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Patients With Coeliac Disease Reported Highter Consumption of Added Sugar and Total Fat Than Healthy Individuals

Nancy **Babio**, PhD, BSc^{1,2}, Mireia **Alcázar**, RD¹, Gemma **Castillejo**, MD³, Miriam **Recasens**, RD¹, Francesc **Martínez-Cerezo**, MD⁴, Vanessa **Gutiérrez-Pensado**, RD¹, Guiomar **Masip** RD¹, Cristina **Vaqué** BSc, PhD, BSc⁵, Anna **Vila-Martí**, PhD, BSc⁵, Miriam **Torres-Moreno** PhD, BSc⁵, Enric **Sánchez**, RD¹, Jordi **Salas-Salvadó**, MD, PhD^{1,2}

¹Human Nutrition Unit, Faculty of Medicine and Health Sciences, Biochemistry & Biotechnology Department, Rovira i Virgili University, and Sant Joan de Reus Hospital, IISPV, Reus, Spain

²Centro de Investigación Biomédica en Red Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

³Pediatrics Gastronterology Unit. Sant Joan de Reus Hospital. Paeditrics Research Unit, Rovira i Virgili University, IISPV, Reus, Spain.

⁴Service of Adult Gastroenterology. Sant Joan de Reus Hospital. Reus, Spain

⁵Faculty of Health Sciences and Welfare. Research Group of Food, Health and Welfare. University of Vic-Central University of Catalonia. Spain.

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Address correspondence and reprint requests to Nancy Babio, RD, PhD. Human

Nutrition Unit, Faculty of Medicine and Health Sciences, Universitat Rovira i Virgili.

C/Sant Llorenç 21, 43201 Reus (Spain). Telephone number: +34 977759312; Fax

number: +34 977759322; e-mail address: nancy.babio@urv.cat

Jordi Salas-Salvadó, MD, PhD. Human Nutrition Unit, Faculty of Medicine and Health

Sciences, Universitat Rovira i Virgili. C/Sant Llorenç 21, 43201 Reus (Spain).

Telephone number: +34 977759312; Fax number: +34 977759322; e-mail address:

jordi.salas@urv.cat

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ABSTRACT

Objectives: To compare the dietary pattern between subjects with coeliac disease (CD) (cases) and subjects without (healthy controls).

Methods: A case-control design study was conducted. A total of 98 subjects with CD (aged 10 to 23 years-old) were matched by age, gender and BMI with 98 non-coeliac participants. A non-consecutive 3-day food record was completed to assess energy, nutrient and food intake and evaluate the participant's adherence to recommendations. Differences in energy, nutrients, food consumption, and compliance with general recommendations between cases and control groups were assessed by Student's t-test. Pearson's chi-squared test was used to compare categorical variables. Socio-demographic, personal and family history data were collected.

Results: Compared to the control group, the CD cases reported a significantly higher consumption of added sugar (P<0.001) and total fat (P<0.017). Mean fiber consumption was below nutritional recommendations in both groups. CD participants consumed significantly lower amounts of foods rich in starch (P<0.001), and higher amounts of foods rich in starch (P<0.001), and higher amounts of foods rich in protein such as meat/fish/eggs (P=0.007). CD subjects showed a significantly lower percentage of adherence to recommendations for folic acid (53.2 vs 70.5; P<0.001), calcium (49.0 vs 56.3; P=0.025), iron (57.4 vs 78.0; P<0.001) and magnesium (50.0 vs 63.9; P<0.001).

Conclusion: The CD subjects showed a more unbalanced diet than controls in terms of added sugars, total fat and micronutrient consumption.

Keywords: coeliac patients, children, adolescents, dietary pattern.

WHAT IS KNOWN

- Coeliac disease (CD) is an immune mediated enteropathy disorder.
- The only recognized treatment for coeliac patients is to adhere to a strictly gluten-free diet.
- Some studies have compared the dietary pattern of subjects with CD and healthy individuals with controversial results.

WHAT IS NEW

- This is the first case-control study to compare the diet of individuals with CD and healthy controls matched by important characteristics that may influence nutritional intake and requirements.
- Subjects with CD consumed a diet higher in total fat and added-sugar, and foods rich in protein and sweetened beverages than non-coeliac healthy individuals.

INTRODUCTION

Coeliac disease (CD) is an immune mediated enteropathy disorder triggered by gluten and characterized by the presence of gluten-dependent clinical manifestations in genetically susceptible individuals (1,2). Coeliac individuals frequently have gastrointestinal symptoms such as diarrhea and malabsorption, and is an important cause of malnutrition (3).

The prevalence of CD in Europe and the United States is approximately 1%, although differences between countries have been reported (4). In Spain the estimated prevalence of CD is about 1/118 in children and 1/389 in adults (5). A strictly gluten-free diet (GFD) is the cornerstone treatment for CD for reducing complications and improving health (6). Adherence to a GFD imposes major restrictions on daily life, and it is often difficult to maintain an appropriate lifestyle (7). This strict diet involves no bread, flour, paste, or other foodstuffs that are the main sources of energy, carbohydrates, iron, calcium, zinc, magnesium and group B vitamins. It is recognized that all restrictive diets are associated with higher risks of nutritional inadequacy, which increases the risk of nutritional deficiencies, particularly in children and adolescents, who are in the acceleration phase of linear growth (8).

