

# The impact of histopathological celiac disease activity on dental enamel defects and dental caries

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## ABSTRACT

**Background:** Celiac disease is an autoimmune chronic disease that affects the human's intestine and subsequently reflects its effect on the entire body health by retardation the absorption and immune mediated complications cause the involvement of oral health. The present study intended to evaluate the impact of the histopathological disease activity upon dental enamel defects and dental caries.

**Subjects and methods:** Forty celiac-diseased patients aged 7-11 years were collected from 3 different teaching hospitals in Baghdad classified by means of the histopathological activity of the intestinal disease according to modified Marsh-Rostami classification. Dental enamel defects were measured by Aine's classification, while dental caries experience and severity were measured using d1-4mfs/t and D1-4MFS/T.

**Results:** The majority of the sample came with partial villous atrophy of the small intestine (Marsh III-a) and almost half of the sample were with no celiac disease specific dental enamel defects (Aine's 0), while Aine's I was the most predominant than Aine's II. Most missed surfaces due to dental caries in permanent teeth came with Marsh II.

**Conclusion:** The more the severity of celiac disease histopathological activity the more the severity of celiac specific dental enamel defects and the less experienced dental caries.

**Key words:** Celiac disease, histopathological activity, dental enamel defects, dental caries. (Received: 10/10/2019; Accepted: 13/11/2019)

## INTRODUCTION

Celiac disease (CD) is a chronic hereditary autoimmune inflammatory disease leading to intestinal damage and malabsorption associated with serious health consequences.<sup>(1)</sup> CD can introduce itself by multiple signs and symptoms starting from diarrhea, weight loss and abdominal pain to extra-intestinal manifestations including dental enamel defects DED.<sup>(2,3)</sup> The only available and acceptable treatment is lifelong strict gluten free diet GFD.<sup>(1)</sup>

Endoscopy for CD diagnosis doesn't provide definitive image for intestinal pathology<sup>(4)</sup> during which multiple biopsies are taken from different sites of the small intestine usually duodenum to submit them for histopathological assay.<sup>(5)</sup> Small intestine has a major role in digestion, secretion and absorption; numerous mucosal folds containing villi increase the surface area of absorption and digestive enzymes production.<sup>(6)</sup> Histological features of the duodenal disease are villous atrophy, crypt hyperplasia, increase a number of intraepithelial lymphocytes and decrease in height of enterocytes.<sup>(7)</sup>

Intestinal epithelial damage is caused by both innate and adaptive immune responses and that intraepithelial lymphocytes, those are elicited by the inflammation caused by gluten and mediated genetically and production of variant immunoglobulin such as tissue transglutaminase, anti-endomesial and anti-gliadin.<sup>(8)</sup> Modified Marsh-Rostami index had been developed to describe intestinal mucosal damage.<sup>(9)</sup> Orally, dental enamel defects DED can be identified in some CD patients and this plays a vital role for dentists to play pointing to the disease for diagnosis.<sup>(10)</sup> When any impaired function of the ameloblasts occurred due to environmental or nutritional deficiency factors, enamel formation would get impaired too.<sup>(11)</sup>

A study by Abdul-Wahid *et al*<sup>(12)</sup> revealed an increase in the presence of unspecific dental enamel defects by the application of the Modified Developmental Defects of Enamel Index for 102 CD patients aged 2-35 years compared to the control group in primary and permanent dentitions while dental caries was experienced at higher extent in the primary teeth only.

Higher DED in CD children was observed as compared to children devoid from the disease<sup>(10,13,14)</sup> in contrast to dental caries that was experienced at lesser extent in CD children.<sup>(13)</sup> Another study showed no significant difference in prevalence of DED between CD children and others without the disease.<sup>(15,16)</sup> Another study reported no significant difference in caries experience in CD children.<sup>(16)</sup>

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The aim of the current study was the estimation of the essential role that the oral cavity plays as a gate of the gastrointestinal tract at which the health of each may logically affects the other's, thus CD was studied in children with mixed dentition to evaluate CD histopathological activity impact on DED and dental caries.

## SUBJECTS AND METHODS

Ethical approval was gained from the Ethical Committee of College of Dentistry/University of Baghdad and consents forms were gained from the patients' parents to be included. The sample of the present study consisted of 40 celiac-diseased (CD) children aged 7-11 years according to the last birthday and date of examination, half of them had been just diagnosed and the rest was committed to gluten free diet. Patients should have been devoid from any other diseases. The study was carried out from November 2018 to March 2019. Patients had been collected from pediatric consultation sections of the gastroenterology of three different teaching hospitals in Baghdad.

