Factors Associated with Dietary Adherence in Celiac Disease: A Nationwide Study

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Key Words

Celiac disease • Adherence • Gluten-free diet

Abstract

Aims: Diagnostics and follow-up of celiac disease have gradually shifted from tertiary centers to secondary and primary health care. In order to establish whether this has affected the success of treatment, and to identify predictors for dietary non-adherence, we carried out a study in a nationwide cohort of treated celiac patients. **Patients and Methods:** 843 biopsy-proven patients, 94 children and 749 adults, were enrolled and interviewed. Adherence to a gluten-free diet was determined by means of an interview and serological testing. **Results:** Altogether, 88% were on a strict gluten-free diet; the rest had occasional dietary transgressions. Younger age at diagnosis, being currently a teenager, and current symptoms were associated with non-adherence. There was no association between non-adherence and place of diagnosis, gender, disease phenotype or severity of symptoms before diagnosis, presence of comorbidities, family history of celiac disease, smoking, duration of diet, use of oats, self-efficacy for the diet or lack of follow-up. **Conclusions:** Good dietary adherence can be achieved also in patients diagnosed and followed in primary health care. In a country with

a high prevalence and good general knowledge of celiac disease, only age at diagnosis and age at present would appear to be major determinants for adherence.

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Introduction

Currently, the treatment of celiac disease is based on life-long exclusion of wheat, rye and barley and other gluten-containing food products from the diet. Adherence to a gluten-free diet is crucial not only for intestinal mucosal recovery and alleviation of symptoms, but also for the prevention of complications such as anemia, osteoporotic fractures and small-bowel lymphoma [1–3]. However, due to the expense and restrictive nature of the treatment, changing eating habits for life may constitute a formidable challenge for many celiac disease patients, and hence compliance with the diet easily remains inadequate [4]. It has been found in clinical practice that 20–80% of patients adhere only partially to the diet, and especially those detected by screening are thought to be at risk of poor adherence [5–11]. Nevertheless, data on factors affecting the long-term dietary control of celiac disease are scant. As non-adherence wastes health-care re-

sources and may cause significant morbidity and even increased mortality [2, 12], it is important to characterize individuals most likely to be non-adherent, and offer them advice and assist them better to follow their diet.

In recent years, active case-finding in at-risk groups and among subjects with atypical symptoms has resulted in an increasing diagnostic rate, and the prevalence of clinically detected celiac disease in Finland is 0.7% [13]. Simultaneously, the diagnostics and follow-up have shifted from tertiary centers to secondary and primary health care [14]. It is not known whether these changes in clinical practice have affected the success of the treatment. To identify factors associated with non-adherence, we carried out a cross-sectional study in a large, nationwide cohort of celiac disease children and adults.

Materials and Methods

Patients and Study Design

The study was conducted in the Departments of Gastroenterology and Alimentary Tract Surgery and Pediatrics, Tampere University Hospital and in the School of Medicine, University of Tampere. Volunteer children (age below 18 years) and adults diagnosed with celiac disease were enrolled in study investigating different clinical, pathogenic and genetic aspects of celiac disease. The participants were recruited by a nationwide search using newspaper advertisements and via national and local celiac disease societies. Approximately 70% of celiac patients in our country are members of celiac societies. Subjects with biopsy-proven celiac disease diagnosed more than one year ago were considered eligible. All participants or in the case of young children their parents were interviewed by phone either by a physician or by a study nurse with expertise in celiac disease, and blood samples were drawn for celiac disease serology. All diagnoses, presenting symptoms and the presence of celiac disease-associated disorders or other comorbidities were confirmed from the patients' medical records. In the present study, particular attention was paid to place of diagnosis, family history of the disease, severity and duration of symptoms at diagnosis, presence of comorbidities, smoking, baseline dietary counseling, duration and strictness of gluten-free diet, possible current symptoms and regular follow-up. Patients were asked to rate the severity of their previous and current symptoms as follows: no symptoms, slight symptoms, moderate symptoms and serious symptoms.