Although several studies have assessed the dietary patterns of children and adolescents with CD (9-15), the potential nutritional imbalances in their diet with respect to nutritional recommendations remain controversial. Several studies have suggested that the dietary intake of CD patients is unbalanced in some nutrients (9,16) compared to healthy subjects. Other studies, however, have found that the diet of subjects with CD is comparable in terms of energy (9,16) and nutrients (10,11,15,17). Furthermore, some studies have found that the mean intake of saturated fatty acids (9,11,15) and sucrose

(9,11) in CD individuals was above recommendations, whereas others have reported higher amounts of carbohydrate and lower amounts of total fat than controls (13).

To the best of our knowledge four of these studies have compared the nutrient intake of subjects with CD and healthy controls (9,13,15,16). They all assessed diet in small samples of children or adolescents, and the control subjects were not matched by variables that may have a considerable influence on energy and nutritional requirements such as sex, age and BMI (body mass index). Their results, then, must be interpreted with caution.

Hence, the aim of the present study was to compare the food and nutrient intake of patients with CD aged between 10 and 23 years-old with non-coeliac healthy controls matched by age, gender and BMI.

METHODS

The Coeliac Disease Eating Attitudes (COEDATTI) study is a case-control crosssectional study that assesses the risk of eating disorders in subjects with CD in comparison with non-coeliac subjects. In the present sub-study, we analyzed differences in food, energy and nutrient intake between those patients diagnosed with CD and their respective matched healthy controls.

From October 2012 to June 2014, the study participants were recruited. Subjects aged between 10 and 23 years old who were diagnosed with CD by both the Paediatric and adult Gastroenterology Unit of the Sant Joan University Hospital in Reus (Spain) were recruited (cases). The CD diagnosis was made by means of compatible duodenal biopsy, presence of specific gluten autoantibodies (anti-endomysium (EmA) and/or anti-tissue transglutaminase IgA were positive in all cases). They were also positive for HLA DQ2 and/or DQ8.

Exclusion criteria were: a) lack of motivation to participate in the study, b) participants who only complied partially with the gluten-free diet or who were reluctant to follow it; c) history of chronic diseases (other than CD) such as diabetes mellitus, inflammatory bowel disease, other digestive disorders, food allergies or diseases that required dietetic advice, d) autism or other cognitive disabilities.

Healthy participants (control group) who had not been diagnosed with coeliac disease and did not meet the mentioned exclusion criteria were also enrolled in the study. The same research team matched the controls (1:1) by age (\pm 1 year), gender and BMI (\pm 1 kg/m²) with CD participants. These subjects were recruited by appealing to the general public, particularly in primary and secondary schools in Reus, Vila-Seca, Cambrils, Barcelona, Lleida, Granollers and Vic (Spain). Once they had been recruited and the patient characteristics known, the matched controls were looked for.

All participants (cases and controls) and legal tutors (for the youngest ones) provided their informed consent. The protocol was approved by the institutional review board of the Sant Joan University Hospital in Reus.

Procedure

All participants with CD were visited on two occasions at the University Hospital of Sant Joan in Reus or in the Human Nutrition Unit at the Faculty of Health Sciences in Reus. Healthy participants (controls) were also interviewed on two occasions in the medical room of their respective schools or, in some cases, at the Human Nutrition Unit if it was more convenient for the participant.

In the first visit, in a face-to-face interview, a trained dietitian collected sociodemographic and personal data, and information about the family history of obesity, history of disease and medication use, presence of eating disorders, and the level of education of their parents or legal tutors. In addition, physical activity during leisure

time was self-reported by the study participants, and categorized according to the Institute of Medicine as:

- Sedentary: Only the physical activities required for independent living.
- Low active: Sedentary + equivalent of 30 minutes walking or low physical activity between one and three times a week.
- Active: Equivalent of 1 hour walking or moderate physical activity between three and five and up to six or seven times a week.
- Very Active: Vigorous physical activity or sports training on a daily basis.

Finally the four levels of physical activity were re-categorized as sedentary (sedentary and low activity), moderately active (moderate) and active or very active (active). At the end of this visit, the dietitian told participants how to complete a non-consecutive

3-day food record (2 workdays and 1 weekend day).

In a second visit, participants delivered the 3-day food record, which was checked by the same dietitian in the presence of the participant and their parents. All participants were also weighed and had their height measured wearing light clothing and using a calibrated scale. BMI was calculated and expressed in kg/m².

Dietary assessment and adherence to nutritional recommendations

We asked the participants to complete the food register in household measures. In order to estimate the sizes of the food portions accurately, the SUVIMAX Photographic Atlas was used by trained dietitians. Subjects with CD were asked to record the brand of all the gluten-free products they consumed. The macro- and micronutrient compositional data provided by those free-gluten product labels were collected in a database specifically developed for the present study.

Once the questionnaires had been collected, the same dietitian encoded each food consumed in grams, and the energy and nutrient intake was estimated using Spanish

food composition tables (18). Then, the percentages of adherence to current recommendations by the Food and Nutrition Board, Institute of Medicine, and the National Academy of Science for folic acid, calcium, zinc, iron, magnesium, sodium, thiamine, pyridoxine and cholecalciferol were calculated (19) by the following formula: (observed data/reference data) *100. The reported frequency of the food group consumed (in portions per day) was also compared to the recommendations of the National Pyramid Guideline using the formula mentioned above (20).

