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(REVIEW ARTICLE)

Impact of risk factors for oral candidiasis in patients with Sjögren's syndrome

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Abstract

Background: Sjogren's Syndrome (SS) is an autoimmune disease in which the body attacks the exocrine glands. The characteristics of this syndrome involve dysfunction and destruction of the exocrine glands, leading to oral manifestations. Patients with Sjogren's Syndrome are at a significantly higher risk of developing oral cavity diseases. Common oral manifestations found in Sjogren's Syndrome include sialadenitis, lichen planus, and salivary swelling.

Material and Methods: The literature review was carried out in Pubmed, ScienceDirect, and Researchgate as well as various relevant sources with the keywords: “Oral Candidiasis", “Sjogren’s Syndrome", "Oral Cavity Lesions”, "Flow Saliva", and "Oral Health."

Conclusion: In patients with Sjogren's Syndrome, the saliva flow tends to decrease, which can increase the risk of higher levels of *Candida albicans* bacteria, thereby raising the likelihood of developing Oral Candidiasis.

Keywords: Oral Candidiasis; Sjogren's Syndrome; Oral Cavity Lesions; Flow Saliva; Oral Health.

1 Introduction

Sjögren's Syndrome is an autoimmune condition where the immune system mistakenly targets the salivary and lacrimal glands, resulting in various oral manifestations [17]. Approximately 0.5 to 1% of the population suffers from Sjögren's Syndrome [2], primarily impacting individuals aged 45 to 55. Notably, women are nine times more frequently affected than men, with a gender ratio of 9:1. The incidence rate varies widely, ranging from 0.1 to 3 cases per 1,000 people. Interestingly, male sufferers of Sjögren’s Syndrome are more prone to developing cancers and have double the mortality risk compared to females, irrespective of the type of malignancy [3].

Common manifestations of Sjögren’s Syndrome involve dry mouth (xerostomia), angular cheilitis, ulcers, lichen planus, erosions, parotid gland inflammation (sialadenitis), dry eyes (xerophthalmia), arthritis, swollen salivary glands, and reduced saliva production (hyposalivation). Saliva contains IgA antibodies, lysozyme, and lactoferrin, which not only moisturize but also protect against pathogens by regulating the oral environment's pH balance [4]. Furthermore, Sjögren's Syndrome predominantly affects women nine times more often than men [5].

In patients with Sjogren's Syndrome, the concentration of immunoglobulins and other electrolytes decreases, making their mucosal surfaces vulnerable to exposure from oral microorganisms like those causing candida infections [6]. The frequency of oral candidiasis among these patients varies greatly—between 0% and 80%—due to several factors including ambiguous symptom presentation, oral care practices, and how oral candidiasis is diagnosed [7].

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2 Material and methods

2.1 Search Strategy

A literature search in both Indonesian and English was conducted using the PUBMED, ScienceDirect, Google Scholar, and ResearchGate databases to identify research on impact of risk factors for oral candidiasis in patients with Sjögren's Syndrome. Studies and literature reviews from 2002 to 2021 were included. The keywords used in the search included: Oral Candidiasis, Sjogren's Syndrome, Oral Cavity Lesions, Flow Saliva, and Oral Health.

3 Results and Discussion

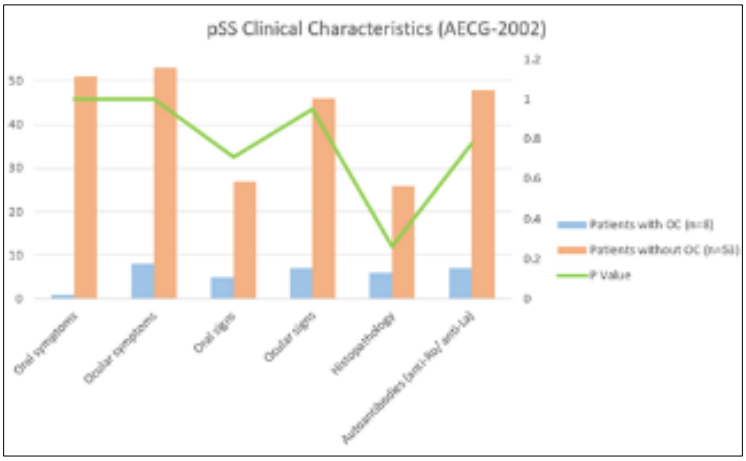

Figure 1 The differences between patients with and without oral candidiasis (OC) based on PSS Clinical characteristics [7].

