

Etiological Factors Related to Denture Stomatitis: A Meta-analysis

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Abstract

Denture stomatitis (DS) is a very common disorder that affects upper denture wearers. Clinically, DS presents erythema and inflammation of the palatal mucosa covered by the denture. The objective of the study was to assess the etiological factors related to DS. A search for articles on etiological factors related to DS was performed in the following electronic databases: PubMed (MEDLINE, Cochrane Library), Web of Science (WoS), and Spanish Medical Index (IME). One thousand five hundred thirty-two articles were found (683 in PubMed, 829 in WoS, and 19 in IME), 340 of them were duplicates. From 330 articles with full-text availability, 306 were excluded for several reasons. Finally, 24 studies were included in this meta-analysis. For dichotomous outcomes, the estimates of effects of an intervention were expressed as odds ratios (ORs) using Mantel-Haenszel method with 95% confidence intervals. Data were processed using the statistical software RevMan 5.3. The most important risk factors for DS were *Candida* species infection (OR: 5.64, $P < 0.001$), denture age over 10 years (OR: 5.36, $P = 0.02$), the existence of denture trauma related to ill-fitting denture (OR: 4.30, $P = 0.02$), night sleeping with the denture (OR: 4.09, $P < 0.001$), poor denture cleaning (OR: 2.81, $P = 0.02$), high carbohydrate intake (OR: 1.83, $P = 0.01$), and female gender (OR: 1.42, $P = 0.02$). The most common microorganisms in DS were the *Candida albicans* fungus and the *Stafilococcus aureus* bacteria. Infection by species of the genus *Candida* seems to be the main etiological factor of DS.

Keywords: Candidiasis, denture/etiology, oral, palate, risk factors, stomatitis

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INTRODUCTION

Denture stomatitis (DS) is a very common disorder that affects superior denture wearers. Clinically, it is characterized by the appearance of areas of erythema and inflammation in the palatal mucosa covered by the denture.^[1] DS is usually asymptomatic, although a small percentage of patients report pain, itching, or a burning sensation. Despite its frequency, its etiology is not completely clear and it is thought to be multifactorial with the participation of various factors.^[2] The prevalence of DS is highly variable according to the populations studied, ranging from 15% to 75% of denture wearers, with a higher incidence in the elderly and women. Institutionalized patients are especially susceptible to DS, possibly due to their impaired immune system, poorer general health, xerostomia, or decreased motor skills leading to the inability to perform good oral and denture hygiene. Among the local etiological factors, the following highlights (1) traumatic factors due ill-fitting denture, increased age of dentures (over 10 years), or the habit of sleeping without removing it; (2) infectious factors,

considering DS as a *Candida*-associated lesion; and (3) hygienic factors due to poor denture cleaning and inadequate oral hygiene. Systemic etiological factors include high carbohydrate intake, smoking, nutritional deficiencies, or drug hyposialia.^[3] Currently, DS is thought to be a response to *Candida* infection, due to the very high prevalence of this fungus in DS patients compared to the rest of the population.^[4] The purpose of this study was to assess the different etiological factors associated with DS.

MATERIAL AND METHODS

The databases PubMed (MEDLINE, Cochrane Library), Web of Science (WoS), and the Database of Information and

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Documentation of Science in Spain (InDICES-CSIC) that includes the Spanish medical index (IME) were searched for studies on etiological factors related to DS. The following terms from the Medical Subject Headings (MeSH) and free text were used for the article search: “stomatitis, denture/etiology,” “DS,” “risk factors,” and “estomatitis prot*.” After this first search, 1532 articles were found (683 in PubMed, 829 in WoS, and 19 in IME) between September 1972 and October 2018, 340 of them were duplicate articles, which left 1192 articles for review. Two researchers (ARA and CGG) independently assessed the titles and abstracts of the articles and then jointly selected the papers that were included in this meta-analysis.

