fungus first isolated in 1844, is characterized as a non-photosynthetic, eukaryotic organism with a cell wall external to the plasma membrane. The plasma membrane contains significant amounts of ergosterol. Candida species exhibit similar cultural characteristics and can metabolize glucose under aerobic and anaerobic conditions.

Several pathogenic variables associated with Candida infection. Key factors facilitating Candida adhesion to epithelial cells include fungal cell wall components (mannose, C3d receptors, mannoprotein, and saccharins), hydrophobicity, and fibronectin binding. Additional factors contributing to infection include germ tube formation,

mycelia presence, intracellular persistence, endotoxins, tumor necrosis factor induction, and proteinase activity. Phenotypic switching in C. albicans has also been implicated.[8]

HOST

LOCAL FACTORS

Impaired salivary gland function is a predisposing factor for oral candidiasis. Saliva's dilutional effect and mechanical removal of organisms from the mucosa play a crucial role in preventing infection. Antimicrobial proteins in saliva, including lactoferrin, sialoperoxidase, lysozyme, histidine-rich polypeptides, and anticandida antibodies, interact with the oral mucosa to prevent Candida overgrowth.

Studies have elucidated the association between inhaled steroid use and increased susceptibility to oral candidiasis, suggesting immunosuppressive effects on cellular immunity and phagocytosis. Reversibility of local mucosal immunity upon cessation of inhaled steroid therapy underscores the importance of monitoring and adjusting treatment regimens.[9]

Oral cancer/leukoplakia and high carbohydrate diets as additional risk factors for oral candidiasis. The presence of glucose in saliva promotes Candida growth, while a high carbohydrate diet enhances its adherence to oral epithelial cells, underscoring the importance of dietary considerations in oral health.[10]

SYSTEMIC FACTORS

Individuals at extremes of life, including the elderly and young children, are more susceptible to infection due to compromised immune function.

Broad-spectrum antibiotics can disrupt the local oral flora, creating an environment conducive to Candida proliferation. Upon discontinuation of antibiotics, the normal oral flora is typically restored. Additionally, immunosuppressive drugs, including antineoplastic agents, have been shown to predispose individuals to oral candidiasis by altering the oral flora, disrupting the mucosal surface, and modifying salivary characteristics.

Additional factors that contribute to the development of oral candidiasis include smoking, diabetes, Cushing's syndrome, immunosuppressive conditions such as HIV infection, malignancies like leukemia, and nutritional deficiencies, particularly vitamin B deficiencies. Studies have reported a significant incidence of oral candidiasis in immunosuppressed individuals, with rates ranging from 15% to 60% in those with malignancies and 7% to 48% in those with HIV infection.[11]

EPIDEMIOLOGY

Oral candidiasis exhibits a homogeneous distribution across genders. The condition is predominantly observed in neonates and infants, with a distinct pattern of incidence. Notably, oral candidiasis is rare in the first week of life, peaks during the fourth week, and subsequently declines in infants over six months old, likely due to the development of host immune competence.[12]

PATHOPHYSIOLOGY

In healthy individuals, the immune system and commensal bacterial flora effectively inhibit Candida growth. However, immunosuppression resulting from conditions such as diabetes, denture use, steroid therapy, malnutrition, vitamin deficiencies, and recent antibiotic use can disrupt this balance, leading to Candida overgrowth and disease.[12]

HISTOPATHOLOGY

The diagnosis of Candida infections typically involves the use of two complementary methods: 10% potassium hydroxide stain, which facilitates the visualization of fungal elements, and culture on Sabouraud dextrose agar, which enables the isolation and identification of Candida species.[13]

The identification of Candida species can be refined using specialized culture media, such as Chromagar Candida. Moreover, molecular diagnostic techniques, including ELISA and PCR, are utilized in cases of invasive candidiasis and to distinguish between Candida dubliniensis and Candida albicans.

HISTORY AND PHYSICAL

Pseudomembranous candidiasis, or oral thrush, is the prototypical presentation of oral candidiasis, although various other manifestations have been documented. Clinically, oral candidiasis can manifest as white or erythematous lesions within the oral cavity.