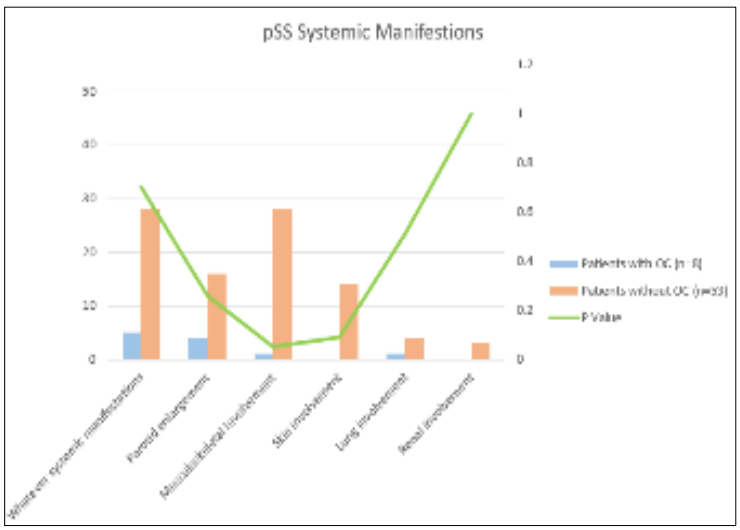

Figure 2 The differences between patients with and without oral candidiasis (OC) based on PSS Systemic Manifestations [7].

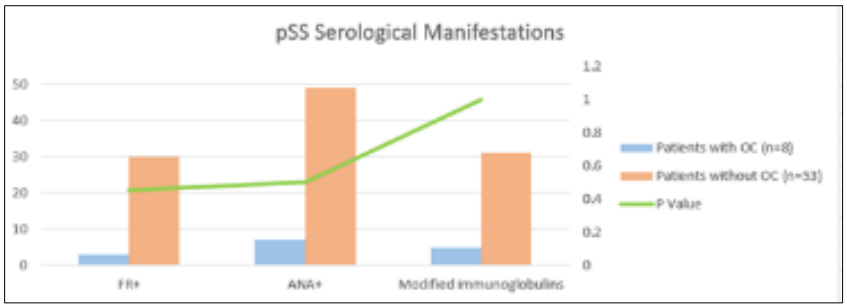

Figure 3 The differences between patients with and without oral candidiasis (OC) based on PSS Serological Manifestations [7].

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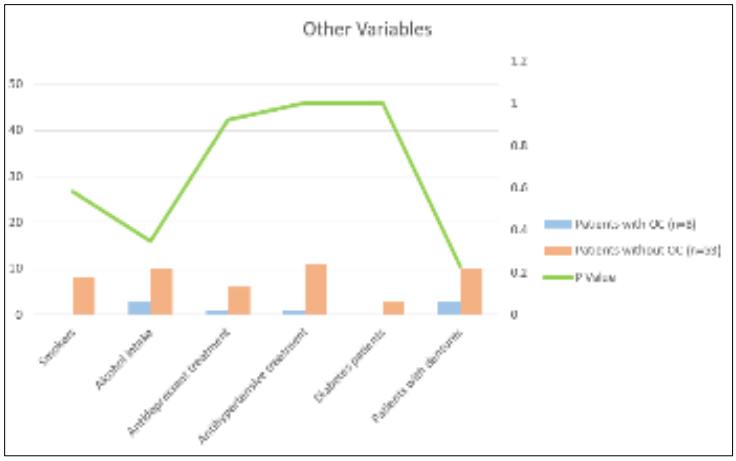

Figure 4 The differences between patients with and without oral candidiasis (OC) based on Other Variables [7].

Figure 1-4 presents data taken from a research journal by Serrano (2020). The table shows a comparison of clinical characteristics, systemic manifestations, serological manifestations, and other variables between patients with and without oral candidiasis (OC). Patients with Sjogren's Syndrome with OC typically do not differ much from patients without. The key differences between the two groups of patients are that patients with musculoskeletal involvement have higher incidence in the "without OC" group.

Table 1 Relationship between oral candidiasis and salivary variables [7].

	Patients with OC (n=8)	**Patients without OC (n=53)**	***P***
UWS Hyposalivation			
Yes	7 (87.5%)	30 (56.6%)	0.09[b]
No	1 (12.5%)	23 (43.4%)	0.09[b]
UWS flow rate mL/min (mean±SD)	0.05±0.11	0.13±0.17	0.15[a]
SWS Hyposalivation			
Yes	7 (87.5%)	27 (50.9%)	0.05[b]
No	1 (12.5%)	26 (49.1%)	
SWS flow rate mL/min (mean±SD)	0.36±0.69	0.73±0.67	0.08[a]

Values are number (%) and mean ± standard deviation (SD). Statistical test: *U-Mann-Whitney test, bFisher's exact test. OC: oral candidiasis; UWS: Unstimulated whole saliva; SWS: stimulated whole saliva.