The disease had been diagnosed according to the European society of pediatric gastroenterology, hepatology and nutrition guidelines<sup>(17)</sup> histopathological findings were collected from the patients' medical reports by means of grading according to Modified Marsh index for histological CD activity.<sup>(9)</sup> All histopathological examinations of all patients included were accomplished in the histology laboratory of Gastroenterology and Hepatology Teaching Hospital/Baghdad. Oral examination had been carried out following the basic principles of WHO (1997).<sup>(18)</sup> Dental enamel defects (DED) had been evaluated descriptively by Aine's classification for CD specific dental enamel defects criteria<sup>(10)</sup> as shown in table (1); those should have been distributed symmetrically and chronologically in all dental arches when all teeth were examined in all dental quadrants. Dental caries dmfs/t and DMFS/T and severity D<sub>1-4</sub>/d<sub>1-4</sub> were examined and recorded according to Muhlemann.<sup>(19)</sup> Descriptive statistics was applied, level of significance was set at 0.05 by SPSS program version 21.

**Table 1: Aine's criteria for celiac disease specific dental enamel defects.**

Grade	Description
<b>0</b>	No defects meet the criteria
<b>I</b>	Defect in color of enamel. Single or multiple creamy, yellow or brown opacities with clearly defined or diffuse margins; in addition a part or the entire surface of enamel is without glaze.
<b>II</b>	Slight structural defects, Enamel surface rough, filled with horizontal grooves or shallow pits; light opacities and discoloration may be found; in addition a part or the entire surface of enamel is without glaze.
<b>III</b>	Evident structural defects, A part or the entire surface of enamel rough and filled with deep horizontal grooves which vary in width or have large vertical pits; large opacities of different colors or strong discoloration may be in combination.
<b>IV</b>	Severe structural defects, the shape of the tooth changed: the tips of cusps are sharp-pointed and/or the incisal edges are unevenly thinned and rough; the thinning of the enamel material is easily detectable and the margins of the lesions are well defined; the lesion may be strongly discolored.

## RESULTS

The sample contained 22 boys and 18 girls, there was no significant difference concerning gender among the groups (Chi- square = 3.671; p = 0.160) and the sample had been considered as one age group.

Grading of CD histopathological activity of the current sample revealed that it was devoid from Marsh I and Marsh III-c while Marsh II, III-a and III-b were presented as 3 (7.50%), 25 (62.50%) and 12 (30.00%) respectively

Aine's classification of dental enamel defects (DED) specific for CD that was used in the present sample revealed that 19 (47.5%) of children were with no defects (grade 0) followed by 17 (42.5%) children with grade I and 4 (10%) children with grade II. Neither Aine's III nor Aine's IV had been found in the present sample Marsh grading of histopathological disease activity in relation to Aine's grading of CD specific dental enamel defects revealed a significant difference among the present grades where there were no enamel defects in Marsh II. On the other hand, the least children with Aine's 0 grades were observed in Marsh III b in contrast to Aine's II enamel defects which were the most frequent in Marsh III-b category (Table 2).

Caries severity and experience were found in D<sub>4</sub>, DS and DMFS components among Marsh II as compared to Marsh III-a and III-b but no

significant difference was observed; the same is applied to ds component concerning primary teeth (Table 3).

Multiple comparisons by Games-Howell as ANOVA post hoc test were applied to MS according to the available three Marsh grades showing no significant difference between Marsh III-a and Marsh III-b mean differences ( $P>0.05$ ) while high significant differences concerning Marsh II mean difference with both Marsh III-a

and III-b ( $P<0.01$ ) was noticeable (Table 4). Dental caries experience and severity showed no significant difference in relation to CD dental enamel defects but the mean values of d<sub>4</sub>, ds, dmfs and dmft for deciduous teeth showed lower results in Aine's II than both Aine's I and Aine's 0. The same was applied to D<sub>4</sub> and DS for permanent teeth as shown in table (5) but no statistical differences were found.

