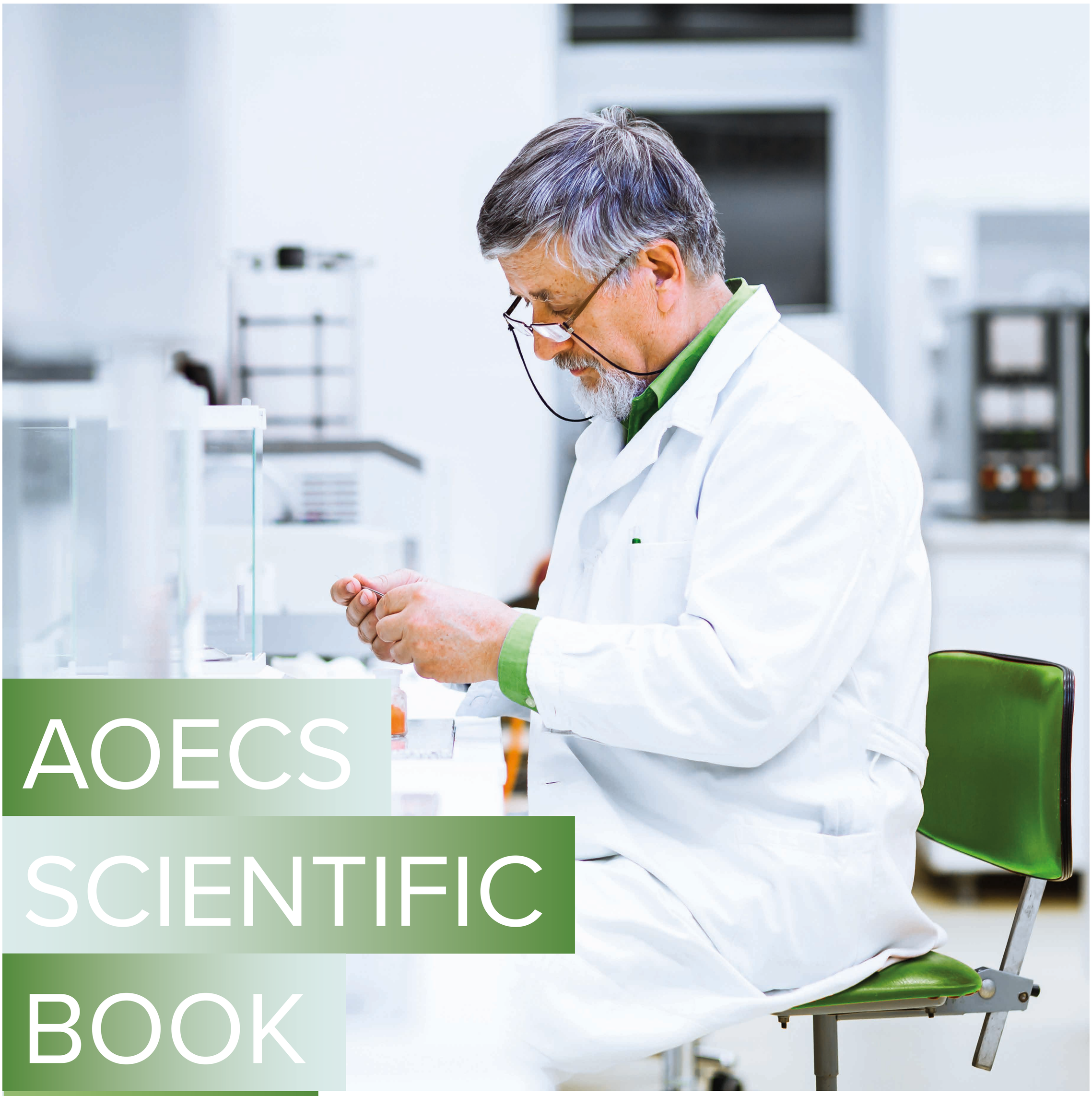
AOECS

Association of European Coeliac Societies



AOECS SCIENTIFIC BOOK 2022

Uniting and empowering coeliac societies in Europe and beyond

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FOREWORD

Coeliac disease is a chronic, multiple-organ, autoimmune disease that affects genetically predisposed individuals when exposed to the ingestion of gluten.

