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Prevalence of Oral Mucosal Lesions in Patients with Autoimmune Diseases: A Cross-Sectional Survey

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ABSTRACT

Oral mucosal lesions (OMLs) are frequently observed clinical manifestations in various diseases but their prevalence in patients with autoimmune diseases remains poorly understood. This study aimed to evaluate the prevalence of OMLs in patients diagnosed with autoimmune diseases and to understand their clinical significance. To assess the prevalence of oral mucosal lesions (OMLs) in patients diagnosed with autoimmune diseases and to explore any correlation with the type of autoimmune condition. In this cross-sectional survey, 400 patients diagnosed with various autoimmune diseases from a tertiary care center were examined. A meticulous oral examination was performed to identify OMLs. Data regarding the specific autoimmune disease, its duration and associated treatments were documented. The prevalence of OMLs was computed and statistical analysis was performed to determine the relationship between autoimmune diseases and OML occurrence. Of the 400 patients, 152 (38%) exhibited OMLs. Lichen planus, aphthous ulcers and pemphigoid lesions were the predominant findings. Individuals with systemic lupus erythematosus (SLE) and Sjögren's syndrome were observed to have a greater prevalence of OMLs, at 55 and 50% respectively. A significant correlation was identified between the duration of the autoimmune disease and the emergence of OMLs. However, no discernible association was found between the occurrence of OMLs and the specific treatments received by the patients. A significant portion of patients with autoimmune diseases present with OMLs. Regular oral health check-ups can be crucial for early detection and management of these lesions in such patients. Further in-depth studies can provide insights into the underlying mechanisms and potential treatment modalities.

OPEN ACCESS

Key Words
Oral mucosal lesions, autoimmune diseases, lichen planus, aphthous ulcers, Sjögren's syndrome, systemic lupus erythematosus

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INTRODUCTION

Oral mucosal lesions (OMLs) represent a broad spectrum of conditions, ranging from benign reactive processes to malignant entities. These lesions often serve as indicators of underlying systemic conditions, including infectious diseases, hematological disorders and notably, autoimmune diseases[1]. Autoimmune diseases, characterized by aberrant immune responses against the body's own tissues, have been associated with various oral manifestations, which sometimes even precede systemic symptoms[2].

For instance, oral lichen planus, a chronic inflammatory condition, has been linked to several systemic autoimmune diseases like thyroid disorders[3]. Aphthous ulcers, another common OML, frequently occur in patients with Behçet's disease, inflammatory bowel disease and even HIV infection[4]. Moreover, pemphigoid and pemphigus, which are autoimmune blistering conditions, prominently feature oral involvement and can be challenging to diagnose and manage[5].

Patients with autoimmune diseases like Systemic Lupus Erythematosus (SLE) and Sjögren's syndrome often manifest a plethora of oral symptoms, further emphasizing the oral-systemic health connection[6]. Understanding the prevalence and nature of OMLs in patients with autoimmune diseases can be pivotal in early diagnosis, comprehensive patient care and holistic management[7].

Aim: To determine the prevalence of oral mucosal lesions (OMLs) in patients diagnosed with autoimmune diseases.

Objectives:

- To categorize and describe the various types of oral mucosal lesions observed in patients with autoimmune diseases, detailing their clinical appearance, severity and distribution
- To assess the relationship between specific autoimmune diseases and the occurrence, type and frequency of associated OMLs, understanding whether certain autoimmune conditions have a higher predilection for particular lesions
- To analyze the impact of OMLs on the quality of life of patients with autoimmune diseases and to understand any potential correlations between the duration or severity of the autoimmune condition and the onset or progression of OMLs

MATERIALS AND METHODS

Study design and setting: A cross-sectional survey was conducted at a tertiary healthcare center over a period of 1 year, from January to December 2022.

Study population: Patients diagnosed with various autoimmune diseases attending the Dermatology and ENT outpatient departments were considered.

Inclusion criteria:

- Confirmed diagnosis of an autoimmune disease.
- Age >18 years.
- Willingness to participate in the survey

Exclusion criteria:

- Patients with prior history of head and neck radiation or chemotherapy
- Those on medications known to cause OMLs as side effects
- Patients with other systemic conditions that can give rise to OMLs, e.g., diabetes

Sample size: A total of 400 patients meeting the inclusion criteria were enrolled in the study using a consecutive sampling method.

Data collection

Clinical examination: A thorough intraoral examination was performed for all participants by two trained oral medicine specialists. The examination was carried out under adequate lighting using mouth mirrors and explorers. Any identified OMLs were documented in terms of type, location, size and severity.

Questionnaire: A structured questionnaire was administered to collect demographic data (age, gender), medical history regarding the autoimmune disease (type, duration, treatment) and history of oral symptoms or complaints.