The clinical manifestations of oral candidiasis encompass a range of lesions, including pseudomembranous and hyperplastic white lesions, as well as erythematous lesions, which comprise atrophic lesions in acute and chronic forms, angular cheilitis, median rhomboid glossitis, and linear gingival erythema.[13]

Beyond the primary categories of oral candidiasis, several rare and distinct entities have been recognized, including cheilocandidiasis, chronic mucocutaneous candidiasis, and chronic multifocal candidiasis, which exhibit unique clinical features and presentation.[14]

ACUTE PSEUDOMEMBRANOUS CANDIDIASIS

Pseudomembranous candidiasis is the most frequently encountered manifestation of oral candidiasis, comprising approximately one-third of cases. This condition predominantly affects vulnerable populations, including newborns, immunocompromised individuals, and the elderly. Furthermore, the use of topical steroids and decreased salivary flow have been identified as additional risk factors.

Pseudomembranous candidiasis typically presents with widespread white patches that can be readily removed with gauze, revealing an underlying erythematous mucosal surface. Histologically, the pseudomembrane is composed of desquamated epithelial cells, fibrin, and fungal hyphae. The lesions commonly occur on the tongue, labial and buccal mucosa, gingival tissues, hard and soft palate, and oropharynx, and are often asymptomatic. However, when symptomatic, patients may report a burning sensation, oral bleeding, and altered taste perception.[15]

HYPERPLASTIC CANDIDIASIS

Hyperplastic candidiasis presents with distinctive clinical features, including slightly elevated, well-circumscribed white plaques situated on the buccal mucosa, potentially extending to the labial commissures. Additionally, the lesions can exhibit nodular or spotted morphologies. A key differentiating feature of hyperplastic candidiasis is the presence of adherent lesions that are resistant to removal.

Hyperplastic candidiasis is associated with an increased risk of malignant transformation, with potential progression to severe dysplasia or frank malignancy. Furthermore, Candida infection in leucoplakia lesions has been demonstrated to elevate the risk of malignancy compared to non-candidal leucoplakias.[15]

ACUTE ATROPHIC CANDIDIASIS

Acute atrophic candidiasis is characterized by the presence of generalized or localized erythematous lesions on the oral mucosa, with a notable propensity for the palatal region. Additionally, the condition may also manifest on the buccal mucosa and the dorsal surface of the tongue.

The clinical presentation of acute atrophic candidiasis may include atrophy of the tongue papillae, accompanied by erythema. Patients frequently report a burning sensation in the mouth or tongue, prompting medical consultation and necessitating consideration in the differential diagnosis of glossodynia.

Acute atrophic candidiasis is frequently observed as a secondary complication of broad-spectrum antibiotic therapy. Nevertheless, a range of additional risk factors have been implicated, including corticosteroid administration, HIV disease, iron deficiency anemia, vitamin B12 deficiency, and uncontrolled diabetes mellitus.[15]

CHRONIC ATROPHIC CANDIDIASIS

Chronic atrophic candidiasis, alternatively known as denture stomatitis, presents as localized erythema of the oral mucosa in the denture-bearing area. Epidemiological studies have reported a significant incidence of this condition, with estimates ranging up to 65%. The clinical presentation of chronic atrophic candidiasis is marked by edematous and erythematous lesions, which are typically limited to the mucosal area in direct contact with the denture. Interestingly, angular cheilitis frequently co-occurs with chronic atrophic candidiasis, suggesting a potential link between these two conditions.

The clinical manifestation of denture stomatitis can be stratified into three distinct categories. Type I is distinguished by petechial hemorrhage and localized inflammatory response, whereas Type II is characterized by erythema of the mucosa subjacent to the denture. Type III is notable for erythema of the central hard palate or papillary hyperplasia of the oral mucosa under the denture. While often asymptomatic, patients may report a sore mouth or oral burning sensation.[15]

MEDIAN RHOMBOID GLOSSITIS

Median rhomboid glossitis is a rare and distinctive manifestation of oral candidiasis, affecting a small fraction of the population. Clinically, it presents as a well-defined, rhomboid-shaped erythematous patch situated centrally on the tongue's dorsum, anterior to the circumvallate papillae. Histopathologically, the lesion is characterized by atrophy of the filiform papillae. Epidemiological studies have identified smoking and inhaled steroid use as significant risk factors for the development of this condition.[16]

The development of a concomitant erythematous lesion on the palate, forming a "kissing" lesion with the lingual lesion, has been observed. This phenomenon is frequently associated with immunosuppression and may serve as a potential surrogate marker for HIV infection, highlighting the need for comprehensive diagnostic evaluation.[17]

ANGULAR CHELITIS

Angular cheilitis is characterized by the presence of erythematous, fissured patches at one or both commissures of the mouth, with bilateral involvement being the typical presentation.