The two inclusion criteria were (a) study types (clinical trial, clinical study, comparative study, meta-analysis, multicenter study, or observational study) ($n = 527$) and (b) articles with full-text availability ($n = 330$). Exclusion criteria were (a) studies on DS treatment ($n = 101$); (b) studies that did not consider denture wearers without DS ($n = 68$); and (c) studies with non-usable data ($n = 137$). Finally, 24 studies were included in this meta-analysis [Figure 1].

Statistical analysis

For dichotomous variables, the odds ratio (OR) with the Mantel–Haenszel Chi-square formula and 95% confidence intervals (95% CI) was used. Heterogeneity was determined according to the Higgins statistic (I^2). In cases of high heterogeneity ($I^2 > 50\%$), the random-effects model was applied. All statistical comparisons were performed with RevMan 5.3 program (The Cochrane Collaboration, Oxford, UK). P values below 0.05 were considered statistically significant.

RESULTS

Figure 2 shows the 17 studies^[5-21] that analyzed whether the detection of species of the genus *Candida* in denture wearers could influence the appearance of DS. DS patients were 5.64 times more likely to be infected by *Candida* species than denture wearers without the disease, finding a statistically significant association (OR = 5.64; 95% CI: 3.16–10.05. $P < 0.001$).

Table 1 presents the detection of different microorganisms in denture wearers with and without DS. Among fungi, *Candida albicans* was the microorganism that appeared more frequently in denture wearers, both with DS (231 patients) and without the disease (95 subjects). Among bacteria, *Streptococcus aureus* was the most frequently detected bacterium in DS patients (138 cases), while in denture wearers without this condition, the most common bacteria were *Streptococcus mutans* (131 cases). The main risk factors related to DS are shown in Table 2.

Twelve studies^[6,7,9,12-14,21-26] considered the gender of denture wearers as a possible risk factor for the development of DS. Women had 1.42 times more likely of DS than men with a statistically significant relationship (OR = 1.42; 95% CI: 1.06–1.90. $P = 0.02$).

Eleven studies^[5,9,12,14,17,21-24,26,27] evaluated the habit of sleeping with the denture in subjects with and without DS, observing that individuals who sleep with their dentures had 4.09 times more likely to have DS. After statistical analysis, statistically significant differences were found (OR = 4.09; 95% CI: 2.05–8.18. $P < 0.001$).