The study protocol was approved by the Ethical Committee of Tampere University Hospital. All study subjects, or in the case of young children their parents, gave written informed consent.

Dietary Assessment

A history of occasional or regular consumption of gluten-containing products and oats was assessed by means of a structured dietary interview [6]. Serologic tests were employed to further monitor disease activity. Serum IgA class endomysial antibodies were measured using an indirect immunofluorescence method with human umbilical cord as substrate [15], and serum IgA class

tissue transglutaminase antibodies by enzyme-linked immunosorbent assay (QUANTA Lite h-tTG IgA, INOVA Diagnostics, San Diego, Calif., USA); a dilution 1:≥5 and a unit value ≥30 were considered positive, respectively. In the case of selective IgA deficiency, the corresponding IgG class antibodies were determined. Patients who reported maintaining a strict gluten-free diet in a structured interview and were found to have negative serology after 2 years on the diet were regarded as strictly adherent [6, 8]. Further, patients who had been on a gluten-free diet less than 2 years were considered adherent if they reported a strict diet upon interview and serum antibody values had decreased from the level found at diagnosis. When possible, the self-assessed adherence was further confirmed from the patients' medical reports; the reported diet was considered strict only if there was inadvertent gluten ingestion less than once in a month [16].

Statistics

Fisher's exact test was used in cross-tabulation in statistical evaluations, and a *p* value <0.05 was considered significant. All statistical calculations were performed using Predictive Analytic Software for Windows (version 18).

Results

Altogether, 94 children and 749 adults with celiac disease were eligible. At the time of the study, their median age was 51 years (range 2–89 years); 76% were female. At diagnosis, gastrointestinal complaints had been the main presenting symptom in 62%, while 16% had suffered from extraintestinal symptoms and 22% were detected by screening in celiac disease at-risk groups. Eight percent of the patients had experienced severe symptoms at diagnosis, 36% moderate symptoms, and in 56% symptoms had been mild or absent. Among adults, 18% of the diagnoses had been established in tertiary centers, 47% in secondary health care and 35% in primary care. In contrast, among children 70% of the diagnoses had been still made in tertiary care and the remainder in secondary care.

In total, 69% of the celiac disease adults were not under any kind of follow-up for their disease, while 95% of the children were being followed. Subjects with celiac disease-associated or other comorbidities were followed no more often than others (data not shown). Of those under regular surveillance, 59% were followed up in primary health care (adults 71%, children 5%). In total, 88% of the patients were found to be keeping to a strict gluten-free diet (adults 90%, children 81%). The rest reported occasional dietary transgressions, but none was completely non-adherent. Altogether, the patients had been a median of 7 years (range 1–48 years) on a gluten-free diet.

Table 1. Demographic data, duration of gluten-free diet, clinical presentation and duration and severity of symptoms at diagnosis and dietary adherence (n = 843)

	Subjects	Adherent %	p value
Gender			0.143
Male	206	86	
Female	637	90	
Age at diagnosis, years			0.01
<13	105	79	
13–17	34	79	
18–64	670	91	
>64	34	85	
Current age, years			0.009
<13	58	86	
13–17	36	72	
18–64	597	89	
>64	152	91	
Duration of diet, years			0.153
<5	295	86	
5–9	209	89	
10–14	142	89	
>15	117	91	
Clinical presentation at diagnosis			0.287
Gastrointestinal symptoms	523	90	
Extraintestinal symptoms	132	87	
Screen-detected subjects ¹	188	86	
Duration of symptoms, years			0.255
Never had symptoms	60	95	
<1	182	90	
1–5	253	87	
5–10	73	86	
>10	235	90	
Severity of symptoms at diagnosis			0.429
Asymptomatic	105	87	
Slight	366	87	
Moderate	303	91	
Severe	68	88	

¹ Family history of celiac disease, type 1 diabetes mellitus, thyroidal disease, selective IgA deficiency, Sjögren's syndrome.

