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Periodontal Treatment Needs and Oral Ulceration in Children and Adolescents with Celiac Disease

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Authors' contributions

This work was carried out in collaboration between the both authors. Author RH diagnosed the celiac patients, author RD examined the oral cavity and record all the dental findings. The two authors worked together in designing the study and writing the manuscript. The both authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: To determine periodontal treatment needs and the incidence of oral ulceration among children and adolescents with celiac disease and to compare their findings with a healthy age and gender-matched control group.
Methods: A prospective study was conducted at King Hussein Medical Center on a total of 86 patients: 43 patients with celiac disease as the study group (comma removed) and 43 healthy age and gender-matched participants as the control group. Both groups were questioned for a history of recurrent mouth ulcers (comma removed) and the frequency of tooth brushing. The dental examination for each patient in both groups included the following: plaque index, gingival index (comma removed) and Community Periodontal Index of Treatment Needs (CPITN). The oral mucosa was examined clinically for any lesion consistent with aphthous ulceration.
Results: There were 26 females and 17 males in each group, with a mean age of 13.2 and 13.3 years respectively. Plaque scores were significantly higher among the study group ($p<0.05$) while the difference in the gingival scores was not statistically significant ($p>0.05$). Recurrent aphthous ulceration (RAS) was positive among 13 (30.23%) celiac

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patients compared to 9 (20.9%) among the control group. However, the result was not statistically significant (p>0.05). CPITN revealed no significant difference between the two groups although the mean index was higher among the celiac group. No one in either group scored 0, while the highest percentage in both groups scored 2. Shallow and deep pockets (scores of 3 and 4) were greater in celiac patients. Overall, the variation between the two groups was not statistically significant.
Conclusion: Oral hygiene status seems worse in celiac patients, which indicates that oral health education programs may be beneficial for these children. Although the need for periodontal treatment and the frequency of RAS are higher in celiac patients, the statistical difference was not significant (p NS).

Keywords: Celiac disease; periodontal treatment needs; oral ulceration; children and adolescents; Jordan.

1. INTRODUCTION

The oral cavity is part of the gastrointestinal tract so it is not surprising that any disorder affecting this system can be manifested in the oral cavity. Celiac Disease (CD) is considered a malabsorption syndrome; the disease more closely resembles a multi-systemic disorder with the intestine as the primary site of the disease, in particular the small intestine's intolerance to gluten [1].

The cause of celiac disease was unexplained until a Dutch pediatrician recognized an association between the consumption of bread and cereals and relapsing diarrhea. This observation was confirmed during the periods of food shortage in the Second World War, the symptoms of patients improving once bread was replaced by non-cereal-containing foods [2]. The toxic agents in the cereals were found to be present in gluten, the primary protein found in wheat. The grains that contain the triggering proteins are wheat, barley and rye.

The disease involves the small bowel, from the duodenum to ileum and is characterized by histological mucosal alterations (more or less severe villous atrophy, crypt hyperplasia and increased lymphocytic infiltration of the lamina propria). Identification of celiac disease is facilitated by widely available serological tests, particularly for anti-endomysial and anti-tissue transglutaminase antibodies, but definite diagnosis requires small bowel biopsies and the demonstration of villous atrophy with improvement or normalization on a gluten-free diet [3].

Screening studies have found a prevalence of 1 in 300 and it has been suggested that the prevalence might be as high as one in 100 individuals [4]. Its prevalence is extremely variable from country to country and predominantly affects white individuals [5]. Several studies have shown that the risk of CD is much higher among first-degree (1:10) than second-degree relatives (1:40) and in people with certain chronic diseases such as Type I juvenile diabetes mellitus and autoimmune diseases (1:60) [6]. CD was not considered as a common diagnosis among children in Jordan, the incidence calculated to be 1:2,800 [7]. However, in a more recent publication using serological tests, the prevalence of celiac disease among schoolchildren in Jordan was estimated to be 1:124 [8].