Over the past 25 years, there has been an increasing prevalence of celiac disease, which affects about 1,3% of the population, while the only available treatment as of today, is the adherence to a strict and life-long gluten-free diet.

The Association of European Coeliac Societies (AOECS) together with its members is committed to work towards improving the lives of coeliacs and their relatives. We do so by promoting a reliable Food Safety Scheme for pre-packaged gluten-free food; enhancing Gluten-free Eating Out Schemes in different countries; raising awareness among policymakers and promoting sound research and innovation within the coeliacs and gluten-free ecosystems.

As part of these efforts, we are proud to offer this first collection of scientific posters to the public, which were presented during the 34th AOECS General Assembly held in September 2022, in Lisbon, Portugal.

We warmly thank all the authors that submitted their posters to this first edition for their inestimable contribution to enhancing intelligence and awareness around coeliac disease, and we invite them to continue their research efforts in this field.

Veronica Rubio
Secretary General, AOECS

ACKNOWLEDGEMENTS

SUBMITTING COELIAC ORGANISATION	TITLE	SUBMITTED BY
Italian Coeliac Society Associazione Italiana Celiachia	**Gluten-free pigmented cereals: chemical characterization and their role in the modulation of inflammatory status in celiac disease**	Fondazione Celiachia Onlus, Università degli Studi di Milano, Milano, Italy; Francesca Colombo, Stefano Piazza, Corinne Bani, Marco Fumagalli, Giulia Martinelli, Enrico Sangiovanni, Patrizia Restani, Mario Dell'Agli, Chiara Di Lorenzo
Coeliac Society of Ireland	**Characteristics of Individuals with Coeliac Disease that Present with Other Autoimmune Conditions**	Sarah Kiernan; Coeliac Society of Ireland
Portuguese Celiac Association Associação Portuguesa de Celíacos	**What about the siblings? Self-regulation, agency, and quality of life in siblings of children with Celiac Disease**	Portuguese Celiac Association, Psychology Research Center, School of Psychology, University of Minho, Portugal; Gabriela Figueiredo, Pedro Rosário, Paula Magalhães
Coeliac Society of Belarus Harmony without gluten	**Evaluation of the nutrition menu for children with celiac disease in educational institutions of the Republic of Belarus**	Yanka Kupala State University of Grodno; Sycheuskaya N. Bashun N. Mikhalchuk L. Harmony without gluten; Lipnitskaya E.
Ukrainian Coeliac Society ВГО Українська Спілка Целіакії	**Features of the intestinal microbiome in patient with gluten-sensitive diseases who are on an agliadin diet**	Yanka Kupala State University of Grodno; Sycheuskaya N. Bashun N. Mikhalchuk L. Harmony without gluten; Lipnitskaya E.
Celiac Disease Foundation United States of America	**Disease Burden and Quality of Life Impacts in Patients With Celiac Disease on a Gluten-Free Diet: An Analysis of the iCureCeliac Registry**	Takeda Pharmaceutical Company Limited, Cambridge, MA Celiac Disease Foundation, Woodland Hills, CA Analysis Group, Inc., Boston, MA
Coeliac Society of Ireland	**The Prevalence of Other Autoimmune Conditions Alongside Coeliac Disease**	Sarah Kiernan; Coeliac Society of Ireland

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Gluten-free pigmented cereals: chemical characterization and their role in the modulation of inflammatory status in celiac disease

Submitted by: Fondazione Celiachia Onlus, Francesca Colombo[1], Stefano Piazza[1], Corinne Bani[1], Marco Fumagalli[1], Giulia Martinelli[1], Enrico Sangiovanni[1], Patrizia Restani[1], Mario Dell'Agli[1], Chiara Di Lorenzo[1]

[1] *Università degli Studi di Milano, Milano, Italy*

Introduction

The important role of oxidative stress and inflammation in celiac disease (CD) has been reported by several authors. In celiac subjects deamidated gliadin peptides activate the innate and adaptive immune response with the production of proinflammatory cytokines and auto-antibodies. In addition, some gliadin regions trigger off the oxidative stress at intestinal level1. Therefore, inflammation and oxidative stress seem to be involved in the molecular mechanisms of CD2.