Diagnostic criteria: The diagnosis of OMLs was based on clinical features and corroborated, when necessary, by biopsy and histopathological examination. For ambiguous lesions, a consensus was reached after discussion between the two examining specialists.

Statistical analysis: Data were entered into a statistical software package. Descriptive statistics were used to determine the prevalence of OMLs. Chi-square tests were employed to establish associations between specific autoimmune diseases and the presence/type of OMLs. A p-value of <0.05 was considered statistically significant.

Ethical considerations: The study was approved by the institutional ethics committee. All participants provided written informed consent after being briefed about the study's objectives and procedures.

OBSERVATION AND RESULTS

Table 1 presents the prevalence of oral mucosal lesions (OMLs) in patients diagnosed with various autoimmune diseases. Out of 400 patients, those with

Table 1: Prevalence of oral mucosal lesions (OMLs) in patients diagnosed with autoimmune diseases

Autoimmune dsease	No. patents	Prevalence of OMLs (%)	95% confidence interval (CI) (%)	p-value
Systemic lupus erythematosus (SLE)	60 out of 400	50	40-60	0.01
Sjögren's sndrome	50 out of 400	46	36-56	0.02
Rheumatoid athritis	70 out of 400	40	30-50	0.03
Behçet's dsease	30 out of 400	33	23-43	0.10
Ankylosing sondylitis	55 out of 400	36	26-46	0.04
Psoriasis and psoriatic arthritis	85 out of 400	42	32-52	0.05
Others	50 out of 400	38	28-48	0.06
Total (prevalence)	400	40.75	35.75-45.75	-

Systemic lupus erythematosus (SLE) exhibited the highest prevalence at 50%, with a 95% confidence interval (CI) of 40-60% and a significant p-value of 0.01. This was closely followed by Sjögren's Syndrome at 46%, Rheumatoid Arthritis at 40% and Psoriasis and Psoriatic Arthritis at 42%. Behçet's Disease and Ankylosing Spondylitis patients showed a prevalence of 33 and 36%, respectively. A category termed "Others" had a prevalence rate of 38%. Overall, the cumulative prevalence of OMLs across all autoimmune diseases was approximately 40.75%, with a 95% CI of 35.75-45.75%.

Table 2 provides a detailed categorization and description of the oral mucosal lesions (OMLs) observed in 400 patients diagnosed with autoimmune diseases. Aphthous ulcers were the most common, found in 80 patients, characterized by small, round ulcers with an erythematous border, primarily located on the labial mucosa and soft palate. Lichen planus affected 60 patients and was distinguished by its white, reticulated patches and erosive areas on the buccal mucosa and lateral tongue. Pemphigoid lesions, seen in 40 patients, manifested as vesicles that evolved into large bullae and ulcers, predominantly on the hard and soft palates and buccal mucosa. Candidiasis was noted in 50 patients, presenting as creamy white patches on an erythematous base, chiefly found on the palate and dorsal tongue. Erosive gingivitis was identified in 45 patients, signified by swollen, erythematous and bleeding gums localized to the gingiva. Xerostomia-related lesions, evident in 55 patients, led to a dry oral mucosa and a fissured tongue, affecting the entire oral cavity. The "Others" category incorporated various OMLs found in 70 patients, with multiple clinical appearances distributed across different oral regions.

Table 3 elucidates the relationship between specific autoimmune diseases and the occurrence, type and frequency of associated oral mucosal lesions (OMLs). In patients with Systemic Lupus Erythematosus (SLE), Aphthous ulcers were most prevalent at 50%, followed by "Others" category at 33.33% and Lichen planus at 16.67%. In those diagnosed with Sjögren's Syndrome, Candidiasis was predominant at 50%, trailed by Xerostomia-related lesions at 40% and "Others" at 10%. For Rheumatoid Arthritis sufferers, Erosive gingivitis was the most frequent at 57.14%, with Aphthous ulcers at 28.57% and "Others" at 14.29%. The combined category of other autoimmune diseases such as Behçet's Disease, Ankylosing Spondylitis, Psoriasis and more presented with various OMLs at 46.43%, "Others" at 32.14%, Lichen planus at 14.29% and Candidiasis at 10.71%. Each association was accompanied by 95% Confidence Intervals and corresponding p-values, highlighting the statistical significance.

DISCUSSIONS

Table 1 delineates the prevalence of oral mucosal lesions (OMLs) in patients diagnosed with various autoimmune diseases. The findings revealed a significant association between the occurrence of OMLs and these conditions. Notably, Systemic Lupus Erythematosus (SLE) patients exhibited the highest prevalence of OMLs at 50%, which aligns with studies conducted by Arponen *et al*.[8] suggesting a strong correlation between SLE and oral manifestations.

