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ORALNE MANIFESTACIJE POVEZANE SA CELIJAKIJOM KOD SIRIJSKIH PACIJENATA: STUDIJA PRESEKA

ASSOCIATION OF ORAL MANIFESTATIONS WITH CELIAC DISEASE IN SYRIAN PATIENTS: A CASE-CONTROL STUDY

Aliaa H Al Shaar[1], Omar H Hamadeh[1], Ayman F Ali[2]

[1]UNIVERZITET U DAMASKU, FAKULTET DENTALNE MEDICINE, KATEDRA ZA ORALNU MEDICINU, DAMASK, SIRIJA
[2]UNIVERZITETE TISHREEN, MEDICINSKI FAKULTET, KATEDRA ZA INTERNU MEDICINE, LATAKIJA, SIRIJA

[1]DEPARTMENT OF ORAL MEDICINE, FACULTY OF DENTAL MEDICINE, DAMASCUS UNIVERSITY, SYRIA
[2]DEPARTMENT OF INTERNAL MEDICINE, FACULTY OF MEDICINE, TISHREEN UNIVERSITY, SYRIA

Sažetak

Uvod: *Celijakija je autoimuno oboljenje koje primarno izaziva unos glutena iz pšenice, ječma i ovsa. Može se manifestovati i simptomima koji ne zahvataju digestivni trakt; činjenica da gastrointestinalne tegobe mogu izostati otežava pravovremenu dijagnozu i smanjuje dijagnostičku prepoznatljivost ove bolesti. Oralne manifestacije predstavljaju važne indikatore u identifikaciji celijakije kod pacijenata. Prepoznajući karakteristične oralne znakove i upućujući pacijente na konačnu dijagnostičku evaluaciju, stomatolozi igraju ključnu ulogu u ranom otkrivanju celijakije. Cilj ove studije bio je da se ispitaju oralne manifestacije povezane sa celijakijom.*
Materijali i metode: *Sprovedena je studija tipa slučaj–kontrola sa sedamdeset ispitanika, koji su bili podeljeni u dve grupe: u prvoj grupi bilo je trideset pet osoba sa dijagnostikovanom celijakijom, a u drugoj trideset pet zdravih ispitanika, koji su činili kontrolnu grupu. Oralni nalazi – rekurentne aftozne stomatitis (engl. Reccurent Aphtosus Ulcers – RAU), blede i ispucale usne, angularni heilitis (žvale), atrofični glositis (glatki jezik) i benigni migrirajući glositis (geografski jezik) – pregledani su pod halogenim osvetljenjem, uz pomoć sterilnog stomatološkog ogledala.*
Rezultati: *U studiji je korišćen X^2 test, koji je ukazao na postojanje značajnih razlika između grupe ispitanika sa celijakijom i kontrolne grupe. Statistički značajna povezanost uočena je između celijakije i RAU-a ($p = 0,000$), [A4.1][MN4.2]atrofičnog glositisa ($p = 0,041$) i benignog migrirajućeg glositisa ($p = 0,000$). Nasuprot tome, između posmatranih grupa nije zabeležena statistički značajna razlika kada je reč o učestalosti pojave bledih i ispucalih usana ($p = 0,066$) i angularnog heilitisa ($p = 0,779$).*
Zaključak: *Rezultati ove studije preseka pružili su uvid u oralne manifestacije povezane sa celijakijom. Takođe, u studiji je istaknut značaj rutinskih stomatoloških pregleda i ranog prepoznavanja oralnih manifestacija kod osoba sa celijakijom, s obzirom na to da one mogu biti važni klinički indikatori pomenutog autoimunog poremećaja.*

Ključne reči: *celijakija, oralne manifestacije, rekurentni aftozni stomatitis*

Corresponding author:
Aliaa H Al Shaar, DDS, Department of Oral Medicine, Faculty of Dental Medicine, Damascus University
E-mail: aliaa.alshaar@damascusuniversity.edu.sy
ORCID: 0009-0003-8114-8399

