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DENTURE STOMATITIS IN DIABETIC SENILE PATIENT : PATHOPHYSIOLOGY AND MANAGEMENT REVIEW

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ABSTRACT : Diabetics are more likely to develop oral disease, such as candidiasis. One of the most prevalent oral manifestation in most denture wearers is *Candida*-associated denture stomatitis. The purpose of this study to explain the pathophysiology and management of denture stomatitis in the diabetic senile patient. Oral candidiasis is the highest prevalence of oral mucosal opportunistic infections. One of the things that can induce oral candidiasis is diabetes mellitus, which is associated with poorly controlled or neglected glycaemic control. Several studies have revealed that *Candida* species biofilms can be found on abiotic surfaces of dentures. The ability of *Candida* Species to infect niche hosts is very diverse, supported by various virulence factors and the internal ability of *Candida* species, the most common species were *C. albicans*. Denture stomatitis in the diabetic senile patient requires proper management to achieve the successful treatment. In conclusion, diabetic senile patients with dentures can increase the risk of denture stomatitis. Good glycaemic control and periodic denture control are needed to minimize the occurrence of denture stomatitis. Proper management of cases of denture stomatitis can reduce the risk of further spreading the infection and morbidity.

Key words : Oral candidiasis, diabetes mellitus, denture stomatitis, elderly well-being, human health, medicine.

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INTRODUCTION

The unpolished denture surfaces have irregular surface topography that can act as reservoirs that provide a nutrient-rich microenvironment for microorganisms to grow. In addition, the denture serves as an excellent incubator for microorganisms such as *Candida* species (Aziz, 2015). There are numerous *Candida* species in the oral cavity, such as *C. albicans*, *C. tropicalis*, and *C. glabrata*, moreover, *C. albicans* is the most prevalent opportunistic fungal species which can be found in the oral cavity ranging from 45-65% of healthy individuals (Farah *et al*, 2010) The prevalence of *Candida* can rise by 60-100% in denture wearers (Loster *et al*, 2012) and this microorganism can shift to its pathogenic state due to the reduction of oxygenation and salivary flow rate to the underlying tissue, which creates an acidic and anaerobic microenvironment that supports the growth of this microorganism. In addition, *Candida* has an excellent affinity towards denture acrylic surfaces with irregular surface topography (Sampaio-Maia *et al*, 2012).

Hydrophobicity is a well-known characteristic of acrylic resin, which significantly contributes to the critical

stage of biofilm formation, adhesion (Lazarin *et al*, 2012). *C. albicans* are often associated with denture stomatitis (Lazarin *et al*, 2012; Darwazeh *et al*, 2010), although non-albicans species such as *C. glabrata*, *C. tropicalis*, *C. krusei*, *C. parapsilosis* and *C. dubliniensis* may also have a role in the development of denture stomatitis (Farah *et al*, 2010; Coenye *et al*, 2011). Various symptoms may be exhibited by denture wearers with candidiasis, such as burning mouth syndrome, painful sensations, taste alterations, speaking discomfort and swallowing difficulty. Denture stomatitis may result in a decline in the patient's quality of life (Bakhshi *et al*, 2012).

Diabetes mellitus is a ubiquitous and rising global health issue that can lead to various of complications. A study reported that diabetes affects nearly 30% of the world's geriatric population. The primary characteristic of this disease is poor glycaemic control which leads to an increased tendency to develop numerous oral diseases such as candidiasis (Soell *et al*, 2007). Furthermore, this review article aims to explain the pathophysiology of denture stomatitis in the elderly with diabetes mellitus and its management.

Oral candidiasis

Oral candidiasis is a common fungal infection caused by the genus *Candida in the oral cavity*. Numerous *Candida* species are found in the oral cavity, including *C. albicans*, *C. glabrata*, *C. guillermondii*, *C. krusei*, *C. parapsilosis*, *C. pseudotropicalis*, *C. stellatoidea*, and *C. tropicalis* (Dangi *et al*, 2010). The most common opportunistic infection in the oral cavity is oral candidiasis. Although the pathogenesis of oral candidiasis is not fully understood, predisposing factors have a significant role in changing species *Candida* from normal flora or known as saprophytic stage to pathogenic organisms or parasite stage (Greenberg *et al*, 2008). It has been described that oral candidiasis is a "disease of the diseased" (Coulthard *et al*, 2008).

