Ministry of Higher Education and Scientific Research

University of Babylon

College of Dentistry

Department of Prosthodontics

Oral Candidiasis Complications in Removable Denture Wearers Infected with Covid-19

Graduation Project

Submitted to the Department of Prosthodontics in partial fulfillment of the requirements for Bachelor degree in Dentistry

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CERTIFICATION OF THE SUPERVISOR

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"Oral Candidiasis Complications in Removable Denture Wearers Infected with Covid-19"

Is prepared by under my supervision at the *Department of Prosthodontics College of Dentistry / University of Babylon* in partial fulfilment of the requirements for B.D.S degree.

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Date: 2024/ /

ACKNOWLEDGMENT

First and fore the most, praises and thanks to Allah for his showers of blessings throughout our research work and complete it easily

Our deepest thanks to the Teaching Staff of the College of Dentistry-University of Babylon for all they have done for us.

We would like to express our deep and sincere gratitude to our research supervisors, *Dr. Ahmed HINDY & Assist.prof. Rasha Jasim Al-Ward* for all of their help, encouragement and support.

It were a great privilege and honor to work under their guidance.

ABSTRACT

Corona Virus Pandemic in 2019 (COVID-19) opened a wide scope of research on the field of oral infection complication. Oral candidiasis is one of the oral infections that accompanied with the wearing of removable dentures. With the introduction of the idea that COVID-19 has a relation to the oral diseases, oral candidiasis gaining increased attention and acknowledgment as an integral component of the severe consequences of COVID-19. The aim of our study is to review and assess the association between Oral Candida infection and COVID-19 in the removable denture wearers.

INTRODUCTION

Coronavirus disease-2019 (COVID-19) pandemic caused by a the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with a wide range of opportunistic bacterial and fungal coinfections.[1] The triad of the most common secondary oral fungal coinfections seen in COVID-19 comprises candidiasis, mucormycosis, and aspergillosis.[2]

Removable Dental prostheses possess the capacity to serve as a reservoir for microorganisms, and the occurrence of elderly individuals who utilize dental prostheses is typically substantial [3].Candida infection is very common in maxillary denture wearers, which might be due to many factors, such as reduced salivary flow, constant friction between the palate and denture, and poor oral hygiene, and it is further aggravated by the presence of systemic conditions such as diabetes and hypertension [4]. Furthermore, fungal organisms belonging to the Candid a genus are widely regarded as opportunistic microorganisms, and patients who are confined to hospitals exhibit a heightened susceptibility to oral candidiasis due to alterations in both the environment and systemic conditions, resulting in disruptions to the natural microbiota and facilitating the onset of opportunistic infection[5].

Candida species are generally found as oral commensals in approximately one-half of the general population. They metamorphose into opportunistic pathogens when adverse conditions supervene, as in SARS-CoV-2 infection, causing both localised and systemic infections.[6] COVID-19 itself and/or the associated contributory factors including corticosteroid therapy, lymphocytopenia, mechanical ventilator support, and other localised factors such as poor oral hygiene, xerostomia, and denture-wearing appear to favour Candida proliferation in the oral cavity.[7]

Denture wearers are generally more prone to suffer recurrent oral candidiasis, also defined in this case as denture stomatitis. Regarding the denture wearers with COVID-19, it has been reported that 60% of them also had denture stomatitis, mainly sustained by C. albicans strains [7]Several cases of oral candidiasis have been reported lately in COVID-19 patients, and it may elevate the associated risks of morbidity and mortality. Therefore, early identification of oral candidiasis in these patients is necessary for successful and effective management.

1. Denture Stomatitis

is a recurring mucosal condition commonly observed in denture wearing individuals. It is defined as a 'chronic erythematous mucosal inflammation of oral tissues underneath a partial or complete removable prosthesis'.[8] The other terms commonly used to refer to this condition are-Chronic atrophic candidiasis, chronic denture palatitis and denture sore mouth. Incidence of occurrence ranges between 11-67% of complete denture wearers with a higher prevalence seen in women.[9] Denture stomatitis has multifactorial etiology, predominant factors being- accumulation of microbial plaque, trauma due to poorly adapted prostheses, presence of micro-porosities on denture surfaces and poor oral hygiene.[10]

1.1 Clinical Features

Denture stomatitis has variable symptoms which differ depending on the severity from completely asymptomatic to pain and irritation.[11] In few cases, Candidial overgrowth can become intense causing discomfort, alteration of taste, dysphagia and a scalding sensation in the mouth[.12] According to the clinical aspects of the lesions, Newtonin 1962 clinically graded denture stomatitis into three progressive stages:[13]

