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Original Article

The Experience of a Gluten-free Diet in Children with Type 1 Diabetes and Celiac Disease

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ABSTRACT

Objective: This study examined overall self-reported adherence to gluten-free diet (GFD) in children with type 1 diabetes and celiac disease (T1DCD) compared to children with celiac disease (CD). Secondary objectives included gaining insight into self-reported symptoms, barriers to adherence, and experience of a GFD between groups.

Methods: Children <18 years old who had been seen at BC Children's Hospital for T1DCD or CD were invited to participate in a web-based questionnaire and medical record review.

Results: A total of 26 children with T1DCD and 46 children with CD participated in the study. The groups' demographics and symptoms of CD were similar; however, a greater proportion of those with T1DCD were asymptomatic at diagnosis (T1DCD 27%; CD 7%; $P = 0.016$). Overall adherence to a GFD was high in both groups (T1DCD 92%; CD 100%; $P = 0.38$) but those with T1DCD reported a significantly less positive effect on their health ($P = 0.006$) and a significantly greater negative effect on activities from a GFD ($P = 0.03$). Children with T1DCD reported more significant barriers to eating gluten-free at home and at restaurants, specifically with social pressure, cost and taste compared to those with CD only.

Conclusion: Children with T1DCD face specific barriers in adherence that are more impactful compared with children living with CD. These children are more often asymptomatic at diagnosis, and they go on to experience different impacts of a GFD spanning across home and social settings. Given the complexity of having a dual diagnosis, CD care should be tailored specifically to children living with T1DCD.

Keywords: *Adolescent; Celiac disease; Child; Gluten-free diet; Patient compliance; Type 1 diabetes mellitus*

Introduction

Celiac disease (CD) and type 1 diabetes (T1D) are both chronic autoimmune diseases. The prevalence of CD is approximately 1% in the general population compared to 5% to 10% in people with T1D (1). CD is characterized by intestinal inflammation caused by an immune response to gluten and treatment involves a lifelong, strict gluten-free diet (GFD). Among those with both T1D and CD (T1DCD), 60% to 70% have asymptomatic or silent celiac disease (2).

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Adherence to a GFD is associated with a variety of positive health outcomes in patients with T1DCD. Youth with T1DCD who were non-adherent to a GFD were found to have a lower quality of life, lower general well-being and higher hemoglobin A1c compared to those who were adherent (3). Upon starting a GFD, several positive outcomes have been described in children with T1DCD including improvements in gastrointestinal symptoms, reduced number of hypoglycemic events and restoration of weight and growth (4,5). A recent study reports no differences in hemoglobin A1c over the first year of starting a GFD but provides evidence that a transition to a GFD is safe for children with T1D, with no differences in hypoglycemic time or adverse events (6). While health benefits from a GFD in children with T1DCD have been described, parents of these children have also reported significant challenges in managing both T1D and CD simultaneously including financial concerns and impact on mental/emotional health (7). Unique or elevated barriers in adherence to a GFD for children with T1DCD, compared to those with CD alone, have not been previously described.

The primary objective of this study was to assess for differences in self-reported adherence to a GFD. Secondary objectives included describing symptoms, specific barriers in adherence to a GFD, and impact on activities of daily living experienced by children with T1DCD, compared to children with CD alone.

METHODS

The study was conducted at British Columbia Children's Hospital (BCCH), which is the province's only tertiary children's hospital. Children were invited to participate if they were <18 years old and had been seen at BCCH for T1DCD or CD. All participants had biopsy-proven CD. A consent letter to introduce the study and gain consent was mailed to 61 patients with T1DCD and 143 patients with CD between August and December 2018. The letter contained a link and a unique participant code that could be used to complete the survey online. Participants aged <13 years were instructed to complete the survey with their parents and those aged >13 years were asked to complete the survey with assistance as needed. As per our Research Ethics Board's requirements, participants had the option to provide consent for a medical record review of their tissue transglutaminase (TTG) and hemoglobin A1c results.

