

Risk Elements Linked to Oral Candidiasis

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Abstract

Introduction: Oral candidiasis is also called oral thrush or oropharyngeal candidiasis. In this condition, the fungus named *Candida albicans* (*C. albicans*) accumulates on the lining of the oral cavity. The typical colonization rate of *C. albicans* varies with age. In neonates it is around 45%; in healthy children ranging between 45–65%; in healthy adults about 30–45%. **Objectives:** This study aimed to find out the risk factors, and symptoms and identify the different types of clinical presentations according to the classifications, as well as trace out the drugs which is commonly being used. **Materials and Methods:** This prospective observational study was conducted at the Shishu Hospital, Shaymoly, Dhaka, and Rajshahi Medical College (RMC), Rajshahi with the ethical clearance of the review board, between January 2016 and December 2016. In this study, 386 patients were enrolled out of which 286 patients were from Shishu Hospital, Shamoly, Dhaka and 100 were from RMC who had the positive clinical features of *Candida* infection. **Results:** Out of the 247(64%) patients had dry mouth. About 62(16%) patients had dental prostheses, such as dentures or fillings. Around 42(11%) patients were using steroid drugs. Almost 259(67%) patients gave a history of unhealthy dietary intake. The systemic factor was that more than 235(61%) patients in our study were belonging two adverse age groups. About 239(62%) patients had malnutrition. Around 127(33%) patients had a history of using long-term antibiotics. In our study 142(37%) patients had a history of Diabetes Mellitus. In the case of 335(87%) cases creamy white lesions on the surface of the tongue. Loss of taste sensation had to 127(33%) cases. **Conclusion:** In the last few decades, a huge amount of clinical data has been recorded on oral candidiasis to its advent with various immunocompromised conditions. With the development of antifungal drugs, this disease has been controlled better than the previous decades.

Keywords: *Candida albicans*, Oral thrush, Risk factors.

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Introduction:

In the oral cavity, *Candida albicans* is most commonly detected on the dorsum surface of the tongue, followed by the palate and buccal mucosa. While *Candida* is a natural organism in the mouth, it can sometimes overgrow and lead to symptomatic infections¹. Oral thrush, a common manifestation, produces creamy white lesions typically located on the tongue or inner cheeks, but it may also spread to the roof of the mouth, gums, tonsils, or the back of the throat². These lesions often cause discomfort and can interfere with normal oral function, especially in more severe cases. *C. albicans* is responsible for around 80% of infections and can colonize the oral cavity either on its own or in combination with other non-albicans

species. The typical colonization rate of *C. albicans* varies significantly with age: in neonates, it is approximately 45%; in healthy children, it ranges from 45–65%; in healthy adults, about 30–45%; in denture wearers, between 50–65%; in patients residing in acute or long-term care facilities (e.g., nursing or residential homes), it rises to 65–88%; and in immunocompromised patients, such as those with HIV or undergoing chemotherapy for acute leukemia, the rates soar to 95% and 90%, respectively^{1,3}. The reasons for these age-related variations in colonization rates remain unclear, but the differences highlight the complex relationship between host factors and *Candida* overgrowth. This study aimed to identify risk factors, evaluate symptoms, classify clinical presentations, and determine the commonly used treatment regimens. Understanding these factors is crucial for the effective management of *Candida* infections.

Aetiology and Pathogenesis:

Candidiasis is caused by the excessive growth of *Candida* species, which are normal commensals in the body. Among these, *C. albicans* is the most frequently isolated species in both healthy and unhealthy individuals. Less commonly, species such as *C. glabrata*, *C. tropicalis*, *C. guilliermondii*, *C. krusei*, *C. parapsilosis*, *C. kefyr*, and *C. dubliniensis* are identified¹⁻⁵. However, colonization by *Candida* in the oral cavity does not necessarily indicate an infection. A significant proportion of healthy individuals continuously harbor *C. albicans* without symptoms^{1,4}. Reported symptom-free oral *Candida* carriage rates vary from 25% to 75% across different populations²⁻⁶. *Candida* species are typically harmless commensals within the normal microbial flora of the mouth, just as they are in the skin, gastrointestinal tract, and vagina⁷⁻⁹. Whether *Candida* remains a benign commensal or proliferates to cause disease is largely determined by the organism's virulence factors and the host's predisposing conditions¹⁰⁻¹². The development of candidiasis is influenced by *Candida*'s virulence factors, which include its ability to adhere to the host's tissues, form germ tubes, switch between phenotypic states, and produce hydrolytic enzymes and toxins¹³⁻¹⁵. However, the most significant factors in the progression of infection are related to the host. During our study, we observed several important host factors that contributed to the onset of *Candida* infection, which are discussed in detail.