Biofilm formation of *C. albicans* on a denture

Biofilms may adhere to living tissues like mucosal surfaces, as well as abiotic surfaces like implanted medical devices, intravascular catheters and oral prosthesis (Darwazeh *et al*, 2010). Poor oral hygiene and poor systemic conditions may allow biofilm accumulation (William *et al*, 2011). *Candida*, *Staphylococcus* and *Streptococcus* create mixed biofilms during denture stomatitis (Dandekeri *et al*, 2013).

Candida biofilm adhesion and formation on the surface of acrylic dentures is influenced by a number of factors, including the inner surface roughness of the prosthesis, salivary pellicle, the interactions of hydrophobic and electrostatic, and the interactions of receptor-ligand (Loster *et al*, 2012; Dandekeri *et al*, 2013; Huh *et al*, 2014). Reports are showing a correlation between denture surface roughness and *C. albicans density*. A study reported that the colonies of *C. albicans* were significantly higher when observed on rough surfaces than smooth surfaces. This study also reported adhesion of *C. albicans* significantly greater in rough surfaces (Huh *et al*, 2014). These results indicate that surface area is increased by surface roughness. Surface roughness may act as a potential microorganism growth location (Lazarin *et al*, 2012; William *et al*, 2011).

Pathogenesis of oral Candidiasis

The capability of *C. albicans* to infect niche hosts is supported by various virulence factors and the internal capabilities of the species. Virulence factors include morphological transitions between yeast and hyphae, adhesins and invasins expression on the cell surface, the formation of biofilm, thigmotropism, phenotypic switching, and hydroxylic enzymes. In addition, internal capabilities include rapid adaptation to environmental pH alterations, metabolic flexibility, a robust nutrient acquisition system, and good stress response (Nicholls *et al*, 2011).

C. albicans has a specific set of proteins such as adhesins hat allow it to adhere to other microorganisms, abiotic surfaces, and host cells (Garcia *et al*, 2011). The protein agglutinin-like sequence (ALS), forming a family of eight members (Als1-7 and Als9) is one of the most important adhesins in the *C. albicans* attachment process. Glycosylphosphatidylinositol (GPI) cell glycoprotein is encoded by ALS genes (Zordan *et al*, 2012; Murciano *et al,* 2012). *In vitro*, the expression of ALS3 gene is increased during oral epithelial cells infection (Naglik *et al*, 2011). Another essential adhesive from *C. albicans* is Hwp1. Another important adhesive from *C. albicans* is Hwp1 (Zordan *et al*, 2012).

C. albicans is an outstanding pathogen due to its two invading-host cell mechanisms, inducing endocytosis and active penetration (Naglik *et al*, 2011). *Candida* expresses invasins on the cell surface, which mediate binding to host ligands such E-cadherin on epithelial cells (Murciano *et al*, 2012) and N-cadherin on endothelial cells (Phan *et al*, 2005) to induce endocytosis, promoting fungal cells to attach to the host cell. Ssa1 and Als3 (acts as an adhesin) are the two invasion that have been discovered so far (Sun *et al*, 2010). Ssa1 is an expressed cell surface member of the heat shock protein 70 (Hsp70). Als3 and Ssa1 bind to E-cadherin and possibly induce endocytosis by a clathrin-dependent mechanism

(Dalle *et al*, 2010).

The ability of *C. albicans* to form biofilms on both abiotic and biotic surfaces is another important virulence factor. Dentures and mucosal cell surfaces are the most common substrates invaded by this species (Fanning and Mitchell, 2012). Biofilm formation is regulated by several transcription factors. These include the transcription factors Bcr1, Tec1 and Efg1 (Fanning and Mitchell, 2012). In a recent study, biofilm formation is controlled by a transcriptional network and further identified a previously unknown regulator of biofilm production. These novel factors include Ndt80, Rob1, and Brg1 (Nobile *et al*, 2012).

C. albicans can utilize a unique mechanism that allows it to switch back and forth between different forms (from budding yeast to pseudohyphae to hyphae) (Farah *et al*, 2010; Darwazeh *et al*, 2010). One of the critical factors in the pathogenic activity of *C. albicans is the* transition morphology from yeast to hyphae is. In the hyphae state, *C. albicans has ability to* produce acidic proteinase that damages the oral mucosa (Loster *et al*, 2012).

