

The Virtual Celiac Symptoms Study: Symptom and gluten-free diet perceptions of adolescents at baseline

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Introduction

- Celiac disease (CeD) is a chronic, systemic autoimmune disorder characterized by autoantibody formation and inflammation of the small intestine in response to gluten ingestion.^{1,2}
- The symptom patterns among adolescent patients with CeD remain unclear.
- Adherence to a gluten-free diet (GFD) is the only management option for CeD; however, many patients continue to experience symptoms due to inadvertent exposure to gluten, which may limit the effectiveness of a GFD.²⁻⁵
- Improved understanding of the symptom patterns experienced by adolescent patients with CeD may help to inform optimal disease management strategies in this patient population.

Objective

- To characterize the symptom patterns and GFD adherence in adolescents with CeD through a prospective observational study (Virtual Celiac Symptoms Study; VCSS). Here, we describe the self-reported symptom patterns and GFD adherence at the time of enrollment to the VCSS.

Methods

Study design

- The VCSS (NCT05309330) observational study was conducted in the USA among adults and adolescents with CeD, from July 25, 2022 to March 4, 2023.
- Participants were recruited by the Celiac Disease Foundation via digital advertisements (email, social media channels, app push notifications, website advertisements and a study microsite).
- At the time of enrollment, participants self-reported information via a smartphone app regarding:
 - demographics and clinical disease characteristics
 - adherence to a GFD, and known and suspected inadvertent gluten exposure
 - occurrence of CeD symptoms
 - healthcare resource utilization.

Inclusion criteria

- English-speaking individuals aged 12 to < 18 years at baseline (for the adolescent cohort) and residing in the USA.
- Diagnosis of CeD for ≥ 1 year, confirmed via self-reported positive biopsy or serology.
- Adherence to a GFD for ≥ 6 months.
- CeD-related symptoms (patient-reported) within the past 3 months.
- Daily access to a smartphone and Internet/Wi-Fi/cellular data.

Exclusion criteria

- Planned or current involvement in any clinical study with an investigational drug, or a surgical procedure or gluten challenge during the 3-month observation period.

Data analysis

- All baseline measures were analyzed using descriptive statistics and R version 4.0.4. The p values were generated using a χ^2 test for categorical variables (or Fisher's exact test when expected value < 5) and analysis of variance (ANOVA) for continuous variables.

Results

Patient demographics and clinical disease characteristics at baseline

- Adolescent participants comprised 142 of the 480 enrolled participants, of which 66.9% self-identified as female and 97.9% were of White race, with a mean (standard deviation; SD) age of 14.5 (1.7) years (Table 1).
- Duration of disease since CeD diagnosis (mean [SD]: 5.4 [3.4] years) and duration of adherence to a GFD (mean [SD]: 5.3 [3.4] years) were similar.
- The most common comorbidities (> 20.0%) were anxiety and depression; however, these were not related to disease severity (Table 1).
- In total, 7.8% of participants reported irritable bowel syndrome as a comorbidity at baseline and no participants reported inflammatory bowel disease or small intestine bacterial overgrowth.

GFD adherence and dietary assessment

- Overall, 78.2% of adolescent participants reported "rarely eating gluten accidentally", 13.4% reported "never eating gluten accidentally or on purpose", 6.3% reported "rarely eating gluten on purpose" and 2.1% reported "eating gluten-containing foods regularly" (Table 1).
- In addition to gluten, 23.2% of adolescents reported additional dietary restrictions, most of whom were following a lactose-free, dairy-free or milk-free diet (Table 1).

CeD symptom profile

- Abdominal pain was the most bothersome and most frequently reported symptom (Figure 1).
- In total, 81.7% of participants reported that they were "likely/extremely likely" to experience CeD symptoms after perceived gluten exposure (Figure 2).
- Over 60.0% of participants described symptom intensity as moderate (33.1%) or severe (30.3%). The remaining participants reported having mild (9.9%) or varying symptom severity (26.8%) (Table 1).
 - At baseline, reported symptom severity was significantly different between males and females ($p = 0.0001$); a higher proportion of males than females reported "mild" symptoms, while a higher proportion of females than males described symptom severity as "severe" or "varies widely" (Table 1).
 - In total, 11.3% of participants reported hospitalization or emergency room (ER) visits due to CeD symptoms in the past year (Table 1).