Survey Design

The T1DCD and CD surveys were designed by and piloted with an interdisciplinary team of pediatric endocrinologists, pediatric gastroenterologists, dietitians, nurses, a statistician, and people living with T1DCD and CD. They were based on a previous questionnaire evaluating adherence to GFD in children with CD and they are yet to be validated (8). The surveys were developed to meet study objectives and questions were evaluated by the aforementioned interdisciplinary team for interpretation and understanding.

Data Collection and Management

The surveys were administered using the Research Electronic Data Capture (REDCap) online database platform. REDCap is a secure, web-based application designed to support data capture for research studies. Laboratory values were collected from medical records for those participants who provided consent.

Statistical Analysis

Results are presented using descriptive statistics. Likert scale results are presented as mean values and standard deviations. A sample size of 16 per group was calculated to provide a power of 80% on the primary outcome assuming an effect size of 0.5. An independent *t*-test (two-sample assuming unequal variances) was used for comparisons between groups. Statistical significance was considered for $P < 0.05$.

Research Ethics

This study was approved by the University of British Columbia Children's and Women's Research Ethics Board (H18-01257).

RESULTS

Demographics

In total, 26/61 children with T1DCD and 46/143 with CD participated in this study yielding response rates of 43% and 32%, respectively. Overall, the groups were similar in age, gender, and area of residence (Table 1). Notable differences include the years since diagnosis of CD, as the T1DCD group had a significantly longer duration since diagnosis ($P = 0.0009$). Additionally, those with T1DCD had more family members who were also on a GFD and, analogously, a greater percentage of T1DCD households were mostly or completely gluten-free (T1DCD 73%; CD 63%). Ninety-two per cent of the patients with T1DCD and 94% of patients with CD met with a dietitian for guidance after their diagnosis of CD. Twenty-four out of 26 participants with T1DCD and 44/46 participants with CD provided consent to access their medical records.

Symptoms

The most common symptoms at diagnosis for both groups were similar (Figure 1). Both groups indicated abdominal pain as the most common symptom (T1DCD 65%; CD 76%), followed by fatigue, diarrhea and nausea/vomiting.

Table 1. Characteristics of participants with type 1 diabetes and celiac disease (T1DCD) and celiac disease only (CD)

Characteristic	T1DCD ($n = 26$)	CD ($n = 46$)	*P*-value
Age, years, mean (SD)	12.8 (3.5)	11.5 (3.8)	NS
Gender, *n* (%)			
Male	11 (42)	16 (35)	NS
Female	15 (58)	30 (65)	
Time since CD diagnosis, years, mean (SD)	7.0 (3.8)	4.6 (2.1)	0.0009
Time since T1D diagnosis, years, mean (SD)	7.2 (4.0)	-	
Area of residence*, *n* (%)			
Urban	8 (31)	20 (45.5)	NS
Suburban	13 (50)	20 (45.5)	
Rural	5 (19)	4 (9)	
Number of family members, mean (SD)			
At home	4.4 (1.0)	4.31 (0.9)	NS
With CD	1.6 (0.7)	1.33 (0.6)	NS
On a gluten-free diet	1.88 (1.2)	1.58 (1.0)	NS
Household Diet Status, *n* (%)			
Partly gluten-free	7 (27)	17 (37)	NS
Mostly gluten-free	18 (69)	24 (52)	
Completely gluten-free	1 (4)	5 (11)	
Hemoglobin A1c, mean (SD)	7.7 (1.2)	-	-
Most recent† TTG, *n* (%)	$n = 13$	$n = 12$	NS
Within reference range	11 (85)	9 (75)	
<3× reference range	13 (100)	10 (83)	

NS, not significant; SD, standard deviation; TTG, tissue transglutaminase.

*Two participants in the CD group did not respond to this question.
†Within 3 months of survey completion.

A smaller percentage of T1DCD, compared to CD, reported having symptoms at diagnosis for the majority of symptom categories. Of note, a much greater percentage of children with T1DCD were asymptomatic at diagnosis (T1DCD 27%; CD 7%).

Both groups shared the same four most common symptoms upon accidental exposure to gluten: abdominal pain (77%; 78%), diarrhea (50%; 30%), nausea/vomiting (35%; 39%), and fatigue (27%; 33%) for T1DCD and CD, respectively (Figure 1).

