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RISK OF EATING DISORDERS IN PATIENTS WITH CELIAC DISEASE

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ABSTRACT

Objectives: Several cases of eating disorders (EDs) have been reported in patients with celiac disease (CD), suggesting that ED could be a comorbidity associated with CD. However, few epidemiological studies have assessed this potential association. We aimed to evaluate the risk of EDs in individuals diagnosed with CD in comparison to healthy controls.

Methods: A total of 98 cases and 98 controls matched for gender, age and body mass index between 10 and 23 years-old were studied. A questionnaire was completed on medical history, and sociodemographic and anthropometric characteristics. Various ED screening self-reported tests were administered.

Results: A total of 61.2% of the study population were girls with a mean age of 15.3±3.7 years-old. Patients with CD scored non-significantly higher on all the ED screening tests than control participants. No differences were observed between study groups in terms of the frequency of individuals who exceeded the clinical cutoff identifying those at risk of ED. Patients with CD above 13 years-old were associated with a 2.15 point increase in the Eating Attitude Test (EAT) score compared to controls [βcoefficient=2.15 SE 1.04; P=0.04] after adjusting for various confounders.

Conclusions: Although being a patient with CD was associated with a significantly higher EAT score in individuals above 13 years old, no clear differences were observed between individuals with CD and controls in terms of risk of ED when other screening tests were used. More studies with larger samples and prospective designs are warranted to confirm these findings.

Key words: celiac disease, eating disorders, Eating Attitude Test.

What is known

- Eating disorders (EDs) may be a comorbidity derived from celiac disease (CD) because food restrictions may focus the attention of patients with CD on food and their body image.
- EDs affect female adolescents between 10 and 19 years old.

What is new

- Being a patient with CD is associated with a significantly higher EAT score in individuals above 13 years old.
- No clear differences were observed between patients with CD and control subjects, in terms of ED, when other screening tests were used.

INTRODUCTION

Celiac disease (CD) is a permanent intolerance to gluten and prolamins found in some cereals such as wheat, barley, rye, spelt, kamut, triticale and, possibly, oats. The disease occurs in genetically predisposed individuals, and is characterized by a severe inflammatory, immune-based reaction, which alters the absorption of macro- and micronutrients (1).

Celiac disease is common in all parts of the world and in all ethnic groups. In Europe and the USA, it affects approximately 1% of the general population. There are some regional differences (2) and it is more frequent in girls (3,4).

The only effective treatment at present is a strict gluten-free diet (5), which means that bread, pasta and other processed foods made from the cereals mentioned above cannot be eaten. This permanent restriction on foods containing gluten may mediate some of the attitudes and eating behaviors of patients with CD (6–8). In this regard, some authors have suggested that eating disorders (EDs) may be a comorbidity associated with CD, because food restriction may focus the attention of patients on food consumption and body image (9)

EDs are psychiatric disorders with a multifactorial origin, which mainly affect female adolescents between 10 and 19 years old (10). They are characterized by abnormalities in eating behavior, severe disturbances in body image and some degree of physical and nutritional disorder (11)

Since the risk of EDs is higher in adolescence, when nutritional requirements are greater, it is very important to identify individuals at high risk in order to prevent the potential deleterious effects on growth and development.

Although several clinical cases of CD patients with anorexia nervosa (12), bulimia (13) and other EDs such as binge eating (14) have been reported, few epidemiological studies have assessed these associations (9,15,16). Therefore, the aim of the present study was to assess the risk of individuals between 10 and 23 years old diagnosed with CD developing EDs in comparison with a group of healthy controls matched for age, gender and body mass index (BMI).

METHODS

Study design

The Coeliac Disease Eating Attitudes (COEDATTI) study is a cross-sectional analysis that assesses the risk of subjects with CD (cases) developing EDs in comparison with healthy non-celiac subjects (controls).

Study population

All participants meeting the inclusion criteria were invited to take part between October 2012 and June 2014. The cases recruited were between 10 and 23 years old and had been diagnosed with CD by both the pediatric and adult Gastroenterology Units of the Sant Joan University Hospital in Reus (Spain). CD was diagnosed by observing features of CD in the duodenal biopsy specimens and the 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) only partial compliance with the gluten-free diet or reluctance 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 require dietetic advice, d) autism or other cognitive disabilities.