For many years, typical celiac disease was the only type described, and was defined by a set of classic clinical malabsorption manifestations of childhood. However, the combination of serological, genetic and histological data has led to the description of other categories of

the disease. These include: a) the atypical type in which the extra intestinal manifestations are predominant, and few or no gastrointestinal symptoms are evident [9]; b) the silent/subclinical type which has no discernable symptoms of celiac disease, but has a positive specific serological test for the disease and biopsy evidence of villous atrophy [10]; and c) the latent type which includes individuals with celiac disease, but who have normal jejunal mucosa and display no or minor symptoms (at least at one point in time) while on a normal, gluten-containing diet [11]. Catassi et al. [12] found that the number of so-called silent celiacs is much higher than the number of patients with classic celiac disease. That study, which was performed on school children in Italy, showed the ratio of asymptomatic to symptomatic cases was a remarkable 7:1 [12].

In order to identify the greatest number of 'atypical' or 'silent' CD patients and prevent long-term complications, it has been suggested that the clinicians should investigate those subjects who present 'indirect' signs of the disease such as chronic anemia, hypertransaminasemia or hyperamylasemia of unknown origin, osteoporosis and autoimmune thyroid disorders [13]. Therefore, clinical knowledge, clinician suspicion in the appropriate setting and a thorough history and examination remain the cornerstone for approaching CD [14].

According to a recent study investigating the burden of celiac disease in the Mediterranean area, a delay in diagnosis is expected to increase mortality; about 600 000 celiac patients will die in the next 10 years and over 44.4% compared to their age and sex-matched controls [15]. Yet further evidence that identifying the greatest number of hidden CD patients and thus preventing long-term complications is paramount to treating and controlling the disease.

The oral cavity including the dentition has also been investigated for this purpose, with most dental research associated with celiac disease focusing on enamel defects. This relationship between enamel defects and CD was first described by Smith and Miller in 1979. Since then, some researchers have found that the prevalence of enamel hypoplasia is not higher in celiac disease patients than in the control group [13], while others have found it significantly more common among CD patients [16].

The other controversial issue in dental literature is the prevalence of recurrent aphthous stomatitis (RAS) among patients with CD. It has been reported that individuals with RAS have an increased prevalence of CD which suggests that oral aphthae may be an early indicator or sign of CD [17]. Other studies, meanwhile, have demonstrated that there are no significant differences between patients with celiac disease and the general population regarding the prevalence of recurrent aphthous stomatitis [18]. However, data from literature is often controversial, probably because of the different geographical origins of patients studied and the lack of adequate controls.

In addition to enamel defects and recurrent aphthous ulcers, Rashid et al. [19] reported delayed eruption, cheilosis, oral lichen planus and atrophic glossitis as other manifestations of celiac disease. The only publication that explored periodontal condition as one aspect of oral health status was performed by Tsami et al. [20], their study had two limitations: the lack of a control group and the fact that the celiac patients included in the study were all compliant with gluten free diet (GFD). Therefore, the objectives of this study were, initially, to determine periodontal treatment needs and the incidence of oral ulceration among children and adolescents with celiac disease, and secondly to compare their findings with healthy age and gender-matched children and adolescents.

2. METHODS

This prospective study was conducted at King Hussein Medical Center (KHMC) on a total of 86 patients: a study group of 43 patients with celiac disease who were regular attendants of the pediatric gastrointestinal clinics at KHMC, and a control group of 43 healthy age and gender-matched children who attended the general dental practice clinic at the out-patients clinic of the same hospital.

For the study group, the level of compliance with a gluten-free diet was recorded as non-compliant or compliant. Both study and control groups were questioned, firstly, on tooth-brushing frequency (which was recorded as follows: 0: never brush their teeth, 1: occasional brushing, 2: once daily brushing and 3: twice or more daily brushing) and secondly, on a history of any recurrent painful ulceration in the oral cavity. This covered intervals of ulceration, from a few months to a few days, the size, color and duration of the ulcer in the mouth. If an ulcer was present while examining the oral cavity, the type of the ulcer was categorized as minor, major, or herpetiform according to the criteria described by Scully and Porter [21].

The dental examination for both groups was carried out by a single examiner at the periodontal clinic in the out-patient clinics at KHMC and included the number of erupting deciduous and permanent teeth (excluding third molars), in addition to the plaque index for all buccal and lingual surfaces of all teeth present according to the following criteria: 0=no plaque; 1=plaque visible only when scraped by an explorer; 2=visible plaque; 3=heavy plaque accumulation [22]. The gingival condition was assessed according to the Gingival Sulcus Bleeding Index based on the presence or absence of bleeding on probing at the mesial and distal sites around each tooth [23]. Periodontal treatment needs were assessed according to the criterion of the Community Periodontal Index of Treatment Needs (CPITN) in which the full dentition is divided into six segments, three in each jaw (one anterior and two posterior). Only the highest score in any given sextant of teeth examined was recorded as follows: 0=healthy periodontium (no treatment); 1=bleeding on probing (only oral hygiene instruction OHI); 2=calculus and iatrogenic marginal irritation (OHI and scaling); 3=shallow pockets up to 5mm (OHI and scaling); 4=deeper pocket from 6mm (OHI and scaling and complex periodontal treatment) [24].