Table 1. Baseline demographics and clinical disease characteristics of adolescent participants of the Virtual Celiac Symptoms Study (2022–2023) stratified by self-reported symptom severity.

	Overall	Self-reported severity of CeD symptoms					p value
		Mild	Moderate	Severe	Varies wildly		
Number of participants, n (%)	142 (100)	14 (9.9)	47 (33.1)	43 (30.3)	38 (26.8)		
Age, years, mean (SD)	14.5 (1.7)	14.9 (1.7)	14.3 (1.7)	14.5 (1.8)	14.6 (1.6)		0.65
Age at CeD diagnosis, years, n (%)							0.58
12-< 18	43 (30.3)	5 (35.7)	12 (25.5)	16 (37.2)	10 (26.3)		
6-< 12	74 (52.1)	7 (50.0)	27 (57.5)	17 (39.5)	23 (60.5)		
< 6	25 (17.6)	2 (14.3)	8 (17.0)	10 (23.3)	5 (13.2)		
White race, n (%)	139 (97.9)	14 (100)	44 (93.6)	43 (100)	38 (100)		0.19
BMI, kg/m², mean (SD)	20.9 (4.3)	21.0 (2.4)	20.9 (4.4)	21.4 (3.8)	20.4 (5.2)		0.80
Sex, n (%)							0.0001
Female	95 (67.0)	5 (35.7)	28 (59.6)	39 (90.7)	23 (60.5)		
Male	47 (33.1)	9 (64.3)	19 (40.4)	4 (9.3)	15 (39.5)		
Education, n (%)							
High school graduate or equivalent	6 (4.2)	0 (0.0)	3 (6.4)	1 (2.3)	2 (5.3)		0.78
Some high school	72 (50.7)	9 (64.3)	22 (46.8)	21 (48.8)	20 (52.6)		0.70
Elementary, junior high or middle school	63 (44.4)	5 (35.7)	22 (46.8)	20 (46.5)	16 (42.1)		0.87
Adherence to a GFD, n (%)^a							
I eat a GFD and never eat gluten accidentally or on purpose	19 (13.4)	3 (21.4)	4 (8.5)	8 (18.6)	4 (10.5)		0.37
I eat a GFD and rarely eat gluten accidentally	111 (78.2)	8 (57.1)	39 (83.0)	32 (74.4)	32 (84.2)		0.16
I eat a GFD and rarely eat gluten on purpose	9 (6.3)	3 (21.4)	2 (4.3)	3 (7.0)	1 (2.6)		0.13
I eat gluten-containing foods regularly	3 (2.1)	0 (0.0)	2 (4.3)	0 (0.0)	1 (2.6)		0.65
Additional dietary restrictions other than gluten, n (%)							
Lactose-free/dairy-free/milk-free	23 (16.2)	2 (14.3)	6 (12.8)	8 (18.6)	7 (18.4)		0.88
Vegetarian	8 (5.6)	0 (0.0)	2 (4.3)	2 (4.7)	4 (10.5)		0.56
Low FODMAP	2 (1.4)	0 (0.0)	0 (0.0)	1 (2.3)	1 (2.6)		0.62
Other ^b	8 (5.6)	0 (0.0)	3 (6.4)	3 (7.0)	2 (5.3)		0.96
No dietary restrictions	109 (76.8)	12 (85.7)	37 (78.7)	32 (74.4)	28 (73.7)		0.84
Comorbidities, n (%)							
Anxiety	56 (39.4)	4 (28.6)	17 (36.2)	19 (44.2)	16 (42.1)		0.70
Depression	30 (21.1)	3 (21.4)	13 (27.7)	4 (9.3)	10 (26.3)		0.12
ADHD	24 (17.0)	2 (14.3)	8 (17.0)	5 (11.6)	9 (23.7)		0.55
Anemia	13 (9.2)	1 (7.1)	3 (6.4)	4 (9.3)	5 (13.2)		0.78
GERD	13 (9.2)	0 (0.0)	4 (8.5)	7 (16.3)	2 (5.3)		0.25
IBS	11 (7.8)	0 (0.0)	2 (4.3)	5 (11.6)	4 (10.5)		0.40
Thyroid disease	8 (5.6)	0 (0.0)	2 (4.3)	2 (4.7)	4 (10.5)		0.56
Type I diabetes	3 (2.1)	1 (7.1)	1 (2.1)	1 (2.3)	0 (0.0)		0.35
Failure to thrive as a small child or difficulty gaining weight at any point, n (%)	51 (35.9)	3 (21.4)	18 (38.3)	16 (37.2)	14 (36.8)		0.70
Hospitalization or ER visit due to CeD symptoms in the past 12 months, n (%)	16 (11.3)	2 (14.3)	3 (6.4)	8 (18.6)	3 (7.9)		0.26

^aSmall discrepancies in percentages are due to rounding errors.