Healthy participants (control group) who had not been diagnosed with celiac disease were also enrolled in the study as controls matched (1:1) for age (±1 year), gender and BMI (±1 kg/m^2) with CD patients. 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).

Given that no studies of this sort have been published before, it was impossible to calculate the sample size required. We decided that this would be a pilot study that can be useful for future work in the same field.

All participants 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.

Procedures

All participants were visited twice at the Sant Joan de Reus Hospital, or at the Human Nutrition Unit at the Faculty of Medicine and Health Sciences in Reus, or their respective educational centres (control participants) if it was more convenient for them. On the first visit, the principal investigator explained the study to the participants and asked them to fill honestly and individually at home the ED screening questionnaires delivered by dietitian. On the same visit, a dietitian collected sociodemographic details, personal data,

the family history of obesity, history of ED or celiac disease and the parent's or tutor's level of education by a face-to-face interview with the participant. At the end of this visit, participants were instructed how to fill in the various ED screening questionnaires to assess the risk of ED and body dissatisfaction. On the second visit, participants delivered the questionnaires, which were then checked with the dietitian.

MEASUREMENTS AND INSTRUMENTS

Anthropometric measurements were taken by trained dietitians. We used calibrated scales and a wall-mounted stadiometer to measure weight and height, respectively, with participants in light clothing and no shoes. The BMI was calculated. Children with underweight, adequate weight or overweight were categorized according to the cut-off points defined by Cole et al (17,18)

In addition, physical activity during leisure time was self-reported by the study participants, and categorized according to the Institute of Medicine (19) as:

- Sedentary: Only 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).

Screening tests

The validated version for the Spanish population of the *Children Eating Attitudes Test* (ChEAT) (20) and the Eating Attitude Test (EAT)-26 (21) were administered. These ED screening questionnaires are based on a scale of 26 items that assess a range of attitudes and behaviours associated with anorexia nervosa and bulimia nervosa. The ChEAT questionnaire was used for children between 10 and 13 years old, and for those over 13 years old the EAT-26 test was used. Each question was scored on a scale of 0 to 3 (based on the replies: always, usually, often, sometimes, rarely and never). Possible scores on the EAT-26 range from 0 to 78. A score of 20 or above indicates that a person may have an eating disorder and in consequence is recommended for further evaluation to confirm the diagnosis.

Sick Control Fat Food (SCOFF). This instrument is a questionnaire consisting of five yes/no questions filled out by patients. It was used for all study participants. Each positive response is given 1 point, and a score over or equivalent to 2 indicates that the individual assessed is at risk of EDs. The Spanish version of this questionnaire has proven to be useful for early detection of EDs in primary care settings (22).

*Bulimia Investigatory Test Edinburgh (*BITE). The version validated for the Spanish population of this test was used (23) for all the participants. It is a self-filled questionnaire designed to identify subjects with symptoms of bulimia.

Body Shape Questionnaire (BSQ). This is a 34-item questionnaire that explores the degree of anxiety that subjects experience about their bodies by assessing attitudinal aspects of body image: dissatisfaction/satisfaction. It is used to discriminate between normal people, people concerned about their image and people with EDs. In this study

the version validated for the Spanish population by Raich et al (1996) was used for all study participants (24).

Figure Drawings Scale (25). This consists of seven male and female pictures of children (10 to 16 years old and 17 to 23 years old) with bodies ranging from the very thin to the obese. The pictures were shown to the subjects and they were asked to identify which of the figures they thought most resembled their body shape and to define which one they wanted to look like. The discrepancy between the two answers was considered to be a measure of body dissatisfaction.

Statistical analysis

The results compare cases and controls by age categories. Continuous variables were presented as means (standard deviation) or medians (25th-75th percentiles). To test for normal distribution, the Kolmogorov-Smirnov statistic was performed. Categorical variables were presented as number (n) and percentages (%). Differences between groups were assessed with Student's t-test when variables were normally distributed and the Mann-Whitney U-test when they were not. The Pearson chi-squared test was used to compare categorical variables. Multiple linear regression models were fitted to assess the risk of celiac patients and control participants having ED. Estimates with β coefficient and 95% confidence interval (CI) were shown. The multiple linear regression models included the following potential confounders: age (years); sex (men vs. women), BMI (kg/m^2); mother's and father's education (university or higher level vs. lower at university level); physical activity (moderate or very active vs. sedentary); alcohol consumption (no, yes); body dissatisfaction (no, yes); history of parental eating disorder (no, yes); history in the use of weight loss or restrictive diets (yes, no). The goodness of

fit was expressed as: R square multiply per 100 (R^2*100), the variance analysis of the model, and its significance (F and P).