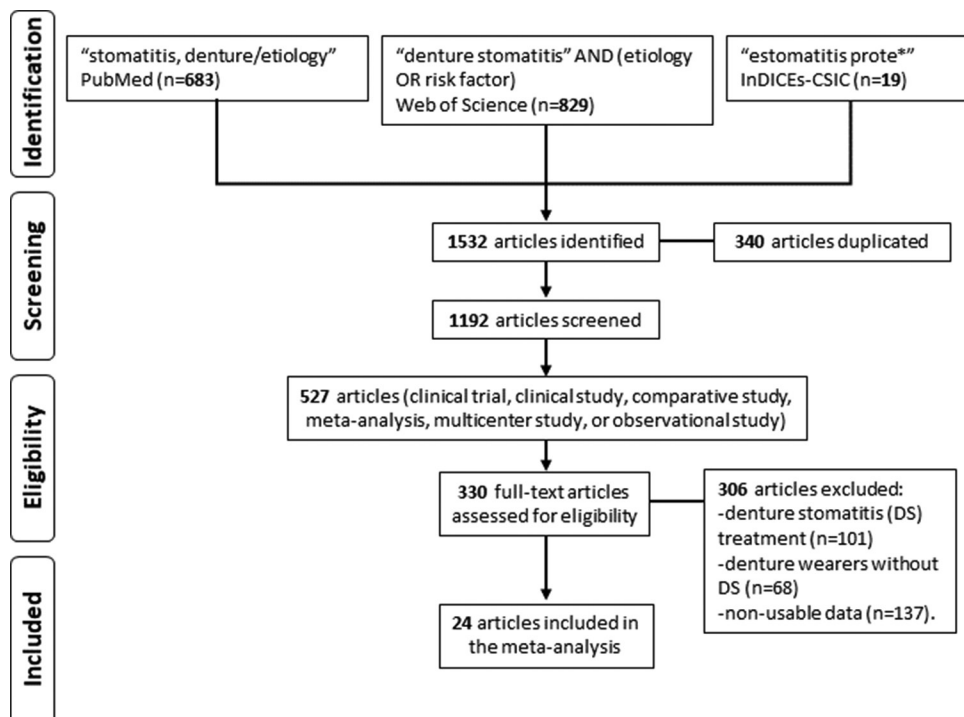


Figure 1: Study flow diagram

Regarding the existence of denture trauma due to its ill-fitting, six studies^[12,17,21-23,28] analyzed this parameter as a possible risk factor, showing that denture trauma increased 4.30 times the DS risk with a statistically significant relationship (OR = 4.30; 95% CI: 1.25–14.82. *P* = 0.02).

Another six studies^[5,12,24,26-28] investigated whether poor denture cleaning could promote DS. Subjects with inadequate cleaning of dentures had 2.81 times more probability of having DS with a statistically significant association (OR = 2.81; 95% CI: 1.15–6.89. *P* = 0.02).

Finally, four other studies^[21-23,28] considered whether denture age over 10 years could increase the DS risk. Individuals with oldest dentures were 5.36 times more likely to develop DS, with statistically significant differences (OR = 5.36; 95% CI: 1.23–23.27. *P* = 0.02).

Table 1: Detection of different microorganisms in denture wearers with and without denture stomatitis

Microorganisms	Denture wearers		Total, <i>n</i> (%)
	With DS, <i>n</i> (%)	Without DS, <i>n</i> (%)	
Fungi			
<i>Candida albicans</i>	231 (70.9)	95 (29.1)	326 (100.0)
<i>Candida glabrata</i>	5 (50.0)	5 (50.0)	10 (100.0)
<i>Candida kefyr</i>	1 (33.3)	2 (66.7)	3 (100.0)
<i>Candida krusei</i>	1 (100.0)	0	1 (100.0)
<i>Candida sphaerica</i>	1 (100.0)	0	1 (100.0)
<i>Candida famata</i>	1 (50.0)	1 (50.0)	2 (100.0)
<i>Candida tropicalis</i>	7 (50.0)	7 (50.0)	14 (100.0)
<i>Candida guilliermondii</i>	0	6 (100.0)	6 (100.0)
<i>Candida lusitaniae</i>	3 (37.5)	5 (62.5)	8 (100.0)
Bacteria			
<i>Streptococcus mutans</i>	28 (17.6)	131 (82.4)	159 (100.0)
<i>Staphylococcus aureus</i>	138 (64.4)	77 (35.6)	215 (100.0)
<i>Staphylococcus epidermidis</i>	13 (68.4)	6 (31.6)	19 (100.0)
<i>Staphylococcus xylosum</i>	7 (77.8)	2 (22.2)	9 (100.0)
<i>Staphylococcus cohnii</i>	1 (100.0)	0	1 (100.0)
<i>Staphylococcus capitis</i>	1 (100.0)	0	1 (100.0)
<i>Staphylococcus chromogenes</i>	0	5 (100.0)	5 (100.0)
<i>Staphylococcus warneri</i>	2 (50.0)	2 (50.0)	4 (100.0)
<i>Haemophilus influenzae</i>	8 (88.9)	1 (11.1)	9 (100.0)
<i>Neisseria meningitidis</i>	2 (50.0)	2 (50.0)	4 (100.0)
<i>Klebsiella pneumoniae</i>	1 (100.0)	0	1 (100.0)

References.^[5,7,10,11,15,16,20] *n*=Number of cases. DS=Denture stomatitis

Concerning high carbohydrate intake assessed by three studies,^[7,10,17] DS patients had a higher intake compared to controls with a statistically significant relationship (OR = 1.83; 95% CI: 1.13–2.99. *P* = 0.01).

