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Relationship Between Steroid and Antibiotic Therapy and the Frequency of Oral Candidiasis

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ABSTRACT

Most fungal infections in the oral cavity are caused by antagonism and immunosuppression. It occurs in patients who suffer from immunodeficiency such as diabetes or diseases that cause a weakened immune system. The frequency of oral thrush has increased significantly in the world with the increase in viral infections and the use of immunosuppressive medications caused by immunodeficiency. Certain species of Candida, such as *Candida albicans*, can cause the fungal infection known as candidiasis. When it affects the mouth, it is called thrush in some countries. Symptoms include white patches on the palate and other areas of the mouth and oral mucosa. Other symptoms may include ulceration and swallowing problems. Aspergillus, a common mold that grows both indoors and outdoors, is the source of aspergillosis, an infection. The majority of people inhale Aspergillus spores on a daily basis without becoming unwell. However, Aspergillus-related health issues are more common in those with lung diseases or compromised immune systems. The primary goal of this investigation is to examine fungal infection in 100 patients with immunodeficiency, particularly those with concomitant and chronic diseases. We found that oral fungal infections, particularly those caused by Candida species, are becoming more common in immunocompromised individuals, including those with autoimmune diseases, diabetes, or those receiving immunosuppressive therapies. Symptoms of these infections are often white lesions in the mouths that can lead to painful ulcers and difficulty swallowing. The increase in the use of corticosteroids combined with the use of broad-spectrum antibiotics has increased the prevalence of oral candidiasis, since these drugs impair host immune response, and affect the balance of oral resident microbiota. As a result, opportunistic fungi such as *Candida albicans* can proliferate and cause infections. The purpose of this study is to determine the relationship between these medications and the incidence of oral fungal infection, especially candidiasis, in immunocompromised patients so that better prophylaxis and treatment strategies can be established. The results of this study indicate a significant association between the types of fungi and the incidence of infection ($P = 0.000$). Furthermore, results showed that females are more frequently infected by *Candida albicans*, with an infection rate of 80%, compared to males at 20%.

1. INTRODUCTION

Most oral fungal infections, also known as oral mycosis, are caused by opportunistic infections. Impairment of host resistance permits local colonization in the oral cavity, which initiates and advances pathogenic conditions. Although many people carry Candida without clinical symptoms, antibiotic treatment can trigger its pathogenic effects, changes in the usual bacterial flora, such as those brought on by broad-spectrum antibiotic treatment, enable *Candida albicans* to multiply and infiltrate tissues, significantly impacting the pathogenicity of the *Candida albicans*. People who have weakened immune systems are also more vulnerable to Candida's harmful consequences. The increased use of immunosuppressive medications and the rise in immunodeficiency virus infections have contributed to the growing prevalence of oral mycosis worldwide [1, 2].

Fungal infections of oral tissues can range from superficial to deep mycotic diseases. The two main types of oropharyngeal candidiasis are as follows. The most prevalent type is called pseudomembranous thrush, which manifests as readily removed white plaques on the tongue, palate, buccal mucosa, or oropharynx. Elderly people frequently get the atrophic form of denture stomatitis when a person has no

natural teeth in their upper jaw, they wear a denture that substitutes all of their upper teeth. Its defining feature is erythema without plaques, typically observed beneath dentures [3]. Candida infections and superficial fungal infections in the mouth are the most commonly diagnosed and reported types. The pseudomembranous variety of oral candidiasis, which appears as white, rub-offable plaques on the palate, tongue, or buccal mucosa, is the most prevalent type. One clinical manifestation of chronic hyperplastic candidiasis (CHC) is the nodular type, an uncommon form of oral candidiasis. The increasing number of oral candidiasis cases is likely due to the growing population of immunocompromised patients. Additionally, dentists with advanced training in diagnosing fungal infections are better equipped to identify and differentiate oral candidiasis from other fungal diseases [3, 4].

