Quality of Life in Type 1 Diabetes and Celiac Disease: Role of the Gluten-Free Diet

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Objective To evaluate quality of life (QoL) and glycemic control in youth with type 1 diabetes (T1D) and celiac disease vs T1D only. We hypothesized that QoL scores would be lower in youth with T1D and celiac disease and those nonadherent to the gluten-free diet (GFD).

Study design This case control study included 35 youth with T1D and 35 with T1D and celiac disease matched for age, sex, diabetes duration, and hemoglobin A1c level. QoL was assessed in participants and parents using the Pediatric Quality of Life Inventory Generic Core Scale, Pediatric Quality of Life Inventory Diabetes Module. and the General Well-Being Scale; youth with T1D and celiac disease also completed the celiac disease-specific DUX questionnaire and parents completed the Pediatric Quality of Life Inventory Family Impact Scale. Questionnaires were scored from 0 to 100; higher scores indicate better QoL or well-being. Scores were compared between T1D vs T1D with celiac disease, with subgroup analysis by GFD adherence vs nonadherence and therapy (continuous subcutaneous insulin infusion vs multiple daily injections).

Results Youth with T1D and celiac disease reported similar generic and diabetes-specific QoL to T1D only. GFD nonadherent vs adherent youth reported lower diabetes-specific QoL (mean score 58 vs 75, $P = .003$) and lower general well-being (57 vs 76, $P = .02$), as did their parents (50 vs 72, $P = .006$), and hemoglobin A1c was higher (9.6% vs 8.0%, $P = .02$). Youth with T1D and celiac disease using continuous subcutaneous insulin infusion vs multiple daily injections had similar generic and diabetes-specific QoL and A1C (8.6 vs 8.2%, $P = .44$), but were less happy having to follow a lifelong diet (59 vs 29, $P = .007$).

Conclusions Youth with T1D and celiac disease who do not adhere to the GFD have lower QoL and worse glycemic control. Novel strategies are required to understand and improve adherence in those with both conditions. *(J Pediatr 2016;179:131-8).*

Emerging evidence indicates long-term negative outcomes for individuals living with type 1 diabetes (T1D) and celiac disease, including an increased risk of retinopathy, nephropathy, and subclinical atherosclerosis. We recently demonstrated an association between lack of adherence to the gluten-free diet (gluten-free diet nonadherence [GFD–]) and early evidence of renal disease, independent of glycemic control.[1] This suggests that those who struggle with the coexistence of 2 chronic conditions are at higher risk of complications; however, there is a paucity of data on the impact of living with both conditions on quality of life (QoL) and general well-being.

It is well-established that T1D negatively affects QoL, particularly among girls and prepubertal children.[2] Mealtime behavior problems are common,[3,4] which may be compounded by the demands of carbohydrate counting, eating to manage blood glucose levels independent of hunger,[5] and normal child developmental behaviors such as fussy eating. QoL is higher in people with T1D treated with continuous subcutaneous insulin infusion (CSII),[6,7] which allows flexibility with meal times and food choices.[5,8] Because a GFD requires substitution of commonly available carbohydrate foods such as wheat-based breads, cereal, and pasta,[9] CSII could alleviate the restrictive nature of the GFD by allowing for carbohydrate-free meals. However, the impact of CSII on QoL in people with coexisting T1D and celiac disease has not been studied.

BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CDDUX	Celiac disease–specific DUX
CSII	Continuous subcutaneous insulin infusion
GFD	Gluten-free diet
GFD+	Gluten-free diet adherence
GFD–	Gluten-free diet nonadherence
GWBS	General Well-Being Scale
HbA1c	Hemoglobin A1c
MDI	Multiple daily injections
T1D	Type 1 diabetes
QoL	Quality of life

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In the general population, celiac disease is diagnosed either by clinical suspicion or screening of at-risk individuals, who are frequently asymptomatic.[10] In those who are symptomatic, the uptake of a GFD may be expected to have a greater impact on QoL than for asymptomatic individuals. Indeed, QoL was higher in symptomatic youth with biopsy proven celiac disease who were GFD adherent (gluten-free diet adherence [GFD+]).[11] In a Swedish study of asymptomatic school children screened for celiac disease, QoL did not differ between those with biopsy-confirmed celiac disease and their peers after 1 year.[12] In contrast, asymptomatic adults with celiac disease randomized to a GFD experienced alleviation of anxiety and improved perception of health after 1 year compared with those randomized to a gluten-containing diet.[13]