Overall Adherence and Impact of a GFD

Hundred per cent of the participants with CD and 92% of participants with T1DCD indicated they are currently on a GFD ($P = 0.38$). The two participants with T1DCD not on a GFD both indicated they had been on a GFD for over 2 years in the past. Among the 25 participants with eligible TTG results (within 3 months of the survey), 17 of 25 were taken before the survey date, while the majority of the remaining values were taken within 1 month following the survey.

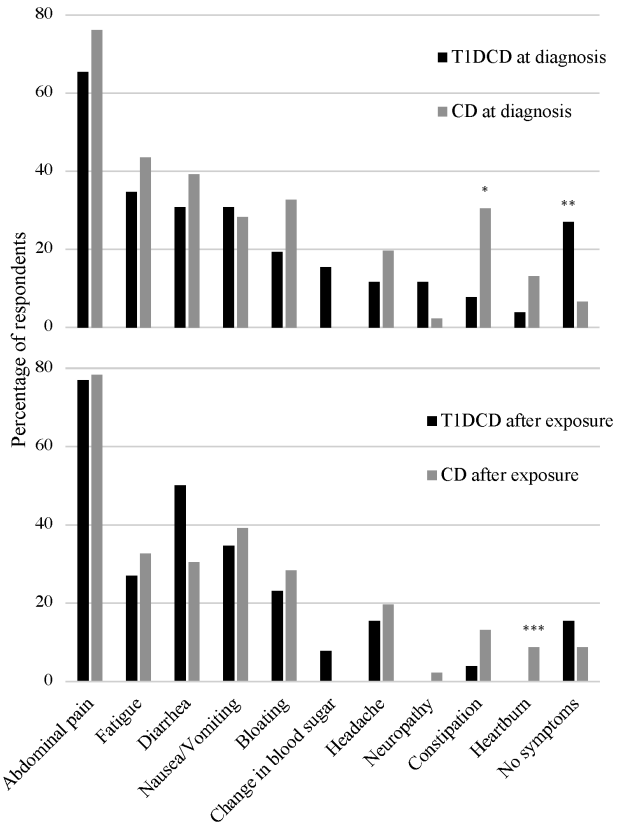

Figure 1. Symptoms experienced at diagnosis of celiac disease and upon accidental exposure to gluten for participants with type 1 diabetes and celiac disease (T1DCD, $n = 26$) and participants with celiac disease only (CD, $n = 46$). *$P = 0.026$, **$P = 0.016$, ***$P = 0.042$.

Overall reported adherence and adherence in various settings, although high for both groups, was lower for T1DCD across all settings (Table 2) but statistical significance was found only for camping ($P = 0.005$). The lowest adherence for those with T1DCD was at restaurants, whereas those with CD reported the lowest adherence at friends' houses.

The effects of a GFD on daily life are depicted in Figure 2. Children with T1DCD had a statistically significant decrease in perceived benefit on health (Likert mean [SD]: T1DCD 3.92 [1.13]; CD 4.56 [0.8]; $P = 0.006$) and activities (T1DCD 2.61 [1.17]; CD 3.24 [1.18]; $P = 0.03$). While not meeting statistical significance, those with T1DCD also reported a greater negative impact of a GFD on the remaining categories when compared to children with CD. Both groups indicated the most positive effect of a GFD was on their health and emotional well-being. Additionally, both groups indicated a negative effect on social life, travel and family finances.

For participants with T1D, there was no perceived impact on overall diabetes management (Likert mean 3.04 [SD 0.98]), diabetes-related symptoms (3.24 [0.98]), and ability to be involved in their own care (3.29 [0.81]) with the Likert scale as follows: 1 = negatively impacted, 3 = not impacted and 5 = positively impacted.

Barriers in Adherence

The T1DCD group had a higher level of difficulty with a GFD at home ($P = 0.0004$) and in restaurant settings ($P = 0.0001$; Table 3) compared to the CD group. Both groups were impacted the most by the same factor for each of the three locations: cost at home and availability of gluten-free foods at school and at restaurants. Youth with T1DCD reported they had the most difficulty with a GFD at restaurants whereas those with CD reported the most difficulty with a GFD at school. Social pressure was a more significant barrier to a GFD for the T1DCD group, both at home ($P = 0.02$) and at restaurants ($P = 0.03$; Table 3). Furthermore, cost caused more difficulty in adhering to a GFD for the T1DCD group in all three environments, with a statistically significant difference noted in the home environment ($P = 0.007$). Availability of gluten-free food at restaurants was the most challenging factor for both T1DCD and CD groups.