Deep fungal infections can display a variety of clinical presentations that are difficult to identify, which makes clinical diagnosis difficult [5]. Candida typically does not cause illness, but when the immune system is weakened or the normal microflora balance is disrupted, *Candida albicans* can become an opportunistic pathogen. It is the primary cause of invasive fungal disease in premature infants, diabetics, and surgical patients, as well as oropharyngeal disease in AIDS patients [5]. The most common symptoms of superficial fungal infections are parageusia, burning sensations in the mouth, pain, and food aversion [4, 6]. Deep fungal infections often present aggressively, with ulceration and bone perforation, due to the spread of microorganisms into deeper tissue layers. The focus of the diagnostic strategy for oral mycotic disorders was on the oral tissues' cytological/histopathological and clinical investigations. Crucially, research using immunogold electron microscopy has shown that this enzyme is secreted by *Candida albicans* throughout the infectious process. According to these findings, phospholipase B plays a crucial role in the pathogenicity of Candida. The majority of the time, fungal diseases that were clinically diagnosed were confirmed by biopsy-based diagnosis. Standard therapeutic care also included microbial isolation, identification, culture, and susceptibility to antifungals [7, 8].

In the absence of clinical oral disease, Candida can be detected cytologically or histologically in healthy individuals, indicating its role as a common commensal depending on the surroundings, this dimorphic yeast can exist in both a hyphal (mycelial) and a yeast phase (blastospore). Since Candida is a frequent commensal of the oral cavity, a microbiology result proving that an oral sample with a positive fungus culture without any clinical symptoms should rule out the diagnosis of oral candidiasis.

Candidiasis is a common infection affecting the human skin, gastrointestinal tract, vagina, esophagus, and vascular system. *Candida albicans*, the organism most frequently responsible for disease, displays a number of virulence factors that contribute to pathogenesis, even though the majority of infections occur in people who are immunocompromised or otherwise impaired. These factors include secreted aspartyl proteases, phospholipases, morphogenesis (the reversible transition from yeast to filamentous forms), and host recognition molecules (adhesins) [9].

When determining the ultimate diagnosis of oral candidiasis, the clinical presentation is crucial. Thus, the clinical examination is a crucial component in the diagnosis of superficial fungal infections such as candidiasis [9].

Oral candidiasis usually manifests as a white, scrapable lesion of the oral cavity. Consequently, when making a differential diagnosis for a scrapable white lesion, oral candidiasis needs to be taken into account. Understanding the mechanisms of C. albicans pathogenesis is crucial. A number of putative virulence factors have been suggested in the enhancement of C. albicans pathogeniclty. These include yeast-tohyphal transition, phenotype switching, thigmotroplsm, molecular mimicry, adhesion factors or surface hydrophobicity, phospholipase production, and the production or an extracellular secreted aspartyl proteinase (Sap) [10]. Additionally, immunological deficiencies can cause Candida spp. to proliferate and give rise to more aggressive species that have greater ability to attach to and enter host tissue cells. The virulence factors of Candida species increase host susceptibility to microbial proliferation and may play a significant role in periodontal disease research. Through a variety of methods, *C. albicans* and oral bacteria interact, either reducing or increasing fungal virulence. The nature of the bacteria's influence on the development of mixed infection with Candida albicans has not yet been conclusively established by published early analyses for some bacteria [11].

This study aims to show the relationship between use of steroids and antibiotics therapy and the frequency of oral mycotic infections since steroids have indicated that they act to block effector mechanisms mediating immunologic injury, e.g., decreasing the function of macrophages and suppressing the generation of cytotoxic lymphocytes [10, 11]. While the effects of steroid and antibiotic therapy on systemic fungal infections are well-documented, their specific impact on oral candidiasis in immunocompromised patients remains understudied.

2. MATERIALS AND METHODS

A hundred swabs (n = 100; males = 19, females = 81) were collected from the mouths that were taken directly from humans who visited specialized dental care from October 2023 to February 2024 (Table 1). Their ages ranged between 10-55 and their weights ranged between 18-85 kg.

Table 1. Number of samples

Genders	Number of Samples
Males	19
Females	81

Saliva samples were collected from the mouth by a sterile swab. The sampling method, which entails gently wiping a sterile cotton swab over the lesional tissue, is straightforward and frequently employed, although it typically does not allow quantification of the infecting Candida and the samples were taken to the microbiology laboratory to be cultured on culture media.

2.1 Isolation and identification of fungi

Saliva samples were initially cultured on culture media to determine the required type. This was done on Sabouraud's Dextrose-Agar (SDA) culture medium and swabs were grown on it.

