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To cite this article: Frida van Megen, Gry I. Skodje, Marianne Stendahl, Marit B. Veierød, Knut E. A. Lundin & Christine Henriksen (2021) High disease burden in treated celiac patients – a web-based survey, *Scandinavian Journal of Gastroenterology*, 56:8, 882-888, DOI: [10.1080/00365521.2021.1930146](https://doi.org/10.1080/00365521.2021.1930146)

To link to this article: <https://doi.org/10.1080/00365521.2021.1930146>



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Published online: 30 May 2021.



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High disease burden in treated celiac patients – a web-based survey

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ABSTRACT

Background: Strict adherence to a gluten-free diet usually leads to clinical and histological remission in celiac disease. Few studies have investigated the prevalence of persistent symptoms in a celiac population. We aimed to study the impact of gastrointestinal symptoms on general health in a large number of treated celiac patients, and describe the prevalence of persistent gastrointestinal symptoms and investigate associated factors.

Methods: Adults with celiac disease filled out background questions, the Celiac Symptom Index (CSI) and the celiac disease adherence test (CDAT) in a web-based national survey. Participants who reported gastrointestinal symptoms during the previous week also recorded the gastrointestinal symptom rating scale-irritable bowel syndrome version (GSRs-IBS). Statistical analysis included chi-squared test, *t*-test, correlation, and linear regression.

Results: Of 3834 participants (82% women; mean age 47 years), 54% reported gastrointestinal symptoms the previous week, and 30% of these had CSI score ≥ 45 , indicative of the relatively poor quality of life (vs. 5% among those without gastrointestinal symptoms). The prevalence of persistent gastrointestinal symptoms (GSRs-IBS ≥ 30) was 40% and the most prominent symptoms were bloating (44%) and pain (37%). Age, sex, symptoms at the time of diagnosis, comorbidity, dietary adherence and CeD-specific health were significantly associated with gastrointestinal symptoms ($p < .001$).

Conclusion: In this national cross-sectional study among participants with celiac disease, persistent gastrointestinal symptoms were frequent, and were associated with a high symptom burden and reduced CeD-specific health. Several factors were associated with gastrointestinal symptoms, but more research is needed to find the cause of persistent symptoms in patients with celiac disease.

Abbreviations: CeD: celiac disease; CDAT: celiac disease adherence test; CI: confidence interval; CSI: celiac symptom index; GI: gastrointestinal; GSRs-IBS: gastrointestinal symptom rating scale-IBS version; IBS: irritable bowel syndrome; PROMs: patient reported outcome measures; QoL: quality of life; REC: Regional Committee for Medical and Health Research Ethics; SD: standard deviation; STROBE statement: strengthening the reporting of observational studies in epidemiology

ARTICLE HISTORY

Received 25 March 2021

Revised 29 April 2021

Accepted 7 May 2021

KEYWORDS

Gastrointestinal; gluten; quality of life; survey; disease burden

Introduction



Celiac disease (CeD) is an immune disease of the small intestine with local, abdominal and general manifestations. The only current treatment is a gluten-free diet, as gluten proteins from wheat, rye and barley trigger CeD [1]. Strict adherence to a gluten-free diet usually leads to clinical and histological remission, reduced risk of gastrointestinal (GI) malignancies and improvements in nutritional status and quality of life (QoL) [2,3]. Still, many patients have continued GI symptoms and/or reduced general health even though they are dietary adherent [4–8].

Persistent GI symptoms in CeD resemble irritable bowel syndrome (IBS), a common functional GI disorder with an

estimated global prevalence of 11% [9]. IBS is characterized by recurrent abdominal pain, bloating and change in frequency and/or appearance of stool [10]. Previous studies found that 20–58% of CeD patients may suffer from persistent IBS-like symptoms [4,7,8,11–13], but there are few large, nationwide studies [7,8,13].

Gluten exposure is a common cause of persistent symptoms in CeD [5,6,14], but rates for strict dietary adherence vary. Strict adherence to a gluten-free diet ranged from 42 to 91% in a 2009 review [15], probably illustrating heterogeneity in dietary adherence assessment and lack of standardized validated methods.

