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The frequency and characteristics of ultra-short celiac disease in children: A single-center experience

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Abstract

Purpose: Due to the patchy nature of mucosal involvement in celiac disease (CD), histopathological changes may be limited to the duodenal bulb in some patients, leading to diagnostic difficulties. This study aimed to investigate the frequency and clinical and serological characteristics of ultra-short celiac disease (USCD) in children.

Methods: Between February 2024 and March 2026, children diagnosed with CD based on separate biopsies obtained from the duodenal bulb and distal duodenum, each placed in separate containers, were included in the study. Patients were divided into two groups: USCD and classic CD.

Results: Of the 78 patients included in the study, 47 (60.25%) were female, and the mean age at diagnosis was 9.58±4.21 years. The median tissue transglutaminase IgA (tTG-IgA) level was 125.50 [IQR: 21.30-200.00] IU/L. Sixteen [20.51%] of the 78 patients had histopathologically confirmed USCD. The median tTG-IgA level was significantly lower in the USCD group compared to the classical CD group (22.50 versus 162.00; $p<0.05$). The most frequent presenting symptom in this group was growth retardation (87.50%).

Conclusion: The rate of isolated duodenal bulb involvement in children was found to be quite high (20.51%). Ultra-short celiac disease is more common in children presenting with fewer classic gastrointestinal findings and tTG-IgA levels below 10xULN; therefore it is critically important to obtain at least one biopsy sample from the duodenal bulb and place it in a separate container. Otherwise, a high percentage of patients may miss duodenal bulb involvement.

WHAT IS KNOWN

Ultra-short celiac disease (USCD) is more common in children presenting with fewer classic gastrointestinal findings

It has been reported that the frequency of USCD varies between 2.4% and 15.6%

ESPGHAN no-biopsy approach for celiac disease (CD) diagnosis is widely adopted in European countries, it is not yet a routine practice in Turkey.

WHAT IS NEW

The most frequent symptom at presentation was found to be growth retardation in the USCD group

The rate of USCD in children was found to be highest value (20.51%) in the literature

No-biopsy criteria were successfully applied in almost 100% of eligible children with CD in Turkey in the present study

Introduction

Celiac disease (CD) is an autoimmune enteropathy triggered by gluten intake in genetically susceptible individuals, characterized by the small intestinal bowel damage [1,2]. It affects approximately 1% of the world population [2,3]. It is known that small intestinal involvement is a patchy in CD [4]. It has been shown that the characteristic histopathological changes may be limited to the duodenal bulb in some patients [5,6]. This condition is called "isolated bulb CD" or "ultra-short celiac disease" (USCD), and was first described by Vogelsang et al. in 2001 [7].

While duodenal bulb biopsies were previously not recommended due to concerns that the duodenal bulb's rich structure of Brunner's glands and lymphoid tissue might lead to difficulties in histological interpretation, current evidence shows that bulb biopsy increases diagnostic sensitivity of CD [8–11]. It is recommended that at least four biopsies from the distal duodenum and at least one from the duodenal bulb are taken in patients suspected of CD due to the patchy involvement [9,12]. Since isolated duodenal bulb involvement may present with milder clinical findings compared to classic CD, the diagnosis is often missed in these patients [13]. The aim of this study is to determine the frequency of USCD and to compare the clinical and serological features of these patients at the time of presentation with those of classic CD.

Material and Methods

This retrospective single-center study was conducted in tertiary pediatric gastroenterology clinic between February 2024 and March 2026. The current study only included patients who have been diagnosed with CD by biopsy. All consecutive patients who were diagnosed with CD according to ESPGHAN 2020 criteria and from whom biopsies were obtained in separate containers from the duodenal bulb and distal duodenum during gastroduodenoscopy were included in the study [12].

Patients diagnosed with selective IgA deficiency, those with insufficient or poorly oriented biopsy samples, and those with autoimmune disease, inflammatory bowel disease, helicobacter pylori infection, or immunodeficiency were excluded from the study. In all patients suspected of having CD, total serum IgA and tissue transglutaminase IgA (tTG-IgA) levels were measured at the initial stage. The cut-off value for tTG-IgA is accepted as 10 IU/L. During gastroduodenoscopy, at least two biopsy specimens from the duodenal bulb and at least four from the distal duodenum were obtained. The bulb and distal duodenum biopsies were placed in separate containers. This practice is of great importance because it is not always possible for the pathologist to histologically distinguish between the bulb and distal duodenum specimens. Histopathological evaluation was performed by experienced pathologists according to the modified Marsh-Oberhuber classification [4,14].