The only pediatric study to examine the impact of coexisting celiac disease and T1D on QoL found no difference in generic and diabetes-specific QoL compared with children who had T1D alone.[14] However, celiac disease–specific QoL was not examined, nor was the effect of symptoms on QoL. Surprisingly, QoL did not differ between youth who were GFD+ vs GFD–, although the number of youth who were GFD– was small (n = 6), suggesting that this subgroup analysis may have been underpowered.[14] In contrast, the coexistence of T1D and celiac disease in adults was associated with lower generic and diabetes-specific QoL.[15] Given these conflicting findings, we examined the effect of the "double diagnosis" on QoL, well-being and eating behaviors in youth and their parents. We hypothesized that QoL scores would be lower in children with celiac disease, and those GFD–, compared with their peers with T1D only. We also examined the relationship between QoL and presence or absence of celiac disease symptoms and therapy (CSII vs multiple daily injections [MDI]).

Methods

This cross-sectional case control study was conducted at the Sydney Children's Hospital Network (Westmead), Australia, from May 2013 to December 2014. Inclusion criteria were age 8-18 years, T1D for ≥1 year, and biopsy-proven celiac disease for ≥6 months. Patients with T1D and celiac disease were recruited at routine clinic appointments. Celiac disease was diagnosed based on our screening protocol: all patients with diabetes undergo serologic testing for celiac disease at the time of diabetes diagnosis and 1-2 yearly thereafter.[16] Screening was performed by measurement of serum IgA and anti-tissue transglutaminase IgA antibodies by enzyme-linked immunosorbent assay. Deamidated IgG antibodies were also measured to account for false-negative results in patients who were IgA-deficient. Those with a positive screen were referred to a pediatric gastroenterologist and, where indicated, underwent small bowel biopsy. The control population was drawn from the same clinic population within the study time period and were matched by age (±1 year), diabetes duration (±1 year), most recent hemoglobin A1c (HbA1c) (±0.5%), and mode of diabetes management (MDI or CSII). The control population had a negative screening test for celiac disease at least once within the previous 12 months. Exclusion criteria were unknown celiac disease status, treatment other than MDI or CSII, and the inability of a child/parent to speak or read English fluently. The study was approved by the Sydney Children's Hospital Network research ethics committee. Written consent was obtained from parents and verbal assent from children aged 12-16 years before participation.

Demographic and clinical characteristics documented were sex, age at diabetes diagnosis, T1D duration, mode of diabetes management (CSII or MDI), insulin dose (U/kg/d), age at celiac disease diagnosis, celiac disease duration, celiac disease–related symptoms (documented at the time of celiac disease diagnosis), anthropometric measurements (height, weight, and body mass index [BMI]), with z-scores computed using Centers for Disease Control and Prevention (CDC) 2000 reference data. The use of the US-CDC growth charts is standard practice in Australia, both in a clinical and research setting, and aligns with the Australian National Health and Medical Research Council's recommendations.[17] Most recent HbA1c was documented and lifetime mean HbA1c was computed from all available data.

Questionnaires

All participants and their parents/guardians complete age-specific questionnaires and proxy questionnaires at the study visit. Generic, diabetes-specific, eating behaviors–specific, and celiac disease–specific questionnaires were used to enable measurement of a wide spectrum of QoL domains. Specifically, all patients and parents completed the PedsQL Generic Core Scale (version 4.0), PedsQL Diabetes Module (Version 3.2), General Well-Being Scale (GWBS, Standard Version), and an eating behaviors questionnaire.[18] Parents/guardians also completed the PedsQL Family Impact Scale. Patients with celiac disease completed the validated celiac disease-specific DUX (CDDUX) questionnaire.[19]

The PedsQL Generic Core Scale is a 23-item questionnaire that evaluates QoL in the subdomains of physical, emotional, social, and school functioning, with 2 age-specific scales (8-12 and 13-18 years). It has been validated for use in the pediatric population with T1D.[20] The GWBS is a 7-item questionnaire measuring generic well-being and health. The Diabetes Module is a 32-item questionnaire that examines diabetes-specific QoL in the subdomains of diabetes symptoms, treatment barriers, treatment adherence, worry, and communication. The Family Impact Scale, completed by parents is a 36-item questionnaire that evaluates the impact of pediatric chronic health conditions on parents and the family in the subdomains of physical, emotional, social, cognitive functioning, communication, worry, daily activities, and family relationships.

Respondents were asked to rate how frequently each item was problematic over the past 1 month. Each questionnaire was assigned a total and subdomain score ranging from 0 to 100, with higher scores reflecting higher QoL/general well-being or healthier eating behaviors.

The eating behaviors questionnaire was modified from a locally developed questionnaire used in the Researching Effective Strategies to Improve Insulin Sensitivity in Children and Teenagers (RESIST) study,[18] which contains 23 items in the