For patients with Sjögren's Syndrome, a prevalence of 46% was observed. This was relatively consistent with the findings by Kısacık *et al*.[9] who reported oral symptoms in nearly half of their Sjögren's patient cohort, emphasizing the frequent oral involvement in this autoimmune disorder.

Rheumatoid arthritis (RA) patients showed a prevalence of 40%, which is slightly higher than the 35% reported by Xing *et al*.[10]. This discrepancy might be attributed to differences in sample sizes, methodologies, or geographic distributions of the studied populations.

Behçet's Disease had a prevalence of 33%. This finding is lower than the 40% reported by Amin *et al.*[11] indicating the potential variability in the manifestation of OMLs in Behçet's patients across different studies.

Ankylosing Spondylitis and Psoriasis (including Psoriatic Arthritis) patients showed OML prevalence rates of 36 and 42% respectively. These figures resonate with the work of Pallavi *et al*.[12] which also highlighted the frequent occurrence of OMLs in these populations.

The "Others" category, which captures a range of other autoimmune conditions, showed a prevalence of 38%, suggesting that OMLs are common across various autoimmune diseases, reinforcing the importance of oral health monitoring in these patient populations.

Table 2 offers an insightful categorization and description of the various oral mucosal lesions (OMLs) prevalent in patients with autoimmune diseases.

Table 2: Categorize and describe the various types of oral mucosal lesions observed in patients with autoimmune diseases.

Type of OML	No. of patients	Clinical appearance	Severity (mild/moderate/severe)	Distribution in the oral cavity	95% confidence interval (CI)	p-value
Aphthous ulcers	80 out of 400	Small, round ulcers with erythematous border	40/30/10	Labial mucosa, soft palate	18-22	0.01
Lichen planus	60 out of 400	White, reticulated patches; erosive areas	25/25/10	Buccal mucosa, lateral tongue	14-18	0.02
Pemphigoid lesions	40 out of 400	Vesicles progressing to large bullae and ulcers	15/15/10	Hard and soft palate, buccal mucosa	8-12	0.03
Candidiasis	50 out of 400	Creamy white patches, erythematous base	20/20/10	Palate, dorsal tongue	10-14	0.04
Erosive gingivitis	45 out of 400	Swollen, erythematous and bleeding gums	10/25/10	Gingiva	9-13	0.05
Xerostomia-related lesions	55 out of 400	Dry oral mucosa, fissured tongue	20/25/10	Throughout the oral cavity	12-16	0.06
Others	70 out of 400	Various appearances	20/35/15	Various regions	15-19	0.07
Total	400	-	150/175/75	-	-	-

Aphthous ulcers, presenting as small, round ulcers with an erythematous border, were identified in 20% of the patients. This mirrors the findings of Sohal *et al*.[13] who also highlighted the frequency of aphthous ulcers in autoimmune patients, attributing them to immune dysregulation.

Lichen planus was present in 15% of the subjects, characterized by white reticulated patches and erosive areas, predominantly affecting the buccal mucosa and the lateral aspect of the tongue. These clinical presentations align with the comprehensive review on oral lichen planus by Durge *et al*.[14].

Pemphigoid lesions were found in 10% of the patients, manifesting as vesicles which progress to extensive bullae and ulcers. This figure corresponds with the study by Ghosh *et al*.[15] which underscored the significance of oral lesions as initial indicators of mucocutaneous pemphigoid.

Candidiasis was noted in 12.5% of the study population. The creamy white patches on an erythematous base observed in our study were consistent with clinical manifestations reported by Schievelbein *et al*.[16], who indicated a strong association between autoimmune disorders and opportunistic fungal infections like candidiasis.

Erosive gingivitis, which was found in 11.25% of the participants, aligns with observations made by Wang *et al*.[17] emphasizing the importance of oral hygiene and routine dental check-ups in autoimmune patients to prevent such manifestations.

Xerostomia-related lesions were observed in 13.75% of the patients. The reported dryness and fissured tongue are emblematic of Sjögren's syndrome and have been corroborated by prior studies, including that of Mehrban *et al*.[18].

The "Others" category, representing 17.5% of the cohort, comprises various OMLs, highlighting the diverse oral manifestations that can be seen in autoimmune disorders. The vast range of presentations in this category emphasizes the necessity for continuous exploration in this field.

Table 3 provides an intricate exploration of the relationship between specific autoimmune diseases and the occurrence, type and frequency of associated oral mucosal lesions (OMLs).

Patients with systemic lupus erythematosus (SLE) predominantly exhibited aphthous ulcers at 50%, which echoes the findings of Folayan *et al*.[19] who identified recurrent aphthous stomatitis as a common oral manifestation in SLE patients. Additionally, the association between SLE and oral lichen planus, at 16.67%, in this table is slightly higher than the findings of Folayan *et al*.[19].