Different in vivo studies have evaluated the oxidative status in celiac patients (both adults and children) observing that the oxidative stress is strongly associated with CD. Particularly, an oxidative imbalance was observed in new diagnosed and non-responder celiac subjects. Although the gluten free diet (GFD) exerts beneficial effects on the oxidative stress at intestinal level of celiac patients, in some cases, the GFD only partially improved the physiological activity of intestinal mucosa in celiac subjects3,4.

Several dietary components possess antioxidant and antiinflammatory properties. Therefore, the consumption of foods rich in antioxidant compounds could potentially mitigate the oxidative stress characteristic of celiac patients, improving their well-being. Rice and corn are the most consumed gluten-free cereals and are often used for the formulation of cereal-based gluten-free products. The pigmented varieties of cereals are generally richer in bioactive compounds (such as anthocyanins and other flavonoids) than the usual ones and are characterized by a higher antioxidant activity. Therefore, the pigmented cereals could represent interesting ingredients for the formulation of functional cerealbased products.

In this context, Celiac Foundation funded in 2019 a project entitled "Naturally gluten free pigmented cereals to modulate the inflammatory status in celiac disease".

The aim of this project was to evaluate the possible antioxidant and antiinflammatory properties of pigmented gluten free cereals in the framework of CD.

Method

Hydro-alcoholic extracts from pigmented rice (Nerone) and corn (Scagliolo Rosso and Rosso Rostrato di Rovetta), previously selected among 19 varieties with different pigmentation, on the basis of their phenolic content, were in vitro digested and characterized in term of phenolic compounds and antioxidant activity, using both spectrophotometric and chromatographic techniques: 1) Folin-Ciocalteu's assay for the quantification of total phenolic content; 2) DPPH (1,1,- diphenyl-2-picrylhydrazyl) assay for the evaluation of antioxidant capacity; 3) High Performance Thin Layer Chromatography (HPTLC) for the separation and semi-quantitative characterization of phenolic substances, assessing in parallel the associated antioxidant activity; 4) High Performance Liquid Chromatography-Diode Array Detector (HPLC-DAD) for the identification and quantification of phenolic compounds.

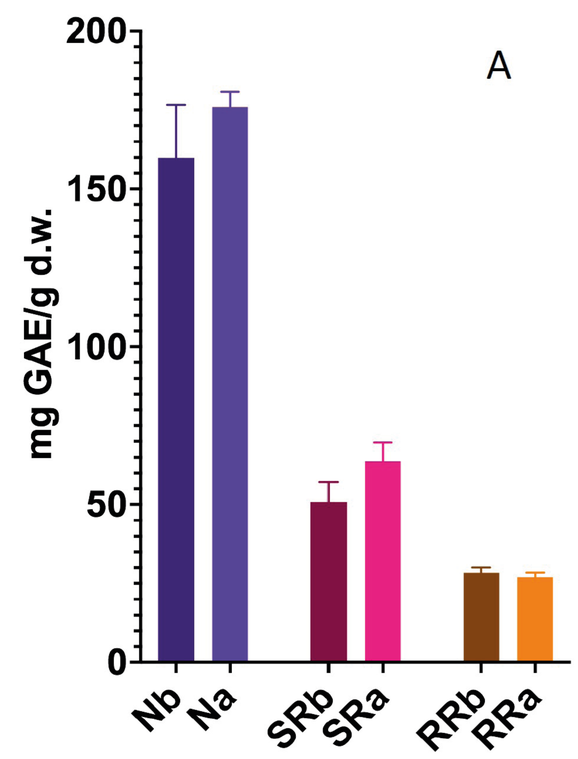
In parallel, for the evaluation of the anti-inflammatory activity of the extracts, Caco-2 cells were treated with digested gliadin in
combination with other proinflammatory stimuli, to mimic a celiac disease-related inflammatory status.