Statistical analysis

Categorical variables are presented as number (n) and percentages (%). Continuous variables were presented as means (standard deviation). To test for normal distribution, the Kolmogorov-Smirnov statistical test was used. Differences in energy, nutrient and food group consumption between cases and controls were assessed by Student's t-test. Pearson's chi-squared test was used to compare categorical variables. In order to exclude a potential influence of parental education on the study outcomes, sensitivity analyses on adjusting for parental education level were performed. Data were processed using the SPSS statistical package (version 22.0, SPSS Inc., Chicago, IL) and P<0.05 were considered statistically significant. To avoid multiple comparison bias and as a sensitivity analysis, we applied Benjamini-Hochberg correction in all results using R 2.14.2 software for Windows.

RESULTS

From a total of 155 and 194 potentially eligible cases and controls, respectively, 113 and 119 cases and controls fulfilled the inclusion criteria. Of these, 13 cases were excluded because they did not complete the second visit, and 2 subjects with a previous diagnosis of eating disorders refused to participate in the study. Then, a total of 98 cases

were matched with 98 controls by age, gender and BMI. The mean age and BMI of the participants were 15.3 ± 3.7 years old and 19.4 ± 2.7 kg/m², respectively.

Table 1 summarizes the main general characteristics of the whole study sample, categorized by cases and controls. Compared to the cases, alcohol consumption was significantly increased in the highest age category of controls. No significant differences in the other general characteristics were observed between cases and controls.

Differences in energy and in macronutrients

The consumptions of energy and macronutrients reported by participants are shown in Table 2. Compared to the control group, CD cases reported a significantly lower consumption of polysaccharides, irrespective of the age group considered. Overall, the case group reported a higher consumption of added sugar (P<0.001) except in the oldest group (P=0.130).

The CD cases consumed significantly higher amounts of total fat (in g/day), except in the oldest category in which the difference did not reach statistical significance (P=0.404).

Differences in micronutrients

Micronutrient consumption and whether it complies with nutritional recommendations is shown in Table 3. If we compare the adherence to recommendations in the whole cohort (case and controls), individuals from both groups met the current nutritional recommendations for thiamine (103.1 vs 119.9; P=0.005), pyridoxine (130.1 vs 146.2; P=0.036) and sodium (94.6 vs 135.5; P<0.001) but not for folic acid (53.2 vs 70.5; P<0.001), calcium (49.0 vs 56.3; P=0.025), iron (57.4 vs 78.0; P<0.001) and magnesium (50.0 vs 63.9; P<0.001).

Differences in the consumption of food groups

Food group consumption and adherence to National Pyramid Guidelines are described in Table 4. No differences between cases and controls were observed with respect to pulses, dairy products, vegetables, oil and fats and fruits consumption. Cases consumed less starch (paste, bread and pastries) than controls in both age categories. They also consumed more foods rich in protein (meat/fish/eggs and red processed meat) and sweetened beverages, although the difference did not reach the statistical significance for sweetened beverages (P=0.052). Individuals from both groups showed a low adherence to National Pyramid Guidelines mainly with respect to those food groups rich in fibre (pulses, vegetables and fruits).

In the whole sample, no significant differences in energy consumption by gender were reported (data not shown). In both groups, the energy provided by added sugar consumption was higher than the upper level recommended by the World Health Organization. Study participants also consumed more energy provided by saturated fatty acids (SFAs) than recommended (<10% of total energy intake).

Although the differences between cases and controls were not significant, total fiber and sodium consumption was, respectively, below and above the current nutritional recommendations in all categories of study subjects.

Results were similar even after the data have been adjusted for parental education (data not shown). When applying the multiple testing correction as a sensitivity analysis, differences were blunted, but the main results remained significant. Only the significant differences in energy intake between cases and controls in those participants between 10 and 13 years were lost (P=0.051).

DISCUSSION

The present study is the first one in which cases and controls have been matched by age, sex and BMI, all of which are important characteristics that may influence nutritional intake and requirements. We found that subjects with CD on a GFD consumed a diet richer in total fat, added sugar, foods rich in protein (meat, fish and eggs) and sweetened beverages than non-coeliac healthy individuals. Both study groups followed an unbalanced diet characterized by a lower consumption of fiber and higher consumption of sodium than recommended. Although neither group of participants (cases and controls) complied with the recommendations for optimal micronutrient intake, the nutrient density for many micronutrients consumed, such as folic acid, calcium, iron, and magnesium, was lower in participants with CD than in controls.

Our findings with regard to the high intake of total fat and added sugar by CD participants are consistent with previous studies that assessed only the diet of patients with CD (10,11), and also with studies comparing CD individuals with controls (15,21). As observed in the youngest individuals in our study Zucotti et al. (13) also found that subjects with CD reported higher intake of carbohydrates. However, in contrast our results, the authors also observed a lower intake of fat in cases compared to healthy participants (13).

As far as total energy intake is concerned, our results in the younger category of participants are in line with those found by Zucotti and coworkers (13), who reported higher energy intakes by cases than controls. However, these differences between cases and controls were not observed in individuals between 14 and 23 years in our study, as has also been shown by other studies (9,21). These discrepancies may be due to differences in age or BMI, or the use of different methodologies for assessing food consumption between studies.