• Punctiform hyperemia (Type I): Pinpoint hyperemic areas which are localized, the chief etiological factor being trauma;

• Diffuse hyperemia (Type II): Diffuse erythematous areas which are generalized .This is most widely seen presentation extending usually over a part or the complete denture bearing region;[14]

• Granular hyperemia (Type III) : Hyperemic mucosa with a nodular appearance which mostly involves the central part of the palate or alveolar ridges. (Figure 1)

F.g.1: Newton's Type scale for the classification of inflammation present in DS- A. Type 1 - Pinpoint hyperemia seen on palate B. Type 2 -Diffuse erythema distributed over palatal denture bearing area C. Type 3- Erythematous mucosa presents a papillary/ pebbly surface and involves the entire vault of the hard palate by (Mansi Nautiyal)

1.2Etiology

This condition is prevalent in denture patients since notable changes in oral environment occur after placement of dentures which disrupt the integrity of oral tissues. Denture stomatitis has multitude of cruses for its initiation and progression, the chief etiological factors being as follows:

1.2.1Trauma

The inflammatory process in denture stomatitis. differs and is dependent on involved tissue type and the manner in which transmitted forces are intensified and concentrated. The histopathological studies conducted on denture-supporting tissue revealed that changes were dependent on intensity of the occlusal pressure. [15] Trauma can arise either from poorly adapted dentures or dentures that lack adequate vertical and horizontal arch relations.[16] Incorrect vertical dimension distributes the load in an uneven manner and produces traumatic contacts which further increase the frequency of denture stomatitis. Cawson came to the conclusion that infection by C. albicans and trauma are predominant causative agents for denture stomatitis. [17] Histological and microbiological analysis of mucosal tissue has proved that trauma has a substantial role for development of this condition.[18]

1.2.2 Nocturnal denture wearing

The combination of reduced salivary flow and highly acidic local environment under a denture surface facilitates increased microbiological aggression which predisposes the mucosa to inflammation.[19] The prevention of adequate oxygenation of the palatal mucosa due to prolonged wear of prostheses at night leads to local trauma to the mucosal tissues. This further makes denture wearers more conducive to mechanical and microbial trauma thereby increasing the likelihood of developing denture stomatitis. [20]

1.2.3 Surface Texture of Denture Base

Various in vitro studies have shown that colonization of denture surface by microorganisms progresses rapidly and Candida species adhere well to the denture base.[21] This occurs since irregularities in denture surface provide an increased opportunity for microorganisms to retain and protect them from shear

forces even during denture cleaning. The denture surface thus acts as a reservoir with these irregularities allowing the entangled microbial cells to attach to the surface irreversibly.[22]

1.2.4 Poor denture hygiene

Wearing dentures predisposes an individual to infection since their usage results in a variation in the oral micro flora. A poly microbial plaque is formed on the denture fitting surface and underlying mucosa.(figure.2) In due course of time, Candida species invades this denture plaque if denture is not cleaned efficiently."[23]

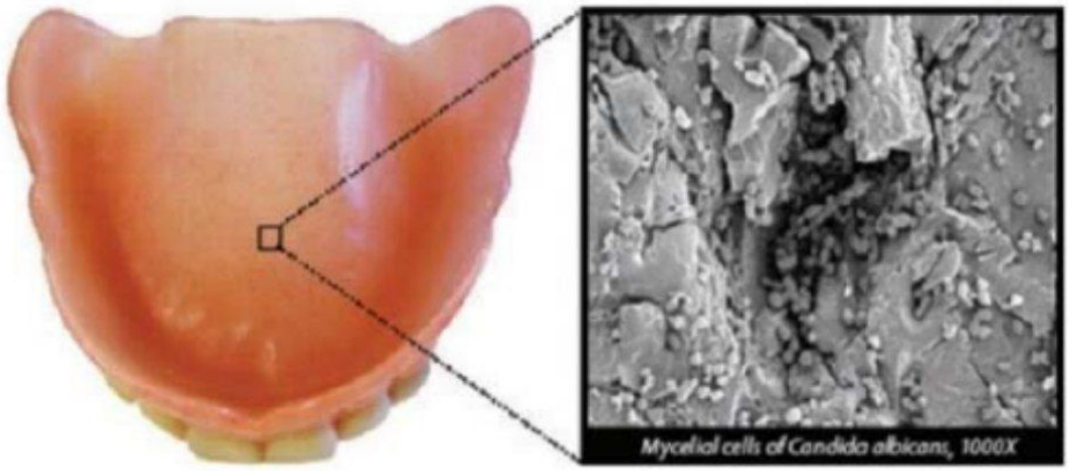


Figure. 2: Microscopic representation of mycelial cells of Candida Albicans invading the denture surface by (Mansi Nautiyal)