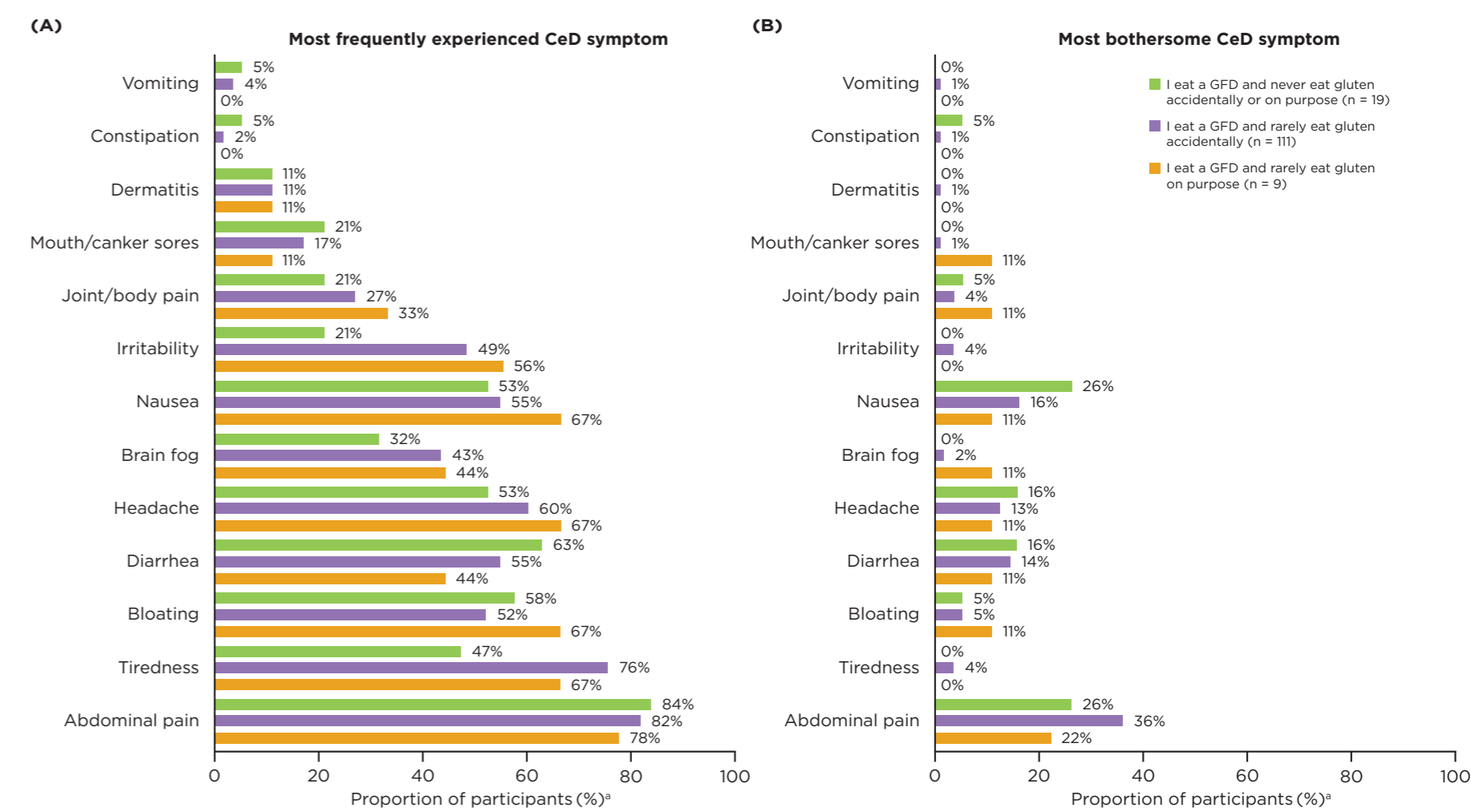
^bNone of the participants reported "eating gluten-free diet sometimes".