Angular cheilitis is characterized by painful and sore lesions. The humid microenvironment created by saliva accumulation in the corners of the mouth facilitates the growth of Candida. Notably, bacterial species, including Staphylococcus aureus and streptococcal species, are also commonly isolated from the lesions[18].

LINEAR GINGIVAL ERYTHEMA

Linear gingival erythema is a specific type of gingival pathology that is frequently encountered in HIV-positive individuals. Interestingly, the presence and severity of LGE may correlate with the progression of HIV disease.

Linear gingival erythema is a clinical entity that can manifest in both immunocompetent children and immunocompromised individuals. Characteristically, the lesion presents as an erythematous line or band situated along the gingival margins of one or more teeth. The pathogenesis of linear gingival erythema involves the interplay of Candida and bacterial infections.[15]

EVALUATION

The diagnosis of oral candidiasis is primarily clinical, entailing a comprehensive examination, medical history, and risk factor assessment. Characteristic lesion morphology, differential diagnosis exclusion, and treatment response evaluation are integral to confirming the diagnosis. The clinical presentations of acute atrophic candidiasis and chronic hyperplastic candidiasis may overlap with those of premalignant or malignant lesions, highlighting the importance of supplemental biopsy in conjunction with empirical antifungal therapy. When antifungal therapy proves ineffective, microbiological cultures and sensitivity testing can provide valuable insights into the underlying etiology, informing subsequent treatment strategies. A range of sampling methods has been developed to detect Candida species in the oral cavity. Method selection is largely determined by clinical presentation.[19]

In addition to confirming candidiasis, testing to diagnose an underlying immunocompromising condition should be considered. Patients may be tested for diseases such as HIV, adrenal insufficiency, malnutrition, steroid use, and diabetes mellitus.[18]

MANAGEMENT

The therapeutic approach to oral candidiasis involves targeted antifungal interventions, calibrated to the patient's specific needs based on the extent of involvement and immunosuppressive status. Topical antifungal therapy constitutes first-line treatment for uncomplicated presentations, with concurrent administration alongside systemic therapy when warranted.

The administration of systemic antifungal therapy is generally restricted to patients who demonstrate a lack of response to topical treatments, those who exhibit adverse reactions to topical therapies, and individuals possessing risk factors that predispose them to the development of systemic mycoses.

The therapeutic management of mild oral candidiasis primarily involves the use of topical antifungal agents, supplemented by rigorous oral hygiene practices. A range of topical antifungal medications is available, including nystatin, miconazole, clotrimazole, and ketoconazole.[19]

The high sucrose content of nystatin oral rinse and clotrimazole troches may pose a drawback for certain patient populations. In such cases, triazole antifungals, including fluconazole and itraconazole, offer a viable alternative, with the convenience of once-daily dosing.

In cases of oral candidiasis associated with diabetes mellitus, or when there is an elevated risk of dental caries, alternative antifungal agents with lower sucrose content are recommended.[20]

In cases of mild or initial oral candidiasis presentation, topical therapeutic interventions are indicated. Clotrimazole troches (10 mg, five times daily) and nystatin oral suspension (100,000 units/mL, 5 mL four times daily) represent two established treatment options.[21]

Moderate to severe oral candidiasis necessitates more aggressive treatment, for which fluconazole is recommended. The regimen entails an initial dose of 200 mg orally, followed by a maintenance dose of 100 mg orally once daily for 7 to 14 days. Importantly, existing evidence supports the safety of fluconazole during lactation.[22]

Notably, a single 150 mg oral dose of fluconazole has been shown to be efficacious in patients with advanced cancer, offering a simplified treatment regimen that mitigates pill burden.[23]

MANAGEMENT OF DENTURES

The importance of denture hygiene cannot be overstated in the treatment of denture stomatitis and, indeed, all manifestations of oral candidiasis.[18]

By maintaining proper denture hygiene, individuals can effectively eradicate Candida colonization from their dentures, thereby eliminating a potential reservoir for fungal infection.[19]