1.2.5 Denture lining materials

Tissue conditioners and soft denture liners commonly called denture lining materials are used in prosthodontics for the management of oral mucosal tissues which are traumatised. Tissue conditioners are composed of polyethylmethacrylate and a mixture of aromatic ester and ethyl alcohol. These are used to preserve the residual ridge and heal irritated hyperemic tissues prior to denture fabrication. Resilient or soft denture liners include silicone

elastomers, plasticized methacrylate polymers, hydrophilic polymethacrylates and fluoropolymers. These are indicated if the patient has abused denture bearing mucosa, defects of palate or inelastic tissue. One of the major problems encountered with these products is that Candida species and other microorganisms grow and proliferate within these materials thereby compromising their surface properties. The fungal colonization arises due to exotoxins and metabolic products produced by the yeast along with increased surface roughness."[24]

1.2.6 Saliva

Saliva has a dual role on Candidial adhesion to polymethylmetacrylate. Some studies have shown that saliva shows a physical cleansing effect and consist of antimicrobial components such as lysozyme, lactoferrin and peroxidase. These constituents interact with Candida species and reduce their adherence and colonization on oral mucosal surfaces.[25] However few other studies have shown that salivary proteins such as mucines and statherins perform the role of receptors for mannoproteins present in Candidial cell wall and promote their adhesion."[26]

1.2.7 Other causes

It has been shown that smoking significantly increases the carriage rate of C. Albicans and results in a higher predisposition for development of Oral Candidiasis. Sugar consumption is another significant cause which leads to Denture Stomatitis.[27] Other systemic factors such as- deficiency of iron, folate, ferritin, vitamin B6 and vitamin B12, HIV infection, prolonged use of corticosteroids, decreased saliva production and radiation therapy for head and neck region also contribute to the development of this condition.[28]

1.3 Diagnosis

Diagnosis of oral candidiasis is often clinical, based on clinical examination, medical history taking, and assessment of risk factors. The diagnosis is made after finding the typical lesion's features, excluding other conditions, and assessing the lesion's response to antifungal treatment. [30] Acute atrophic candidiasis and chronic hyperplastic candidiasis resemble premalignant or malignant lesions; therefore, a biopsy is recommended on top of the empirical treatment. [30]

Several methods have been developed to obtain a sample from the oral cavity to identify Candida species. The selection of the method mostly depends on the clinical findings.

- If visible lesions can be identified, taking a swab with a plain microbial swab or an imprint with a sterile foam pad is recommended. [29]

- If no specific lesion is identified, but a Candida infection is suspected, collecting a whole saliva sample in a sterile container or the oral rinse technique is advised. [29]

- If denture stomatitis is suspected, a sample should be obtained from both the internal surface of the denture and palatal mucosa, as sampling from the oral mucosa alone may be negative. [29]

1.4 Management of Dentures

Denture hygiene is particularly important in treating denture stomatitis; however, it must be indicated in managing all forms of oral candidiasis to eradicate the *Candida* colonization from dentures, which acts as a reservoir.[30]