The results obtained were expressed as absolute values with corresponding percentages. Differences between the celiac patients and the control group were tested using χ^2 tests and independent sample *t*–tests. In all of evaluations *p* values less than 0.05 were considered statistically significant.

3. RESULTS

Out of the total of 43 patients in each of the study and control groups, there was 26 females (60.5%) and 17 (39.5%) males. The mean age of the patients was 13.2±2.85 years for the study group and 13.4±2.74 years for the control group, with a range of 8-18 years in both groups.

Although tooth-brushing frequency was not satisfactory among both groups, the percentage of patients who never brush their teeth or brush occasionally was 86.1% in the celiac patients compared to 65.1% in the control group, while patients who brush once or twice

daily accounted for 13.9% among the study group compared to 34.9% among the control group (Table 1). This difference was statistically significant *(p < 0.05)*.

Table 1. Differences in the brushing habits between the study and control group

Tooth Brushing frequency	Celiac No. (%)	Control No. (%)
Never	13 (30.3%)	0
Occasional	24 (55.8%)	28(65.1%)
Once	5 (11.6%)	8(18.6%)
Twice	1(2.3%)	7(16.3%)
Total no. of patients	43	43

Plaque scores were significantly higher among the study group (*p<0.05)*. However, the difference in the gingival scores between the study and control groups was not statistically significant (*p>0.05)*. General assessment of the periodontal treatment needs as assessed by CPITN revealed no significant difference between the celiac and control groups although the mean index was higher among the celiac group. Differences in the means of indices are presented in Table 2.

Table 2. Differences in plaque and gingival indices and CPITN between the study and control groups

Variable	Group	No.	Mean	Std. deviation	Std. error mean	*Sig. (2-tailed)*
Plaque Index	study	43	1.4812	.43817	.06682	*0.012 Sig.*
	control	43	1.2434	.42131	.06425	
Gingival index	study	43	.8093	.23055	.03516	*0.23 N.S*
	control	43	.7549	.18675	.02848	
CPITN	study	43	1.7119	.78758	.12010	*0.14 N.S*
	control	43	1.4878	.60472	.09222	

Table 3 shows the percentage variation, according to the CPITN scores, between the celiac and control groups with the mean index for each group. It can be noted from the table that no one in either group achieved a score of 0 (no need for periodontal treatment), while the highest percentage in both groups was for a score of 2. Shallow and deep pockets (3 and 4) were greater in celiac patients. However, the variation between the two groups was not statistically significant.

Table 3. Differences in CPITN scores between the celiac and control groups with the mean index for each group

	CPITN 0	CPITN 1	CPITN 2	CPITN 3	CPITN 4	Mean index
Study (43)	0	14	15	11	3	1.71±0.79
%		32.5%	34.88%	25.58%	6.97%	
Control (43)	0	12	25	4	2	1.49±0.6
%		27.9%	58.13%	9.30%	4.65%	

The presence or history of recurrent aphthous ulceration was positive among 13 (30.23%) celiac patients compared to nine (20.9%) among the control group. However, the result was not statistically significant (*p>0.05)*. Ulcers observed in oral examinations were all of a minor

type (Fig. 1). Out of the 13 celiac disease patients with ulcers, four were non-compliant and nine were compliant with GFD.

Fig. 1. Minor aphthous ulcer appears in the lower labial mucosa of a celiac disease child

The compliance of celiac disease patients with GFD revealed that 34.8% of the patients were non-compliant, while 65.2% were compliant. Differences in the mean indices for each group are presented in Table 4. No significant difference was found between the compliant and non-compliant patients with regard to recurrent apthous stomatitis.