Two out of the three most commonly identified factors that make it easier to follow a GFD were shared between groups: availability of gluten-free foods (T1DCD 85%; CD 72%) and social support (T1DCD 62%; CD 72%). Additionally, 42% of those with T1DCD reported someone else at home following a GFD to be another important factor that makes it easier to follow the diet themselves, while 39% of participants in the CD group selected the occurrence of symptoms when they eat gluten to be the next most important factor that aids them in following a GFD.

Regarding factors that make it difficult to follow a GFD, both groups selected less availability of gluten-free foods (T1DCD 65%; CD 48%) and cross-contamination (T1DCD 46%; CD 70%) as two of their top three factors. Those with T1DCD selected cost (46%; CD 26%), whereas those with CD selected difficulty explaining to others (48%; T1DCD 27%), for example, when ordering food at a restaurant, as the third most important factor.

Table 2. Reported adherence to a gluten-free diet in various locations

Location	T1DCD ($n = 26$)	CD ($n = 46$)	*P*-value
Home	4.64 (0.97)	4.80 (0.58)	NS
School	4.46 (1.22)	4.73 (0.65)	NS
Restaurants	4.31 (1.26)	4.75 (0.77)	NS
Parties	4.38 (1.18)	4.70 (0.76)	NS
Friends' houses/ sleepovers	4.42 (1.18)	4.63 (0.92)	NS
Summer camp	4.67 (1.00)	4.91 (0.29)	NS
Camping	4.42 (1.26)	4.97 (0.17)	0.005
Other activities	4.42 (1.25)	4.80 (0.66)	NS

Participants rated their adherence to a gluten-free diet in each location as 1 = never, 2 = rarely, 3 = sometimes, 4 = most of the time, or 5 = always eating gluten-free. Mean (SD) values are reported.

NS, not significant.

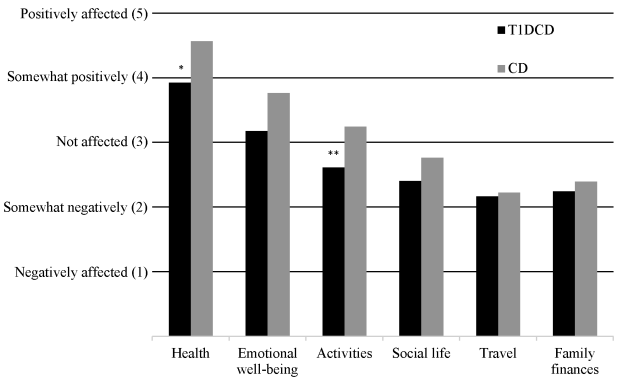

Figure 2. Effects of a gluten-free diet on daily living. Participants with type 1 diabetes and celiac disease (T1DCD) or celiac disease only (CD) were asked to score each factor from 1 = negatively affected to 5 = positively affected by a gluten-free diet. Mean values are represented. *$P = 0.006$, **$P = 0.03$.

Discussion

To our knowledge, this study represents the first comparison of GFD adherence and GFD barriers between children with T1DCD and CD. While prior studies on T1DCD have primarily focused on the prevalence of CD in T1D patients or clinical outcomes of adherent versus non-adherent patients, this study compares adherence to a GFD and barriers in adherence *between* children with T1DCD and those with CD (3,4,9,10). Here, we report no statistically significant difference in reported adherence to a GFD for youth with T1DCD and CD ($P = 0.38$); however, youth with T1DCD face increased barriers in adherence across multiple settings. This study illuminates unique characteristics of children with T1DCD and the specific barriers in adherence that they face, providing novel insights for those providing care to these children and their families.