Younger age at diagnosis and current age were related to dietary non-adherence. In particular, those currently in their teens were likely to be non-adherent (table 1). In contrast, neither the place of diagnosis, gender, clinical presentation of the disease, duration and severity of symptoms before diagnosis, presence of comorbidities, family history of celiac disease, smoking, duration of gluten-free diet, dietary counseling from a dietitian, regular follow-up, self-efficacy for the diet nor consumption of oats were associated with adherence (tables 1–3). Al-

Table 2. Family history of celiac disease, presence of celiac disease-associated conditions or other comorbidities and smoking and adherence to gluten-free diet (n = 843)

	Subjects	Adherent, %	p value
Celiac disease in the family			0.224
Yes	505	88	
No	330	90	
Other food intolerance			1.000
Yes	171	89	
No	672	89	
Type 1 diabetes			0.530
Yes	26	77	
No	817	89	
Malignancy			0.117
Yes	34	97	
No	809	88	
Psychiatric disease			0.387
Yes	31	94	
No	812	89	
Osteoporotic fracture			0.149
Yes	31	97	
No	812	88	
Presence of comorbidity			0.284
Yes	590	88	
No	253	91	
Smoking, current or previous			0.494
Yes	608	89	
No	219	89	

though there was no significant difference, patients with osteoporotic fracture or malignancy showed particularly good adherence (table 2). Of note, subjects betraying frequent dietary transgressions also experienced more clinical symptoms (table 3); in a separate analysis, this could be seen only in adults. Otherwise, there were no differences between children and adults in the factors related to dietary adherence.

Discussion

Our main finding was that the decentralization of celiac disease diagnostics and follow-up from tertiary centers to primary health care in recent decades has not affected the success of treatment. We also showed that, in a country with a good general knowledge and a high prevalence of celiac disease, only current age and age at diagnosis were major factors associated with dietary adherence. In particular, teenage patients showed more non-adherence than others. Previously, poor coping among

Table 3. Place of celiac disease diagnosis, dietary counseling, maintenance and place of follow-up, use of oats, current symptoms, self-efficacy for the diet and adherence to gluten-free diet (n = 843)

	Subjects	Adherent, %	p value
Place of diagnosis			0.584
Primary care	199	88	
Secondary care	370	90	
Tertiary care	269	88	
Dietary counseling			0.048
No advice	211	93	
Dietitian	558	87	
Other	74	92	
Regular follow-up			0.748
No follow-up	522	90	
1–2 years	233	87	
3–5 years	72	87	
Place of follow-up			0.145
Primary care	174	90	
Secondary/tertiary care	121	83	
Use of oats			0.561
Yes	701	89	
No	133	89	
Current symptoms			0.001
No symptoms	642	91	
Slight	184	82	
Severe	12	83	
Self-efficacy for the diet			0.719
Yes	803	89	
No	40	93	

adolescents has also been noted in a small Italian study [5], and in some adult studies older patients have been more adherent than younger [17–20]. Elsewhere, no such association has been found [6, 8, 21, 22]. Besides current teenagers, in our study patients diagnosed in childhood also showed more dietary non-adherence. Ciacci et al. [23] detected better adherence in patients diagnosed after 20 years of age, whereas in another study the same applied to children diagnosed before the age of 4 years [24]. Again, there are studies where no association has been observed between age at diagnosis and dietary adherence [6, 8, 21]. Though somewhat inconsistent, the results indicate that adolescence in particular is a sensitive period to adapt and maintain a gluten-free diet. At that age, parents may still have a major role in the treatment, and it may be challenging for a teenager to take more self-responsibility. Also, considerable changes such as new place of education and residence often occur at the same time. With this in mind, health care professionals should pay particular attention to adolescent celiac patients. In ac-

cord with most previous studies [17, 18, 23], we observed no significant difference between genders in adherence.