Studies show that CeD patients have reduced QoL compared to the general population, and poor gluten-free diet

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This article has been corrected with minor changes. These changes do not impact the academic content of the article.

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adherence and IBS-like symptoms seem to be contributing factors [11,16,17]. However, studies assessing QoL and GI symptoms in CeD are sparse, vary in design and often have poorly validated outcomes [1,18,19]. Recently, the disease-specific patient-reported outcome measures (PROMSs) for general health, specific symptoms and dietary adherence have become available, enabling larger samples of patients with appropriate methodology [1,18].

In Norway, 98% of the population has internet access [20], and the use of social media is common, facilitating studies in a larger number of patients *via* digital patient communities. CeD affects 1–2% of the population [21] (50,000–100,000 Norwegians).

Moreover, Norwegian patients with a verified CeD diagnosis receive governmental reimbursement through the public health care system, meaning that study patients who receive reimbursement have confirmed CeD.

In this national cross-sectional study, our primary aim was to study the impact of GI symptoms on general health in a large sample of treated CeD patients. Our secondary aim was to describe the prevalence of persistent GI symptoms and investigate associated factors.

Methods

Study design and participants

The cross-sectional web-based ‘Survey about celiac disease and health’ was performed in October 2018. We invited adult CeD patients (age 18–75) on a strict gluten-free diet for at least 12 months, and with biopsy verified diagnosis, or serology verified in childhood/adolescence [22]. We also asked whether they received governmental reimbursement. Participants were invited through digital patient communities, and the Norwegian Celiac Association (~9500 members) invited participants by e-mail and the association’s journal.

Variables

Background characteristics were obtained from the survey. The Norwegian counties were categorized according to the Regional Health Authorities: Northern, Central, Western and Southeastern [23].

GI symptoms were assessed by the question: “Did you experience GI symptoms during the previous week?” Answering “yes” on this question created a subgroup that was asked to fill out the Gastrointestinal Symptom Rating Scale, IBS version (GSRS-IBS) [24]. A total score \geq of 30 was empirically set as the cut-off for GI symptoms (range 13–91) based on our previous experience [25,26]. A mean score \geq of 4 defined moderate to severe symptoms for the five sub-dimensions; satiety, abdominal pain, diarrhea, constipation and bloating [24,26].

General health and disease-specific symptoms were assessed by celiac symptom index (CSI) [27]. CSI total score range is 16–80 and \leq 30 indicates high QoL and excellent gluten-free diet adherence, while \geq 45 indicates relatively

poor QoL and worse gluten-free diet adherence [27]. Scores 31–44 were interpreted as moderately reduced QoL.

Gluten-free diet adherence was measured using the 7-item celiac disease adherence test (CDAT), where a total score of \leq 12 is considered ‘adequate adherence’ (range 7–35) [28]. Self-rated dietary adherence was also assessed by the question: ‘How well do you adhere to a gluten-free diet?’ (very well, pretty well, fair, not well, do not adhere).

The Norwegian version of the questionnaires CSI and CDAT were previously translated, re-translated and approved by the original author Dr. Leffler. The survey was pilot tested in 17 Norwegian Celiac Association members, and minor changes were made in CSI and CDAT. In CSI: ‘hunger pain’ was changed to ‘cramps associated with an empty stomach’ in item seven, and ‘food cravings’ was changed to ‘urge to eat’ in item ten. In CDAT: ‘generally intended’ was added in parenthesis in items four and five.

Statistical methods

Descriptive results are presented as mean (standard deviation (SD), range) and frequency (%). Independent samples *t*-test and chi-squared test were used to compare two groups. We estimated Pearson’s correlation coefficient, *r*, with 95% confidence interval (CI). Logistic regression was used to compare participants with and without GI symptoms when adjusting for age, sex and comorbidity. Multiple linear regression analysis was used to study associations between GSRS-IBS and years since diagnosis, symptoms at the time of diagnosis, comorbidity, CDAT and CSI. We adjusted for age and sex, and analyses of CDAT and CSI were also adjusted for comorbidity. All tests were two-sided, and $p < .05$ was considered statistically significant. IBM SPSS Statistic version 27 (SPSS Inc. Chicago, IL) was used for statistical analyzes.