Unlike Zucotti et al. (13), we did not find significant differences in the amount of carbohydrate consumption between cases and controls (13). Although in our study, subjects with CD presented similar intakes of total carbohydrates to controls, subjects with CD consumed higher amounts of added sugar and lower amounts of starch. This could be partially explained by the fact that subjects with CD reported a higher consumption of sugar-sweetened beverages than controls. In addition, because of the higher prices, the lack of economic support provided to families, and the tastelessness of gluten-free products coeliac patients may tend to consume other products that are more rich in lipids and/or protein such as eggs, meat, fish, and sweetened beverages instead of gluten-free substitute products (22).

Consistent with other studies (10,11,15), CD participants consumed less fiber, although the differences between groups were not statistically significant, and both groups were under the national nutritional recommendation as observed in other healthy cohorts using the same age categories (23). This in part can be explained because Gluten-free cereals tend to have lower amounts of dietary fiber, and CD subjects have a low intake of fruits and vegetables.

Also consistent with other studies, both groups of participants in our study did not comply with the national nutritional recommendations for several micronutrients (9,13,15). Although Kautto et al. (15) suggested that micronutrient intakes were usually comparable between individuals with CD and controls, they considered that subjects with CD generally have a worse nutrient density (amount of nutrients per kcal) than controls, as we also observed in our study. In this regard, our results showed that subjects with CD consumed significantly higher amounts of food rich in iron such as meat/fish and eggs, but even so intake of iron was lower than in the control group. This finding should be interpreted cautiously, because many gluten-free products are not

labeled for iron content. However, this may also be because food rich in starch is usually fortified with several micronutrients, whereas the gluten-free products are not. The main strength of the present study is that the sample is larger than that of other studies on nutritional deficiencies in CD patients. Another strength of our study is that CD subjects were matched by three important characteristics that may influence food intake and nutritional requirements, which made it possible to study differences between the two different populations independently of these characteristics.

Our study, of course, does have some limitations. First, the National food composition tables do not contain gluten-free products. To obtain this information the data provided on the gluten-free product labels were collected in a database specifically created for the present study. Unfortunately, the data available on the micronutrient profile of glutenfree products consumed by our population were limited, which means that the total micronutrient consumption in our CD population was underestimated. The second limitation is inherent to the nature of cross-sectional studies: causal relationships cannot be established. Third, there is a potential risk of desirability bias. For instance, consciously or unconsciously patients might be more prone to socially desired responding because they visit their pediatrician on a regular and long-term basis, unlike the controls, who only visited the study team twice and had no ongoing relation with the researchers after the end of the study. On the other hand, the controls who were willing to participate in the study might be more educated and this might be associated with better nutritional behaviour. Nevertheless, after adjusting for parental education results were similar. Finally, it is uncertain whether our findings can be generalized to younger or older individuals from other geographical locations.

In conclusion, the CD subjects proved to have a more unbalanced diet than controls in terms of consumption of added sugars, total fats and micronutrients with respect to

recommendations. The results of the present study suggest that subjects with CD have a more unbalanced diet, which could be prevented through nutritional education in childhood, in which not only teaches them how to choose foods properly, but also emphasizes the importance of complying with nutritional recommendations in the long term.

REFERENCES

- Husby S, Koletzko S, Korponay-Szabó IR, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr 2012;54:136–60.
- Fasano A, Catassi C. Coeliac disease in children. Best Pract Res Clin Gastroenterol 2005;19:467–78.
- Hill ID, Dirks MH, Liptak GS, et al. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2005;40:1–19.
- Catassi C, Gatti S, Fasano A. The new epidemiology of celiac disease. J Pediatr Gastroenterol Nutr 2014;59 Suppl 1:S7-9
- 5. Casellas F. Enfermedad celíaca. Med Clin (Barcelona) 2006;126:137–42.
- Martin U, Mercer SW. A comparison of general practitioners prescribing of gluten-free foods for the treatment of coeliac disease with national prescribing guidelines. J Hum Nutr Diet 2014;27:96–104.
- Kinos S, Kurppa K, Ukkola A, et al. Burden of Illness in Screen-detected Celiac Disease Children and their Families. J Pediatr Gastroenterol Nutr 2012;55:412-6.
- 8. Kinsey L, Burden ST, Bannerman E. A dietary survey to determine if patients with coeliac disease are meeting current healthy eating guidelines and how their diet compares to that of the British general population. Eur J Clin Nutr 2008;62:1333–42.
- 9. Mariani P, Viti MG, Montouri M, et al. The Gluten-Free Diet: A Nutritional Risk Factor for Adolescents with Celiac Disease? J Pediatr Gastroenterol Nutr 1998;27:519-23.