**Table 2: Celiac disease dental enamel defects according to Aine's classification in relation to the histopathological disease activity measured by modified Marsh-Rostami classification.**

			Aine's classification			FEPT*	p	Total
			0	I	II			
Marsh	II	N.	3.00	0.00	0.00	9.452	0.025**	3.00
		%	15.79	0.00	0.00			7.50
	III a	N.	14.00	10.00	1.00			25.00
		%	73.68	58.82	25.00			62.50
	III b	N.	2.00	7.00	3.00			12.00
		%	10.53	41.18	75.00			30.00
<b>Total</b>		<b>N</b>	19.00	17.00	4.00			40.00
		<b>%</b>	47.50	42.50	10.00			100.00

\*Fissure Exact Probability Test

\*\*Significant<0.05

**Table 3: Dental caries experience and severity for primary and permanent teeth according to Marsh grading**

Dental caries	Marsh grading							
	II		III-a		III-b		F	p
	Mean	SE	Mean	SE	Mean	SE		
<b>d1</b>	0.333	0.333	0.080	0.080	0.000	0.000	1.102	0.343
<b>d2</b>	1.333	1.333	0.240	0.166	0.917	0.434	2.069	0.141
<b>d3</b>	1.333	1.333	1.480	0.361	1.500	0.469	0.011	0.989
<b>d4</b>	6.333	6.333	6.040	1.498	5.667	1.676	0.015	0.985
<b>ds</b>	9.333	9.333	7.840	1.520	7.750	1.670	0.053	0.949
<b>ms</b>	0.000	0.000	1.400	0.614	2.083	1.145	0.514	0.602
<b>fs</b>	0.000	0.000	0.000	0.000	0.167	0.167	1.177	0.319
<b>dmfs</b>	9.333	9.333	9.160	1.785	10.000	2.514	0.033	0.968
<b>dmft</b>	5.333	5.333	5.080	0.848	5.667	0.956	0.072	0.931
<b>D1</b>	0.667	0.667	1.520	0.289	1.167	0.241	0.772	0.470
<b>D2</b>	0.000	0.000	0.880	0.211	1.250	0.446	1.359	0.269
<b>D3</b>	2.000	0.000	1.200	0.294	0.750	0.179	1.357	0.270
<b>D4</b>	4.333	2.603	1.600	0.408	1.417	0.645	2.073	0.140
<b>DS</b>	7.000	2.082	4.680	0.577	4.583	0.783	0.931	0.403
<b>MS</b>	3.333	3.333	0.000	0.000	0.000	0.000	8.556	0.001
<b>FS</b>	0.000	0.000	0.040	0.040	0.833	0.833	1.068	0.354
<b>DMFS</b>	10.333	5.364	5.000	0.648	5.417	1.171	2.334	0.111
<b>DMFT</b>	4.667	0.667	4.440	0.597	4.417	0.733	0.010	0.990

Table 4: Multiple comparisons of missing component (MS) of DMFS among the three available Marsh grades.

Games-Howell test for MS among Marsh grades			
(I) Marsh	(J) Marsh	Mean Difference (I-J)	P
III-a	III-b	0.00000	1.000
	II	-3.33333	0.002**
III-b	II	-3.33333	0.003**

\*\* Highly significant &lt; 0.01

Table 5: Dental caries experience and severity in primary and permanent teeth in relation to Aine's grades of celiac disease enamel defects.

Aine's grade	0.00		1.00		2.00		F	P
	Mean	SE	Mean	SE	Mean	SE		
d <sub>1</sub>	0.053	0.053	0.118	0.118	0.000	0.000	0.247	0.782
d <sub>2</sub>	0.684	0.375	0.412	0.173	0.250	0.250	0.325	0.724
d <sub>3</sub>	1.211	0.347	1.647	0.428	2.000	1.414	0.472	0.627
d <sub>4</sub>	5.895	1.629	6.882	1.857	2.250	1.931	0.681	0.512
ds	7.842	1.794	8.824	1.954	4.500	2.630	0.506	0.607
ms	1.053	0.614	2.059	0.964	1.250	1.250	0.432	0.652
fs	0.000	0.000	0.118	0.118	0.000	0.000	0.665	0.520
dmfs	8.789	1.907	11.00	2.565	5.750	3.376	0.606	0.551
dmft	5.053	0.966	5.824	1.102	4.000	2.309	0.326	0.724
D <sub>1</sub>	1.421	0.299	1.353	0.331	1.000	0.408	0.173	0.841
D <sub>2</sub>	0.789	0.237	1.059	0.337	1.000	0.707	0.223	0.801
D <sub>3</sub>	1.263	0.285	1.118	0.331	0.500	0.289	0.610	0.549
D <sub>4</sub>	2.263	0.675	1.353	0.383	1.000	1.000	0.885	0.421
DS	5.053	0.664	4.882	0.701	3.500	1.555	0.475	0.625
MS	0.526	0.526	0.000	0.000	0.000	0.000	0.540	0.588
FS	0.053	0.053	0.000	0.000	2.500	2.500	4.363	0.113
DMFS	6.000	1.084	4.882	0.701	6.000	3.342	0.337	0.716
DMFT	4.737	0.606	4.235	0.662	4.000	1.826	0.205	0.815