The swabs were incubated for 48 hours at 37°C. After the end of the time for fungal growth, various fungi appeared, including Candida and Aspergillus, and there were dishes in

which no fungus grew. Candida was isolated by making additional culture dishes to hatch it on the same SDA culture medium to obtain Candida without contamination. Then, the Candida was transferred to a second culture medium (chrome agar) and kept it throughout the course of 24 hours at 37°C.

2.2 Examination under a microscope

On a glass slide, a drop of (KOH) solution was applied; the Candida taken from the culture medium placed on it and covered with a cover slip will be ready to be read under the microscope on the lens 40 x. Under the microscope, the Candida cells appeared, but they were not clear as required.

KOH was replaced with human blood serum. The serum was separated from the blood and then put the serum alone from the coagulated blood. We put Candida in the serum and left it in the incubator for 3 hours. After 3 hours, a drop of the mixture was put on the slide mixed with Candida. We read it under the microscope and it appeared to us in a clearer picture.

Oral fungal infections such as oral candidiasis have become more common because of the increased use of immunosuppressive drugs and the burgeoning population of immunocompromised individuals throughout the world. The disruption of balance between the host's immune system and microbial flora in immunocompromised patients encourages the opportunistic fungi such as *Candida* to the oral cavity and infects the host [12]. In humans, the most common *Candida* species found in both healthy oral mucosa and in OC is *C. albicans* due to its adherence properties and greater level of pathogenicity. *C. albicans* is a dimorphic yeast, which may exist in both hyphal and yeast forms depending on the environment. *C. albicans* is isolated in more than 80% of oral lesions. Other species that have been implicated include *C. dubliniensis, C. glabrata, C. krusei, C. kefyr, C parapsilosis, C. stellatoidea*, and *C. tropicalis* [12].

Oral candidiasis often presents with white lesions on the mucous membranes, which can be scraped off. Most commonly, these infections occur after treatment with steroids or antibiotics because the medications reduce the immune response of the body, leading to increased fungal growth. For example, steroids suppress macrophage function and reduce the functional activity of cytotoxic lymphocytes so that the host is more susceptible to fungal infections. Although there is much known about the effects of steroids and antibiotics on systemic fungal infections, there is a question as to their specific effect on oral candidiasis in the immunocompromised individual [13].

3. RESULTS AND DISCUSSION

The smooth, spherical, white to cream-colored colonies that grew on SDA were visible (Figure 1). According to study [14], colonies of *Candida spp*. exhibit certain phenotypic traits when grown on the medium.

The above-described outcome aligns with the findings of Ellis et al. [14], with the appearance of colonies with a creamy, glossy color, smooth and circular in shape, supply the proper growing environment.

The isolated species gave positive results from interaction with gram stain, where the cells appeared ovoid to spherical or ovoid to elongated or cylindrical in the yeast form of the fungus. This outcome agreed with the findings of Ellis et al. [14]. Moreover, the appearance of blue-dyed Candida cells was attributed to the dye's ability to preserve the peptidoglycan layer in the cell wall [14].

After the isolated species of Candida were cultured for 24 to 48 hours on the previously specified medium at a temperature of 37°C, colonies displayed different colors. Each species exhibited a distinct color, confirming that this medium serves as a reliable differential medium for diagnosing Candida species (Figures 2 and 3). Specifically, *C. albicans* appeared green, *C. tropicalis* appeared blue, *C. parapsilosis* appeared purple, and C. *krusei* appeared pink (Figure 4).

Candida can be isolated from the mouth and is considered one of the most crucial fungi in the field of fungal diagnosis, as the staining properties of the medium aid in accurate identification.