Materials and Methods:

This prospective observational study was conducted at the Shishu Hospital, Shamoly, Dhaka, and Rajshahi Medical College (RMC), Rajshahi with the ethical clearance of the review board, between January and December 2016. In this study, 386 patients were enrolled out of which 286 patients were from Shishu Hospital, Shamoly, Dhaka and 100 patients were from RMC who had the positive clinical features of *Candida* infection. Age of the participants was between five and 72. Structured questionnaires were used for patient interviews.

Results and Discussion:

Risk factors:

-Local and systemic factors in the host can increase susceptibility to infection by *Candida* species. These predisposing factors that we noted during our study period are elaborated below and summarized in Table-I.

Local Factors:

- Dry Mouth (247 patients, 64%): Out of the total number of patients, 247 (64%) experienced dry mouth (Figure 1). The reduction in saliva production is a significant risk factor for oral candidiasis, as saliva plays a crucial role in controlling microbial growth. Salivary components, such as enzymes and antimicrobial proteins, naturally inhibit the overgrowth of *Candida*. Without sufficient saliva, these protective mechanisms are weakened, creating an environment conducive to *Candida* colonization and infection³. Dental Prostheses (62 patients, 16%): Approximately 62 patients (16%) had dental prostheses, including dentures or dental fillings (Figure 1). These prosthetic devices can provide surfaces where *Candida* organisms can adhere and thrive, particularly if oral hygiene is inadequate. Dental prostheses can create small pockets or niches that retain moisture and food particles, which encourage fungal growth, making the oral cavity more susceptible to *Candida* infections³. Steroid Use (42 patients, 11%): Around 42 patients (11%) were using steroid medications (Figure 1). Corticosteroids, commonly prescribed for inflammatory or autoimmune conditions, can temporarily suppress the immune responses in the oral cavity. This immune suppression alters the oral microbiome by reducing the body's ability to control fungal organisms, including *Candida*. The disturbance in the oral flora, combined with a weakened immune response, can lead to an imbalance, allowing *Candida* species to overgrow and cause infection⁴. Unhealthy Dietary Habits (259 patients, 67%): Nearly 259 patients (67%) reported having unhealthy dietary patterns (Figure 1). Diets high in sugars, carbohydrates, sweets, and dairy products are known to lower the pH level in the oral cavity, making it more acidic. This acidic environment promotes the growth of *Candida* by providing ideal conditions for the fungi to thrive. Furthermore, a poor diet lacking essential nutrients can weaken the immune system, further predisposing patients to fungal infections such as candidiasis⁸.

Table I: Local and Systemic factors of oral candidiasis

List of local factors	List of systemic factors
1. Impaired local defense mechanisms	1. Impaired systemic defense mechanisms
2. Decreased saliva production	2. Primary or secondary immunodeficiency
3. Smoking	3. Immunosuppressive medications
4. Atrophic oral mucosa	4. Endocrine disorders- Diabetes
5. Mucosal diseases	5. Malnutrition
6. Topical medications – corticoids	6. Malignancies
7. Decreased blood supply	7. Congenital conditions
8. Radiotherapy	8. Broad-spectrum antibiotic therapy
9. Poor oral hygiene	
10. Dental prostheses	
11. Altered or immature oral flora	

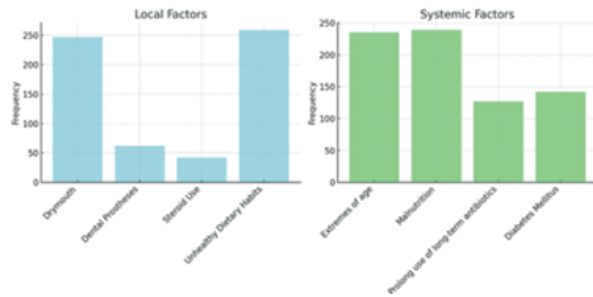


Figure 1: The bar diagrams displaying the frequency of local and systemic factors.

On the left side, the local factors such as "Dry mouth" and "Unhealthy Dietary Habits" with the highest occurrences. On the right-hand side, systemic factors such as "Malnutrition" and "Extremes of age" have similarly high frequencies.

Systemic factors:

- More than 235 (61%) patients in our study were belonging two adverse age groups. Extremes of age may be one of the predisposing factors for individuals to candidiasis owing to immature or weakened immunity, along with variations in the *Candida* carriage rates¹⁶.
- About 239 (62%) patients had malnutrition (Figure 1). Malnutrition, particularly iron but also in other nutrients such as essential fatty acids, folic acid, vitamins A and B6, magnesium, selenium, and zinc, are often associated with the increased risk of oral candidiasis. A deficiency of Iron may cause the fungistatic action of transferrin and other iron-dependent enzymes used in the suppression of fungal overgrowth in the oral cavity¹⁷.
- Around 127 (33%) patients had a history of using long-term antibiotics (Figure 1). Prolonged use of such broad-spectrum antibiotics (e.g. co-amoxiclav), or immunosuppressants (e.g. azathioprine) may alter the local oral flora by killing off the bacteria and suppressing the immune system. This results in a favorable environment for the growth of *Candida*¹⁷.
- In our study 142 (37%) patients had a history of Diabetes Mellitus (Figure 1). Oral and invasive candidiasis is more frequently reported in patients who have endocrine disorders, such as diabetes and Cushing's syndrome. Additionally, in immunodeficiency conditions such as AIDS; and also in patients receiving chemotherapy and radiotherapy for the treatment of carcinoma¹⁸.