Reported adherence to a GFD was high: 92% and 100% in children with T1DCD and CD, respectively. For children with CD, other Canadian studies have found overall, self-reported adherence ranging from 69% to 95% (11,12). For patients with T1DCD, previous studies suggest that adherence, both self-reported and by dietician or serological assessment, varies

Table 3. Effects of various factors on the ability to eat gluten-free in three common settings

Factor	Home			School			Restaurants		
	T1DCD	CD	*P*-value	T1DCD	CD	*P*-value	T1DCD	CD	*P*-value
Taste	2.72	2.50	NS	2.44	2.47	NS	2.80	2.13	0.0400
Availability	2.36	2.39	NS	3.21	3.24	NS	3.92	3.41	NS
Cost	3.48	2.63	0.0070	2.83	2.47	NS	3.56	2.93	NS
Social Pressure	2.61	1.91	0.0200	2.48	2.48	NS	2.71	2.03	0.0300
Labeling	2.60	2.50	NS	2.42	3.02	NS	3.50	3.07	NS
Food Prep	2.25	2.30	NS	2.79	2.95	NS	2.71	2.03	NS
Overall	2.67	2.37	0.0004	2.70	2.77	NS	3.20	2.60	0.0001

Participants ranked each of the indicated factors as 1 = never, 2 = rarely, 3 = sometimes, 4 = most of the time, or 5 = always makes it difficult to eat gluten-free at home, at school, and at restaurants. Mean values are reported.

NS, not significant.

greatly, from 25% to 69% (13–16). Self-reported adherence has been shown to overestimate true adherence in comparison to evaluation by a registered dietitian (12). However, the high rates of adherence reported for both groups in this study are supported by participants with available recent TTG results, among whom 85% of T1DCD and 75% of CD had TTG levels within reference range. While a majority of participants in both groups reported seeing a dietitian after diagnosis of CD, we recognize that follow-up for both groups is different. For those with CD only, follow-up at BCCH consists of two to three visits (the first at 6 to 12 months post-diagnosis and 12 months afterwards) in the Celiac Clinic before being referred back to their community physician. Those with T1DCD will have had regular follow-up with their multidisciplinary endocrinology team, which includes ongoing contact with a dietitian. This may result in increased support for those with T1DCD in following GFD compared to their peers with CD only.

A much larger proportion of youth with T1DCD, compared to those with CD, were diagnosed while they were clinically asymptomatic, which is expected due to routine screening for CD every 2 years in children with T1D at BCCH and is consistent with previous studies (2). Thus, patients with silent CD may be captured soon after their T1D diagnosis, and indeed it has been previously found that CD diagnosis in children and young adults most often occurs within 5 years of T1D diagnosis (10,17). It is interesting to consider if the significantly longer duration of CD in those with T1DCD in our study could have an impact on outcomes and adherence. Schiepatti et al. found in adults with CD that GFD adherence varies only slightly and generally improves over time (18). In the same study, they noted that strict, long-term adherence is associated with the presence of classical symptoms such as diarrhea and weight loss at diagnosis, which were found less frequently in our T1DCD group (18).

High rates of asymptomatic CD in patients with T1D have also been reported in the CD-DIET study by Mahmud et al. which found that these patients with T1DCD can feel overwhelmed in managing the substantial lifestyle implications of both diseases despite facilitated access to no-cost care (6). Modified clinical approaches may well be needed to support families of asymptomatic children with CD, compared to children with symptomatic CD (19). Herein lies a potential need for a difference in approach between the T1DCD subset compared to the larger group of youth with CD.

Another important difference in this study between youth with T1DCD compared to CD alone is the lower perceived benefit of a GFD in children with T1DCD. Children with T1DCD had less perceived benefit to their health ($P = 0.006$) and more negative effect on activities ($P = 0.03$) compared to youth with CD only. Additionally, while not statistically significant, the T1DCD group reported either less perceived benefit or similarly a greater negative impact of a GFD across all other categories: emotional well-being, social life, travel and family finances. This is consistent with previous research reporting a lower quality of life, social functioning and general health in adults with T1DCD compared to T1D only (20), and here we demonstrate it for the first time in children with T1DCD.