Patients with a biopsy result of Marsh type 2 or 3 were considered to have CD. Based on histopathological findings, patients were divided into two groups.

1. group USCD: Patients with Marsh type 2 or 3 lesions in the bulb and Marsh type 0 or 1 lesions in distal duodenal biopsies.

2. group classic CD: Patients with Marsh type 2 or 3 detected in distal duodenal biopsies, with or without bulb involvement.

Demographic characteristics, symptoms at presentation, tTG-IgA levels at diagnosis, total IgA, other laboratory parameters, and histopathological reports of the patients were retrospectively reviewed.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) software. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were expressed as number and percentage. For comparing continuous variables between two independent groups, Student's t-test was used for data showing normal distribution, and Mann-Whitney U test was used for data not showing normal distribution. The Chi-square test was used for comparing categorical variables. A p-value less than 0.05 was considered statistically significant.

Ethics Committee Approval

The study was approved by the Gaziantep City Hospital Clinical Research Ethics Committee *(March 18, 2026/29)*, and was conducted in accordance with the principles of the Helsinki Declaration. Written informed consent was not obtained because the study was retrospective in nature.

Results

Of the 78 patients included in the study, 47 (60.25%) were female, and the mean age at diagnosis was 9.58±4.21 years. The median tissue transglutaminase IgA (tTG-IgA) level was 125.50 (IQR: 21.30-200.00) IU/L (Table 1). No IgA deficiency was detected in any patient.

Table 1: Demographic and laboratory characteristics of patients

Variables	Patients [n=78]
Age [years]*	9.58±4.21
Sex [f/m]	47/31
Height [cm]*	128.59±21.98
Weight [kg]*	28.84±16.51
Hemoglobin[g/dL]*	12.55±1.61
MCV *	76.55±7.31
Ferritin#	10.00 [IQR: 5.97-18.17]
tTG IgA [IU/L] #	125.50 [IQR: 21.30-200.00]
Total IgA [mg/dL]*	142.63±70.31

*Data are presented as mean ∓ SD

#Data are presented as median [IQR: Q1-Q3]

tTG IgA: tissue transglutaminase IgA

Sixteen (20.51%) of the 78 patients had histopathologically confirmed USCD. The remaining 62 patients (79.49%) formed the classic CD group (Table 2). All patients in the USCD group had Marsh 3 lesions in the duodenal bulb, while 14 patients (87.50%) had Marsh 0, and 2 patients (12.50%) had Marsh 1 in the distal duodenum.

Table 2: The comparison of two groups in terms of demographic and laboratory features of USCD group and classic CD group patients

Variables	1. group-USCD [n=16]	2. group-Classic CD [n=62]	p
Age [years] *	10.50±4.58	9.34±4.12	0.370
Sex [f/m]	9/7	32/34	0.228
Height [cm]*	130.44±22.15	128.11±22.09	0.711
Weight [kg]*	32.63±19.83	27.87±15.57	0.383
Hemoglobin*	13.01±0.93	12.44±1.73	0.081
Ferritin#	14.00 [IQR: 8.25-21.47]	10.00 [IQR: 5.67-27.10]	0.202
tTG IgA [IU/L]#	22.50 [IQR: 17.63-155.75]	162.00 [IQR: 26.48-200.00]	0.018

* Data are presented as mean ∓ SD

Data are presented as median [IQR: Q1-Q3]

USCD: Ultra-short celiac disease

CD: Celiac disease

tTG IgA: tissue transglutaminase IgA

The median tTG-IgA level was significantly lower in the USCD group compared to the classical CD group (22.50 vs. 162.00 IU/L; $p<0.05$) (Table 2). In 75.00% of those with USCD, the tTG-IgA level was less than 10 times the upper limit of normal (10xULN). The most frequent presenting symptom in this group was growth retardation (87.50%). There were no patients presenting with chronic diarrhea or constipation in the USCD group (Table 3). The incidence of anemia was higher in the classical group compared to the USCD group (25.80% vs 12.5%).