Diabetes mellitus in senile patients

According to the American Diabetes Association (ADA), diabetes is a group of diseases defined by hyperglycemia caused by defects in insulin secretion, insulin function, or both which cause organ dysfunction and damage such as the eyes, kidneys, nerves, heart and blood vessels. DM is a syndrome in which glucose, lipid and protein metabolism are all disrupted caused by inadequate insulin secretion or decreased tissue sensitivity to insulin (Barrett *et al*, 2010). Diabetic patients have an increased tendency to manifest oral diseases such as candidiasis, which is linked to poor glycemic regulation (Soell *et al*, 2007). DM can also lead to xerostomia, which can accelerate candidal colonization and oral candidiasis. The association of dentures and diabetes may increase the incidence of candidiasis (Barbeau *et al*, 2003).

Diabetes mellitus is a chronic metabolic disease that leads to several disorders. *Candida* colonization is more common in diabetic patients (Kumar *et al*, 2005) and many studies have found that diabetic patients have a higher ubiquity of *Candida* colonization in the oral cavity than non-diabetic patients (Soell *et al*, 2007). In addition, the condition of decreased salivary flow rate in diabetic patients, especially geriatric patients, is an important predisposing factor (Hoseini *et al*, 2017). The reduction of the quality and quantity of saliva leads to inadequate oral self-cleansing mechanisms. In addition, this condition leads to a decrease in oral innate immunity, especially in the composition of salivary sIgA, which can lead to opportunistic candida infections (Brown *et al*, 2020).

Treatment and prevention of denture stomatitis

Periodic preservation and evaluation of oral hygiene conditions are vital preventive measures of oral candidiasis. The initial success of this preventive intervention is dependent on good cooperation between denture users and dentists. Denture wearers' oral hygiene entails a thorough cleansing of the oral cavity tissue as well as the denture in use (Gracia-Cuesta *et al*, 2014). Denture cleansers are effective in killing microorganisms, one of which is *Candida* species and has been confirmed by several studies (Volety *et al*, 2021).

The use of antifungal drugs can also be used as a treatment in cases of denture stomatitis. The recommended antifungal agents for treating oral candidiasis include topical administration such as nystatin, amphotericin, miconazole, and clotrimazole (Loster *et al*, 2012; Darwazeh *et al*, 2010; Bakhshi *et al*, 2012; Dangi *et al*, 2010; William *et al*, 2011; Brondani *et al*, 2012; Petrovic *et al*, 2014). The drug selection is determined by various factors, including the patient's medical history, oral symptoms, and application technique forecasts (Farah *et al*, 2010). It is essential to identify the causal species in order to begin therapy with antifungal medications as soon as possible (Sampaio-Maia *et al*, 2012). Denture stomatitis is often treated with nystatin, which is the standard treatment (Bakhshi *et al*, 2012). Dentures must be detached during treatment because the drug acts topically and must reach the tissue directly (Dangi *et al*, 2010). Treatment with systemic antifungal drugs may be required if the treatment is still unsuccessful (Farah *et al*, 2010). In xerostomia patients, therapeutic medication levels in the oral cavity might be difficult to attain with systemic therapy (Salim *et al*, 2013).

Probiotic microorganisms have been used to inhibit the growth of pathogenic microbes in the treatment of oral candidiasis in the latest decades. Probiotics such as *Lactobacillus rhamnosus* GG, *Lactobacillus rhamnosus* LC705, *Propionibacterium freudenreichii* and *Shermanii* JS stuffed in cheese were utilized in a recent study. This probiotic cheese revealed a decrease in oral *Candidiasis*' prevalence in elderly and its use is also possible for patients with hyposalivation (Thein *et al*, 2009).

Denture stomatitis associated with diabetic senile patient

In industrialized nations, rising life expectancy has contributed to a rise in the senior population. This condition is best accompanied with improvements in life quality.

As the population of the elderly grows, so will the number of persons who require removable dentures to rehabilitate stomatognathic function and enhance patients' quality of life (Coenye *et al*, 2011). Globally, the adult population's tooth loss rate is estimated to be somewhere between 7 to 69 percent (Felton *et al*, 2011). Older adults who tend to have decreased manual dexterity suitable for removing oral debris from prostheses are more susceptible to bacterial and fungal opportunistic infections in the oral mucosa (Brondani *et al*, 2012).