Table 4. Variation in the means of indices according to the compliance with GFD

Compliance with GFD	*No (%)*	*Age*	*PI*	*GI*	*CPITN*
Not compliant	15 (34.8)	12.71	1.63	0.83	1.74
Compliant	28 (65.2)	13.45	1.42	0.75	1.70

4. DISCUSSION

The existence of an association between gastrointestinal disorders and oral manifestation has been well documented in the literature. Crohn's disease, celiac disease and ulcerative colitis may occasionally be associated with recurrent aphthous stomatitis [25]. Symptoms reported to be associated with Crohn's disease include hypertrophy and swelling of the lips, gingival soft tissue swelling which resembles epulis fissuratum, and cobblestone appearance of the buccal mucosa and palate [26]. In addition to oral ulceration, celiac disease has also been associated with enamel defects but the results are controversial; manifestation related to the periodontium in celiac disease patients was only reported in one publication [20].

This study investigated the periodontal treatment needs and the incidence of oral ulceration of children and adolescents with mixed and permanent dentition who were diagnosed with celiac disease, and compared their oral findings with an age and gender-matched control group. Gender distribution in this study {females (60.5%) vs. (39.5%) males} found a predisposition of females to celiac disease. This finding was less than that reported by Sedghizadeh et al. [18] who found that 79% of celiac disease group were females [19], while more than that reported by Nusier et al. [8] who found that only 56.3% of celiac school children in Jordan were females.

In this current study, poor oral hygiene behavior was noticed in both groups although it was slightly worse in the CD group. In addition, the mean plaque index among the celiac patients was significantly higher than that of the control group, a finding which reflects the inferior tooth-brushing habits among patients with celiac disease in the study. Avsar and Kalayci [16] showed no significant difference in tooth-brushing habits between celiac and control groups. Note that other variables which may affect this issue such as socio-economic status and education levels of the parents were not assessed in the present study.

Recent research in Israel compared oral health, bacterial colonization and salivary buffering capacity of children with CD receiving GFD, recently diagnosed CD, and control group. The results revealed lower plaque scores in children with CD receiving GFD that could not be explained by salivary properties or bacteria but rather by better oral hygiene [27].

The first and only report regarding the periodontal status of celiac disease patients was published by Tsami et al. [20], who found that the periodontal treatment needs of children and adolescents with CD were high; 60.01% needed treatment of gingivitis and only a few (34.29%) had a healthy periodontium. They also found that the periodontal treatment need index, the simplified gingival index and the hygiene index showed a statistically significant correlation with the presence of a coexisting disease, the frequency of tooth-brushing, gum bleeding with brushing and oral malodor [20]. The limitations of their study included the lack of a control group and the fact that the celiac patients were all compliant with GFD. To obviate these limitations, a comparison with healthy pediatric patients and also with celiac patients who are not compliant with GFD would have been necessary.

In the present study the periodontal treatment needs of celiac disease patients was compared with a healthy age and gender-matched group, the results of which showed no significant difference between them, although the mean index was higher among the celiac group. No one in either group recorded a CPITN score of 0 which means that there was no need for periodontal treatment. The majority of children in both groups showed bleeding on probing or calculus which indicates a greater need for oral hygiene instruction and scaling, although the percentage of those who scored CPITN 1 and 2 were greater among the control group than the celiac patients (86% vs. 67.4%). Celiac patients with shallow and deep pockets (CPITN 3 and 4) were greater than control group counting 32.57% vs. 14.95%.

The periodontal treatment needs among celiac disease patients in this study compared to those concluded by Tsami et al., (2010) revealed the following results: score 0 (0% vs. 34.3%), score 1 (32.5% vs. 28.6%), score 2 (34.9% vs. 31.4%), score 3 (25.6% vs. 5.7%), and score 4 (6.9% vs. 0%). While the results for scores 1 and 2 are comparable, those for scores 0, 3 and 4 highlight a big difference between the patients in the two studies. It can be concluded from this that, in general, the current study indicates a greater need for periodontal therapy for celiac sufferers, although this may possibly reflect the inferior periodontal health status among Jordanian compared to Greek celiac disease children and adolescents.