Table 3: Comparison of symptoms between two groups

Presenting symptoms or characteristics	1. group-USCD [n=16]	2. group-Classic CD [n=62]
Growth retardation	14 [87.5%]	45 [72.58%]
Refractory iron deficiency anemia	1 [6.25%]	-
Abdominal pain	1 [6.25%]	1 [1.61%]
Constipation	-	2 [3.23%]
Abdominal distention	-	1 [1.61%]
Diarrhea-constipation attacks	-	1 [1.61%]
Precocious puberty	-	1 [1.61%]
Family history	-	8 [12.90%]
Turner syndrome	-	1 [1.61%]
Type 1 diabetes mellitus	-	1 [1.61%]
Growth retardation+ abdominal pain	-	1 [1.61%]

USCD: Ultra-short celiac disease; CD: Celiac disease

Discussion

In the present study, the frequency of USCD in children with CD was found to be 20.51%. This rate is the highest value reported in the literature. The most important findings of the current study were significantly lower tTG-IgA levels in the USCD group, the fact that the vast majority of these patients had tTG-IgA levels below 10xULN, and that none of the USCD patients reached tTG-IgA ≥ 10xULN. In addition, the most frequent symptom at presentation in the USCD group was growth retardation, and no classic gastrointestinal symptoms were detected in this group.

Because CD exhibits patchy involvement, it is recommended that at least four biopsies from the distal duodenum and at least one from the bulb be obtained during routine endoscopy to avoid false negative

results and to make a definitive diagnosis [9,12,15]. It has been reported that the characteristic lesions are seen only in the duodenal bulb in approximately 10% of celiac patients [6,16]. In our study, at least four biopsies from the distal duodenum and at least two from the duodenal bulb were obtained to make a definitive diagnosis in patients suspected of CD, and the distal duodenum and bulb biopsies were placed in separate containers. It has been reported that the frequency of USCD varies between 2.4% and 15.6% [5,6,13,17–21]. In the current study, this rate was 20.51%, which is the highest value reported in the literature. These differences between studies may be due to differences in patient population characteristics (age, geographic region, genetic factors, autoimmune disease), biopsy protocols (number of biopsies taken from the bulb, sending them in separate containers), and pathological evaluation criteria. In particular, Bonamico et al. [5] suggested that the reason for the low incidence of USCD in their multicenter study may be due to the lack of standardization of biopsy practices in different centers. The routine collection of bulb biopsies in separate containers in our center may have enabled us to detect isolated bulb cases at a higher rate. Furhermore, Behl et al. [17] also emphasized the importance of sending bulb and distal duodenum biopsies in separate containers and showed that demonstrated that in roughly one-third of the instances, even a skilled pathologist was unable to differentiate between bulb and distal duodenum biopsies.

It has been reported that children with USCD are diagnosed at an older age, present with milder symptoms, higher weight, and have fewer classic gastrointestinal findings (diarrhea, anemia) [11,17,18]. In addition to that, it has been reported that those with USCD have milder malabsorption findings and a lower frequency of anemia [7,11,17]. Consistent with literature, the mean age was higher in the USCD group; however, this difference did not reach statistical significance. Diarrhea and constipation were not observed in the USCD group. In line with the literature, the most frequent presenting symptom in our patients in the USCD group was growth retardation [87.50%]. In addition to that, the incidence of anemia was higher in the classical group compared to the USCD group (25.80% vs 12.5%).

The literature highlights that tTG-IgA levels are significantly lower in the USCD group, and in most patients have lower tTG-IgA levels (below 10xULN) [12,13,18,22]. Consistent with the literature, 75.00% of our patients with USCD had tTG-IgA levels below 10xULN, and no patient had levels ≥ 10xULN. These findings indicate that the ESPGHAN 2020 non-biopsy diagnostic criteria will be insufficient to detect this patient group. It has been reported that the diagnosis rate of USCD increased from 4.6% to 12.4% with the use of no-biopsy diagnostic criteria [13,14].

