Early Dietary Fiber Intake Reduces Celiac Disease Risk in Genetically Prone Children: Insights From the TEDDY Study

Dietary fibers belong to a group of complex carbohydrates that are neither digested nor absorbed in the small intestine and serve as the primary substrate for gut bacteria. They are crucial in supporting gut barrier integrity and function, interacting with the immune system, and promoting greater diversity in gut microbiota composition, particularly during early life.[1,2]

Celiac disease, an autoimmune disorder, is driven by dietary gluten in genetically susceptible individuals carrying the HLA DQ2 and/or DQ8 risk-haplotypes. Prospective observational studies following children with these genetic markers from birth up to 14 years reveal that celiac disease predominantly develops during the first decade in life; however, a second peak in later life cannot be ruled out. Its incidence is associated with higher gluten intake and a greater number of infections during early childhood.[3] A recent review of mechanistic studies on celiac disease pathogenesis highlights the potential involvement of gut microbiota diversity and gut barrier function pathways.[4] Although gluten-containing grains are important sources of dietary fiber, it remains unclear if dietary fiber is associated with celiac disease.

This study examined the quantity and timing of dietary fiber intake in children up to 5 years of age who were at genetic risk for celiac disease, assessing its relationship with their subsequent risk of developing the condition. The analysis included 6520 children carrying the HLA-DQ2 and/or DQ8 risk haplotypes who were prospectively followed for a total 61,669 person-years to age 13 years in The Environmental Determinants of Diabetes in the Young (TEDDY) study (see Supplementary Methods).[5] Among these children, 479 were diagnosed with celiac disease (incidence rate 7.8 per 1000 person-years; 95% CI, 7.2-8.6), at a median age of 3.3 years (Q1-Q3, 2.1- 5.4 years). Dietary fiber intake increased from mean (±SD) 4.4 ± 3.8 g/1000 kcal/d at age 6 months to 8.8 ± 2.8 g/1000 kcal/d by age 5 years (Supplementary Table 1).

Dietary fiber intake from 6 months to 3 years of age was inversely associated with the subsequent risk of celiac disease in models unadjusted for the concurrent gluten intake and to 2 years of age in models adjusted for gluten intake (Figure 1*A*). In contrast, no association was observed between dietary fiber intake to 4 and 5 years of age and the risk of celiac disease regardless of whether models accounted for the gluten intake. The inverse relationship between dietary fiber intake up to 2 years of age and celiac disease risk persisted after adjusting for all food sources of dietary fiber and when excluding one food group at a time from the model (Figure 1*B*).

The TEDDY study is the first observational study on children at genetic risk for celiac disease to demonstrate that higher dietary fiber intake during the first 2 years of life is associated with a lower risk of developing the condition later. Notably, this inverse association remained, with a stronger effect size, after adjusting for the total intake of fiber-rich foods and systematically excluding individual food groups. This suggests that the amount of fiber itself drives the observed effect, regardless of its food source or other compounds present in these foods. Importantly, the association was only evident during the first 2 years of life as no effect was observed with fiber after this period. These findings highlight a potential role of dietary fibers in modulating celiac disease risk, although the causality of this relationship requires validation through further mechanistic studies.

In a population-based cohort study, Norwegian children of mothers with higher pregnancy dietary fiber intake were found to have a lower risk for developing celiac disease.[6] However, data from a subset of participants indicated that maternal fiber intake did not predict levels of short chain fatty acids or microbiota diversity in the infant's stool, suggesting that the association might be attributed to the child's own fiber intake. Other studies have observed an inverse relationship between a "prudent" dietary pattern, rich in fiber-rich foods after weaning, and celiac disease autoimmunity in children from the general population.[7] Similarly, a dietary pattern low in fiber from oats, legumes, and root vegetables at age 2 years was positively associated with celiac disease in at-risk children.[8] None of these studies accounted for the dietary fiber intake in their analysis.

A key strength of TEDDY is the prospective study design, involving children monitored across six clinical sites in four countries under a standardized study protocol. This included the repeated and detailed collection of harmonized dietary data and regular screening for celiac disease. Such a design enabled the investigation of the amount and timing of dietary fiber intake in relation to the initial appearance of celiac-specific autoantibodies, preceding the clinical diagnosis of celiac disease. The extensive collection of relevant data also allowed for adjustment of known and plausible confounders, enhancing the robustness of the findings. Additionally, the use of joint modeling enabled participants with incomplete data to contribute to the analyses, unlike traditional survival model, thereby reducing the risk of bias from missing data.