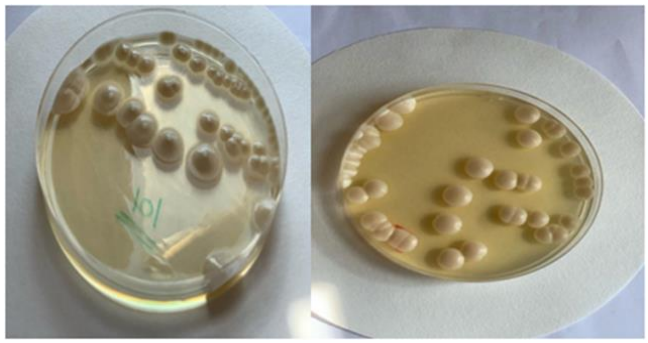

Figure 1. *C. albicans* development on SDA medium for seven days at 37°C

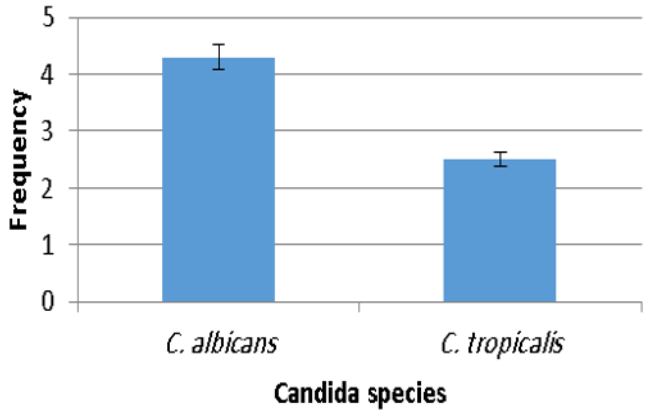

Figure 2. The frequency of Candida species isolated from mouth of immunocompromised patients

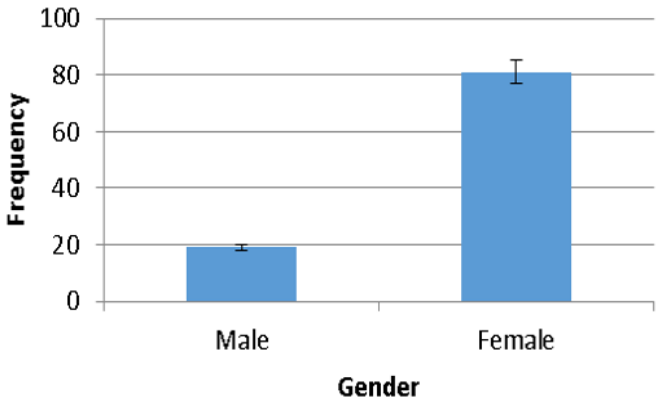

Figure 3. Female were the most frequently infected with Candida

The test results showed that all isolates belonging to the type *C. albicans* formed germ tubes when incubated at a temperature of 37°C in 0.5 cc of human blood serum for two to three hours, but all other species *C. tropicalis*, *C. parapsilosis*, *C. krusei* did not form tubes (Figure 5).