Ethics, approval and pretesting

The study was conducted in accordance with the Helsinki Declaration and approved by the Regional Committee for Medical and Health Research Ethics (REC) [29] 24 August 2018, with the identification 2018/1055, REC South East B.

All authors have reviewed and approved the final manuscript.

Results

After exclusion of 293 persons without definite CeD diagnosis or with disease duration $<$ 1 year, the final study sample consisted of 3834 participants. There was a female predominance (82%), and the mean (SD) age was 47.0 (range 19–79) years (Table 1). Biopsy verified CeD diagnosis was reported by 97%, while 2.6% reported a diagnosis based on serology tests from childhood/adolescence, and 99% received governmental reimbursement. GI symptoms the previous week were reported by 54%. Females and younger participants were most likely to report GI symptoms ($p < .001$). There were also differences between the groups for ‘region of residence’, ‘first-degree family members with CeD’, ‘years since diagnosis’, ‘symptoms at

Table 1. Participant characteristics and gastrointestinal (GI) symptoms the previous week.

	Total (n = 3834)	GI symptoms during the previous week		p-value ^a
		Yes (n = 2057)	No (n = 1777)	
Sex, n (%)				
Female	3146 (82.1)	1746 (55.5)	1400 (44.5)	<.001
Male	688 (17.9)	311 (45.2)	377 (54.8)	
Age (years), mean (SD)	47.2 (15.5)	46.5 (15.0)	48.1 (16.1)	<.001
Region of residence, n (%)				
Northern Norway	278 (7.3)	157 (56.5)	121 (43.5)	.04
Central Norway	547 (14.3)	316 (57.8)	231 (42.2)	
Western Norway	946 (24.7)	503 (53.2)	443 (46.8)	
Southeastern Norway	2063 (53.7)	1081 (52.4)	982 (47.6)	
Diagnosis, n (%)				
Biopsy	3736 (97.4)	2000 (53.5)	1736 (46.5)	.36
Serology in childhood/adolescence	98 (2.6)	57 (58.2)	41 (41.8)	
Governmental reimbursement, n (%)				
Yes	3782 (98.6)	2020 (53.4)	1762 (46.6)	.06
No	48 (1.3)	36 (75.0)	12 (25.0)	
Do not know	4 (0.1)	1 (25.0)	3 (75.0)	
First-degree family members with CeD, n (%)				
Yes	1538 (40.1)	801 (52.1)	737 (47.9)	<.001
No	1851 (48.3)	974 (52.6)	877 (47.4)	
Do not know	445 (11.6)	282 (63.4)	163 (36.6)	
Years since diagnosis, n (%)				
1–5	1201 (31.3)	685 (57.0)	516 (43.0)	<.001
6–10	875 (22.8)	493 (56.3)	382 (43.7)	
>10	1758 (45.9)	879 (50.0)	879 (50.0)	
Years of symptoms prior to diagnosis, n (%)				
No symptoms	342 (8.9)	190 (55.6)	152 (44.4)	.71
<1	403 (10.5)	217 (53.8)	186 (46.2)	
1–5	1314 (34.3)	715 (54.4)	599 (45.6)	
6–10	466 (12.2)	253 (54.3)	213 (45.7)	
>10	1309 (34.1)	682 (52.1)	627 (47.9)	
Symptoms at time of diagnosis, n (%)				
Yes	3123 (81.4)	1782 (57.1)	1341 (42.9)	<.001
No	494 (12.9)	181 (36.6)	313 (63.4)	
Do not know	217 (5.7)	94 (43.3)	123 (56.7)	
Self-reported severity of symptoms after exposure to gluten, n (%)				
No symptoms	202 (5.3)	69 (34.2)	133 (65.8)	<.001
Little	594 (15.5)	251 (42.3)	343 (57.7)	
Some	821 (21.4)	456 (55.5)	365 (44.5)	
Pretty much	951 (24.8)	552 (58.0)	399 (42.0)	
Very much	1266 (33.0)	729 (57.6)	537 (42.4)	
Comorbidity, all, n (%)				
Yes, one or more	2237 (58.3)	1356 (60.6)	881 (39.4)	<.001
No	1597 (41.7)	701 (43.9)	896 (56.1)	
Comorbidity, type, n (%) ^b				
Autoimmune thyroid disease	607 (15.8)	350 (57.7)	257 (42.3)	
Irritable bowel syndrome	453 (11.8)	388 (85.7)	65 (14.3)	
Rheumatic disorder	360 (9.4)	222 (61.7)	138 (38.3)	
Fatigue	355 (9.3)	257 (72.4)	98 (27.6)	
Mental illness	293 (7.6)	205 (70.0)	88 (30.0)	
Osteoporosis	247 (6.4)	145 (58.7)	102 (41.3)	
Fibromyalgia	246 (6.4)	178 (72.4)	68 (27.6)	
Dermatitis herpetiformis	168 (4.4)	94 (56.0)	74 (44.0)	
Inflammatory bowel disease	111 (2.9)	79 (71.3)	32 (28.7)	
Diabetes type 1	97 (2.5)	40 (41.2)	57 (58.8)	
Sjogren's	63 (1.6)	34 (54.0)	29 (46.0)	
Diabetes type 2	57 (1.5)	40 (70.2)	17 (29.8)	
Multiple sclerosis	19 (0.5)	13 (68.4)	6 (31.6)	
Other	824 (21.5)	508 (61.7)	316 (38.3)	