- Hopman EGD, le Cessie S, von Blomberg BME, et al. Nutritional management of the gluten-free diet in young people with celiac disease in The Netherlands. J Pediatr Gastroenterol Nutr 2006;43:102–8.
- Öhlund K, Olsson C, Hernell O, et al. Shortcomings in children on a gluten-free diet. J Hum Nutr Diet 2010;23:294–300.
- 12. Wild D, Robins GG, Burley VJ, et al. Evidence of high sugar intake, and low fibre and mineral intake, in the gluten-free diet. Aliment Pharmacol Ther 2010;32:573–81.
- Zuccotti G, Fabiano V, Dilillo D, et al. Intakes of nutrients in Italian children with celiac disease and the role of commercially available gluten-free products. J Hum Nutr Diet 2013;26:436–44.
- 14. Shepherd SJ, Gibson PR. Nutritional inadequacies of the gluten-free diet in both recentlydiagnosed and long-term patients with coeliac disease. J Hum Nutr Diet 2013;26:349–58.
- 15. Kautto E, Ivarsson a., Norström F, et al, Hörnell a. Nutrient intake in adolescent girls and boys diagnosed with coeliac disease at an early age is mostly comparable to their non-coeliac contemporaries. J Hum Nutr Diet 2014;27:41–53.
- Ferrara P, Cicala A, Tiberi E, et al. High fat consumption in children with celiac disease. Acta Gastroenterol Belg 2009;72:296–300.
- 17. Salazar J.C, Espín B, Rodríguez A, et al.Nutritional assessment of gluten-free diet. Is gluten-free diet deficient in some nutrient? An Pediatr 2014;81:33–9.
- Farrán A, Zamora R, Cervera P. Tablas de composición de alimentos del CESNID. Mc Graw-Hill/Interamericana - Edicions Universitat de Barcelona; 2003.
- Dietary Reference Intakes (DRIs): Estimated Average Requirements Food and Nutrition Board, Institute of Medicine, National Academies; 2011.

- 20. Generalitat de Catalunya: Departament d'Educació i Departament de Salut. Guia de l'alimentació saludable a l'etapa escolar. Departament de Salut; 2013.
- Ferrara P, Cicala M, Tiberi E et al. High fat consumption in children with celiac disease.
 Acta Gastroenterol Belg. 2009;72:296–300.
- Martin J, Geisel T, Maresch C, et al. Inadequate Nutrient Intake in Patients with Celiac Disease: Results from a German Dietary Survey. Digestion 2013;87:240–6.
- 23. Llull R, del Mar Bibiloni M, Martínez E et al. Compliance with the 2010 nutritional objectives for the Spanish population in the Balearic Islands' adolescents. Ann Nutr Metab 2011;58:212-9.

Table 1. General characteristics of study participants

	TOTAL sample			10-13 years-old			14-23 years-old		
	Cases	Controls	P-	Cases	Controls	Р-	Cases	Controls	Р-
	n = 98	n = 98	value	n = 45	n = 45	value	n = 53	n = 53	value
Age, mean \pm SD	15.2 ± 3.7	15.4 ± 3.7	0.932	11.9 ± 1.3	12.1 ± 1.4	1.000	17.9 ± 2.6	18.1 ± 2.8	0.940
Girls/Teenagers, % (n)	61.2 (60)	61.2 (60)		57.8 (26)	57.8 (26)		64.2 (34)	64.2 (34)	
BMI in kg/m² , mean \pm (SD									
Girls	19.3 ± 2.6	19.4 ± 2.5	0.936	18.2 ± 2.5	18.3 ± 2.1	1.000	20.2 ± 2.4	20.2 ± 2.4	0.990
Boys	19.5 ± 3.2	19.4 ± 3.0	0.936	18.0 ± 2.7	18.0 ± 2.6		21.0 ± 2.9	20.8 ± 2.7	0.940
Level of physical activity									
Sedentary, % (n)	26.5 (26)	16.3 (16)		22.2 (10)	13.3 (6)		30.2 (16)	18.9 (10)	
Moderately active, % (n)	40.8 (40)	49.0 (48)	0.440	48.9 (22)	62.2 (28)	1.000	34.0 (18)	37.7 (20)	0.661
Active or very active, % (n)	32.7 (32)	34.7 (34)		28.9 (13)	24.4 (11)		35.8 (19)	43.4 (23)	
Smoking habit, % (n)	7.1 (7)	4.1 (4)	0.859	0.0 (0)	2.2 (1)	1.000	13.2 (7)	5.7 (3)	0.661
Alcohol consumption, % (n)	16.3 (16)	33.7 (33)	0.040	0.0 (0)	2.2 (1)	1.000	33.3 (16)	60.4 (32)	0.002
Father's education									
University or higher, % (n)	29.6 (29)	38.2 (34)	0.440	26.7 (12)	35.0 (14)	1.000	32.1 (17)	40.8 (20)	0.661
Lower at university, % (n)	70.4 (69)	61.8 (55)		73.3 (33)	65.0 (26)		67.9 (36)	59.2 (29)	
Mother's education									
University or higher, % (n)	32.0 (31)	42.6 (40)	0.440	28.9 (13)	33.3 (14)	1.000	34.6 (18)	50.0 (26)	0.656
Lower than university, % (n)	68.0 (66)	57.4 (54)	•	71.1 (32)	66.7 (28)		65.4 (34)	50.0 (26)	
Time of CD diagnosis in years, mean \pm SD	9.3 ± 5.1	-		7.8 ± 3.7	-		10.8 ± 6.0	-	

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Abbreviations: SD, Standard deviation; BMI, Body Mass Index; CD, coeliac disease