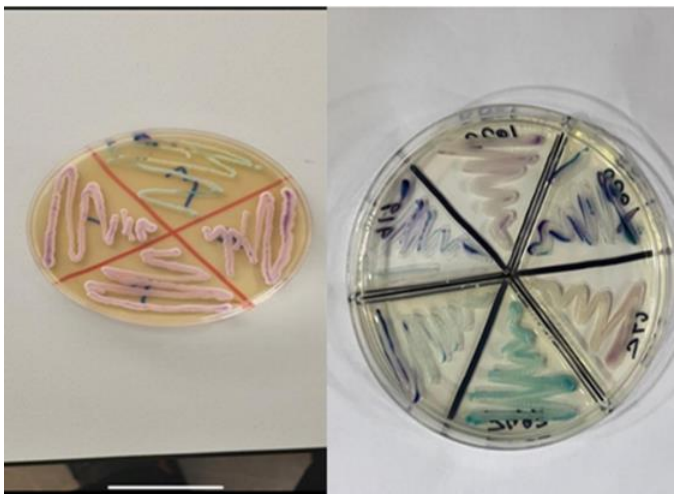

Figure 4. Candida species on chromogenic agar

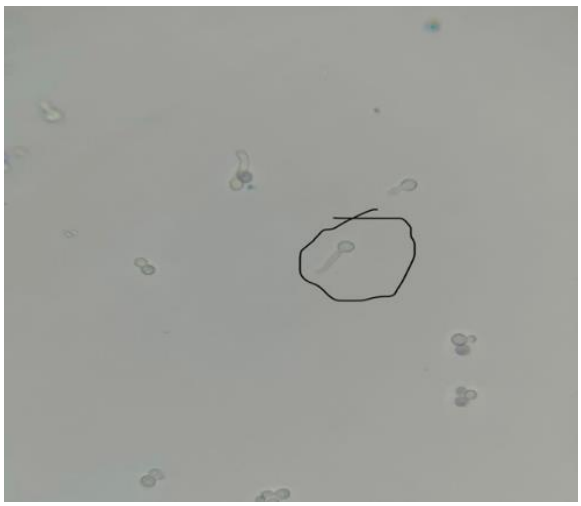

Figure 5. Germ tubes indicated by an arrow for *C. albicans*

These results are consistent with the study by Ellis et al. [14], whose study results showed that only Germ tubes can be formed by C. *albicans*,

In addition to being thought to be crucial for yeast nutrition, the germ tube is thought to play a significant role in the penetration of the layer of epithelial cells lining the body and tissues and access to the bloodstream. Type *C. albicans* can only form the germ tube in this test and in the presence of the stimulus (serum) that works to form it around the yeast cell [15]. Protease, phospholipase, esterase, and hemolytic activities were among the virulence factors tested for *Candida albicans* isolates; each isolate exhibited varying levels of activity for these factors [15].

Steroids, particularly systemic corticosteroids such as prednisone, are known to suppress the immune system's inflammatory response. Prolonged or high-dose steroid therapy can weaken the body's immune defenses, making individuals more susceptible to infections, including fungal infections like candidiasis [16].

Corticosteroids inhibit the function of immune cells such as lymphocytes, macrophages, and neutrophils, which play a crucial role in the body's defense against pathogens. This suppression of immune function can create an environment conducive to the overgrowth of Candida species in the oral cavity [17].

Individuals receiving long-term systemic steroid therapy, such as those with autoimmune diseases, organ transplants, or chronic inflammatory conditions, are at increased risk of developing oral candidiasis [18]. Inhaled corticosteroids are prescribed to treat chronic obstructive pulmonary disease (COPD) and asthma may also predispose individuals to oral candidiasis, especially if proper mouth hygiene is not maintained [19].

Additionally, broad-spectrum antibiotics have the potential to upset the body's microbial equilibrium, including the oral microbiota. This disruption can lead to the overgrowth of opportunistic pathogens such as Candida species, resulting in oral candidiasis [20].

Antibiotics can eliminate beneficial bacteria that normally compete with Candida species for resources and help maintain a healthy microbial balance in the oral cavity. Without these protective bacteria, Candida species can proliferate and cause infection [21].

Individuals receiving broad-spectrum antibiotics, particularly for prolonged periods or repeatedly, are at increased risk of developing oral candidiasis. However, a previous inaccurate diagnosis and inappropriate treatment may be the cause of systemic candidosis's severe nature. Systemic fungal infections are present in around one-third of febrile neutropenic patients who do not improve after a week of antibiotic treatment [22]. Antibiotic use in older adults, individuals with weakened immune systems, or those with underlying medical conditions may further elevate the risk [22]. Theoretically, immunocompromised people or long-term users of steroids and broad-spectrum antibiotics are more likely to develop oral candidosis as a secondary infection [22].

The use of steroids and antibiotics together, such as in the treatment of certain inflammatory or infectious conditions can further increase the risk of oral candidiasis. The immunosuppressive effects of steroids combined with the disruption of the oral microbiota by antibiotics create an environment highly conducive to fungal overgrowth [23].

Prolonged systemic corticosteroid use, and especially prednisone, can increase susceptibility to oral candidiasis.

Although a significant portion of the population has oral Candida, very few go on to develop OC. As a result, the pathophysiology of OC might be influenced by variables other than the fungus's characteristics, like host factors and other risk factors. Inflammation and mucosal damage weaken the integrity of the epithelium, creating an atmosphere that is favorable for fungal invasion. A favorable environment for Candida growth is created by dysregulation in both innate and adaptive immunity, according to molecular insights into the immunocompromised state. An in-depth analysis of Candida species [24].

Immunosuppressive effects are seen with the use of corticosteroids, as they prevent the immune cells—lymphocytes, macrophages and neutrophils—all of which are very important in protection against infections, including fungal ones: Candida. Corticosteroids weaken these responses and in an immunocompromised mouth, they create the perfect environment for an overgrowth of Candida in the mouth and the development of oral fungal infection. This is especially

true for persons on long term steroid therapy, who may have an autoimmune disease or have received organ transplant [24].