SD: standard deviation; chi-squared test is used for all variables except for age (independent sample t-test).

^aComparing participants with and without GI symptoms.

^bMore than one answer is possible.

the time of diagnosis', 'self-reported severity of symptoms after exposure to gluten' and 'comorbidity'.

Ongoing symptoms and general health

The mean (SD) CSI score was 34.2 (11.0), and 41% had scores indicative of high QoL and excellent gluten-free diet adherence, while 19% had scores indicative of relatively poor QoL

and worse gluten-free diet adherence (Figure 1). Participants with GI symptoms the previous week had significantly higher CSI scores than those without GI symptoms (mean 39.4 vs. 28.1), also after adjustment for age, sex and comorbidity ($p < .001$). Among participants with GI symptoms, 30% had CSI scores indicative of relatively poor QoL and worse gluten-free diet adherence (vs. 5% among those without GI symptoms).

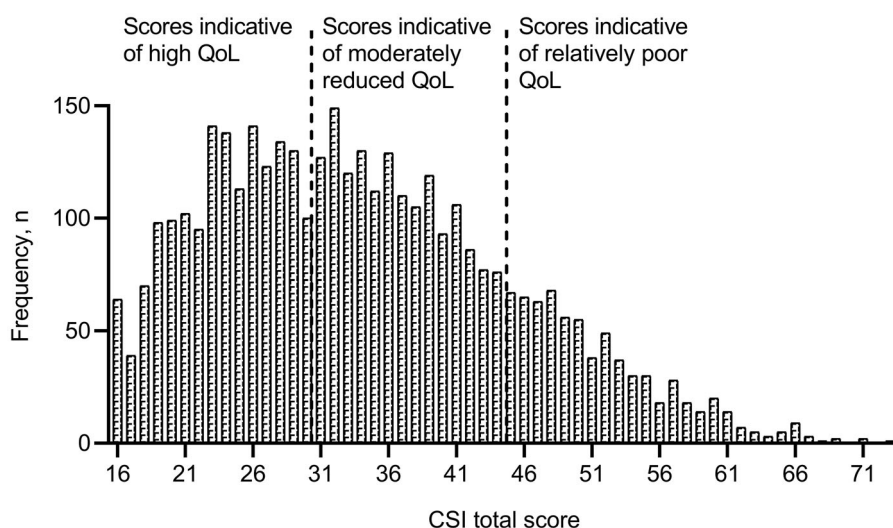


Figure 1. Celiac Symptom Index (CSI, total score range 16-80), $n = 3834$. QoL, quality of life. Score ≤ 30 is associated with high QoL and excellent gluten-free diet adherence, score ≥ 45 is associated with relatively poor QoL and worse gluten-free diet adherence and score 31-44 is associated with moderately reduced QoL.