Table 2. Energy and macrona	TOTAL			10-	-13 years-old		14-23 years-old		
	Cases	Controls	P-value	Cases	Controls	P-value	Cases	Controls	P-value
	n = 98	n = 98		n = 45	n = 45		n = 53	n = 53	
Energy, kcal/day, mean ±	2141 ± 615	2019 ± 520	0.270	2253 ± 642	1975 ± 452	0.051	2045 ± 580	2056 ± 574	0.924
SD									
Carbohydrates									
g/day, mean \pm SD	229 ± 76.6	215 ± 63.7	0.605	243 ± 79.8	211 ± 55.6	0.056	209 ± 70.7	219 ± 70.1	0.703
% of total energy intake	41.9 ± 6.1	42.6 ± 6.2	0.605	43.0 ± 5.7	42.7 ± 5.4	0.858	40.9 ± 6.3	42.6 ± 6.8	0.561
Polysaccharides									
g/day, mean \pm SD	37.9 ± 26.4	81.9 ± 37.4	0.004	36.4 ± 24.2	73.9 ± 32.8	0.006	39.3 ± 28.3	88.7 ± 39.9	0.009
% of total energy intake	7.2 ± 4.5	16.3 ± 6.5	0.004	6.7 ± 4.3	14.8 ± 5.5	0.006	7.6 ± 4.6	17.6 ± 7.0	0.009
Fiber									
g/day, mean ± SD	15.8 ± 6.2	16.2 ± 6.6	0.739	15.7 ± 6.3	15.0 ± 5.8	0.767	15.8 ± 6.1	17.1 ± 7.2	0.703
Free sugar									
g/day, mean ± SD	92.1 ± 37.9	74.9 ± 27.2	0.004	102.6 ± 36.7	76.1 ± 24.2	0.006	83.2 ± 36.9	73.3 ± 29.7	0.468
% of total energy intake	17.5 ± 5.6	15.0 ± 4.4	0.004	18.6 ± 5.4	15.8 ± 4.3	0.025	16.5 ± 5.6	14.3 ± 4.3	0.144
Protein									
g/day, mean \pm SD	84.2 ± 23.9	83.8 ± 24.2	0.910	85.6 ± 24.7	83.1 ± 26.0	0.767	83.0 ± 23.4	84.4 ± 22.7	0.924
% of total energy intake	16.1 ± 3.2	16.9 ± 3.7	0.270	15.4 ± 2.8	16.9 ± 3.4	0.056	16.7 ± 3.5	16.8 ± 4.0	0.924
Fats									
g/day, mean ± SD	96.0 ± 31.3	85.9 ± 27.7	0.049	108 ± 29.0	84.7 ± 25.5	0.025	92.0 ± 32.8	86.9 ± 29.6	0.704
% of total energy intake	40.2 ± 5.9	38.1 ± 5.9	0.046	40.5 ± 5.5	38.5 ± 5.7	0.148	39.9 ± 6.2	37.7 ± 6.1	0.310
MUFA									
g/day, mean \pm SD	33.1 ± 12.6	34.7 ± 14.0	0.739	33.3 ± 12.0	34.7 ± 15.7	0.767	34.4 ± 13.1	34.8 ± 12.5	0.924
% of total energy intake	14.4 ± 4.3	15.5 ± 4.3	0.231	13.5 ± 4.2	15.6 ± 4.3	0.051	13.3 ± 4.2	15.4 ± 4.3	0.924
PUFA									
g/day , mean \pm SD	10.5 ± 6.7	10.2 ± 4.4	0.739	11.4 ± 8.3	9.8 ± 4.4	0.414	9.7 ± 4.8	10.4 ± 4.4	0.704
% of total energy intake	4.4 ± 2.2	4.5 ± 1.5	0.739	4.6 ± 2.6	4.4 ± 1.5	0.858	4.3 ± 1.7	4.6 ± 1.4	0.704
SFA									
g/day, mean \pm SD	28.5 ± 11.5	27.5 ± 9.8	0.670	31.3 ± 10.6	27.4 ± 7.0	0.077	26.2 ± 11.9	27.5 ± 11.7	0.789
% of total energy intake	11.9 ± 2.8	12.2 ± 2.6	0.670	12.5 ± 2.4	12.6 ± 2.0	0.884	11.4 ± 3.1	11.8 ± 3.0	0.704

Table 2. Energy and macronutrient intake in cases and controls by age categories

Abbreviations: Kcal, Kilocalories; g, grams; SD, Standard deviation; MUFA, Monounsaturated fatty acids; PUFA = Polyunsaturated fatty acids; SFA = Saturated fatty acids