^cOther dietary restrictions include kosher, low caffeine, low carb, low fat, low fiber, low sodium, low sugar, no artificial sweeteners, no banana, no coconut, no corn, no eggs, no oats, no peanuts, no pork/pork products, no shellfish, no soy, no tree nuts and pescatarian. ADHD, attention-deficit/hyperactivity disorder; BMI, body mass index; CeD, celiac disease; ER, emergency room; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; GERD, gastroesophageal reflux disease; GFD, gluten-free diet; IBS, irritable bowel syndrome; SD, standard deviation.

Key messages

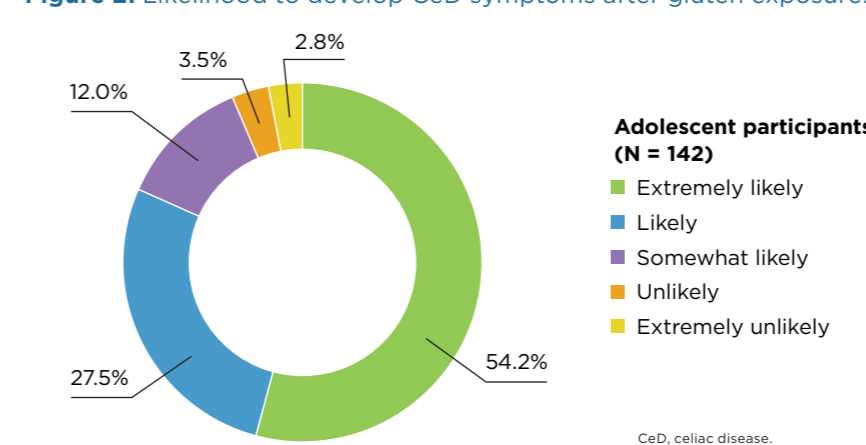
- Despite reported adherence to a gluten-free diet (GFD), adolescents with celiac disease (CeD) continued to experience symptoms, especially after inadvertent gluten exposure.
- Abdominal pain was the most bothersome and most frequently reported symptom among adolescents with CeD.
- This study highlights the need for further understanding of CeD symptoms in adolescents on a GFD and additional treatment options for this patient population.

Figure 1. Most frequent (A) and most bothersome (B) CeD symptoms reported at baseline among adolescent participants of the Virtual Celiac Symptoms Study (2022–2023) stratified by level of adherence to a GFD.



^aTotal number of adolescent participants was 139 because none of the participants reported "eating gluten-free diet sometimes" and participants who reported "eating gluten-containing foods regularly" (n = 3) were not included in this analysis. CeD, celiac disease; GFD, gluten-free diet.

Figure 2. Likelihood to develop CeD symptoms after gluten exposure.



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Disclosures

EL and DA serve as consultants for Takeda Pharmaceuticals. LMM was an employee of Takeda Development Center Americas, Inc. at the time of this study and holds Takeda stock. DAL is an employee of Takeda Development Center Americas, Inc. and receives stock or stock options. JRM, SS and ES are employees of Analysis Group, Inc., which received research support from Takeda Development Center Americas, Inc. MG is an employee of the Celiac Disease Foundation, which received financial support from Takeda Development Center Americas, Inc.

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Limitations

- Participant eligibility was based on a self-reported confirmed diagnosis of CeD and adherence to a GFD; therefore, there may have been some inaccuracies.
- The study population may not be representative of all US patients with CeD, because participants were recruited through advocacy organization channels and, therefore, are likely to be better informed about their disease and more compliant with its management.
- The experience among adolescent patients with CeD in countries other than the USA may differ.
- The results presented here are applicable only to adolescent patients with CeD and may not be translatable to adults. The adult cohort of this study has been evaluated in separate analyses.⁶

Conclusions

- Although adolescent participants with CeD reported adherence to a GFD, symptom occurrence in this population was still high, with most participants reporting their symptoms as moderate or severe and over one-tenth reporting CeD-related hospitalizations or ER visits.
- Despite stratifying occurrence of CeD symptoms by GFD adherence, this analysis observed no clear trends in symptom experience between participants who were on a GFD and reported "eating gluten accidentally" and those who reported "eating gluten on purpose".
- This study highlights the need for further understanding of the factors leading to adolescent patients experiencing CeD symptoms despite adherence to a GFD.