Data were processed using the SPSS statistical package (version 19.0, SPSS Inc., Chicago, IL) and P<0.05 was considered statistically significant.

RESULTS

Of the 155 and 194 potentially eligible cases and controls, respectively, 113 and 119 fulfilled the inclusion criteria. Of these, 13 cases were excluded because they did not complete the second visit, and 2 cases had been previously diagnosed with EDs and refused to participate in the study. Finally, the study sample consisted of 98 cases and 98 non-celiac subjects (control group) with a mean age of 15.3 ± 3.7 years old and a mean BMI of 19.4 ± 2.7 kg/m^2. A total of 61.2% (n=120) of the study population were girls. Table 1 shows the characteristics of the whole study sample categorized by age groups, and compares cases and controls. Alcohol consumption was significantly higher in controls than in cases (P=0.01). The cases had a significantly higher prevalence of family history of ED (P=0.01). No significant differences were observed between cases and controls in the other general characteristics.

The scores for the ED screening tests are shown in Table 2. Cases scored non-significantly higher on all the ED screening tests used than control participants. No differences were observed between study groups in terms of the frequency of individuals who exceeded the clinical cutoff identifying those at risk of ED. The frequency of body dissatisfaction showed no statistically significant differences between cases and controls (data not shown).

Table 3 shows the various multivariable linear regression models for evaluating the relationship between ED risk in cases and controls. Being a celiac patient above 13 years old was positively associated with an increase in the score on the EAT screening test compared to being a control [β coefficient = 2.15 (1.04); P=0.04] after adjusting for various confounders. No significant associations were observed in the other screening tests. Being moderately active or active and a smoker was positively associated with a higher SCOFF score (R^2.100= 11%; $F_{12, 195}$= 1.937; P=0.03). Being moderately active or active and having a history of dietary restrictions for weight loss was positively associated with a higher BITE score (R^2.100= 26%; $F_{12,195}$= 5.526; P<0.001)

DISCUSSION

This study is the first to have assessed the associations between the risk of EDs in patients with CD and healthy control subjects matched for age, gender and BMI. The prevalence of family history of ED was significantly higher in cases than controls. After adjustments had been made for potential confounders, being a patient with CD above 13 years was associated with a higher EAT score. The screening tests showed no clear differences between cases and control subjects in terms of the risk of ED.

Cases had an increased risk of a higher EAT score than healthy controls, a result that was consistent with previous studies (9,15,16). However, unlike other authors (9,16) we found no differences between cases and controls in terms of the mean scores of the screening test or the frequency with which individuals scored over the clinical cut-off. It should be pointed out that the median age of our study sample (196 participants) was 15.3 years old, substantially different from the median of 29 years old of the study sample of

other authors. These discrepancies may arise from differences in age, the study design, the screening test used or other non-controlled variables The onset of ED is usually between 18 and 21 years old (10) so this may be the reason for the lack of differences in the ED test scores when we take the whole population into account. In addition, the study design or screening tests used in these studies were also different. For example, Karwautz and coworkers (9) conducted a systematic study on the prevalence and clinical manifestations of ED among 283 adolescent patients with CD (210 girls, aged 14.8 ±3.0 years old; 73 boys, aged 13.9 ±2.7 years old) and found that 4.8% were affected by ED, all of whom were girls. On the other hand, we assessed only the risk of having EDs while they assessed prevalence and clinical manifestations using a two-stage design (screening and structured interview for ED pathology). The screening tests used were the Eating Disorder Inventory and the Eating Disorder Examination Questionnaire and the cases were matched for sex and age, but not for BMI. We decided to control for BMI because a higher BMI is known to be a strong key factor associated with the risk of developing ED. In fact, Micali et al. (8) found ED to be a comorbidity of CD particularly in those with a higher BMI. On the other hand, Arigo and coworkers examined psychiatric comorbidities in 177 women with CD who were over the age of 18. A total of 22% (n=39) scored in the clinically meaningful range of ED symptoms. They also used the Eating Disorders Examination Questionnaire and compared the result with the frequency of ED in the general population without matching cases and controls as we did (15). Passantini and coworkers (16) used only the EAT-26 test and they found a significantly higher score in patients with CD than we did. Again, the reason for the discordant result might be that their study sample was older (29.2 years-old) than ours.