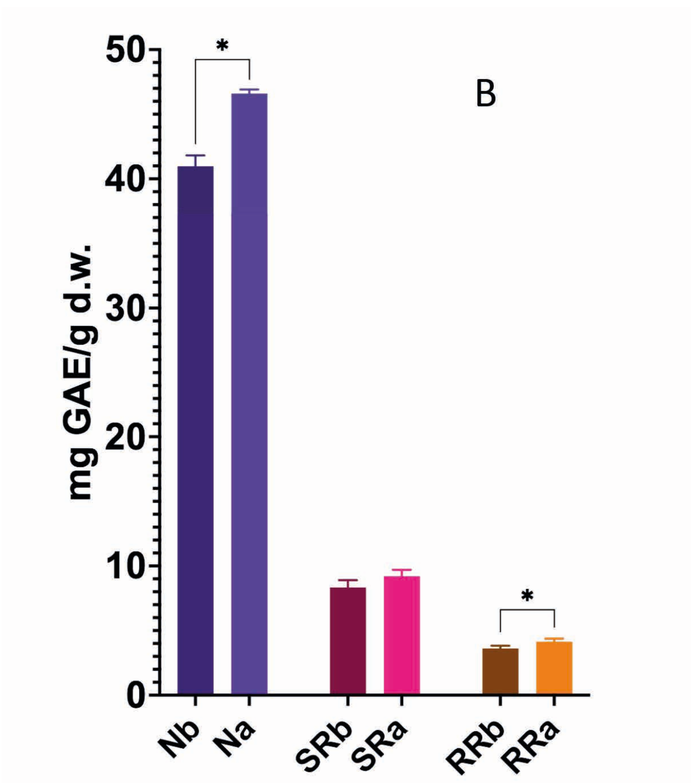
Results

Extracts from pigmented cereals showed different quantitative and qualitative anthocyanins composition; the in vitro digestion determined a significant reduction in the total anthocyanins content (-23% for Scagliolo Rosso corn, -73% for Nerone rice). On the contrary, no significant difference ($p>0.05$) in term of phenolic compounds content was observed after digestion and an increase in term of antioxidant activity was measured (Chart 1).

Chart 1 –

Total Phenolic Content (A) and antioxidant capacity (B) measured in cereal extracts before and after digestion





*GAE: equivalent of gallic acid. N: Nerone rice, SR: Scagliolo Rosso corn, RR: Rosso Rostrato di Rovetta corn, b: before in vitro digestion, a: after in vitro digestion, * $p<0.05$*

During the in vitro digestion, the stability of phenolic compounds and the slight increase of antioxidant activity could be explained by the transformation of anthocyanins into bioactive small compounds, such as benzoic acid derivatives.

To study the potential antiinflammatory effects of extracts at intestinal level, the direct effect of gliadin alone or in combination with typical cytokines of autoimmune diseases (IFN-γ and IL-1β) was investigated monitoring CXCL10, a chemokine overexpressed in the intestinal mucosa of CD patients and involved in the activation and recruitment of leukocytes. Gliadin, in combination with IFN- γ and IL-1β enhanced the release of CXCL10, that was inhibited by all the tested extracts (IC50s<200 µg/mL), both before and after digestion. CXCL10 is controlled by Nuclear Factor kappa B (NF-κB) pathway, which was partially inhibited by all the extracts at the highest concentration tested (200 µg/mL). The additional involvement of other mechanisms demands specific investigations.

Conclusion

During this project, different analytical methods and an in vitro model, suitable to study the inflammation status associated to CD, were developed. This study underlines the potential antioxidant and antiinflammatory activities of pigmented cereals at the gut level. These results could be useful to partially clarify the role of dietary phenolic compounds in the protection of intestinal mucosa in CD. Moreover, the results obtained could promote the use of pigmented cereals among celiac subjects, improving their quality of life.