Furthermore, antibiotic therapy with broad band use of antibiotics can unsettle the natural balance of bacteria in the oral cavity, permitting Candida reproduction. Antibiotics not only kill bad bacteria, but also kill good bacteria that ordinarily compete with Candida for resources. This is because Candida can flourish when these protective bacteria are wiped out leading to oral candidiasis. The most notorious effect is in those, for example the elderly or immune compromised who receive these antibiotics for long, repeated periods of time [25].

The risk of oral candidiasis is increased even further when corticosteroids and antibiotics are combined. Corticosteroids have immunosuppressive effect which coupled with the microbial disruption caused by antibiotics make Candida overgrowth ideal. Because fungal infections can go unnoticed in their early stages due to mild symptoms, patients receiving both treatments should be watched closely for symptoms of fungal infections. Oral fungal infections that occur in immunocompromised people are held in significant risk when individuals use both of the medications at the same time [26].

Other than that, corticosteroid therapy, even when given for relatively long periods of time, also impairs mucosal immunity, the body's first line of defense against microbial colonization. These impairments allow Candida to adhere more easily to the mucosal surfaces of the oral cavity, and to proliferate. However, patients who are treated with long term corticosteroid medications, as in the case of some inhaled corticosteroids used in asthma or COPD, are at greater risk of development of oral candidiasis if they neglect good oral hygiene [27, 28].

Disruption of normal oral flora by broad spectrum antibiotics is a key factor in in increasing the risk of oral candidiasis. Without the beneficial bacteria that normally keep the Candida species under control, antibiotics leave a space open for the population of Candida to grow out of control. But the risk is even higher for people with weakened immune systems (for example, people being treated for cancer or older adults who are more susceptible to infections). Repeated or prolonged use of antibiotics, especially broad spectrum, has been associated with increased incidence of fungal infection [29].

Oral candidiasis has a broad spectrum of clinical manifestations, from mild symptoms (as burning sensations and discomfort), to more severe forms (painful lesions or ulcers) they can spread into tissues deep in immunocompromised individuals and cause much damage. Early diagnosis is difficult because the initial symptoms can be subtle or nonspecific. Therefore, patients on corticosteroid or antibiotic therapy need regular oral examinations. Although *Candida albicans* is a commensal colonizer of the human oral mucosa, it is the cause of fungal infections in hosts with weakened immune systems. In oropharyngeal candidiasis linked to cancer treatment, the interaction between *Candida albicans* and the local oral mucosal bacterial flora, including mitis group streptococci, can be crucial. Oropharyngeal candidiasis and severe dysbiotic alterations in mucosa-associated bacterial communities are caused by antibiotic-mediated depletion of oral commensals, which also exposes different interactions between mucosa-associated bacteria and Candida albicans in the upper and lower gastrointestinal tract [30-32].

4. CONCLUSIONS

The use of steroids and antibiotic therapy can compromise the immune system and disrupt the balance of microorganisms in the oral cavity, predisposing individuals to oral candidiasis. Healthcare providers should be aware of these potential risks and consider preventive measures, such as oral hygiene practices and antifungal prophylaxis, in patients at increased risk of developing oral candidiasis during steroid or antibiotic therapy.

The development of *C. albicans* biofilms has significant adverse clinical consequences, mostly because the cells within the biofilms are resistant to antifungal treatment. As a result, biofilm formation is now generally regarded as one of the primary virulence traits of *Candida albicans* and a main cause of the unacceptably high fatality rates linked to candidiasis.

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REFERENCES

[1] Barnett, J.A. (2008). A history of research on yeasts 12: medical yeasts part 1, *Candida albicans*. Yeast, 25(6): 385-417. https://doi.org/10.1002/yea.1595

[2] Bharatha, A., Kandamaran, L., Krishnamurthy, K. (2021). Commentary: "Fungal infections of oral cavity: Diagnosis, management, and association with COVID-19". SN Comprehensive Clinical Medicine, 3(9): 2002-2003. https://doi.org/10.1007/s42399-021-01017-9

[3] Shibata, T., Yamashita, D., Hasegawa, S., Saito, M., Otsuki, N., Hashikawa, K., Tahara, S., Nibu, K.I. (2011). Oral candidiasis mimicking tongue cancer. Auris Nasus Larynx, 38(3): 418-420. https://doi.org/10.1016/j.anl.2010.11.007

[4] Dangi, Y.S., Soni, M.L., Namdeo, K.P. (2010). Oral candidiasis: A review. International Journal of Pharmacy and Pharmaceutical Sciences, 2(4): 36-41.