There is a potential risk of misreporting dietary fiber intake in TEDDY, as it relied on parent- reported food records. These records captured intake over 3 days, which may not fully represent an individual's habitual diet.[9]

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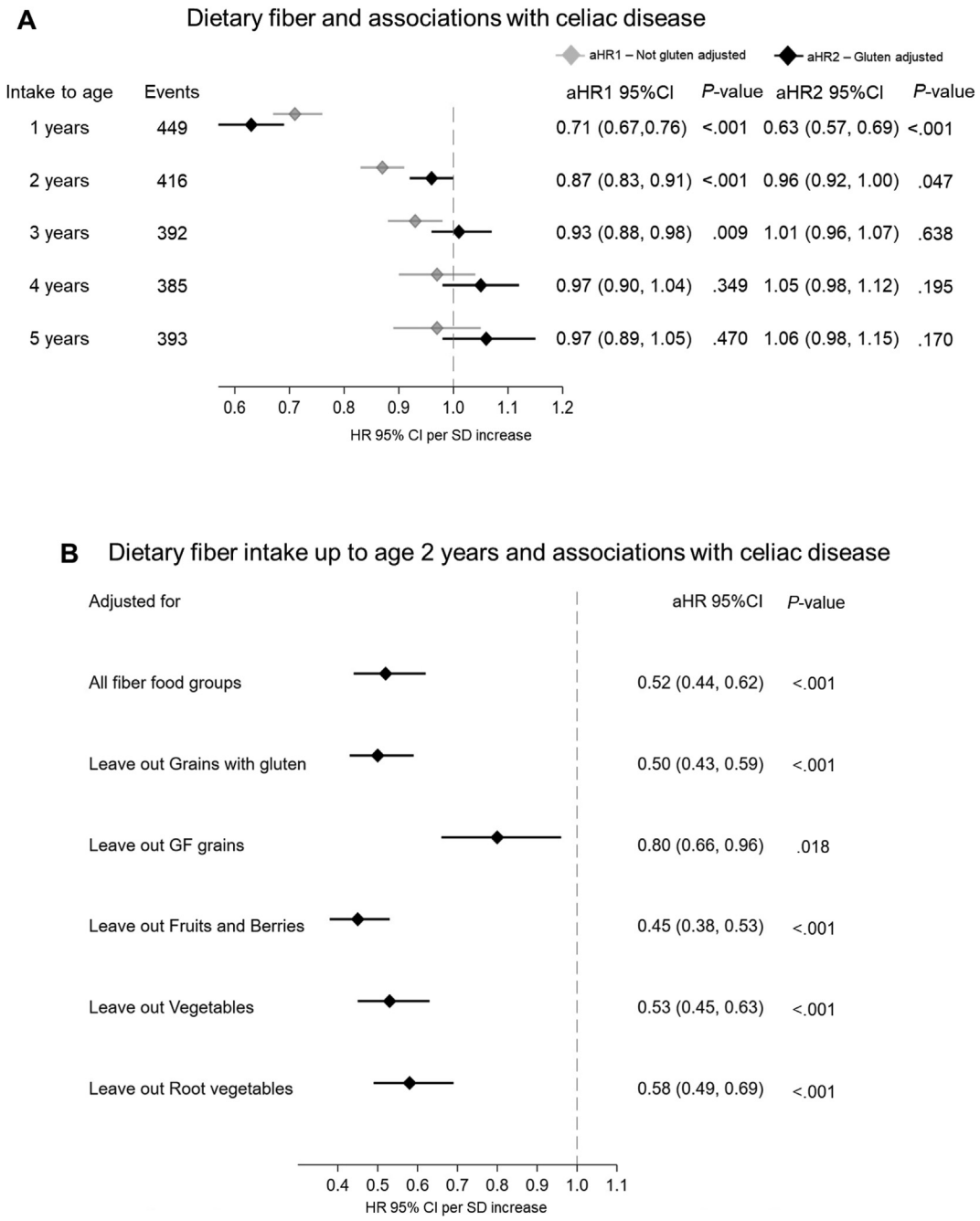

Figure 1. (*A*) Associations between a standard deviation increase in dietary fiber intake daily and the risk of celiac disease by age 13 years investigated by using joint modeling in children at genetic risk. Dietary fiber intake was assessed by repeated 3-day food records collected up to the age of 5 years. (*B*) The effect of food sources of fiber on the association between a standard deviation increase in dietary fiber intake daily and the risk of celiac disease by the age of 13 years was investigated using joint modeling in 6306 children at genetic risk. Dietary fiber intake was assessed by repeated 3-day food records collected up to age 2 years. All models in *A* and *B* were adjusted for sex, HLA risk group, country of residence, having a first-degree relative with celiac disease, breastfeeding duration (proxy for dietary fiber in human milk), probiotic use up to age 2 years, and number of reported gastrointestinal infections up to age 3 years (all restricted up to the age of exposure). aHR, adjusted hazard ratio; CI, confidence interval; GF, gluten-free; SD, standard deviation.