To prevent Candida colonization and mitigate the risk of denture stomatitis, patients are advised to maintain rigorous denture hygiene practices. This includes daily cleaning and disinfection of dentures, as well as removing them for a minimum of six hours nightly.[18]

Optimal denture disinfection can be achieved through soaking in chlorhexidine solution, followed by air drying. This dual approach effectively reduces Candida colonization, as air exposure has been shown to inhibit Candida growth on denture surfaces.[19]

The management of denture stomatitis, topical application of miconazole to the internal surface of dentures, subsequent to cleaning and disinfection, has been shown to be an effective therapeutic strategy.

The combination of nystatin and chlorhexidine digluconate is contraindicated due to their antagonistic interaction, which results in the inactivation of both agents and a subsequent loss of therapeutic effectiveness.[19]

SPECIFIC CONSIDERATIONS

ACUTE PSEUDOMEMBRANOUS CANDIDIASIS IN INFANTS

The therapeutic approach to acute pseudomembranous candidiasis in breastfed infants involves the concurrent administration of topical antifungal agents to both the infant and the mother's nipples, irrespective of maternal symptomatology. In cases where the mother's nipples exhibit signs of thrush, adjunctive systemic antifungal therapy with fluconazole is typically prescribed.[24]

The therapeutic regimen for oral candidiasis in breastfed infants and their mothers typically involves the topical administration of nystatin oral suspension to the infant's oral lesions. Additionally, miconazole 2% cream is applied to the mother's nipples, albeit as an off-label indication for the treatment of oral candidiasis in lactating women.[25]

ACUTE ERYTHEMATOUS CANDIDIASIS

A significant proportion of acute erythematous candidiasis cases are attributed to the use of antibiotic therapy. Notably, discontinuation of the offending antibiotic agent typically results in spontaneous resolution of the candidiasis, thereby eliminating the need for additional therapeutic measures.

In instances where symptoms of acute erythematous candidiasis are more pronounced, systemic fluconazole may be prescribed at a dosage of 50 mg once daily for a duration of one week.[18]

ANGULAR CHELITIS

The treatment regimen for angular cheilitis often incorporates the use of topical creams possessing both antifungal and corticosteroid properties, which collectively serve to mitigate symptoms and facilitate resolution.

The therapeutic regimen for angular cheilitis typically involves the application of miconazole cream, which can be prescribed as a single agent or in combination with hydrocortisone. Treatment should be maintained for an additional 10 days after the complete resolution of lesions to prevent recurrence.In addition to treating angular cheilitis and concomitant oral lesions, it is essential to address any underlying dietary deficiencies to ensure comprehensive management and prevent recurrence.

The topical application of mupirocin cream to the anterior nares has been shown to be an effective strategy for decolonizing Staphylococcus aureus, thereby disrupting this critical reservoir.[19]

CHRONIC HYPERPLATIC CANDIDIASIS

The management of chronic hyperplastic candidiasis entails a multifaceted approach, incorporating antifungal therapy with fluconazole (50 mg daily for 7-14 days) and lifestyle modification, specifically smoking cessation, to optimize treatment outcomes.

Patients diagnosed with chronic hyperplastic candidiasis must be counselled regarding the inherent risk of malignant transformation, highlighting the necessity for vigilant surveillance and regular follow-up appointments.[18]

LINEAR GINGIVAL ERYTHEMA

The therapeutic regimen for linear gingival erythema involves a combination of mechanical, antimicrobial, and antiretroviral interventions, including debridement, chlorhexidine mouthwash, optimized antiretroviral therapy, and antifungal therapy, to effectively manage this condition.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of erythematous oral candidiasis necessitates consideration of various conditions that present with similar clinical manifestations, including oral mucositis, erythroplakia, thermal burns, erythema migrans, and anemia, to facilitate accurate diagnosis and targeted therapeutic interventions.[26]

The differential diagnosis of oral candidiasis encompasses a broad spectrum of conditions, including oral hairy leukoplakia, angioedema, aphthous stomatitis, herpes gingivostomatitis, herpes labialis, measles (Koplik spots), perioral dermatitis, Stevens-Johnson syndrome, histiocytosis, blastomycosis, lymphohistiocytosis, diphtheria, esophagitis, syphilis, and streptococcal pharyngitis.