	Total			10	-13 years-old		14-23 years-old		
	Cases n = 98	Controls n = 98	P-value	Cases n = 45	Controls n = 45	P-value	Cases n = 53	Controls n = 53	P-value
Folic acid									
μ g/day, mean \pm SD	187.0 ± 103.2	244.9 ± 93.9	0.002	166.70 ± 80.7	228.6 ± 84.2	0.004	204.2 ± 117.0	258.7 ± 105.3	0.023
% compliance	53.2 ± 28.1	70.5 ± 28.2	0.002	55.6 ± 26.9	75.3 ± 28.2	0.004	51.2 ± 29.1	66.4 ± 27.9	0.015
Calcium									
mg/day, mean ± SD	601.9 ± 252.3	681.2 ± 259.8	0.038	624.2 ± 249.9	649.0 ± 232.0	0.627	583.0 ± 255.2	708.6 ± 280.6	0.027
% compliance	49.0 ± 21.2	56.3 ± 24.1	0.035	48.0 ± 19.2	49.9 ± 17.8	0.627	49.8 ± 23.0	61.8 ± 27.4	0.027
Zinc									
mg/day, mean ± SD	17.3 ± 6.7	20.0 ± 6.5	0.009	17.7 ± 7.5	18.9 ± 5.1	0.486	17.0 ± 6.0	21.0 ± 7.4	0.007
% compliance	194.1 ± 77.3	222.6 ± 67.9	0.010	207.3 ± 87.2	219.4 ± 62.1	0.506	182.8 ± 66.5	225.4 ± 73.0	0.006
Iron									
mg/day, mean ± SD	7.5 ± 3.0	10.1 ± 3.3	0.002	7.1 ± 2.6	10.0 ± 3.1	0.004	7.8 ± 3.3	10.3 ± 3.5	0.004
% compliance	57.4 ± 29.2	78.0 ± 34.5	0.002	54.9 ± 22.1	77.2 ± 27.7	0.004	59.5 ± 34.2	78.7 ± 39.6	0.018
Magnesium									
mg/day, mean ± SD	184.6 ± 71.7	235.0 ± 65.5	0.002	183.4 ± 76.9	225.4 ± 56.0	0.011	185.6 ± 67.6	243.2 ± 72.2	0.003
% compliance	50.0 ± 20.0	63.9 ± 18.4	0.002	48.3 ± 21.1	59.1 ± 14.1	0.011	51.6 ± 19.1	67.9 ± 20.6	0.003
Sodium									
mg/day, mean ± SD	1419 ± 739	2033 ± 778	0.002	1455 ± 846	1900 ± 6417	0.011	1389 ± 642	2146 ± 868	0.003
% compliance	94.6 ± 49.3	135.5 ± 51.9	0.002	97.0 ± 56.0	126.7 ± 42.7	0.011	92.6 ± 42.8	143.1 ± 57.9	0.003
Thiamin									
mg/day, mean ± SD	1.1 ± 0.5	1.2 ± 0.4	0.009	1.0 ± 0.4	1.2 ± 0.4	0.007	1.1 ± 0.5	1.2 ± 0.4	0.276
% compliance	103.1 ± 43.2	119.9 ± 39.8	0.009	103.1 ± 39.5	128.5 ± 40.9	0.009	103.0 ± 46.5	112.6 ± 37.7	0.276
Pyridoxine									
mg/day, mean ± SD	1.5 ± 0.7	1.7 ± 0.6	0.038	1.5 ± 0.6	1.7 ± 0.5	0.181	1.6 ± 0.7	1.8 ± 0.6	0.192
% compliance	130.1 ± 55.1	146.2 ± 51.3	0.040	134.9 ± 55.8	152.7 ± 54.0	0.192	126.1 ± 54.8	140.7 ± 48.7	0.192
Cholecalciferol									
mg/day, mean ± SD	1.6 ± 1.5	1.8 ± 1.8	0.307	1.5 ± 1.4	1.7 ± 1.5	0.447	1.7 ± 1.6	1.9 ± 2.0	0.567
% compliance	32.1 ± 30.1	37.0 ± 35.5	0.307	29.1 ± 27.3	34.9 ± 30.6	0.447	34.7 ± 32.4	38.7 ± 39.5	0.567

Table 3. Micronutrients consumption and compliance with nutritional recommendations in cases and controls by age categories

Abbreviations: µg, micrograms; mg, milligrams; SD, standard deviation; % compliance, percentage compliance to recommendation of Dietary Reference Intake for Individuals stated by the Food and Nutrition Board, Institute of Medicine, National Academy of Science: Folic acid: 9-13y 300µg/d (both sex); 14-30y 400µg/day (both sex). Calcium 9-18y 1300mg/d (both sex); 19-30y: 1000mg/d (both sex); 19-30y: 1000mg/d (both sex); 14-30y 400µg/day (both sex); 14-18y 11mg/d (male) and 15mg/d (female); 19-30y 8 mg/d (female). Iron 9-13y 8mg/d (both sex); 14-18y 11mg/d (male) and 15mg/d (female); 19-30y 8 mg/d (male) and 19-30y 18mg (female). Magnesium: 9-13y (both sex) 240mg/d; 14-18y 400mg/d (male) and 360 mg/d (female); 19-30y 410mg/d (male) and 310mg/d (female). Sodium: 1500mg/d (all study population). Thiamin: 9-13y 0.9 mg/d (both sex); 14-30y 1.2 mg/d (male); 10-18y 1.0 mg/d (female); 19-30y 1.1mg/d (female). Pyridoxine 9-13y 1.0 mg/d (both sex); 14-30y 1.3mg/d (male); 14-18y 1.2 mg/d (all study population).