Abstract

Introduction: *Celiac disease is an autoimmune condition that is primarily elicited by the ingestion of gluten from wheat, barley and oats. Celiac disease may present with extra-intestinal symptoms despite the absence of gastrointestinal complaints, complicating timely diagnosis and leading to underrecognition. Oral manifestations are valuable indicators for identifying patients with celiac disease. In this context, dentists are pivotal in the early detection of celiac disease by recognizing characteristic oral signs and referring patients for definitive diagnostic evaluation. The objective of this study was to explore the oral manifestations associated with celiac disease.*
Materials and Methods: *A case-control study was conducted involving 70 participants grouped as follows: 35 individuals diagnosed with celiac disease and 35 individuals representing the control group. Oral findings—recurrent aphthous ulcers (RAU), pallor and fissured lips, angular cheilitis, atrophic glossitis, and geographic tongue—were examined under halogen illumination using a sterile dental mirror.*
Results: *The study employed chi-square analysis to identify significant differences between the celiac disease group and the control groups. Significant associations were detected between celiac disease and recurrent aphthous ulcerations ($p = 0.000$), atrophic glossitis ($p = 0.041$), and geographic tongue ($p = 0.000$). However, no significant difference was observed in the incidence of pallor and fissured lips ($p = 0.066$) and angular cheilitis ($p = 0.779$) between the two groups.*
Conclusion: *The outcomes of this cross-sectional study provide valuable insights into the oral manifestations associated with celiac disease. The study underscores the significance of routine dental examinations and the early identification of oral manifestations in individuals diagnosed with celiac disease, as they may serve as crucial clinical indicators of the underlying autoimmune disorder.*

Key words: *celiac disease, oral manifestations, recurrent aphthous ulcers*

Introduction

Celiac disease, an autoimmune disorder affecting the gastrointestinal tract in genetically susceptible individuals, can manifest at any age as a result of the immune response to gluten found in wheat, barley and oats. Intestinal damage leads to malabsorption of crucial nutrients, resulting in vitamins (vitamin D), minerals (iron, calcium), and folic acid deficiencies, contributing to conditions such as osteoporosis, delayed growth, enamel degradation, and oral manifestations[1]. Diagnosis of celiac disease involves initial serological tests followed by histological examination of duodenal biopsies. The sole treatment for celiac disease currently entails strict adherence to a lifelong gluten-free diet[2]. Primary symptoms of celiac disease typically include chronic diarrhea, abdominal pain, weight loss, and muscle weakness[3]. Typically, the disease may manifest with symptoms outside the digestive system such as short stature, non-responsive anemia, dermatitis herpetiformis, and joint pain, alongside various oral manifestations including recurring oral ulcers, pale and fissured lips, angular cheilitis (is an inflammation at the commissures of the lips), atrophic glossitis (is characterized by the partial or complete absence of filiform papillae on the dorsum of the tongue), and geographic tongue (there is the recurrent appearance and disappearance of red areas on the tongue)[4,5]. Although there is a clear association between celiac disease and oral manifestations, the current medical literature lacks conclusive research establishing a direct connection between oral signs and celiac disease. Dentists have a vital role in detecting celiac disease through its atypical or extra-intestinal presentations. The presence of these oral manifestations can assist in identifying celiac disease even when digestive symptoms are absent[6,7]. The prevalence of celiac disease in the general population ranges from 0.5% to 1%, with a high proportion of undiagnosed cases until adulthood[8]. The prevalence of celiac disease in Arab countries was investigated in a review study, which included 35 studies from 12 Arab countries published between 1996 and 2019. The highest prevalence of celiac disease was in Saudi Arabia (3.2%), and the lowest prevalence was in Tunisia (0.1%)[9]. This study aimed to investigate the prevalence of oral manifestations associated with celiac disease in individuals from the Syrian Arab Republic, specifically in the city of Damascus.

Materials and Methods

A case-control study was conducted in Damascus, Syrian Arab Republic between September 2022 and April 2023. This study represents the first of its kind in this region. Patients visiting Gastroenterology Clinic of Damascus hospital and the Department of Oral Medicine at the Faculty of Dentistry, Damascus University were included in the study. Ethical approval for the study was obtained from the Ethics Committee at Damascus University under approval number DN-241023-8-H7.

Inclusion and exclusion criteria involved individuals diagnosed with celiac disease confirmed by duodenal biopsy, aged 18 years and above, with no history of systemic diseases other than celiac disease. The control sample comprised individuals matched for age and gender with the study sample, with no history of any digestive diseases. None of the participants were on any medication regimen or had any systemic diseases, such as hemolytic anemia or chronic renal failure.

This study comprised 70 individuals, allocated into two groups as follows: 35 patients diagnosed with celiac disease and 35 individuals representing the control group. The allocation of participants into these groups was determined using the G*Power 3.1.9.2 program with a significance level set at 0.05, confidence level at 0.95, and a size effect of 0.8.