PROGNOSIS

The prognosis for oral candidiasis is optimistic when patients receive evidence-based treatment. However, relapses can occur due to various factors, including non-adherence to treatment regimens, inadequate denture maintenance, and the failure to address underlying or predisposing factors.[27]

COMPLICATIONS

Oral candidiasis can potentially progress to pharyngeal involvement, characterized by dysphagia and respiratory distress, although this is uncommon in immunocompetent hosts. Immunocompromised individuals, particularly

those with HIV/AIDS, are at heightened risk of systemic dissemination and associated complications, including candidal esophagitis..

REFERENCES

1. Fangtham M, Magder LS, Petri MA. Oral candidiasis in systemic lupus erythematosus. Lupus. 2014 Jun;23(7):684-90. doi: 10.1177/0961203314525247. Epub 2014 Mar 5. PMID: 24598219.
2. Williams D, Lewis M. Pathogenesis and treatment of oral candidosis. J Oral Microbiol. 2011 Jan 28;3. doi: 10.3402/jom.v3i0.5771. PMID: 21547018; PMCID: PMC3087208.
3. Manning DJ, Coughlin RP, Poskitt EM. Candida in mouth or on dummy? Arch Dis Child. 1985 Apr;60(4):381-2. doi: 10.1136/adc.60.4.381. PMID: 4004318; PMCID: PMC1777234.
4. Arendorf TM, Walker DM. The prevalence and intra-oral distribution of Candida albicans in man. Arch Oral Biol. 1980;25(1):1-10. doi: 10.1016/0003-9969(80)90147-8. PMID: 6996654.
5. Fraser VJ, Jones M, Dunkel J, Storfer S, Medoff G, Dunagan WC. Candidemia in a tertiary care hospital: epidemiology, risk factors, and predictors of mortality. Clin Infect Dis. 1992 Sep;15(3):414-21. doi: 10.1093/clind/15.3.414. PMID: 1520786.
6. Hellstein JW, Marek CL. Candidiasis: Red and White Manifestations in the Oral Cavity. Head Neck Pathol. 2019 Mar;13(1):25-32. doi: 10.1007/s12105-019-01004-6. Epub 2019 Jan 29. PMID: 30693459; PMCID: PMC6405794.
7. Benito-Cruz B, Aranda-Romo S, López-Esqueda FJ, de la Rosa-García E, Rosas-Hernández R, Sánchez-Vargas LO. Oral Candida isolates and fluconazole susceptibility patterns in older Mexican women. Arch Gerontol Geriatr. 2016 Jul-Aug;65:204-10. doi: 10.1016/j.archger.2016.04.001. Epub 2016 Apr 9. PMID: 27088219.
8. Kanbe T, Li RK, Wadsworth E, Calderone RA, Cutler JE. Evidence for expression of the C3d receptor of Candida albicans in vitro and in vivo obtained by immunofluorescence and immunoelectron microscopy. Infect Immun. 1991 May;59(5):1832-8. doi: 10.1128/iai.59.5.1832-1838.1991. PMID: 1826896; PMCID: PMC257923.
9. Garber GE. Treatment of oral Candida mucositis infections. Drugs. 1994 May;47(5):734-40. doi: 10.2165/00003495-199447050-00003. PMID: 7520855.
10. Ohman SC, Jontell M. Treatment of angular cheilitis. The significance of microbial analysis, antimicrobial treatment, and interfering factors. Acta Odontol Scand. 1988 Oct;46(5):267-72. doi: 10.3109/00016358809004776. PMID: 3063051.
11. Epstein JB, Truelove EL, Izutzu KT. Oral candidiasis: pathogenesis and host defense. Rev Infect Dis. 1984 Jan-Feb;6(1):96-106. doi: 10.1093/clinids/6.1.96. PMID: 6369482.
12. Mahajan B, Bagul N, Desai R, Reddy M, Mahajan A, Shete A, Risbud A, Mane A. Pseudomembranous Type of Oral Candidiasis is Associated with Decreased Salivary Flow Rate and Secretory Immunoglobulin A Levels. Mycopathologia. 2015 Aug;180(1-2):75-80. doi: 10.1007/s11046-015-9874-5. Epub 2015 Feb 15. PMID: 25682023.
13. Coronado-Castellote L, Jiménez-Soriano Y. Clinical and microbiological diagnosis of oral candidiasis. J Clin Exp Dent. 2013 Dec 1;5(5):e279-86. doi: 10.4317/jced.51242. PMID: 24455095; PMCID: PMC3892259.
14. Odden K, Schenck K, Koppang H, Hurlen B. Candidal infection of the gingiva in HIV-infected persons. J Oral Pathol Med. 1994 Apr;23(4):178-83. doi: 10.1111/j.1600-0714.1994.tb01109.x. PMID: 8046655.