[5] Pires-Gonçalves, R.H., Miranda, E.T., Baeza, L.C., Matsumoto, M.T., Zaia, J.E., Mendes-Giannini, M.J.S. (2007). Genetic relatedness of commensal strains of *Candida albicans* carried in the oral cavity of patients' dental prosthesis users in Brazil. Mycopathologia, 164: 255-263. https://doi.org/10.1007/s11046-007-9052-5

[6] Carmello, J.C., Alves, F., G.Basso, F., de Souza Costa, C.A., Bagnato, V.S., Mima, E.G.D.O., Pavarina, A.C. (2016). Treatment of oral candidiasis using Photodithazine®-mediated photodynamic therapy in vivo. PloS ONE, 11(6): e0156947. https://doi.org/10.1371/journal.pone.0156947

[7] Ge, Y.P., Lu, G.X., Shen, Y.N., Liu, W.D. (2011). In vitro evaluation of phospholipase, proteinase, and esterase activities of Candida parapsilosis and Candida metapsilosis. Mycopathologia, 172(6): 429-438. https://doi.org/10.1007/s11046-011-9440-8

[8] Ma, G. (2000). Potential role of phospholipases in

virulence and fungal pathogenesis. Clinical Microbiology Reviews, 13: 22-43. https://doi.org/10.1128/cmr.13.1.122

[9] Yang, Y.L. (2003). Virulence factors of Candida species. Journal of Microbiology Immunology and Infection, 36(4): 223-228.

[10] Abu-Elteen, K.H., Elkarmi, A.Z., Hamad, M. (2001). Characterization of phenotype-based pathogenic determinants of various *Candida albicans* strains in Jordan. Japanese Journal of Infectious Diseases, 54(6): 229-236.

[11] Sardi, J.C., Duque, C., Mariano, F.S., Peixoto, I.T., Höfling, J.F., Gonçalves, R.B. (2010). Candida spp. in periodontal disease: A brief review. Journal of Oral Science, 52(2): 177-185. https://doi.org/10.2334/josnusd.52.177

[12] Vila, T., Sultan, A.S., Montelongo-Jauregui, D., Jabra-Rizk, M.A. (2020). Oral candidiasis: A disease of opportunity. Journal of Fungi, 6(1): 15. https://doi.org/10.3390/jof6010015

[13] Fangtham, M., Magder, L.S., Petri, M.A. (2014). Oral candidiasis in systemic lupus erythematosus. Lupus, 23(7): 684-690. https://doi.org/10.1177/0961203314525247.

[14] Ellis, D., Stephen, D., Helen, A., Rosemary, H., Roben, B. (2007). Description of Medical Fungi. Second Edition. Mycology Unit, Women's and Children's Hospital, Australia.

[15] Al-Obaidi, H.M.J., Mohammed, S.H. (2022). Molecular characterization of yeasts isolated from the urinary tract of pregnant women in Kirkuk City. Journal of Pharmaceutical Negative Results, 13(3): 881-885. https://doi.org/10.47750/pnr.2022.13.S03.135

[16] Al-Dabbagh, S. (2020). Isolation and diagnosis of *Candida albicans* from oral cavity of local chicken and detection some of the virulence factors in Mosul city. In Proceedings of the 1st International Multi-Disciplinary Conference Theme: Sustainable Development and Smart Planning, IMDC-SDSP 2020. https://doi.org/10.4108/eai.28-6-2020.2298159

[17] Puebla, L.J. (2012). Fungal Infections in Immunosuppressed Patients. Immunodeficiency.