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Acknowledgments

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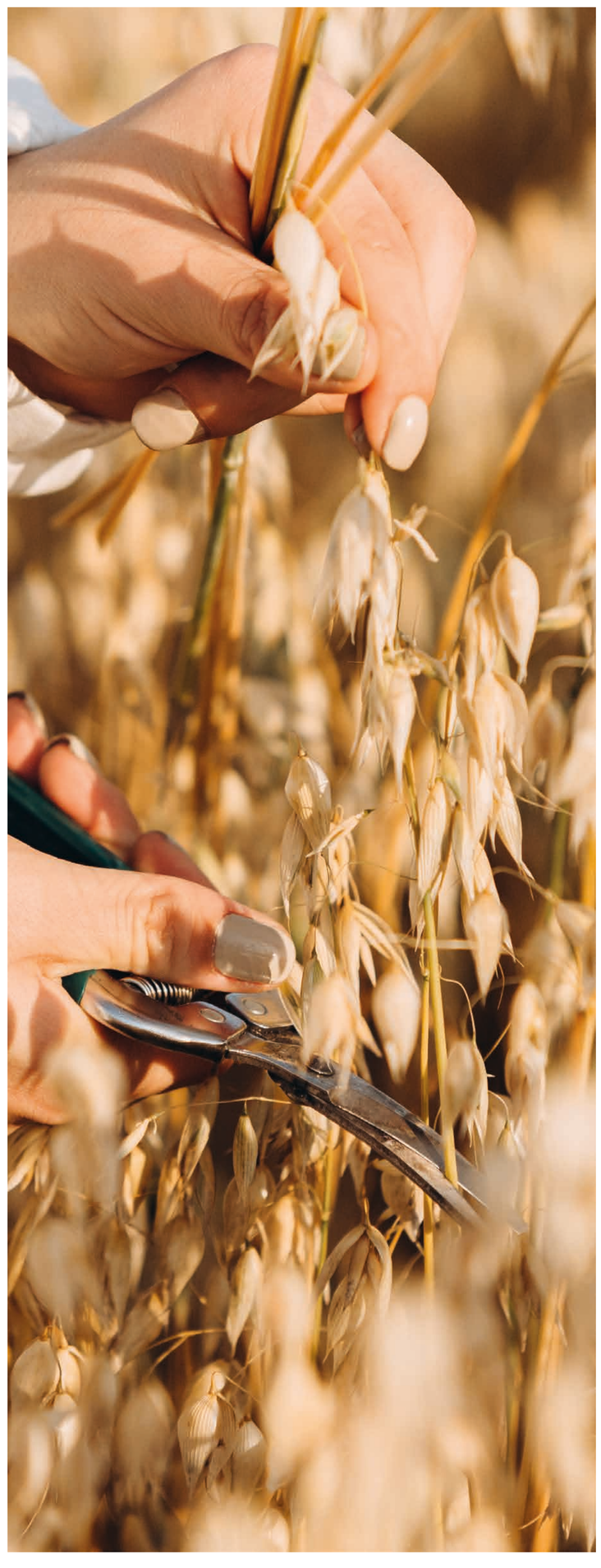

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Characteristics of Individuals with Coeliac Disease that Present with Other Autoimmune Conditions

Submitted by: Sarah Kiernan from the Coeliac society of Ireland

Introduction

Autoimmune conditions, such as coeliac disease, cause an inappropriate immune response(1, 2). Individuals with an autoimmune condition have an increased risk of developing secondary autoimmune conditions(3). Like coeliac disease, other autoimmune conditions are more prevalent in females than in males (4) but limited research investigates the association between sex and the co-occurrence of coeliac disease and other autoimmune conditions. There is little research investigating age and development of other autoimmune conditions with coeliac disease. This study aims to compare the sex and age of individuals with coeliac disease that present with another autoimmune condition and those that do not present another autoimmune condition.

Method

A survey was designed in survey monkey and circulated to the 3,381 active members of the Coeliac Society of Ireland over a 2-week period.

Participants

Only adults were included in this study. Although the coeliac society comprises of gluten intolerant members, only those with coeliac disease and dermatitis herpetiformis were included.

Survey Questions

Questions asked, members their sex, year of birth, if they had another autoimmune condition, names of autoimmune conditions they had and year of both coeliac disease diagnosis and year of other autoimmune condition diagnosis.