Symptoms:

With the informed consent of the patients, we conducted a detailed evaluation of symptoms in both adults and children throughout the study. The findings revealed a range of oral manifestations, varying in severity and impact on daily activities:

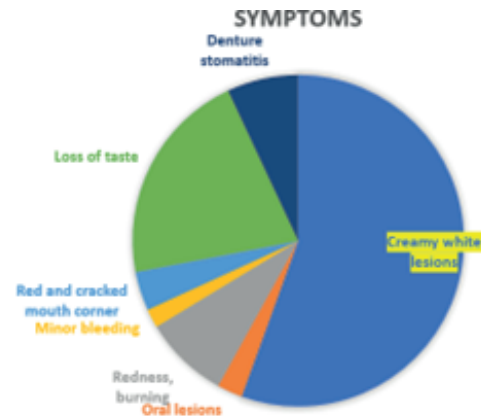


Figure 2: Common symptoms found in oral candidiasis.

- Creamy white lesions were the most common symptom, found in 335 patients (87%) (Figure 2). These lesions appeared on the tonsils, gums, and roof of the mouth, and occasionally extended to the surface of the tongue. The appearance of these lesions often prompted concerns of oral infection or inflammation.
- From Figure 2, approximately 15 patients (4%) exhibited slightly raised oral lesions, which closely resembled the texture and appearance of cottage cheese. These lesions were less common but were still a notable symptom for a subset of the patients.
- Redness, burning, or pain in the oral cavity was reported by 50 patients (13%), with some describing the discomfort as severe enough to interfere with eating and swallowing (Figure 2). This subset experienced significant disruptions to their nutrition intake due to the intensity of their symptoms.
- In 11 patients (3%), attempts to scrape or rub the lesions resulted in minor bleeding, indicating a degree of fragility in the affected areas. This bleeding further complicated the management of their symptoms and increased the risk of secondary infections.
- The corners of the mouth were found to be red and cracked in 23 patients (6%), a condition commonly associated with discomfort while opening the mouth, speaking, or eating (Figure 2). This symptom often exacerbated pain and hindered proper oral hygiene.
- Loss of taste perception was reported by 127 patients (33%) (Figure 2), a significant symptom that impaired their overall eating experience and possibly affected nutritional intake. The loss of taste had both physical and psychological impacts, as it diminished appetite and altered daily eating habits.
- Lastly in Figure 2, denture stomatitis, characterized by redness, irritation, and pain under dentures, was noted in 42 patients (11%). This condition was particularly concerning for patients who relied on dentures for daily function, as it limited their ability to wear them comfortably and maintain proper oral health.

These findings highlight the diversity and severity of oral symptoms observed, emphasizing the need for timely diagnosis and effective management strategies to alleviate patient discomfort and prevent further complications.



Figure 3: Oral thrush

Types of Oral Candidiasis:

We considered Oral candidiasis into three different groups as follows for our work during the study period:

Table II: Types of Oral Candidiasis

Acute candidiasis	Chronic candidiasis	Angular cheilitis (stomatitis)
<ul style="list-style-type: none"> • Acute pseudomembranous. • Acute atrophic (erythematous). 	<ul style="list-style-type: none"> • Chronic hyperplastic (Candidial leukoplakia). • Denture induced (chronic atrophic (erythematous)). • Median rhomboid glossitis. 	<ul style="list-style-type: none"> • Pseudomembranous.

i. Acute Pseudomembranous Candidiasis: During a visual examination, we observed that the lesions could be wiped away, leaving behind an erythematous mucosal surface that may bleed slightly¹⁸.

ii. Erythematous Candidiasis: Clinically, we identified localized erythematous areas, most commonly on the dorsum of the tongue and palate, and less commonly on the buccal mucosa. These areas were painful. This variant, previously referred to as "antibiotic sore mouth," is frequently associated with prolonged use of broad-spectrum antibiotics. These antibiotics reduce the oral bacterial population, creating an environment that fosters *Candida* overgrowth^{8,10-12}. This form is sometimes termed "atrophic candidiasis," where the term "atrophic" is used to describe the red areas. The redness may result not only from reduced epithelial thickness (atrophy) but also from increased vascularity¹⁹.