Salivary pH was also studied in denture wearers.^[7,10,17,18] DS patients had a lower pH (5.32) versus subjects without DS (5.95), finding statistically significant differences (*P* < 0.001).

Finally, three studies^[12,17,25] analyzed the possible influence of smoking habit, observing a greater number of smokers among DS patients, although no statistically significant association was found (OR = 1.13; 95% CI: 0.24–5.31. *P* = 0.88).

DISCUSSION

Twenty-four studies on the possible etiological DS-related factors have been included in the present meta-analysis.

The etiology of DS is multifactorial involving local and systemic factors.^[9] Among these risk factors include *Candida* species infection, female gender, higher denture age, denture trauma, continued use of the denture to sleep, poor denture hygiene, high carbohydrate intake, an acidic salivary pH, and smoking habit.

Different *Candida* species, mainly *C. albicans*, may be found in the oral microbiota in a large percentage of healthy people. Denture wear increases both *Candida* infection of the oral tissues and the probability of DS.^[1] According to this study, DS patients were 5.64 times more likely to be infected by *Candida* species with statistically significant differences (*P* < 0.001). The seventeen studies^[5-21] that analyzed *Candida* detection found a higher prevalence of *Candida* in DS patients compared to denture wearers without DS.

Denture also constituting a *Candida* reservoir and the porosity of the denture acrylic base promotes *Candida* adhesion due to biofilms production.^[14] These biofilms adhere to the denture surface, forming plaque deposits, which provide a source of continuous exposure of the oral mucosa to the microorganisms contained in them.^[20]

Candida infection has been reported as the most common causative agent of DS.^[3] Nevertheless, other studies do not attribute to *Candida* infection such a relevant etiological role in DS. Cankovic *et al.*^[9] did not find *Candida* growth as an important risk factor in the development of DS. Similarly, Emami *et al.*^[12] did not observe any significant relationship between DS and the presence of *Candida* species. Martori

Table 2: Other etiological risk factors related to denture stomatitis

Factor	<i>n</i>	Reference value	OR (95% CI)	<i>I</i> ² (%)	<i>P</i>
Gender	12	Female	1.42 (1.06-1.90)	28	0.02*
Night sleeping with denture	11	Yes	4.09 (2.05-8.18)	85	<0.001*
Denture trauma	6	Yes	4.30 (1.25-14.82)	92	0.02*
Denture hygiene	6	Poor	2.81 (1.15-6.89)	74	0.02*
Denture age	4	>10 years	5.36 (1.23-23.27)	93	0.02*

*Statistically significant. *n*=Number of studies; OR=Odds ratio; CI=Confidence interval; *I*²=Higgins statistic for heterogeneity

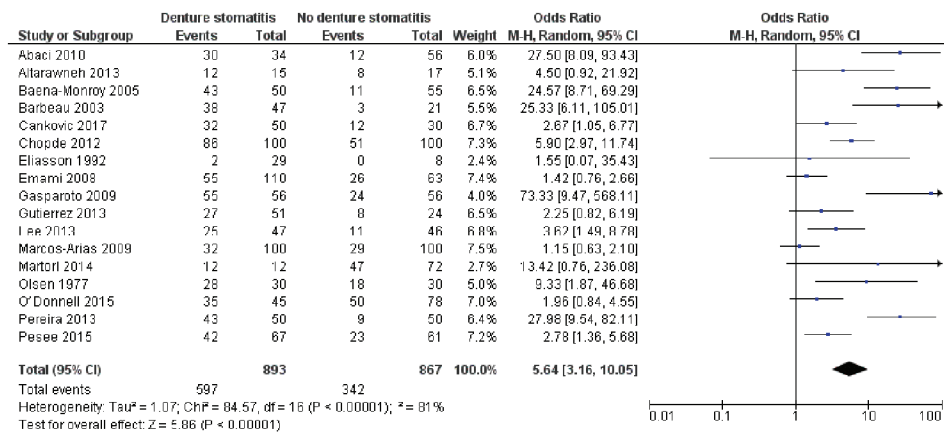


Figure 2: Study data and forest plot graph for genus *Candida* species detection in denture wearers with and without denture stomatitis