Table 2. Coeliac disease adherence test (CDAT) and self-reported adherence to a gluten-free diet, by GI symptoms the previous week, $n = 3834$.

	Total	GI symptoms during the previous week		Univariable p -value	Multivariable p -value
		Yes	No		
CDAT (mean, SD)	13.4 (3.5)	14.2 (3.4)	12.5 (3.3)	$<.001^a$	$<.001^c$
Self-rated adherence, n (%)				.003 ^b	.001 ^c
Very well	3395 (88.6)	1783 (52.5)	1612 (47.5)		
Pretty well	385 (10.0)	240 (62.3)	145 (37.7)		
Fair	35 (0.9)	23 (65.7)	12 (34.3)		
Not well	9 (0.2)	6 (66.7)	3 (33.3)		
Do not adhere	10 (0.3)	5 (50.0)	5 (50.0)		

SD: standard deviation.

^aIndependent sample t -test.

^bChi-squared test.

^cLogistic regression, adjusted for age, sex and comorbidity.

Adherence to a gluten-free diet

The mean (SD) CDAT score was 13.4 (3.5) (Table 2), and 44% had ≤ 12 , indicating adequate adherence. Self-rated adherence was very well in 89%. Participants with GI symptoms the previous week had higher CDAT scores than those without (mean 14.2 vs. 12.5), also after adjustment for age, sex and comorbidity ($p < .001$). In contrast, participants with GI symptoms reported significantly better self-rated adherence compared to those without GI symptoms, also after adjustment for age, sex and comorbidity ($p < .001$).

Severity and type of GI symptoms

Among the 2057 (54%) participants who reported GI symptoms the previous week, 1545 had a total GRS-IBS score ≥ 30 , giving a prevalence of persistent GI symptoms of 40% in the total study sample. The most prominent symptoms were bloating and pain (Table 3).

Factors associated with severity of GI symptoms

Age was weakly negatively correlated with GRS-IBS ($r = -0.07$), and GRS-IBS was lower in men than in women

Table 3. Mean (standard deviation, SD) per sub-dimension of gastrointestinal symptom rating scale-irritable bowel syndrome version (GRS-IBS), and frequencies (%) of moderate to severe discomfort (GRS-IBS ≥ 4), $n = 2057$.

	Mean (SD)	GRS-IBS ≥ 4 , n (%)
Bloating	3.67 (1.39)	905 (44.0)
Pain	3.25 (1.14)	759 (36.9)
Constipation	2.67 (1.65)	579 (28.1)
Diarrhea	2.97 (1.30)	491 (23.9)
Satiety	2.35 (1.52)	420 (20.4)

Missing values: pain, 6; constipation, 2; diarrhea, 1; satiety, 10.

(mean difference -3.50 , 95% CI $(-5.00, -2.00)$, $p < .001$). GRS-IBS scores were significantly higher in participants with symptoms at the time of diagnosis and with comorbidity (adjusted regression coefficients (95% CIs) were 5.45 (3.56, 7.33) and 4.74 (3.60, 5.88), respectively). GRS-IBS was significantly positively associated with CDAT and CSI ($p < .001$) (Table 4).

Discussion

This national cross-sectional survey among almost four thousand treated CeD patients showed that persistent GI

Table 4. Simple linear regression (univariable) and multiple regression (multivariable) analysis for the association between GSRS-IBS and listed variables.

	Univariable B (95% CI)	p-value	Multivariable B (95% CI)	p-value
Years since diagnosis		.251		.058 ^b
1–5 years	–1.04 (–2.29, 0.21)		–1.55 (–2.82, –0.27)	
6–10 years	–0.26 (–1.63, 1.12)		–0.81 (–2.19, 0.58)	
>10 years	Reference		Reference	
Symptoms at time of diagnosis		<.001		<.001 ^b
No	Reference		Reference	
Yes	4.97 (3.07, 6.86)		5.45 (3.56, 7.33)	
Do not know	–0.004 (–3.09, 3.08)		0.67 (2.40, 3.74)	
Comorbidity ^a	4.46 (3.34, 5.58)	<.001	4.74 (3.60, 5.88)	<.001 ^b
CDAT	1.27 (1.13, 1.42)	<.001	1.17 (1.02, 1.32)	<.001 ^c
CSI	0.81 (0.77, 0.86)	<.001	0.83 (0.79, 0.87)	<.001 ^c

Regression coefficient, B, and 95% confidence interval (CI), $n = 2057$.