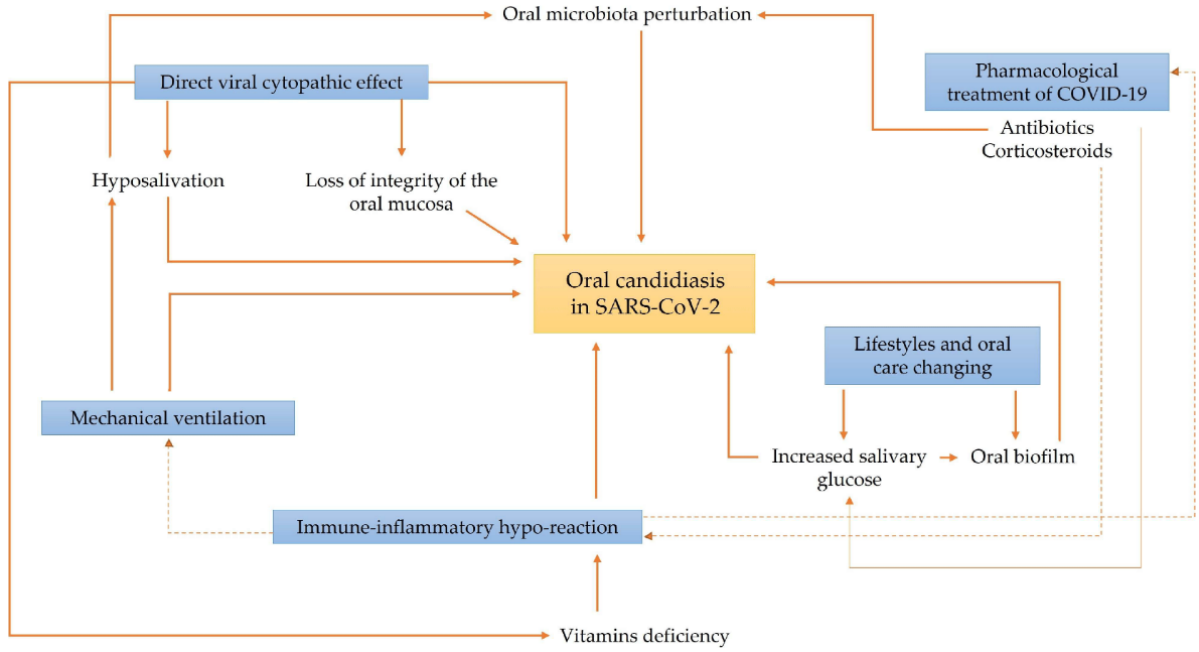
- Patients must clean and disinfect their dentures daily and remove them for at least six hours every night.[29]

- Dentures should be soaked in chlorhexidine and allowed to dry, as air also kills *Candida* adhered to dentures.[30] Hypochlorite can be used instead of chlorhexidine in dentures with no metallic components.[29]
- Dentures must be taken out every time an antifungal rinse is used and, in established cases of chronic atrophic candidiasis, soaked in chlorhexidine before placing them back in the mouth.[30]
- In denture stomatitis cases, patients should be recommended to apply topical miconazole to the dentures' internal surface and place them back in the mouth.[29]
- Mixing an antifungal agent with a denture liner is recommended for denture wearers that cannot hold antifungal rinse in their mouth for long enough.[30]
- Nystatin and chlorhexidine digluconate combination inactivates both; hence, it is contraindicated.[30]

2.The Relation of Oral Cavity in the Morbidity or Mortality of Individuals Infected with SARS-CoV-2:

Oral microorganisms are associated not only with the development of oral diseases, such as denture stomatitis caused by Candida, periodontitis, or caries [31], but they can also lead to an increased risk for several systemic diseases, including aspiration pneumonia, gastrointestinal infection, pleural infection, and bacterial endocarditis [31]. In addition, infectious processes in the oral cavity can induce a systemic inflammatory process and thus affect various organs and pathologies.

Factors that promote infection include enhanced adherence of Candida spp. to acrylic, reduced saliva flow under the surfaces of the denture fittings, improperly fitted dentures, poor oral hygiene, and a high carbohydrate diet [36].Fungi of the genus Candida are considered opportunistic microorganisms and are known to be a potential cause of nosocomial infections [37], which can aggravate pre-existing conditions [35]. Hospitalized patients show a stronger predisposition to oral candidiasis due to environmental and systemic changes which alter the natural microbiota and favor the emergence of opportunistic infections [38].These patients are also likely to undergo several treatments which can further increase their susceptibility to infection, such as intensive care unit (ICU) hospitalization, use of broad-spectrum antibiotics and corticosteroids, and intubation. Any preexisting chronic diseases (diabetes, hypertension, etc.) render these patients further immune compromised [37].



There are various factors associated with COVID-19 that predispose patients to fungal infections (Fig. 2)[56]

Together, these factors make SARS-CoV-2 patients particularly susceptible to the development of oral and oropharyngeal candidiasis (OPC).Although Candida pneumonia in immunosuppressed patients is rare, the presence of Candida in the respiratory tract of immunosuppressed patients should not be disregarded because it may lead to increased morbidity or mortality [39].

Considering the disease progression of COVID-19 and its severity, most infected patients have one or more of the several systemic (e.g., lymphocytopenia, ICU admission, invasive or noninvasive ventilation, use of broad-spectrum antibiotics, use of corticosteroids, immunosuppression) or local risk factors (e.g., use of dental prostheses, inadequate hygiene habits, reduced salivary flow due to the use of medication) that favor Candida proliferation and infection.In cases for which treatment is not performed or is ineffective, for example, in fluconazole-resistant Candida or in immune-compromised patients, oral candidiasis can spread from the oropharynx to the esophagus or systematically through the bloodstream or upper gastrointestinal tract. The resulting candidemia has been shown to have significant morbidity and a mortality rate of 71–79% [45]. It is therefore important to consider the treatment management of these patients in the hospital environment. Individuals who

develop severe COVID-19 may require mechanical ventilation, Mechanical ventilation apparatuses are associated with an increased risk of nosocomial pneumonia, specifically VAP (Ventilator-associated pneumonia) [44]. This type of pneumonia is an important cause of morbidity and mortality in ICU patients [37, 42] and has been associated with the microbiota of the oral cavity and the oropharynx. For example, the presence of periodontitis has been shown to be associated with an increased risk of developing VAP [54].