The potential relationship between cases and the risk of ED may be explained by the fact that patients with CD are more aware of diet because they have to avoid the symptoms associated with the pathology. Likewise, as we observed in our sample, the presence of a history of ED or having a high BMI were other risk factor of developing ED (26) as well as being moderately active or active. Exercise increases prior to, and during an eating disorder (27), and is a method of weight and shape control (28).

The present study has both strengths and limitations. One important strength is that the cases were matched for sex, age and BMI, which are three well-known risk factors of ED (8,10,29) and this last parameter was measured by healthcare professionals during the first visit. Furthermore, the ED screening tests were self-report questionnaires so there was no need to have a face-to-face interview, which often involves a greater risk of bias. The main limitation of the present analysis is its cross-sectional nature, which does not allow any causal relationship between ED risk in patients with CD to be established.

In summary, although being a case was associated with a significantly higher EAT score in individuals above 13 years old, screening tests found no clear differences between cases and controls in terms of the risk of ED. Further prospective studies with larger samples are warranted to confirm these findings. Nevertheless, healthcare professionals are advised to incorporate an ED screening tool in order to identify early ED in patients with CD.

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Table 1. General characteristics of study participants

	TOTAL sample			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**
Age, mean ± SD	15.2 ± 3.7	15.4 ± 3.7	0.70	11.9 ± 1.3	12.1 ± 1.4	0.32	17.9 ± 2.6	18.1 ± 2.8	0.78
Girls/Teenagers, % (n)	61 (60)	61 (60)		57 (26)	57 (26)		64 (34)	64 (34)	
BMI in kg/m^2, mean ±(SD									
Girls	19.3 ± 2.6	19.4 ± 2.5	0.94	18.2 ± 2.5	18.3 ± 2.1	0.88	20.2 ± 2.4	20.2 ± 2.4	0.99
Boys	19.5 ± 3.2	19.4 ± 3.0	0.87	18.0 ± 2.7	18.0 ± 2.6	0.98	21.0 ± 2.9	20.8 ± 2.7	0.82
Weight									
Underweight, % (n)	13 (13)	11 (11)		6 (3)	11 (5)		18 (10)	11 (6)	
Adequate, % (n)	70 (69)	69 (68)	0.81	6 (29)	55 (25)	1.00	75 (40)	81 (43)	0.29
Overweight, % (n)	16 (16)	19 (19)		28 (13)	33 (15)		5 (3)	7 (4)	
Level of physical activity									
Sedentary, % (n)	26 (26)	16 (16)		22 (10)	13 (6)		30 (16)	18 (10)	
Moderately active, % (n)	40 (40)	49 (48)	0.21	48 (22)	62 (28)	0.39	34 (18)	37 (20)	0.39
Active or very active, % (n)	32 (32)	34 (34)		28 (13)	24 (11)		35 (19)	43 (23)	
Smoking habit, % (n)	7 (7)	4 (4)	0.54	0 (0)	2 (1)	1.00	13 (7)	5 (3)	0.32
Alcohol consumption, % (n)	16 (16)	33 (33)	0.01	0.0 (0)	2 (1)	1.00	33 (16)	60 (32)	<0.001
Father's education									
University or higher, % (n)	29 (29)	38 (34)	0.22	26 (12)	35 (14)	0.48	32 (17)	40 (20)	0.41
Lower than university, % (n)	70 (69)	61 (55)		73 (33)	65 (26)		67 (36)	59 (29)	
Mother's education									
University or higher, % (n)	32 (31)	42 (40)	0.14	28 (13)	33 (14)	0.82	34 (18)	50 (26)	0.16
Lower than university, % (n)	68 (66)	57 (54)		71 (32)	66 (28)		65 (34)	50 (26)	
Time of CD diagnosis in years, mean ± SD	9.3 ± 5.1	-		7.8 ± 3.7	-		10.8 ± 6.0	-	
History of parental obesity, % (n)	13 (16)	2 (2)	0.30	17 (8)	17 (8)	1.00	15 (8)	5 (3)	0.20
History of parental eating disorder, % (n)	12 (12)	2 (1)	0.01	9 (65)	2 (1)	0.11	11. (6)	1 (1)	0.11
History of weight loss diets, % (n)	4 (4)	2 (2)	0.41	0 (0)	4 (2)	0.49	7 (4)	0 (0)	0.12