15. Millsop JW, Fazel N. Oral candidiasis. Clin Dermatol. 2016 Jul-Aug;34(4):487-94. doi: 10.1016/j.clindermatol.2016.02.022. Epub 2016 Mar 2. PMID: 27343964.
16. Redman RS. Prevalence of geographic tongue, fissured tongue, median rhomboid glossitis, and hairy tongue among 3,611 Minnesota schoolchildren. Oral Surg Oral Med Oral Pathol. 1970 Sep;30(3):390-5. doi: 10.1016/0030-4220(70)90320-8. PMID: 5270895.
17. Goregen M, Miloglu O, Buyukkurt MC, Caglayan F, Aktas AE. Median rhomboid glossitis: a clinical and microbiological study. Eur J Dent. 2011 Aug;5(4):367-72. PMID: 21912494; PMCID: PMC3170022.
18. Lewis MAO, Williams DW. Diagnosis and management of oral candidosis. Br Dent J. 2017 Nov 10;223(9):675-681. doi: 10.1038/sj.bdj.2017.886. PMID: 29123282.
19. Akpan A, Morgan R. Oral candidiasis. Postgrad Med J. 2002 Aug;78(922):455-9. doi: 10.1136/pmj.78.922.455. PMID: 12185216; PMCID: PMC1742467
20. Blatchford NR. Treatment of oral candidosis with itraconazole: a review. J Am Acad Dermatol. 1990 Sep;23(3 Pt 2):565-7. doi: 10.1016/0190-9622(90)70256-h. PMID: 2170476.
21. Lyu X, Zhao C, Yan ZM, Hua H. Efficacy of nystatin for the treatment of oral candidiasis: a systematic review and meta-analysis. Drug Des Devel Ther. 2016 Mar 16;10:1161-71. doi: 10.2147/DDDT.S100795. PMID: 27042008; PMCID: PMC4801147.
22. Kaplan YC, Koren G, Ito S, Bozzo P. Fluconazole use during breastfeeding. Can Fam Physician. 2015 Oct;61(10):875-6. PMID: 26759844; PMCID: PMC4607332.
23. Lagman R, Davis M, LeGrand S, Walsh D, Parala A, Gamier P, Cothren B, Cheema B, Gopal S, Rybicki L. Single-Dose Fluconazole Therapy for Oral Thrush in Hospice and Palliative Medicine Patients. Am J Hosp Palliat Care. 2017 Aug;34(7):645-649. doi: 10.1177/1049909116643927. Epub 2016 May 4. PMID: 27188880.
24. Brent NB. Thrush in the breastfeeding dyad: results of a survey on diagnosis and treatment. Clin Pediatr (Phila). 2001 Sep;40(9):503-6. doi: 10.1177/000992280104000905. PMID: 11583049.
25. Su CW, Gaskie S, Jamieson B, Triezenberg D. Clinical inquiries. What is the best treatment for oral thrush in healthy infants? J Fam Pract. 2008 Jul;57(7):484-5. PMID: 18625176.
26. Patil S, Rao RS, Majumdar B, Anil S. Clinical Appearance of Oral Candida Infection and Therapeutic Strategies. Front Microbiol. 2015 Dec 17;6:1391. doi: 10.3389/fmicb.2015.01391. PMID: 26733948; PMCID: PMC4681845.
27. Mueller SW, Kedzior SK, Miller MA, Reynolds PM, Kiser TH, Krsak M, Molina KC. An overview of current and emerging antifungal pharmacotherapy for invasive fungal infections. Expert Opin Pharmacother. 2021 Jul;22(10):1355-1371. doi: 10.1080/14656566.2021.1892075. Epub 2021 Apr 21. PMID: 33878996.