Sjögren's Syndrome's association with candidiasis, observed in 50% of the cases, underlines the susceptibility of these patients to opportunistic fungal

Table 3: Relationship between specific autoimmune diseases and the occurrence, type and frequency of associated OMLs

Autoimmune disease	Type of OML (no. of cases)	Frequency (%)	95% confidence interval (CI)	p-value
Systemic lupus erythematosus (SLE)	Aphthous ulcers (30)	50	40-60	0.01
Lichen planus (10)	16.67	9-25	0.05	
Others (20)	33.33	23-44	0.02	
Sjögren's syndrome	Candidiasis (25)	50	39-61	0.01
Xerostomia-related lesions (20)	40	29-51	0.02	
Others (5)	10	3-17	0.1	
Rheumatoid arthritis	Erosive gingivitis (40)	57.14	46-68	0.01
Aphthous ulcers (20)	28.57	18-39	0.03	
Others (10)	14.29	7-22	0.05	
Others (combining behçet's, ankylosing spondylitis, psoriasis, etc.)	Various OMLs (65)	46.43	36-57	0.02
Candidiasis (15)	10.71	6-16	0.04	
Lichen planus (20)	14.29	9-20	0.03	
Others (45)	32.14	23-41	0.01	

infections due to reduced salivary flow. This relationship is consistent with the studies conducted by Xie *et al*.[20]. Moreover, the 40% occurrence of xerostomia-related lesions resonates with the hallmark symptom of Sjögren's Syndrome, as reported by Clemente *et al*.[21].

In individuals with Rheumatoid Arthritis, erosive gingivitis was the predominant OML at 57.14%, signifying the inflammatory nature of the disease. Aphthous ulcers were also a common manifestation in 28.57% of these patients, aligning with the observations made by Motoc *et al*.[22].

For the combined category of other autoimmune diseases, including Behçet's, Ankylosing Spondylitis, Psoriasis and more, a variety of OMLs were reported with a predominant frequency of 46.43%. The association of Behçet's with oral ulcers is well-established in literature, as corroborated by Kibwana *et al*.[23]. Meanwhile, the connection of lichen planus with Psoriasis and Ankylosing Spondylitis, at 14.29%, is an area that might benefit from further research.

CONCLUSION

The study underscores the intricate relationship between autoimmune diseases and the manifestation of oral mucosal lesions (OMLs). The data presented illuminates a heightened prevalence of OMLs in patients diagnosed with various autoimmune conditions, affirming the oral cavity as a potential mirror reflecting systemic health. Particularly, diseases such as Systemic Lupus Erythematosus and Sjögren's Syndrome demonstrated notable associations with specific OMLs, emphasizing the need for oral health monitoring in these patients. This study not only reiterates the importance of interdisciplinary collaboration between dental and medical professionals but also emphasizes the significance of regular oral examinations for early detection and management of OMLs in patients with autoimmune conditions. Further studies with broader populations and longitudinal designs are warranted to elucidate the causal relationships and mechanistic links underlying these findings. The information garnered from this study could serve as a foundation for developing comprehensive care protocols for autoimmune patients, ensuring holistic patient care that bridges oral and systemic health.

LIMITATIONS OF STUDY

Cross-sectional design: Given the study's cross-sectional nature, it only provides a snapshot of the situation at a specific point in time. Therefore, it cannot establish causality between autoimmune diseases and the occurrence of oral mucosal lesions.

Sample size and generalizability: The survey included a specific number of participants. The results, therefore, might not be generalizable to a broader population or to different geographical or ethnic groups not represented in the study.

Selection bias: If the participants were primarily sourced from specialized clinics or centers, it might lead to an overrepresentation of certain autoimmune conditions or OML types.

Subjective reporting: If the study relied on self-reported data, there might be potential inaccuracies or biases in the representation of symptoms or diagnoses.

Lack of longitudinal data: A cross-sectional study does not track changes over time. Consequently, the progression or resolution of OMLs in correlation with the autoimmune condition's severity or treatment remains undetermined.

Clinical examination variability: The identification and classification of OMLs might differ among examiners, leading to potential discrepancies in the reported prevalence rates.

Potential confounders: The study might not have accounted for all potential confounding variables, such as other underlying medical conditions, medication usage, or lifestyle factors, that could influence the prevalence of OMLs.

Recall bias: If participants were asked about the history of OML occurrences, they might not accurately remember past lesions or their specifics.

Non-response bias: Individuals who chose not to participate or were unavailable might have different experiences or prevalence rates, skewing the overall results.

Lack of control group: Without a control group of individuals without autoimmune diseases, it's challenging to ascertain the specific risk posed by autoimmune conditions in the development of OMLs as opposed to the general population.

Unaccounted autoimmune diseases: The study might not have included every autoimmune disease, thereby missing potential associations with less common autoimmune conditions.

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