In line with our previous observations in screen-detected patients [6, 25], the clinical presentation of celiac disease at diagnosis had no effect on adherence, and also some other groups have obtained corresponding results [8, 21]. In contrast, Fabiani et al. [5] detected poorer adherence in screen- than in symptom-detected celiac adolescents, but the study in question was small, and both patient groups showed very poor adherence. There is usually a particular reason why a person is screened for celiac disease, for example belonging to an at-risk group. In such cases, even asymptomatic patients might be motivated to adapt a strict diet, for example in order to prevent possible complications of untreated disease. In any case, the fact that good adherence can be achieved in screen-detected subjects in at-risk groups supports intensified serological screening for such individuals. Consistently with Edwards et al. [26], non-adherent adults here evinced more current symptoms, this probably a being consequence rather than a cause. This would imply that many celiac patients may tolerate a certain amount of symptoms produced by inadvertent or deliberate gluten ingestion.

There was no association between celiac disease-related or other comorbidities and dietary adherence. Similarly, Leffler et al. [8] detected no effect of autoimmune or psychological comorbidities on adherence in celiac adults. However, in contrast to the present observations, they found higher adherence among patients with other food intolerance; this discrepancy might in fact be explained by differences in study cohorts. In a study by Adolorato et al. [27], psychological support reduced depression and dietary non-adherence in celiac patients; in the present and in two other studies [8, 17], no association was seen between psychiatric comorbidities and non-adherence. Interestingly, patients with osteoporotic fracture or malignancy showed very high adherence. This may reflect an aim to optimize celiac disease treatment in the presence of severe complication or comorbidity.

Somewhat surprisingly, lack of dietary counseling was not associated with dietary non-adherence; this was also observed in a recent adult study [8]. Nowadays, information regarding gluten-free products is easy to obtain in the internet and via different advocacy groups; better labeling and availability of products in food stores and restaurants may also have reduced the impact of dietary counseling. In addition, health care professionals may sometimes provide limited information on the treatment of celiac disease [28, 29]. Interestingly, in one earlier study

dietetic counseling proved beneficial in white Caucasian but not in South Asian patients [30], this suggesting that cultural factors may have a significant influence on the outcome. Such results emphasize that dietary counseling should be individually tailored and given by dietitians with expertise in celiac disease. Whether the counseling is implemented in primary care or in specialized centers seems to be less important.

Neither the maintenance nor duration of regular follow-up of celiac disease was associated with dietary adherence, indicating that, once achieved, good adherence remains [6, 8]. These results suggest that the follow-up of celiac disease in adults might be focused predominantly on subjects with coping problems. In children, the situation is different; due to rapid changes in development even short-term dietary transgressions can lead to permanent complications, and regular follow-up is thus mandatory [31, 32]. Interestingly, in our study adult patients diagnosed and followed in primary care evinced adherence equal to that in subjects who were under hospital care. This is important, since it will in the future be impossible to manage the increasing number of celiac patients only in tertiary and secondary centers. These observations cannot be directly generalized to pediatric patients, since here only 5% of them were being followed in primary care settings. In one recent study, children followed by primary care physicians showed poorer adherence than those followed by specialists [33], and this issue remains to be addressed in future studies. When interpreting our results, it is important to realize that in Finland there have been nationwide celiac disease care guidelines already since 1997 [34]. According to the guidelines, adult patients can be diagnosed in primary centers by general practitioners who themselves perform endoscopies. In contrast, all celiac children are diagnosed in secondary and tertiary centers by pediatric gastroenterologists.

The main strengths of our study were its nationwide coverage and the large number of celiac disease patients participating. In addition, adherence was defined meticulously by both dietary interview and serological testing, which is important in that patients may easily underestimate their inadvertent gluten intake when approached through questionnaires only [8, 21, 35]. Limitation of the study was that a substantial number of participants were recruited via celiac societies. This may cause selection bias to the results and limit the accessible patient population [29]. In theory, the high overall adherence noted in this study might also have caused false-negative associations by a ceiling effect, but due to the large cohort size, we still had more than a hundred non-adherent participants.

To conclude, our results showed that good dietary adherence in celiac disease can be attained irrespective of place of diagnosis and subsequent follow-up of the disease. In addition, in a country with a high prevalence, there are only a few major determinants for adherence, the most important being age at diagnosis and age at present.

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Disclosure Statement

None of the authors declare a conflict of interest.

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