The participants received comprehensive details on the study's objectives and procedures, and written informed consent was obtained from each individual. Additionally, the patient has granted consent for the publication of their case details and images. Demographic information encompassing age, gender, the patients' history, medication intake, and oral lesions was methodically documented. A sole examiner, adequately trained, meticulously examined the oral cavity using a sterile dental mirror under halogen light in a clinical setting. The examiner meticulously assessed the presence of various oral manifestations, such as recurrent aphthous ulcerations (RAU), atrophic glossitis, pallor and fissured lips, geographic tongue, and angular cheilitis. The clinical presentation of each oral condition—including lesion size, frequency of episodes, and associated discomfort—was systematically recorded. The documented clinical appearances were based on both the patients' medical history and

observed clinical manifestations, ensuring reliability in the assessment process while minimizing examiner variability and bias.

Data were tabulated and analyzed using SPSS software (SPSS Version 20, IBM SPSS Inc., Chicago, IL, USA). Statistical tests, such as the chi-square, were used to test the research hypotheses. Results presented in appropriate tables were considered significant if the p-value was < .05.

Results

This case-control study included 70 participants, divided equally into two groups: 35 patients diagnosed with celiac disease and 35 healthy controls. The mean age of the celiac group was 36.45 ± 9.63 years, while the control group had a mean age of 36.00 ± 9.63 years, as shown in Table 1. Gender distribution was similar across groups.

As illustrated in Table 2 and Figure 1, recurrent aphthous ulcers were found in 85.3% of patients with celiac disease (n = 29), compared to 38.2% of controls (n = 13). This difference was statistically significant (χ^2 = 15.941, p < 0.001).

Atrophic glossitis was observed in 32.4% of celiac patients (n = 11), versus 11.8% of controls (n = 4), showing a significant association (χ^2 = 4.191, p = 0.041). Geographic tongue was present in 73.5% of patients with celiac disease (n = 25) and 26.5% of controls (n = 9), also statistically significant (χ^2 = 15.059, p < 0.001).

In contrast, no significant difference was found between the two groups in the occurrence of pallor and fissured lips (χ^2 = 3.376, p = 0.066) or angular cheilitis (χ^2 = 0.780, p = 0.779). These findings are detailed in Table 2 and further illustrated in Figures 2–5.

Table 1. Descriptive statistics of this study

Groups				Male		Female	
	Number	average age	Standard deviation	number	percentage	number	Percentage
Control	35	36	9.63	12	35.8%	22	64.7%
Celiac	35	36.45	9.63	13	38.2%	20	58.8%

Table 2. Descriptive analysis and study of the presence of a significant difference

Variables in the celiac group		Number	Percentage	Variables in the control group		Number	Percentage	Chi-square test	P-value	Significance test
Recurrent aphthous ulcerations	No	5	14.7%	Recurrent aphthous ulcerations	No	21	61.8%	15.941	0.000	There is a statistically significant difference
	Yes	29	85.3%		Yes	13	38.2%			
Atrophic glossitis	No	23	67.6%	Atrophic glossitis	No	30	88.2%	4.191	0.041	There is a statistically significant difference
	Yes	11	32.4%		Yes	4	11.8%			
Geographic tongue	No	9	26.5%	Geographic tongue	No	25	73.5%	15.059	0.000	There is a statistically significant difference
	Yes	25	73.5%		Yes	9	26.5%			
Pallor and fissured lips	No	26	76.5%	Pallor and fissured lips	No	27	79.4%	3.376	0.066	There is no statistically significant difference
	Yes	14	41.2%		Yes	7	20.6%			
Angular cheilitis	No	26	76.5%	Angular cheilitis	No	25	73.5%	0.78	0.779	There is no statistically significant difference
	Yes	8	23.5%		Yes	9	26.5%			