iii. Hyperplastic Candidiasis: We found that almost all patients presenting with this variant were smokers. The lesions were well-demarcated, slightly elevated, and consisted of adherent, homogeneous, or nodular white plaques that could not be wiped away. This variant is sometimes referred to as "candidial leukoplakia." The most common site for these lesions was the commissural region of the buccal mucosa, with the dorsum of the tongue being less frequently involved¹⁰⁻¹².

iv. Denture Stomatitis (Denture-associated Erythematous Candidiasis): In this variant, patients primarily reported slight soreness or a burning sensation. Denture stomatitis is often associated with angular cheilitis and median rhomboid

glossitis. It is characterized as a chronic inflammation of the mucosa that bears the denture²⁰.

v. Median Rhomboid Glossitis: This condition was characterized by an erythematous, rhomboid-shaped area located on the midline of the dorsum of the tongue, just anterior to the circumvallate papillae. Although it was once considered a developmental anomaly, current evidence indicates that it may represent an acquired form of chronic oral candidiasis⁵.

vi. Angular Cheilitis: This condition appeared as an erythematous lesion, commonly observed in denture-wearing patients with a reduced vertical occlusal dimension. Additionally, nutritional deficiencies, such as iron or vitamin B12 deficiency, have been implicated in the development of these lesions⁷.

Management of oral candidiasis

We observed that the effective management of oral candidiasis could be achieved by adhering to the following guidelines: (1) Diagnosis should be based on a thorough medical and dental history, alongside clinical manifestations, and confirmed through laboratory tests such as direct wet mount smear, staining, culture, or molecular testing. (2) Addressing and correcting predisposing factors plays a key role in controlling the infection. (3) Maintaining proper oral hygiene can significantly reduce the risk of developing oral candidiasis. (4) The appropriate use of antifungal drugs, as prescribed by a doctor based on the severity of the infection is crucial for effective treatment.

Antifungal Agents: We analyzed the commonly used antifungal agents for treating candidiasis, which are divided into three main categories depending on the nature of the lesion and the patient's immunological status:

Polyenes (nystatin and amphotericin B);

Ergosterol Biosynthesis Inhibitors – including azoles (miconazole, clotrimazole, ketoconazole, itraconazole, and fluconazole), allylamines, thiocarbamates, morpholines, and the DNA analog 5-fluorocytosine; and newer Agents such as Caspofungins^{14,15}. In healthy patients, superficial oral candidiasis can be treated topically, while in immunocompromised patients, both topical and systemic treatments may be required.

Topical Antifungals:

Topical antifungal agents are typically the first choice for treating uncomplicated, localized candidiasis in patients with normal immune function. These drugs achieve high concentrations in the oral epithelium when applied directly were used commonly to the patients. Polyenes function by directly binding to ergosterol in the fungal cell membrane, leading to cytoplasmic leakage and eventual fungal cell death¹⁶. Nystatin or amphotericin B solutions are commonly used for 4 weeks. In cases of recurrence, treatment may be extended to at least 4–6 weeks.

Topically administered miconazole gel is effective in treating uncomplicated infections in generally healthy patients, with treatment continuing for 1 week after the patient's symptoms have resolved.

Systemic antifungals:

We noted that systemic antifungals are typically used for disseminated candidiasis and/or in immunocompromised patients. Fluconazole and itraconazole are the most commonly administered oral antifungal agents. The oral solution of these drugs also has a topical effect. Azoles, a class of antifungal drugs, work by inhibiting the fungal enzyme lanosterol demethylase, which is crucial for ergosterol synthesis. Among the azoles, fluconazole achieves particularly high concentrations in saliva, making it an ideal antifungal agent for treating oral infections¹⁵.

However, one of the significant risks associated with fluconazole and other azoles is the development of resistant *Candida* strains¹⁷. For cases where fluconazole resistance is encountered, itraconazole solution can be administered at a dosage of 200 mg daily or Posaconazole suspension may be used at a dosage of 400 mg twice daily for 3 days, followed by 400 mg daily for up to 28 days, as recommended¹⁸⁻²⁰.

Prognosis:

The prognosis for oral candidiasis is generally good, both in inpatient and outpatient settings, when appropriate and effective treatment is administered. However, relapse is more common in patients who fail to properly remove and clean their dentures or who are unable to resolve the underlying causes or predisposing factors for the infection.

Conclusion:

In recent decades, a large amount of clinical data has been accumulated on oral candidiasis, particularly its association with various immunocompromised conditions. The development of antifungal drugs has significantly improved the control of this disease compared to previous decades. However, the emergence of drug-resistant *Candida* strains underscores the ongoing need for research into newer and more effective antifungal agents. In addition, the development of a vaccine against *Candida* species is becoming increasingly important in addressing this persistent issue.

Conflict of Interest: None.

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