Previous studies have reported that patients with USCD may exhibit normal mucosa or only intraepithelial lymphocytosis in the distal duodenum, and that this condition does not progress to extensive disease over time [12,17,18]. In a study by Demir et al. [18], Marsh 1 lesions was detected in 15 of 35 USCD patients, therefore a second biopsy was performed on those patients to make a definitive diagnosis. Ultra-short celiac disease was diagnosed in 6 patients, Marsh 3 lesions were detected in the bulb of these 6 patients, there was no pathology in the distal duodenum, and these patients did not progress to extensive CD over time. In our study, all patients with USCD had Marsh 3 lesions in the bulbus, while Marsh 0 lesions were observed in 75% of cases and Marsh 1 in 25% of cases in the distal

duodenum. However, since control endoscopic biopsy was not performed on these patients during follow-up, we could not comment on whether the distal duodenum lesions progressed in these patients. Also, since gluten exposure is greater in the bulbus, the distal duodenum may not have been affected for this reason [23].

It has been shown that duodenal bulb biopsy increases the diagnostic sensitivity of CD by 7% to 11.4% [6,12,17,19–21]. The most important clinical conclusion of our study is that taking bulb biopsies in separate containers increases diagnostic sensitivity, and that bulb biopsies should always be taken in separate containers during endoscopy, especially in children presenting with low tTG-IgA levels and atypical symptoms [e.g., growth retardation].

Strengths and Limitations of the Study

The current study has several strengths, as it focuses on USCD, a topic rarely addressed in the literature, evaluates biopsies from the bulb and distal duodenum in separate containers, and applies a standardized endoscopy protocol at a tertiary hospital.

However, the retrospective, single-center nature of the study, and the relatively small number of patients, particularly in the USCD group, and the lack of long-term follow-up data represent important limitations. The fact that no patient in the USCD group underwent a second endoscopy limits the ability to comment on whether USCD progresses over time.

Conclusions

This study showed that the incidence of USCD in children was 20.51%, the highest rate reported in the literature. In the USCD group, tTG-IgA levels were significantly lower, and the vast majority of these patients did not meet the diagnostic criteria without biopsy. We recommend that duodenal bulb biopsies be taken in separate containers, especially in children with mild clinical signs of CD and tTG-IgA levels below 10xULN, as this increases the diagnostic sensitivity of CD, and helps prevent missed diagnoses of USCD. Therefore, taking multiple biopsies from the bulb and distal duodenum in separate containers during endoscopy should be the standard approach in all children suspected of CD.

Statements and Declarations

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draft of the manuscript was written by Ahmet Rauf Goktepe and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval: *This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Gaziantep City Hospital (March 18, 2026/29).* ***Informed consent:*** Written informed consent was not obtained because the study was retrospective in nature.

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References

1. Tjon JM, van Bergen J, Koning F (2010) Celiac disease: how complicated can it get? Immunogenetics 62:641-51. https://doi.org/10.1007/s00251-010-0465-9
2. Sahin Y (2021) Celiac disease in children: A review of the literature. World J Clin Pediatr 10:53-71. https://doi.org/10.5409/wjcp.v10.i4.53.
3. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, Kelly CP, Ahuja V, Makharia GK (2018) Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 16:823-836.e2. https://doi.org/10.1016/j.cgh.2017.06.037
4. Marsh MN (1990) Grains of truth: evolutionary changes in small intestinal mucosa in response to environmental antigen challenge. Gut 31:111-114. https://doi.org/10.1136/gut.31.1.111
5. Bonamico M, Thanasi E, Mariani P, et al. Duodenal bulb biopsies in celiac disease: a multicenter study. J Pediatr Gastroenterol Nutr 47:618-622. https://doi.org/10.1097/mpg.0b013e3181677d6e.
6. Rashid M, MacDonald A (2009) Importance of duodenal bulb biopsies in children for diagnosis of celiac disease in clinical practice. BMC Gastroenterol 9:78. https://doi.org/10.1186/1471-230X-9-78.
7. Vogelsang H, Hanel S, Steiner B, Oberhuber G (2001) Clinical and histological presentation of celiac disease in adults and children: is there a difference? Wien Klin Wochenschr 113:926-30.
8. Hill ID, Dirks MH, Liptak GS et al (2005) Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 40:1-19. https://doi.org/10.1097/00005176-200501000-00001
9. Hill ID, Fasano A, Guandalini S, Hoffenberg E, Levy J, Reilly N, Verma R (2016) NASPGHAN clinical report on the diagnosis and treatment of gluten-related disorders. J Pediatr Gastroenterol Nutr 63:156-165. https://doi.org/10.1097/MPG.0000000000001216
10. Taavela J, Popp A, Korponay-Szabo IR et al (2016) A prospective study on the usefulness of duodenal bulb biopsies in celiac disease diagnosis in children: urging caution. Am J Gastroenterol 111:124-133. https://doi.org/10.1038/ajg.2015.387
11. Doyev R, Cohen S, Ben-Tov A, Weintraub Y, Amir A, Galai T, Moran-Lev H, Yerushalmy-Feler A (2019) Ultra-short celiac disease is a distinct and milder phenotype of the disease in children. Dig Dis Sci