et al.^[17] stated that although the presence of *Candida* species in the oral cavity was significantly associated with DS, this association was no longer statistically significant after including other factors in the analysis, such as sugar consumption and salivary pH.

C. albicans is a commensal microorganism that exists in the oral microbiota of healthy individuals dentate or edentulous.^[2] Numerous studies^[5-21] linked *C. albicans* fungal infection to DS. However, since more than 1000 different microorganisms may colonize the surface of the denture,^[19] it is quite likely that bacteria also play a role in the condition. *C. albicans* is usually the main etiologic infectious agent of DS,^[13-16,18-21,23] but other species from other genera of fungi and bacteria may be implicated.^[5,7,10,11,15,16,20]

In the present study, it was found that the fungus *C. albicans* was the most isolated species in denture wearers, both with and without DS. Among the bacteria, *S. aureus* was the most frequently isolated in denture wearers with DS and *S. mutans* in denture wearers without the disease.

Therefore, determining the presence of *Candida* in the oral cavity of subjects with and without DS allows establishing the concentration of microorganisms necessary to differentiate between a state of health or disease in a denture wearer. These concentrations of microorganisms directly influence the severity of DS. Moreover, patients with high *Candida* concentrations in their oral cavity may require broader therapeutic initiatives to prevent or, where appropriate, treat DS according to its severity.^[15]

The possible influence of gender as a DS risk factor was also analyzed in the present study. A higher prevalence in the female gender was observed, women were 1.42 times more likely to have DS, with a statistically significant association ($P = 0.02$). Of the 12 studies that studied this parameter, nine^[9,12-14,21-23,25,26] found a higher prevalence in females, while three^[6,7,24] observed it in males.

Pereira *et al.*^[20] argue that women are more prone to this disease which may be due to hormonal changes that occur

in association with menopause, which are reflected in the quantitative and qualitative composition of the oral microbiota. Conversely, others justify the possible higher prevalence in males of the existence of harmful habits, mainly tobacco consumption, which is a predisposing factor to candidiasis, including DS.^[6]

Regarding the habit of sleeping with the denture, it was observed that the individuals who slept with their dentures were 4.09 times more likely to have DS, with statistically significant differences ($P < 0.001$). The 11 studies^[5,9,12,14,17,21-24,26,27] that examined this habit agreed in pointing out that sleeping with the denture increased the DS risk. This could be explained by the fact that when dentures are used continuously, the beneficial effects of saliva are nullified, including its cleaning action.^[26] In this same sense, Emami *et al.*^[12] noted that the continuous and nightwear of the dentures raised the frequency of DS. These authors explain this finding by the fact that nighttime use can decrease the protective effect of saliva, the cleaning action of the tongue, and the good oxygenation of the mucosa, which are key factors in the resistance of the mucosa to mechanical and microbiological aggression. Cankovic *et al.*^[9] considered continuous use of the dentures at night to be the main direct risk factor for the development of DS. However, other authors, such as Pesee and Arpornsuwan,^[21] did not observe a significant relationship between the prevalence of DS and the use of the dentures at night.

In this study, denture trauma related to ill-fitting ones increased the DS risk by 4.3 times, with a statistically significant association ($P = 0.02$). All studies^[12,17,21-23,28] confirmed this direct relationship between denture trauma and DS.