However, the study mitigated this limitation by using repeated food records for each child. Unlike commonly used food frequency questionnaires, food records provide more detailed quantified dietary data, offering a better reflection of habitual intake at a group level. A further limitation was the lack of data on specific types of dietary fibers, which may vary in their metabolic effects. As a proxy, the analysis adjusted for food sources of dietary fiber, which supported the study's findings. Despite these measures, the results should be interpreted cautiously, and the potential protective effects of dietary fiber intake on the celiac disease risk need to be validated in future clinical prevention trials.

Higher dietary fiber intake during the first 2 years of life was associated with a lower risk of celiac disease in children at genetic risk. Although this effect was modest, it was independent of gluten intake and other components found in fiber-rich foods in the child's diet.

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2025.01.241.

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Data Availability

All data from The Environmental Determinants of Diabetes in the Young (https://doi.org/10.58020/y3jk-x087) reported here will be made available for request at the NIDDK Central Repository (NIDDK-CR) website, Resources for Research (R4R), https://repository.niddk.nih.gov/.

Supplementary Methods

The TEDDY study follows 8676 children with HLA risk genotypes associated with type 1 diabetes and celiac disease from birth to 15 years of age across Colorado, Georgia, and Washington states in the United States, and Sweden, Finland, and Germany in Europe.[5] For this study, 6520 children (75.1%) who were screened for celiac disease at least once and with more than one completed food record between ages of 6 months and 5 years were included. German children were excluded because their dietary fiber intake had not been harmonized with the TEDDY nutrient database. All caregivers provided consent for newborn screening and follow-up participation, and the study was approved by regional ethics boards in each country.

Screening for celiac disease began at the age of 2 years by measuring tissue transglutaminase autoantibodies (tTGAs) using radiobinding assay. If a child tested positive for tTGA, previously collected samples, as per the study protocol, were analyzed to identify the closest time point of seroconversion to tTGA positivity. Children with a tTGA level of greater than or equal to 30 U/L or celiac-associated symptoms were referred to their health care provider for clinical evaluation. Celiac disease was diagnosed if the child remained persistently tTGA positive and had a small intestinal biopsy showing a Marsh score greater than or equal to 2 (n = 431; 89.2%), or, in cases where a biopsy was not performed, if two consecutive tTGA samples greater than or equal to 100 U/L were collected at least 3 months apart (n = 52; 10.8%).[e1]

A total of 50,996 3-day food records (two weekdays, one weekend day) collected quarterly to semiannually between 6 months to 5 years of age were used to estimate the average daily intake of total dietary fiber in grams.[e1] Caregivers reported the child's food and drink intakes in amounts using a booklet with photos and graphics along with common measurement cups to estimate portion sizes. Trained dietitians and nutritionists entered the intake data into digital software databases. Dietary fiber intake was calculated based on information from each national food database. Composite foods and dishes were deconstructed into individual ingredients, which were then categorized into sources of dietary fiber such as fruits and berries, gluten-containing grains, gluten-free grains, vegetables, and root vegetables. Dietary fiber from supplements (used in 0% to 1.6% of the cohort at each age) were also recorded and included in the total fiber intake. The contribution of dietary fibers from human milk was estimated using the duration of breastfeeding reported in repeated questionnaires as a proxy. Data on dietary fiber and food group intakes were harmonized within TEDDY databases to enable cross-country analysis.

Associations between longitudinal trajectories of dietary fiber intake and the risk of developing celiac disease were analyzed using joint models of longitudinal and time-to-event data with shared parameters. The models were defined by age at which dietary fiber intake was measured (at 6 months to 1, 2, 3, 4, and 5 years) with dietary fiber intake treated as a continuous, time-dependent variable. Time-varying covariates were energy-adjusted using the nutrient density approach (dividing intake by daily energy intake and multiplying by 1000) and standardized to a mean of 0 and a standard deviation of 1. All joint models were evaluated based on the "current value" association parameters of fiber intake. Data were structured using the counting process with risk sets defining the periods when subjects were at risk for the outcome at each visit month. The time of seroconversion to tTGA positivity was used as the time to celiac disease. Subjects were censored either at the end of the 13-year follow-up period or at their last clinic visit if they did not seroconvert to tTGA positivity. Random coefficient mixed effect submodels were adjusted for the energy intake at the corresponding food record, with or without gluten intake, and the number of gastrointestinal infections were reported during the first 3 years in life.[3] The time-to-event Weibull submodel was adjusted for sex, family history of celiac disease, HLA genotypes, country of residence, use of probiotic supplements to the age of 2 years (because of potential interactions with dietary fiber), and duration of breastfeeding.