[18] Hirayama, D., Iida, T., Nakase, H. (2017). The phagocytic function of macrophage-enforcing innate immunity and tissue homeostasis. International Journal of Molecular Sciences, 19(1): 92. https://doi.org/10.3390/ijms19010092

[19] Xiao, J.L., Xu, G.C., de Hoog, S., Qiao, J.J., Fang, H., Li, Y.L. (2020). Oral prevalence of candida species in patients undergoing systemic glucocorticoid therapy and the antifungal sensitivity of the isolates. Infection and Drug Resistance, 13: 2601-2607. https://doi.org/10.2147/IDR.S262311

[20] Khijmatgar, S., Belur, G., Venkataram, R., Karobari, M.I., Marya, A., Shetty, V., Chowdhury, A., Gootveld, M., Lynch, E., Shetty, S., Shenoy, S., Chaithra, K., Chowdhury, C.R. (2021). Oral candidal load and oral health status in chronic obstructive pulmonary disease (COPD) patients: A case-cohort study. BioMed Research International, 2021(1): 5548746. https://doi.org/10.1155/2021/5548746

[21] Li, H., Miao, M.X., Jia, C.L., Cao, Y.B., Yan, T.H., Jiang, Y.Y., Yang, F. (2022). Interactions between *Candida albicans* and the resident microbiota. Frontiers in Microbiology, 13: 930495. https://doi.org/10.3389/fmicb.2022.930495

[22] Griffith, A., Mateen, A., Markowitz, K., Singer, S.R., Cugini, C., Shimizu, E., Wiedman, R., Kumar, V. (2022). Alternative antibiotics in dentistry: Antimicrobial peptides. Pharmaceutics, 14(8): 1679. https://doi.org/10.3390/pharmaceutics14081679

[23] Lu, S.Y. (2021). Oral candidosis: Pathophysiology and best practice for diagnosis, classification, and successful management. Journal of Fungi, 7(7): 555. https://doi.org/10.3390/jof7070555

[24] Youssef, J., Novosad, S.A., Winthrop, K.L. (2015). Infection risk and safety of corticosteroid use. Rheumatic Diseases Clinics of North America, 42(1): 157-176. https://doi.org/10.1016/j.rdc.2015.08.004

[25] Jørgensen, M.R. (2024): Pathophysiological microenvironments in oral candidiasis. APMIS, 132(12): 956-973. https://doi.org/10.1111/apm.13412

[26] Saadh, M.J., Hsu, C.Y., Mustafa, M.A., Mutee, A.F., Kaur, I., Ghildiyal, P., Ali, A.J.A., Adil, M., Ali, M.S., Alsaikhan, F., Narmani, A., Farhood, B. (2024). Advances in chitosan-based blends as potential drug delivery systems: A review. International Journal of Biological Macromolecules, 273: 132916. https://doi.org/10.1016/j.ijbiomac.2024.132916

[27] Gümrü, B., Akkitap, M.P. (2022). Oral candidiasis as a local adverse effect of inhaled corticosteroids: What the dental practitioner should know. Black Sea Journal of Health Science, 5(1): 107-115. https://doi.org/10.19127/bshealthscience.943993

[28] Pappas, P.G., Lionakis, M.S., Arendrup, M.C., Ostrosky-Zeichner, L., Kullberg, B.J. (2018). Invasive candidiasis. Nature Reviews Disease Primers, 4(1): 4. https://doi.org/10.1038/nrdp.2018.26

[29] Tsui, C., Kong, E.F., Jabra-Rizk, M.A. (2016). Pathogenesis of *Candida albicans* biofilm. FEMS Pathogens and Disease, 74(4): ftw018. https://doi.org/10.1093/femspd/ftw018

[30] Tan, G.S.E., Hsu, L.Y. (2018). Overview of fungal infections.Reference Module in Biomedical Sciences. https://doi.org/10.1016/B978-0-12-801238-3.98320-X

[31] Vanani, A.R., Mahdavinia, M., Kalantari, H., Khoshnood, S., Shirani, M. (2019). Antifungal effect of the effect of Securigera securidaca L. vaginal gel on Candida species. Current Medical Mycology, 5(3): 31-35. https://doi.org/10.18502/cmm.5.3.1744

[32] Bertolini, M., Dongari-Bagtzoglou, A. (2019). The relationship of *Candida albicans* with the oral bacterial microbiome in health and disease. In: Oral Mucosal Immunity and Microbiome, pp. 69-78. https://doi.org/10.1007/978-3-030-28524-1_6