Figure 1. The occurrence of oral lesions in the study sample

Figure 2. Recurrent oral ulcer in a patient with celiac disease

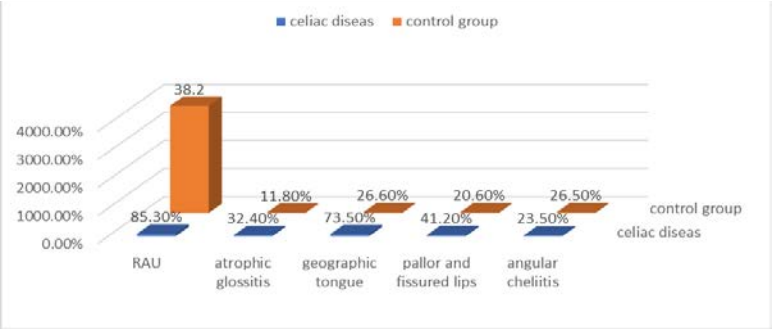

Figure 3. Atrophic glossitis in a patient with celiac disease

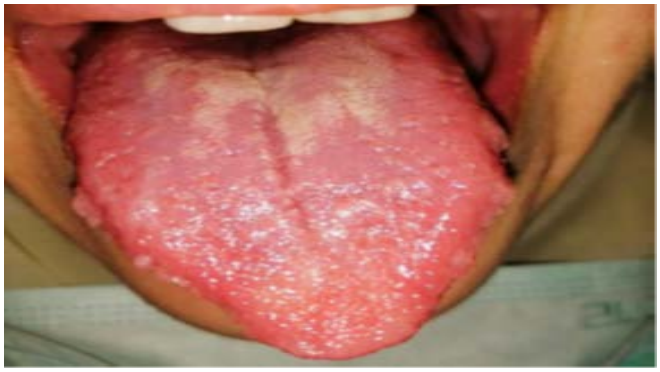

Figure 4. Geographic tongue in a patient with celiac disease

Figure 5. Angular cheilitis in a patient with celiac disease

Discussion

Celiac disease is a chronic autoimmune disorder of the small intestine, characterized by villous atrophy and triggered by gluten ingestion in genetically susceptible individuals. Although classical gastrointestinal symptoms such as diarrhea, malabsorption, and weight loss were once hallmark indicators, their prevalence has declined, and many patients—particularly adults—now exhibit a non-classical or asymptomatic form. This atypical presentation contributes significantly to delayed or missed diagnoses. The anatomical and functional interplay between the gastrointestinal tract and the oral cavity has highlighted a frequent association between celiac disease and extra-intestinal manifestations, notably oral soft tissue lesions. These oral signs, particularly common among individuals with nonclassical celiac disease, emphasize the pivotal role of dental examinations in facilitating early detection and improving clinical outcomes[10].

Recurrent aphthous ulceration (RAU) is a common oral lesion in patients with celiac disease, characterized by painful ulcers bordered by an erythematous halo. Its unclear etiology is attributed to immune dysregulation, genetic factors, and deficiencies in iron, folic acid, or vitamin B12[11]. In this study, RAU was the most frequently observed manifestation, occurring in 85.3% of cases, which is consistent with previous literature[12–14]. In contrast, the other studies reported no statistically significant difference in the occurrence of recurrent aphthous ulcers in patients with celiac disease compared to the control group[3,15,16].

However, variations in prevalence across studies may reflect differences in patient age, geographic distribution, or diagnostic criteria. While earlier research predominantly focused on younger individuals, the current findings suggest significant RAU expression in adults, raising questions about age-related trends. Further research is essential to clarify the pathophysiological mechanisms and to determine the role of nutrient deficiencies and malabsorption in RAU development within this population[17].

Atrophic glossitis and geographic tongue also appeared significantly more often in the celiac group compared to controls, supporting findings from earlier literature. These conditions may reflect the impact of nutrient malabsorption, especially iron and vitamin B-complex deficiencies commonly associated with untreated celiac disease[6,12,18].

Conversely, angular cheilitis and pallor and fissured lips did not differ significantly between groups, in contrast to some published reports, suggesting that these features may be less specific indicators of celiac pathology[6,7,19].

Limitations

This study was subject to several methodological limitations. First, the relatively small sample size may restrict the generalizability of the findings to broader populations. However, the sample was deliberately selected to align with a parallel investigation examining serum and salivary levels of tissue transglutaminase enzyme (tTG) in celiac patients and matched controls, which required strict inclusion criteria and sample matching across both research arms[20].

Second, oral examinations were conducted by a single trained examiner, which may introduce observer bias despite efforts to ensure consistency and standardization of assessment procedures. The use of one examiner was necessitated by the need for clinical continuity and data harmonization with the concurrent biochemical study.

While these constraints should be considered when contextualizing specific outcomes, the integrated design offers a unique opportunity to correlate clinical oral findings with immunological markers. Future studies are recommended to involve larger and more diverse populations, employ multiple calibrated examiners, and incorporate longitudinal monitoring to further validate and expand upon these results.

Conclusion

This study highlights a significant association between celiac disease and specific oral manifestations such as recurrent aphthous ulcers, atrophic glossitis, and geographic tongue. These findings reinforce the critical role of dental practitioners in the early detection of systemic conditions, particularly when gastrointestinal symptoms are absent.

Routine oral examinations in dental settings should incorporate screening protocols for identifying patterns indicative of celiac disease and other systemic diseases. Dentists should be trained to recognize these manifestations and refer patients for further medical evaluation when appropriate.

Future research is recommended to include larger and more diverse populations, assess serum nutritional levels, and control for dietary factors to better understand the underlying mechanisms linking oral health with systemic disease. Such efforts will contribute to more integrated approaches between dentistry and general medicine, ultimately improving patient outcomes.

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Conflicts of Interest

The authors declare no possible conflict of interest

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