Table 1 shows the relationship between oral candidiasis and saliva. The results will be discussed in more detail in the discussion section. Patients with stimulated whole saliva have lower flow in the "with OC" group.

3.1 Hyposalivation in Sjogren's Syndrome

Hyposalivation is a prominent symptom of Sjögren's Syndrome. When saliva production is below normal levels, both the quantity and composition of saliva are affected, which can disrupt the balance of normal oral microflora [8]. Patients who are more susceptible to oral candidiasis may experience this due to a deficiency in salivary protective factors [9]. Reduced saliva flow, loss of buffering capacity, and decreased levels of salivary proteins such as histamine, mucin, immunoglobulin A (IgA), and statherin elevate the risk of opportunistic infections, particularly those caused by *Candida albicans*. Oral candidiasis can either be asymptomatic or manifest as a cracked tongue, rhomboid tongue, non-specific ulcers, prosthetic stomatopathy, or generalized candidiasis. It typically presents as chronic candidiasis, while pseudodiphtheritic candidiasis is less frequently observed. In a study by Yan et al., 87% of patients with primary Sjögren's Syndrome were found to have candidiasis, with 42% of these cases exhibiting mixed features. In addition to C. albicans, other fungal species identified included C. tropicalis, C. glabrata, and C. parapsilosis [10].

3.2 Salivary Flow Rate Analysis

In a 2020 study conducted by Serrano, the data revealed that Unstimulated Whole Salivary flow rate (UWS) and Stimulated Whole Salivary flow rate (SWS) were lower, though without reaching statistical significance. Additionally, another investigation noted that as UWS declined, the count of *Candida albicans* increased [10]. This research demonstrated that among patients with oral candidiasis, 87.5% exhibited hyposalivation during stimulated whole salivary flow rate testing compared to only 50.9% of those with healthy mucosa among patients diagnosed with Sjögren's Syndrome. Furthermore, a similar pattern was observed where 87.5% of oral candidiasis patients also showed hyposalivation during unstimulated whole salivary flow rate tests, indicating an association between hyposalivation and oral candidiasis [13]. Patients suffering from Sjögren's Syndrome are particularly susceptible due to their inherently low salivary production rates, thereby increasing their risk of developing oral candidiasis [9].

3.3 Relationship Between Saliva pH and *Candida albicans*

In individuals with Sjögren's Syndrome, the reduced salivary pH could result from both low salivary flow rates and diminished buffering capabilities. Furthermore, ongoing harm to the salivary gland tissue may directly influence saliva pH production. Research conducted by Serrano in 2020 found that patients with Oral Candidiasis exhibited lower pH levels ranging from 4.40 to 2.91 compared to those without this condition whose pH ranged from 5.19 to 2.80. There is an association between *Candida albicans* quantities and saliva pH; specifically, lower saliva pH correlates with higher amounts of *Candida albicans* present. However, no substantial link was observed between varying pH ranges and Candida growth due to confounding factors such as oral hygiene products like toothpaste or mouthwash which can counteract decreased pH values in patients [9].

While a high number of Candida cells might indicate potential clinical oral candidiasis, there are currently no definitive guidelines specifying exactly how many candida cells would definitively cause visible symptoms [11]. A commonly referenced benchmark is around 266 Colony-Forming Units per milliliter (CFU/mL) of C. albicans in saliva samples. Based on Serrano's research in 2020, every patient exhibiting clinical signs of candidiasis had counts exceeding this threshold. Consequently, further investigations are needed to explore how many C. albicans cells correlate with clinical manifestations of oral candidiasis so that an accurate threshold can be established for diagnosing infections [12].

4 Conclusion

Hyposalivation is a primary manifestation in patients with Sjogren's Syndrome and significantly impacts oral health. Reduced saliva flow not only reduced the volume, but also altered the composition of saliva. So, reduced the protective factor that potentially increased infection risk, especially for *Candida albicans* infection that can cause oral candidiasis. In patients with Sjogren's Syndrome, reduced saliva flow increases the risk of higher *Candida albicans* levels, thereby raising the likelihood of developing oral candidiasis. The diminished salivary production limits the oral cavity's natural defense mechanisms, making it easier for fungal infections like *Candida albicans* to proliferate and cause oral lesions. Overall, the understanding relationship between hyposalivation and *Candida albicans* infections is crucial in managing patients with Sjogren's Syndrome to prevent and address serious oral health complications.

Compliance with ethical standards

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Disclosure of Conflict of interest

All authors declare that there are no conflicts of interest regarding the publication of this document.

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