2.1 Types Candidiasis In COVID-19 Patients:

In COVID-19 patients, two commonly seen candidal infections include oral candidiasis (thrush) and candidemia.These can complicate the COVID-19 infection and even increase its spread rate, leading to high mortality [55]. Therefore, early diagnosis of candidal infections is important to establish effective treatment strategies.

1- Oral Candidiasis: Also called thrush, is commonly seen in denture wearers, diabetics, and patients on steroid therapy. [45]
Oral candidiasis may cause [45]:
-White patches on the inner cheeks, tongue, roof of the mouth, and throat
-Redness or soreness in the mouth
-Dry feeling in the mouth
-Loss of taste
-Pain while eating or swallowing
-Cracking and redness at the corners of the mouth

2-Candidemia: A bloodstream infection with Candida that can occur in hospitalized COVID-19 patients receiving corticosteroid therapy. [57]
Candidemia may cause :
-Fever
-Chills
-Other symptoms can develop if the infection spreads to other parts of the body, such as the heart, brain, eyes, bones, or joints.

2.2 How Can the Risks of Candidiasis in Hospitalized Patients Be Reduced or treated?

All hospitalized patients should undergo an examination of the oral cavity regardless of the reason for hospitalization. However, in COVID-19 patients, examination of the oral cavity is even more important to reduce morbidity and mortality from opportunistic infections such as prosthetic candidiasis. For people who wear prostheses, a good starting point would be to collect the patient's oral anamnesis before removing the prostheses and performing a complete mouth examination, including an inspection of the soft and hard palate as well as the oral mucosa [29].
The timely detection of oral candidiasis, prosthetic stomatitis, or OPC and the identification of etiologic agents in COVID-19 patients are important to optimize therapeutic results [37]. It is important that doctors, nurses, and professionals who care for elderly patients be aware of the risk factors, diagnosis, and treatment options for oral candidiasis [29].

- In cases where uncomplicated oral candidiasis is identified, improved oral hygiene and topical antifungals are generally suitable treatments.
- The drugs indicated for the treatment of C.albicans infections are topical antifungals, such as nystatin (in the form of lozenges, suspensions, or mouthwashes) and should be used as a rinse 4 times a day for 2 weeks, or disinfectant agents such as 0.12 or 0.2% chlorhexidine [39]. However, systemic antifungal therapy is recommended in patients with recurrent intolerance to topical treatment and patients at high risk of developing systemic infections. In these cases, 2 drugs can be used: clotrimazole, in the form of an oral tablet or 10 mg pills, administered 5 times a day for 14 days, or fluconazole, at a dosage of 50–100 mg daily for 7–14 days, or in the case of stomatitis prosthetic, a dosage of 50 mg for 14 days, administered concomitantly with local antiseptic treatment for the prostheses [29]. Nystatin is recommended as the drug of choice due to its effectiveness, absence of serious side effects by oral use, and reduced cost compared to other drugs [49].

RESULTS

Based on the evidence reviewed, C. albicans infection is the main candidiasis infection associated with dentures and has a negative impact on COVID-19 patients by increasing the associated morbidity and mortality. Hospital staff can benefit from a greater awareness of the negative effects that unsatisfactory oral health can have on COVID-19 patients.

Careful monitoring of oral lesions should be instituted through interdisciplinary telemedicine and tele consultation to aid in primary diagnosis, thereby avoiding personal attendance during the pandemic.

Increased awareness and more routine diagnostic strategies are needed for early diagnosis of these infections, which is vital for improving survival. Lastly, we need increased focus on prevention, which could start with restricting access to dexamethasone over the counter to prevent overuse, and improved, broadly accessible care for diabetes.

Conclusions

Denture stomatitis is a multifactorial condition seen mostly in the upper jaw, especially on the palatal mucosa. The management of the condition must be comprehensive starting with proper diagnosis of the causative and risk factors and then directing the treatment toward the most significant factors, which are patient specific to be Continue .

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