	Total			10	-13 years-old		14-23 years-old		
	Cases	Controls	P-value	Cases	Controls	P-value	Cases	Controls	P-value
	n = 98	n = 98		n = 45	n = 45		n = 53	n = 53	
Starch (P/D)	3.1 ± 1.7	5.0 ± 2.2	0.007	3.1 ± 1.7	4.8 ± 2.0	0.011	3.2 ± 1.6	5.2 ± 2.3	0.007
g/day	216.0 ± 102.4	298.6 ± 136.5	0.007	206.6 ± 98.2	278.2 ± 109.1	0.015	224.6 ± 106.4	316.3 ± 155.3	0.007
% compliance with CR	75.4 ± 43.0	119.8 ± 53.0	0.007	87.4 ± 49.3	133.8 ± 56.4	0.015	64.3 ± 33.2	107.7 ± 47.1	0.007
Pulses (P/D)	0.2 ± 0.3	0.2 ± 0.5	0.583	0.2 ± 0.3	0.2 ± 0.3	0.852	0.2 ± 0.3	0.3 ± 0.6	0.771
g/day	16.4 ± 21.4	18.7 ± 34.7	0.592	15.5 ± 20.9	14.7 ± 18.3	0.852	17.3 ± 22.0	22.1 ± 44.0	0.771
% compliance with CR	20.5 ± 29.0	23.9 ± 48.0	0.583	21.3 ± 29.5	20.2 ± 26.1	0.852	19.9 ± 28.8	27.1 ± 60.7	0.771
Dairy products (P/D)	2.0 ± 1.0	1.8 ± 1.0	0.305	2.1 ± 0.9	1.7 ± 0.8	0.150	1.8 ± 1.0	1.8 ± 1.1	0.893
g/day	332.7 ± 179.7	302.4 ± 164.1	0.253	357.1 ± 160.0	310.1 ± 145.7	0.285	310.3 ± 195.0	295.8 ± 179.4	0.889
% compliance with CR	68.3 ± 37.0	60.2 ± 34.6	0.253	85.4 ± 37.7	$69.6\pm~33.6$	0.150	53.0 ± 29.0	52.4 ± 33.8	0.927
Sweetened beverages (P/D)	0.9 ± 1.0	0.6 ± 0.7	0.149	0.9 ± 1.0	0.7 ± 0.7	0.507	0.9 ± 1.0	0.6 ± 0.6	0.169
g/day	178.7 ± 203.4	129.6 ± 135.6	0.149	176.0 ± 208.5	143.9 ± 149.0	0.507	181.2 ± 200.7	117.4 ± 123.3	0.169
Vegetables (P/D)	0.8 ± 0.6	0.9 ± 0.6	0.305	0.6 ± 0.4	0.8 ± 0.6	0.358	1.0 ± 0.6	1.0 ± 0.6	0.771
g/day	101.3 ± 70.2	114.6 ± 76.5	0.305	79.5 ± 54.7	96.7 ± 79.3	0.358	121.4 ± 77.1	129.8 ± 71.3	0.771
% compliance with CR	32.4 ± 22.5	36.7 ± 24.5	0.305	25.4 ± 17.5	30.9 ± 25.4	0.358	38.8 ± 24.7	41.5 ± 22.8	0.771
Oil and fats (P/D)	2.9 ± 1.5	2.6 ± 1.7	0.288	2.8 ± 1.5	2.5 ± 2.0	0.507	3.0 ± 1.6	2.6 ± 1.3	0.453
g/day	30.9 ± 18.0	26.7 ± 18.0	0.253	30.1 ± 17.3	26.1 ± 21.9	0.493	31.8 ± 18.9	27.3 ± 13.7	0.453
% compliance with CR	61.5 ± 31.3	55.6 ± 35.8	0.305	59.8 ± 32.1	55.0 ± 42.6	0.629	63.2 ± 30.7	56.2 ± 28.6	0.526
Fruits (P/D)	0.9 ± 0.8	1.1 ± 0.9	0.305	0.8 ± 0.7	1.1 ± 0.8	0.150	1.1 ± 0.9	1.0 ± 0.9	0.927
g/day	140.2 ± 116.8	160.2 ± 131.4	0.305	120.7 ± 101.1	166.9 ± 126.2	0.150	158.0 ± 127.9	154.6 ± 136.6	0.927
% compliance with CR	37.4 ± 31.1	42.7 ± 35.0	0.305	32.2 ± 27.0	44.5 ± 33.6	0.150	42.1 ± 34.1	41.2 ± 36.4	0.927
Meat/Fish/Eggs (P/D)	3.0 ± 1.3	2.5 ± 1.2	0.026	3.1 ± 1.4	2.6 ± 1.3	0.179	3.0 ± 1.1	2.5 ± 1.2	0.161
g/day	220.2 ± 77.1	188.6 ± 77.3	0.026	223.5 ± 84.0	190.4 ± 70.5	0.150	217.2 ± 71.0	187.1 ± 83.2	0.169
% compliance with CR	121.7 ± 50.3	101.7 ± 49.0	0.026	122.0 ± 57.2	102.0 ± 51.7	0.179	121.3 ± 43.0	101.4 ± 47.0	0.161

Abbreviations: P/D, portions/day; g/day, grams/day; % compliance with CR, percentage of compliance with current recommendations using the National Pyramid Guideline: The starch group included paste, bread, tubers and pastries; Dairy products included milk and yogurt, cheese and other dairy products; Oil and fats included nuts, oils and other fats; Meat, fish and eggs included lean meat, poultry meat, fish, eggs and processed red meat.