In the elderly, it is often found with accompanying systemic diseases such as diabetes mellitus, which causes hyperglycaemia. A large percentage of older individuals have abnormal glucose levels. Pre-diabetes or diabetes affects three-quarters of the aging demographic, while diabetes affects one-third of the geriatric adult. However, the majority of type 2 diabetes patients in their latter years go undetected. Among the total number of patients over 65 years old, data on the number of diabetes was 45.6% of undiagnosed cases. Diabetes affects more than twice as many elderly people as it does middle-aged and younger people. Between 2005 and 2050, the number of diabetes cases detected among those aged 65 and older is expected to grow by more than fourfold, owing to rising disease incidence and an aging population (Dankner *et al*, 2009). In addition, the problem that often arises in elderly patients is the loss of their teeth. Several recent studies have confirmed that elderly patients are more likely to lose their teeth. Tooth decay and periodontal diseases are the leading oral diseases and the main causative factors for tooth extraction so that they require denture treatment to restore chewing function (Fure, 2003).

Diabetic individuals are more likely to have oral disease symptoms such candidiasis, which is linked to poor glycaemic management and therapeutic dentures. This tendency can lead to xerostomia, which is caused by elevated high glucose levels in the mouth or immunological dysregulation. Another risk factor is the usage of full denture, which can promote colonization and biofilm formation of Candida, as well as oral candidiasis. Denture stomatitis can be exacerbated by the combination of dentures and diabetes (Soell *et al*, 2007; Barbeau *et al*, 2003).

A study comparing *Candida* species between diabetic and non-diabetic dental prosthesis users exhibited that diabetic prosthesis users had an increased prevalence rate of oral candidiasis. This finding represents a significant comparison with non-diabetic patients (Lotfi-Kamran *et al*, 2009). At the same time, several additional researches have discovered a positive correlation between *C. albicans* colonization and diabetic condition (Farah *et al*, 2010). Glycaemic control appears to be a more important component than illness presence, since poor control can lower salivary flow and pH, raising salivary glucose levels (Dangi *et al*, 2010). The saliva of diabetic patients fosters the development of *C. albicans* in vitro, and diabetic patients' denture surfaces have a larger number of Candida species than non-diabetic people (Hoshing *et al*, 2011). In addition, any changes in quantity and quality of salivary flow in diabetic individuals may function as risk factors for *Candida* species pathogenicity (Dangi *et al*, 2010).

Candida infections are commonly found in people who wear dentures. Acrylic material in dentures is a major predisposing factor of oral candidiasis because it acts as a reservoir of infection. In healthy edentulous populations, Candida species found in oral cavity range from 20% to 50%, whereas denture users have as many as 75% (Radford *et al*, 1998). Oral candidiasis manifests itself in various forms, such as atrophic glossitis, median rhomboid glossitis, denture stomatitis, and angular cheilitis (Budtz-Jorgensen *et al*, 2000).

The pattern of alveolar bone resorption in diabetic patients tends to be faster and causing considerable bone damage and unstable dentures (Wu *et al*, 2015). Frictional irritation of the palatal mucosa can be caused by unstable dentures, which makes it easier for Candida to invade the epithelium's surface layers. Occasionally, to cushion the acrylic denture material against the mucosa, a denture soft-liner can be utilized. However, this soft-liner is an easy surface for *Candida* accumulation (William *et al*, 2011).

Oral candidiasis associated with denture stomatitis, although if asymptomatic, must therefore be approached with care because this condition might serve as a reservoir into an even more widespread infection and promote alveolar bone resorption and more severe infections. Due to the multiple etiology of the disease and the lack of effectiveness of antifungal medications, therapy has become tough and complex (Petrovic *et al*, 2014; Hoshing *et al*, 2011). Therapeutic strategies include topical and systemic antifungal medications, as well as plaque management on dentures and oral mucosa (Petrovic *et al*, 2014). Therefore, therapy should be focused on identifying and addressing, if feasible, the underlying causes which could influence or lead to oral candidiasis, via a comprehensive history taking (Farah *et al*, 2010).

CONCLUSION

From this review, it can be concluded that diabetic

patients with dentures are more likely to develop oral candidiasis. Adequate glycaemic control followed with periodic denture control are needed to minimize the occurrence of oral candidiasis. As prevention, excellent oral hygiene and adequate prosthetics after-care are required, one of which is the use of a denture cleanser. Proper handling of cases of oral candidiasis can reduce the risk of further spreading the infection.

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