SD, Standard deviation; BMI, Body Mass Index; CD, celiac disease

Table 2. Median [IQR] scores of the screening eating disorders tests

	Case **n= 98**	**Control** **n= 98**	**P-value**
SCOFF (from 0 to 5), % scored ≥ 2 (n)	7 (7.0)	6 (6.0)	0.78
EAT (from 0 to 26), Median [IQR]	4.0 [2.0-8.0]	3.0 [2.0-7.0]	0.28
ChEAT (from 0 to 26), Median [IQR]	3.0 [2.0- 4.0]	4.0 [1.0-8.0]	0.41
BITE (from 0 to 30), Median [IQR]	2.0 [1.0-4.0]	3.0 [1.0-4.0]	0.22
BSQ (from 34 to 204),			
Median [IQR]	43.0 [37.0-62.0]	53.0 [40.0-66.0]	0.10
Moderate or minor preoccupation, % (n)	11 (7.0)	8 (5.0)	0.54

IQR, interquartile range; EAT, Eating Attitudes Test; ChEAT, Children Eating Attitudes Test; SCOFF, Sick Control Fat Food; BITE, Bulimia Investigatory Test Edinburgh; BSQ, Body Shape Questionnaire

Table 3. Risk of having eating disorders in cases-controls according to different screening tests

	SCOFF			EAT			ChEAT			BITE		
	β coefficient	Standard error	P-value	β coefficient	Standard error	P-value	β coefficient	Standard error	P-value	β coefficient	Standard error	P-value
Control-Case	0.00	0.12	0.99	2.15	1.04	0.04	-1.66	1.03	0.11	-0.01	0.46	0.98
Age (years)	0.031	0.23	0.17	0.07	0.22	0.74	- 0.37	0.43	0.39	0.15	0.09	0.09
Sex (men, women)	0.031	0.023	0.15	1.44	1.11	0.20	1.05	1.12	0.35	0.18	0.48	0.71
BMI (kg/m^2)	0.03	0.03	0.23	0.17	0.24	0.47	0.38	0.26	0.15	0.30	0.10	<0.001
Mother's education	0.21	0.13	0.10	-0.67	1.11	0.55	0.92	1.19	0.44	-0.04	0.50	0.94
Father's education	0.04	0.13	0.76	0.66	1.14	0.57	- 0.28	1.20	0.82	0.71	0.52	0.17
Physical activity (sedentary, moderate to active)	0.11	0.14	0.06	2.78	1.17	0.02	- 1.33	1.41	0.35	1.36	0.54	0.01
Smoking (no, yes)	0.01	0.26	<0.001	-0.58	1.68	0.73	--	--	--	1.66	1.01	0.10
Alcohol consumption (no, yes)	-0.11	0.17	0.54	0.69	1.15	0.55	- 1.32	6.74	0.85	-0.18	0.67	0.79
Body dissatisfaction (no, yes)	0.23	0.15	0.12	0.82	1.20	0.49	-3.09	1.69	0.07	-0.14	0.58	0.98
History of parental eating disorders (no, yes)	-0.36	0.23	0.12	-0.59	1.99	0.77	0.41	2.22	0.85	-0.87	0.89	0.33
History of weight loss diets, (no, yes)	0.29	0.23	0.22	2.82	1.77	0.11	- 0.79	3.85	0.84	2.78	0.91	0.003
Model goodness of fit	R^2.100= 11%			$R^{2,}$ .100= 17%			R^2.100= 11%			R^2.100= 26%		

	$F_{12, 195}$= 1.937 P=0.03	$F_{12,105}$= 1.695 P=0.08	$F_{11, 89}$= 0.909 P=0.53	$F_{12,195}$= 5.526 P<0.001

BMI, Body Mass Index; ED, eating disorder; SCOFF, Sick Control Fat Food; EAT, Eating Attitudes Test; ChEAT, Children Eating Attitudes Test; BITE, Bulimia Investigatory Test Edinburg