## DISCUSSION

Celiac disease (CD) had been proved to be accompanied by several systemic and dental defects. Dental enamel defects (DED) are permanent and won't be corrected after gluten free diet (GFD). Early diagnosis of CD patients by dentists can be performed by DED since most CD patients are atypical.<sup>(14, 20)</sup> In the present study almost half of the sample had no CD specific enamel defects, however, most of the defects were enamel opacities (Aine's I). This comes in agreement with a study by Shahraki *et al* when studying wider range of sample age (3-16 years) and larger sample size (65) of CD patients.<sup>(14)</sup> Structural abnormalities were also present at lesser extent as Aine's II was in 10% of the sample which contained no Aine's III or IV and this comes in an agreement with a Turkish study that reported no Aine's III or IV in 60 CD patients' ages 6-16 years.<sup>(21)</sup> The present study revealed that the least intestinal damage (Marsh II) came with no CD specific DED while the more intestinal damage (Marsh III-a and III-b) came with more CD specific DED and this comes in

contrast with what Aine *et al* showed by studying adults enamel defects in relation to the degree of histological damage although children cannot be compared to adults.<sup>(22)</sup>

Yet, no specific mechanism was established explaining DED in CD patients;<sup>(23)</sup> nutritional deficiency specially hypocalcemia and a normal serum concentration of calcium had been found during diagnosis of CD children,<sup>(13)</sup> immune mediated as the primary causative factor<sup>(25,26)</sup> and DED as a hereditary condition and/or affected by environmental circumstances.<sup>(24)</sup> Dental caries is one of the most mentioned infectious diseases human beings suffer from.<sup>(27)</sup> An Iraqi study illustrated an increased salivary IgA in caries free children as compared to caries active in the same age group of the present study<sup>(28)</sup> while another Iraqi study illustrated an important protective roles of salivary immunoglobulins especially IgA and IgM against dental caries in normal kindergarten children,<sup>(29)</sup> since CD is an autoimmune disease that salivary immunoglobulins are logically suspected to be

elevated and dental caries was, in the present study, experienced at lesser extent in a more severe intestinal damage and saliva by itself can be used non-invasively to mirror blood.<sup>(30)</sup> It is wise to investigate salivary immunoglobulins seeking for dental caries protective factors in CD children since patients with increased DED had decreased dental caries.<sup>(21)</sup>

The present study has arrived at the conclusion that the more the severity of the intestinal mucosal damages in CD children the more the presence of specific dental enamel defects, although no severe enamel defects or intestinal damage was recorded and less extracted permanent teeth due to dental caries in the more intestinal villous atrophy cases as compared to the mild ones.

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**الخلاصة**

الخلفية: إن مرض مناعي ذاتي كداء الحنطة يؤثر على صحة الأمعاء لدى الإنسان و ينعكس على صحة جسمه بشكل كامل عن طريق سوء الإمتصاص و مضاعفات ذات أسباب مناعية تؤثر على صحة الفم كإختلال تكوين ميناء الأسنان و تسوس الأسنان. الأشخاص والطرق: تم جمع 40 مريض مصاب بداء الحنطة بأعمار (7-11) سنة من ثلاث مستشفيات مختلفة في بغداد و بإعتماد التقسيم حسب شدة المرض بالنسبة لفعاليته من الناحية النسيجية - المرضية لغشاء الأمعاء حسب تقسيم Marsh- Rostami المعدل و خلل ميناء الأسنان عن طريق تقسيم Aine الخاص بداء الحنطة كذلك تجربة تسوس الأسنان وشدتها. النتائج: أن غالبية العينة كانت تعاني من Marsh III-b. غالبية العينة كان لديها 0 Aine's I. Aine كان الأغلب في العينة Aine II. كان الأغلب عند المصابين ب Marsh II-b. أغلب الأسنان الدائمة المفقودة بسبب التسوس كانت مصاحبة Aine II. الإستنتاج: كلما زادت شدة المرض نسيجياً كلما زادت شدة الإختلال في تكوين ميناء الأسنان و قل تسوس الأسنان. الكلمات المفتاحية: داء الحنطة, الفعالية النسيجية – المرضية, مارش, إختلال ميناء الأسنان, آين, تسوس الأسنان.