The less beneficial impact on health in T1DCD that we observed may be explained by characteristics that differ between T1DCD and CD in our study. Asymptomatic children with CD, compared to children with symptomatic CD, may well notice less benefit from the rigors of a GFD, whereas adhering to a GFD may negatively affect family finances, participation in activities and social pressure. Alternately, for the children who are symptomatic at diagnosis of CD, adherence to a GFD can lead to the resolution of CD symptoms; however, those children with T1DCD still combat the daily health perturbations associated with their T1D.

The more negative impact of a GFD on activities for the T1DCD group is also instructive for those working with this

population. It has been reported that parents of children with T1D only may be fearful of allowing their children to participate in activities alone and may feel overwhelmed with daily responsibilities (21). It is understandable that adding a GFD for a child with T1D may further complicate participation. Correspondingly, parents of children with T1DCD report lower social functioning scores for their children in comparison to parents of children with T1D only (22). Nonetheless, as physical activity remains a cornerstone for improving the overall health of all children, it is incumbent on health educators to consider ways to facilitate this for children with T1D *and* CD (21,22).

The single most significant barrier to adherence for both T1DCD and CD groups was shared between them: availability of gluten-free food at schools and restaurants. This finding is in line with previous reports in children with CD (8,23,24). Cost was a major barrier to adherence for both groups, but more significantly for those with T1DCD when at home. Increased cost for T1DCD may arise because gluten-free options are often higher in carbohydrates and sugar, requiring families to search for specialty gluten-free foods that fall in line with healthy T1D self-management. This also associates with our findings that a greater proportion of families with T1DCD report a 'mostly gluten-free' status, but fewer are able to achieve a 'completely gluten-free' status compared to their peers with CD. This suggests that while a significant portion of families with T1DCD are attempting to follow a GFD, they may be facing increased barriers in completely excluding gluten. Perhaps the lower level of 'completely gluten-free' status in T1DCD families contributes to the finding of increased social pressure at home for youth with T1DCD as they navigate the complex setting of diabetes and celiac meal planning with family members who may not have either disease.

Similarly, children with T1DCD report significantly more challenges at restaurants regarding availability and cost of gluten-free food, which may be because choice becomes limited to avoid high glycemic and gluten-containing foods. Simultaneously managing both health conditions may also result in those with T1DCD having less time or ability to access the tax credit and other financial support options intended to decrease the financial burden of a GFD. Endeavouring to understand more about the social pressure that youth with a dual diagnosis face and acknowledging the impact of availability and increased cost on families may be useful starting points toward improving the ability for children with T1DCD to thrive while adhering to a GFD.

Limitations of our study include the fact that families participating in this study may be different from families that did not respond. Additionally, those who are adherent to a GFD may be more inclined to participate, thus introducing responder bias and positively affecting our adherence data. Self-reported results of symptoms at diagnosis may be impacted by the length of time since CD diagnosis. For the burden of increased cost of a GFD, children aged >13 years who completed the questionnaire by themselves may not have a complete understanding of their family's financial situation. Additionally, this study is limited by the significant proportion of participants who did not have recent serological results and therefore confirmation of the high rates of adherence cannot be extrapolated to all participants. Finally, all participants were seen at BC Children's Hospital in Vancouver, British Columbia, and the results of our study may not be generalizable to children in other locations who are receiving care from other providers or who are in settings where availability of gluten-free products is different.

In conclusion, our study is the first to demonstrate the differences in barriers in adherence for youth with T1DCD compared to CD. While overall reported adherence to GFD was similar between both groups, we have identified specific barriers in adherence that are more impactful on children living with T1DCD. The results of our study point to the need for a difference in approach to care for youth with both T1D and CD given the complexity of their dual diagnosis.

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AUTHOR CONTRIBUTIONS

R.K.: Conceptualization, Methodology, Formal analysis, Writing—original draft, Writing—review and editing, Visualization, Project administration. A.Fu.: Methodology, Writing—review and editing. C.B.: Methodology, Writing—review and editing. A.Fo.: Methodology, Formal analysis, Writing—review and editing. B.E.H.: Conceptualization, Methodology, Formal analysis, Writing—original draft, Writing—review and editing, Supervision.

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CONFLICT OF INTEREST

The funding organization(s) played no role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

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