^aDichotomous variable ('no' is reference).

^bAdjusted for age and sex.

^cAdjusted for age, sex and comorbidity.

symptoms were frequent (40%), and were associated with a high symptom burden and reduced QoL.

Our findings are partly in concordance with previous studies, depending on the assessment methods. A US study found that 52% had IBS-like symptoms at the time of diagnosis, and 22% still had symptoms one year after initiating a gluten-free diet [8]. A Finnish study found that 23% of long-term well-treated CeD patients had persistent GI symptoms [7]. Furthermore, the prevalence of persistent GI symptoms in our study was higher compared to a meta-analysis from 2013, which showed a pooled prevalence of IBS-like symptoms (ROME criteria) [30] of almost 30% among CeD patients strictly adherent to a gluten-free diet [31].

Among participants with GI symptoms, as many as 30% had CSI scores indicative of reduced CD-specific health, which is associated with poor QoL and worse gluten-free diet adherence. These findings are in line with previous smaller studies reporting reduced QoL and ongoing symptoms in treated CeD patients [4,11], although there seems to be a gender difference [16]. However, Silvester et al. found reduced health and ongoing symptoms in only 8% one year after initiating a gluten-free diet [8]. This contrasts with our finding, possibly due to methodologic differences.

Over half of our participants reported comorbidity, most commonly thyroid disease, IBS, rheumatic disorder and fatigue. The association between CeD and other autoimmune conditions is well known [3], including type 1 diabetes [32] and autoimmune thyroid disease [33]. We asked about actual diagnoses, however, there is a possibility that some of the reported comorbidities are self-perceived. Additionally, the true occurrence of some of the comorbidities is questionable. Both fatigue and IBS could possibly be a symptom of CeD rather than a diagnosis by itself. According to the ROME criteria [30], organic GI disease should be excluded before a diagnosis of IBS can be made. Two previous and comparable surveys, the *Canadian Celiac Health Survey* [16] and *Characteristics of Adult Celiac Disease in the USA: Results of a National Survey* [34], found that many participants received one or more diagnoses before the CeD diagnosis was made, most commonly anemia, stress, IBS and chronic fatigue syndrome. Furthermore, in the US survey, nearly 40% of the

participants were previously diagnosed with IBS, which contrasts with our finding of 11% [34]. CeD might predispose to symptoms resembling IBS [4], possibly due to low-grade inflammation [8,31,35,36].

Adequate adherence to a gluten-free diet according to CDAT was unexpectedly low (44%). In comparison, two US surveys reported adequate adherence of 76% and 96%, by use of CDAT [8,37]. On the other hand, we found a very high rate of self-reported adherence (89% very well). However, self-reported adherence is known to overestimate compliance [38,39]. Furthermore, we found that self-rated adherence was higher in participants with GI symptoms the previous week compared to participants without GI symptoms. In contrast, participants with GI symptoms had lower adherence according to CDAT, which is in line with previous studies who found that gluten intake is the most common cause of persistent symptoms [5,6,14]. The variation in dietary adherence can be explained by the different assessment tools. CDAT measures non-specific symptoms, self-efficacy, risk behaviour and perceived ability to adhere to a gluten-free diet [28], and thereby measure the risk of gluten consumption rather than actual gluten intake. Additionally, the tool is validated in a US population, and one can speculate whether the tool fits more to a society where eating outside of the home is more common than in Norway.