The primary etiological factor for periodontal disease is microbial dental plaque. The main organisms linked with deep destructive periodontal lesions are *P. gingivalis*, *P. intermedia*, Bacteroides forsythus, *A. actinomycetemcomitans* and *T. denticola* [28]. Consequently, periodontal pathogens are essential for periodontal disease initiation; however, the extent and severity of tissue destruction are largely dependent on the nature of the host-microbial interactions. In recent years, there has been intense interest in potential associations between periodontal disease and various systemic diseases and conditions that may alter

the host response and increase the risk for periodontal disease. Celiac disease is well-known to be caused by genetic and environmental factors. The only well-defined environmental factor necessary for CD to develop is obviously gluten. However, the composition of intestinal microbiota, seem to play a role in CD as reported by Collado et al. in 2009 who found that patients with CD have a dysbiosis in their digestive tract characterized by a larger rate of Bacteroides spp. and a smaller rate of Bifidobacterium spp. and B. longum when compared with healthy controls, and this dysbiosis did not seem to normalize after a gluten free diet was introduced [29]. In view of the fact that microbial etiology plays a role in the etiology of periodontal disease as well as CD, research concerns with the microbes associated with both diseases would be of interest for further studies.

Recurrent aphthous stomatitis (RAS) comprises recurrent bouts of one or several rounded, shallow, painful ulcers at intervals of a few months to a few days in people who are otherwise well [21], and affects at least 20% of the population. Gastrointestinal disorders, particularly celiac disease and Crohn's disease, are among the predisposing factors in about 3% of patients [30].

RAS has three main presentations: minor, major and herpetiform ulcers [21]. Minor RAS is the most common and affects about 80% of sufferers. It presents as a number (one to five) of small, round or oval ulcers (less than 5mm in diameter) appearing on the non-keratinized mucosa, usually with a grey–white pseudomembrane and an erythematous halo that heal within 10–14 days without scarring. Major RAS is more severe and less common. In this case, the ulcers may exceed 1cm in diameter, persist for up to six weeks and often heal with scarring. Herpetiform ulceration is the least common and is characterized by multiple recurrent crops of widespread, small, painful ulcers. There may be up to 100 ulcers at any given time, each measuring 2–3mm in diameter, although they tend to fuse to become large and irregular.

This study revealed that only the minor type of recurrent aphthous ulceration was observed in both the study and control groups. The percentage was higher among the celiac group but the difference was not statistically significant (30.2% vs. 20.9%). These results are ('in' deleted) consistent with Bucci et al. who found that even though RAS was more prevalent in celiac patients than the healthy controls (33.3% vs. 23.4%), the difference was not statistically significant. They also noticed that more than a third of celiac subjects suffering from RAS benefited from a gluten-free diet [31]. Sedghizadeh et al. [18] also found no significant differences between celiac and control subjects in the prevalence of recurrent aphthous stomatitis, which lead them to mention that they could not conclude that RAS is a clinical manifestation of CD, or that CD is a risk indicator for RAS.

In contrast, other researchers support the association between CD and aphthous ulcers, and have concluded that CD should be added to the differential diagnosis of aphthous ulcers. Campisi et al. [32] suggested that recurrent aphthous-like ulcers should be considered a risk indicator for celiac disease (comma removed) and that a gluten-free diet leads to ulcer amelioration. Campisi et al. [33] examined the frequency of oral lesions in celiac disease patients and assessed their usefulness in making celiac disease diagnosis. They examined 197 celiac disease patients and 413 controls and concluded that the overall prevalence of oral soft tissue lesions was higher in celiac disease patients (42%) than in the controls. However, the positive-predictive value of these lesions for celiac disease diagnosis was low. They also found that RAS was greater in celiac (21% vs. 17%) with disappearance of the ulcers for 89% of the patients after 1 year of gluten-free diet. In the present study the patient were not examined for this purpose prior to altering their diet and strict to GFD. However

there was no significant difference between the compliant and non-compliant patient with regard to RAS [33].

4.1 Limitation of the Present Study

The small sample size, particularly of the CD group, does not facilitate a comparison between the GFD compliant and non-compliant subjects with respect to the variables under investigation.

5. CONCLUSION

In conclusion, oral hygiene status seems worse in celiac patients which indicates that oral health education programs may be beneficial for children and adolescents with celiac disease in Jordan. The need for periodontal treatment and the frequency of RAS are higher in celiac patients but the difference is not statistically significant.

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CONSENT

All authors declare that written informed consent was obtained from the parents of participants in the study.

ETHICAL APPROVAL

All authors hereby declare that the study was approved by the ethical committee of the Royal Medical Services.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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