64:167-172. https://doi.org/10.1007/s10620-018-5323-x

12. Husby S, Koletzko S, Korponay-Szabo I, et al (2020) European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. J Pediatr Gastroenterol Nutr 70:141-156. https://doi.org/10.1097/MPG.0000000000002497
13. Wang QY, Jantchou P, Dirks M, Lavoie SB, Oligny LL, Dal Soglio D, Patey (2025) Low TTG-IgA associated with isolated bulb pathology in pediatric celiac disease: Implications in a no-biopsy approach era. J Pediatr Gastroenterol Nutr 80:678-685. https://doi.org/10.1002/jpn3.12474
14. Oberhuber G, Granditsch G, Vogelsang H (1999) The histopathology of coeliac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol 11:1185-1194. https://doi.org/10.1097/00042737-199910000-00019
15. Pais WP, Duerksen DR, Pettigrew NM, Bernstein CN (2008) How many duodenal biopsy specimens are required to make a diagnosis of celiac disease? Gastrointest Endosc 67:1082-1087. https://doi.org/10.1016/j.gie.2007.10.015
16. Sharma A, Mews C, Jevon G, Ravikumara M (2013) Duodenal bulb biopsy in children for the diagnosis of coeliac disease: Experience from Perth, Australia. J Paediatr Child Health 49:210-214. https://doi.org/10.1111/jpc.12123
17. Behl S, Khan MR, Ismail Y, Swantek C, Chen ZE, Murray JA, Absah I (2023) The Characteristics of Isolated Bulb Celiac Disease in Children. J Pediatr Gastroenterol Nutr 77:79-85. https://doi.org/10.1097/MPG.0000000000003799
18. Demir AM, Hizal G, Berberoğlu Ateş B, Akbaba B, Kırsaçlıoğlu CT, Hızlı Ş, Karakuş E (2026) Ultra-short celiac disease in children: histological and autoimmune features. Eur J Pediatr 185:68. https://doi.org/10.1007/s00431-025-06724-2
19. Boschee E, Lacson A, Turner J, Yap J (2020) Duodenal Bulb Histology in Paediatric Celiac Disease: A Case-Control Study. J Can Assoc Gastroenterol 3:210-215. https://doi.org/10.1093/jcag/gwz014
20. Levinson-Castiel R, Hartman C, Morgenstern S, et al (2011 The role of duodenal bulb biopsy in the diagnosis of celiac disease in children. J Clin Gastroenterol 45:26-29. https://doi.org/10.1097/MCG.0b013e3181e04d26
21. Weir DC, Glickman JN, Roiff T, Valim C, Leichtner AM (2010) Variability of histopathological changes in childhood celiac disease. Am J Gastroenterol 105:207-212. https://doi.org/10.1038/ajg.2009.557
22. Gidrewicz D, Trevenen CL, Lyon M, Butzner JD (2017) Normalization time of celiac serology in children on a gluten-free diet. J Pediatr Gastroenterol Nutr 64:362-367. https://doi.org/10.1097/MPG.0000000000001270
23. Dickson BC, Streutker CJ, Chetty R (2006) Coeliac disease: an update for pathologists. J Clin Pathol 59:1008-1016. https://doi.org/10.1136/jcp.2005.035345