Adequate gluten-free diet adherence was associated with a lower GSRS-IBS score, which is in line with previous findings [5,14]. GI symptoms are also associated with poorer QoL, and a positive correlation between dietary adherence and QoL is previously found [11,17]. In contrast, a clinical study by Silvester et al. did not find a significant correlation between patients fulfilling ROME criteria and adherence to a gluten-free diet [8]. Furthermore, we found that women had a significantly higher GSRS-IBS score than men, which is also in line with previous findings [4,7]. Similarly, IBS is also shown to be more common in females [9]. Comorbidity also predicted GSRS-IBS score in our study, as participants suffering from comorbidity were more likely to have a higher GSRS-IBS score than those without comorbidity. Others have also reported an association between comorbidity and reduced QoL [40]. Furthermore, we found a lower GSRS-IBS

score with a longer duration of CeD, which supports previous findings [4,7]. Lastly, symptoms at the time of diagnosis were associated with a higher GSRS-IBS score.

Previously, a range of different methodologies has been used to assess GI symptoms in CeD [1,18]. The standardized validated tool GSRS-IBS is commonly used [24]. However, a cut-off for the presence or severity of GI symptoms is not established, as GSRS-IBS is developed to assess responsiveness to change. Furthermore, studies exploring QoL in CeD also use a variety of different tools for assessment, and generic instruments like the short form 36 health survey questionnaire are widely used [41]. Comparability of GI symptoms and QoL in CeD patients is therefore difficult, and generic instruments may possibly not adequately reflect challenges in CeD. A strength in our study is the use of the disease-specific questionnaire CSI [27], which includes both intestinal and extraintestinal symptoms. We found a significant positive association between CSI and GSRS-IBS, which is not surprising, as several of the questions in CSI relate to GI symptoms. Obviously, another reason for this association could be the direct impact of GI symptoms on general health. Others have found that abdominal symptoms can impair QoL in CeD [4,11,12], and opposite, it has also been suggested that reduced QoL in CeD is a predictor for abdominal symptoms [42].

A large number of participants is a strength of the present study, and all Norway counties were represented. To limit selection bias, we invited people through different channels and used a general title ('Survey about celiac disease and health'). We believe that the study sample resembles a population of 'true' CeD because as many as 99% of the participants received reimbursement, meaning they had biopsy or serology (from childhood/adolescence) verified CeD. To compare, the previously mentioned Canadian and US surveys found a prevalence of 86% and 75% of biopsy verified CeD, respectively [16,34]. Moreover, our participants were not recruited from health care, and thereby more likely to represent a real-life CeD population.

A standardized dietetic assessment is considered the most objective and non-invasive method for monitoring adherence to a gluten-free diet [43,44]. CDAT is found to be highly correlated with expert dietitian evaluation and performs better than serology anti-tissue transglutaminase antibodies [35]. However, biopsy histology is considered the gold standard to measure CeD activity [44], but due to the nature of the design in this study, we were not able to compare self-reported adherence with nutritional, serological or histological assessment. Therefore, gluten intake cannot be excluded as the cause of ongoing symptoms in our study. Another limitation of this study is the lack of assessment of dietary intake, for example, known triggers of IBS symptoms like FODMAPs. Others have shown that a gluten-free diet is lower in fiber and several micronutrients, and higher in saturated fat and as compared to a gluten-containing diet [45–47]. However, it is unknown whether this less healthy profile of the gluten-free diet is related to ongoing GI symptoms in patients with celiac disease.

In conclusion, this study highlights the high prevalence of persistent GI symptoms and high symptom burden in treated adult CeD patients. There is a need for follow-up of patients with ongoing symptoms and reduced general health despite a strict gluten-free diet and should include evaluation of dietary adherence by a clinical dietician, assessment of serology and histology, and investigation of other causes of ongoing symptoms like refractory CeD and malignancies. More research is needed to find possible causes and treatment methods for the supposedly large group of patients with ongoing symptoms despite remission of CeD. Large randomized trials are needed to find out whether IBS treatment, like for example the low FODMAP diet, can treat ongoing symptoms in CeD.

Acknowledgements

We thank all participants for the valuable sharing of their experience. We would also like to thank the Norwegian Celiac Association for contributions to the development of the survey, and for distributing the survey.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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