To investigate the potential confounding effects of other compounds in fiber-rich foods and the impact of specific types of fiber, joint models incorporating food sources were analyzed, focusing on intakes up to the age of 2 years. Leave-one-out models were also fitted for which one food group was excluded from the model at a time. Random intercept mixed-effect submodels were adjusted for intakes of fruits and berries, gluten-containing grains, gluten-free grains, vegetables, and root vegetables. The time-to-event submodel was adjusted for sex, family history of celiac disease, HLA genotypes, and country of residence. The analysis was performed using Stata statistical software and package stjm and R Core Team (2024) version 4.3.3 with JM R package.

Supplementary Reference

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Supplementary Table 1. Characteristics of Children Enrolled in the Environmental Determinants of Diabetes in the Young (TEDDY) Study by Cohort and Celiac Disease

Characteristic factor	Study cohort n = 6520	Children without celiac disease[a] n = 5243	Celiac disease n = 479
Female, n (%)	3199 (49.0)	2470 (47.1)	294 (61.4)
Country, n (%)			
United States	2809 (43.1)	2315 (44.2)	170 (35.5)
Sweden	2127 (32.6)	1627 (31.0)	224 (46.7)
Finland	1584 (24.3)	1301 (24.8)	85 (17.8)
HLA genotype, n (%)			
High-risk[b]	1370 (21.0)	851 (16.2)	236 (49.3)
Moderate-risk[c]	2561 (39.3)	2058 (39.3)	161 (33.6)
Low-risk[d]	2589 (39.7)	2334 (44.5)	82 (17.1)
Family member with celiac disease,[e] n (%)	111 (1.7)	69 (1.3)	22 (4.6)
Dietary fiber intake by age in months, mean g/1000 kcal (SD)			
6	4.4 (3.8)	4.5 (3.9)	4.0 (3.2)
9	8.7 (4.0)	8.7 (4.0)	8.7 (3.5)
12	9.6 (3.7)	9.6 (3.8)	9.6 (3.3)
18	9.3 (3.2)	9.3 (3.3)	9.1 (3.1)
24	8.8 (3.0)	8.8 (3.0)	8.6 (2.8)
30	8.8 (3.0)	8.8 (3.0)	8.6 (2.8)
36	8.8 (2.8)	8.8 (3.0)	8.3 (2.7)
42	8.8 (2.8)	8.8 (2.8)	8.3 (2.8)
48	8.7 (2.8)	8.8 (2.8)	8.3 (2.7)
54	8.9 (2.8)	8.9 (2.9)	8.5 (2.7)
60	8.8 (2.8)	8.8 (2.8)	8.0 (2.4)
Gluten intake by age in months, mean g/1000 kcal (SD)			
6	0.4 (0.9)	0.4 (0.8)	1.4 (0.9)
9	1.7 (1.8)	1.7 (1.7)	2.0 (1.8)
12	3.1 (2.2)	3.1 (2.2)	3.6 (2.3)
18	4.0 (2.2)	4.0 (2.1)	4.5 (2.6)
24	4.2 (2.1)	4.1 (2.1)	4.5 (2.2)
30	4.3 (2.1)	4.2 (2.1)	4.1 (2.2)
36	4.3 (2.1)	4.4 (2.0)	3.6 (2.5)
42	4.4 (2.1)	4.5 (2.0)	3.2 (2.6)
48	4.5 (2.2)	4.7 (2.0)	2.7 (2.6)
54	4.6 (2.3)	4.8 (2.1)	2.7 (2.9)
60	4.7 (2.3)	4.9 (2.0)	2.3 (2.7)

[a]Children negative for persistent tissue transglutaminase autoantibodies and celiac disease.
[b]DQ2/DQ2, including HLA genotypes DR3*0501/0201*DR3*0501/0201.
[c]DQ2/DQ8 including HLA genotypes DR4*030X/0302*DR3*0501/0201.
[d]Including HLA genotypes DR4*030X/0302*DR4*030X/0302, DR4*030X/0302*DR4*030X/020X, DR4*030X/0302*DR8*0401/0402, DR4*030X/0302*DR1*0101/0501, DR4*030X/0302*DR13*0102/0604, DR4*030X/0302*DR4*030X/0304, DR4*030X/0302*DR9*030X/0303, and DR3*0501/0201*DR9*030X/0303.
[e]Parent or sibling, data collected at age 9 months.