Various studies have shown that the development of DS is related to the lack of stability of the denture, which leads to a greater traumatic effect and the rupture of the integrity of the palatal mucosa, opening a door of entry to tissue colonization by part of the microorganisms.^[12,23]

In the present study, poor denture hygiene caused a 2.81-fold increase in the probability of DS, with a statistically significant

relationship ($P = 0.02$). Of the six studies that investigated the hygiene degree of the denture, four^[5,24,27,28] proved the influence of poor hygiene on the DS risk, and on the other hand, two other^[12,26] did not observe it.

Inadequate hygiene habits, both oral and denture, favor the accumulation of plaque in the oral cavity and the consequent increase in the concentrations of the different microorganisms of the oral microbiota. This finding increases the probability of the development of various infectious diseases, including DS.^[27] Good instruction in specific dental prosthesis hygiene techniques that are different from oral hygiene takes special relevance to minimize the DS risk.^[5]

In this study, patients with denture age over 10 years had a 5.36 higher risk of DS, finding a statistically significant association ($P = 0.02$). All the studies^[21-23,28] that considered this variable showed that the older the prosthesis, the greater the probability of DS.

Certain parallelism has been observed between the use of dentures for long periods and poorer denture hygiene, and there was also a higher prevalence of DS. This prevalence was much lower in patients with new dentures.^[22] Prolonged use of the dentures could lead to wear of the denture base material, which would increase porosity and the appearance of fissures that would facilitate the formation and accumulation of biofilms in it.^[26]

In the present study, it was also evidenced that the DS patients had a high carbohydrate intake compared to healthy denture wearers with statistically significant differences ($P = 0.01$). Several studies^[7,10,17] pointed to this relationship between sugar consumption and DS.

Furthermore, DS patients also had a lower salivary pH, with a statistically significant association ($P < 0.001$). Three studies^[7,10,17] supported this finding of a lower pH in DS patients. The acidic pH acts in two ways: first, it creates an ideal microenvironment for the colonization and growth of *C. albicans* colonies and second, it increases the ability of this fungus to adhere to oral epithelial cells and prosthetic materials due to the acidophilic nature of the different *Candida* species.^[7] In the oral cavity, this acidic microenvironment is located, above all, in the lingual dorsum and the supporting palatal mucosa of the denture, two areas of frequent location of candidal lesions.^[10]

In this study, although a greater number of smokers with DS were observed, tobacco consumption had no significant influence on the risk of the disease ($P = 0.88$). The action of tobacco is controversial. Tobacco consumption can induce the keratinization of the oral mucosa, making it less prone both the trauma and the loss of mucosal integrity, necessary for microorganisms to penetrate and colonize tissues; on the other hand, smoking patients are more susceptible to candidiasis because fungi take advantage of its toxic substances to infect oral tissues.^[17]

Denture stomatitis treatment is mainly based on a) avoiding dental trauma using a well-fitting denture or replacing old dentures; b) keeping an adequate both oral and denture hygiene with daily denture cleaning and/or denture disinfection with high concentration antiseptic agents; c) removing the denture to sleep, and d) the use of antifungal drugs beneath the denture.^[10]

Due to the high heterogeneity of some analyzes included in this meta-analysis, the results should be interpreted with caution. The differences between the studies may be due to the different methodologies used in their execution, the different techniques used in collecting samples, or the particular characteristics of the study populations.

CONCLUSIONS

In this study, the most important DS risk factors were *Candida* species infection (OR: 5.64, $P < 0.001$), denture age over 10 years (OR: 5.36, $P = 0.02$), the existence of denture trauma related to ill-fitting denture (OR: 4.30, $P = 0.02$), night sleeping with the denture (OR: 4.09, $P < 0.001$), poor denture cleaning (OR: 2.81, $P = 0.02$), high carbohydrate intake (OR: 1.83, $P = 0.01$), and female gender (OR: 1.42, $P = 0.02$). The most common microorganisms in DS were the *Candida albicans* fungus and the *S. aureus* bacteria.

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Conflicts of interest

There are no conflicts of interest.

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