Analysis

Responses were analysed with SPSS version 27.0 software. Categorical variables were summarized by descriptive statistics, including total numbers, averages and percentages with associations were analysed using the chi-square test of independence. Pearson correlation was run to assess the relationship between years since coeliac disease diagnosis and number of other autoimmune conditions diagnosed.

Chart 1 – Prevalence of other autoimmune conditions in a coeliac population across the sexes.

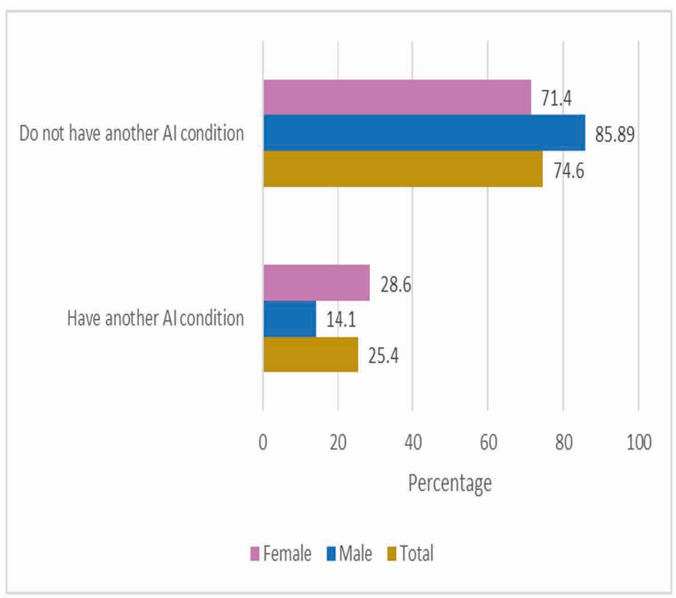

Chart 1; Indication of the number of males, females and total population who reported and did not report diagnosis of another autoimmune condition alongside coeliac disease. Numbers charted are percentages of the female, male and total population.

Chart 2 – Prevalence of other autoimmune conditions in each age group of the population.

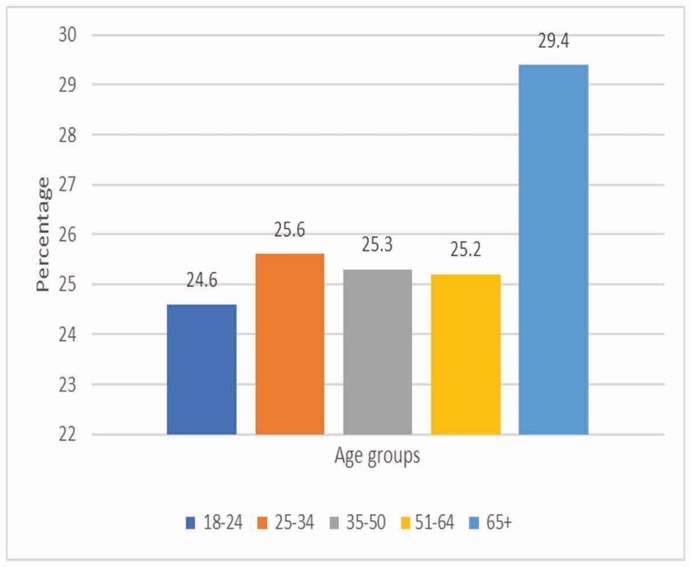

Chart 2; Indication of the proportion of each age group who reported diagnosis of another autoimmune condition alongside coeliac disease. Numbers charted are percentages of each age group.

Results

78% of 677 responders were female. A higher proportion of females (28.6%) reported another autoimmune condition than males (14.1%) with a statistically significant difference between number of males and females reporting another autoimmune condition ($p<0.001$). There was no significant difference between age group of coeliac disease diagnosis and diagnosis of another autoimmune condition ($p=0.986$). Highest prevalence of other autoimmune condition was reported in the 65+ coeliac diagnosis age group category (29.6%) which was the oldest age category of coeliac diagnosis. This suggests with age, chances of coeliac disease and another autoimmune condition co-occurring increases. There was a weak negative correlation between years since coeliac disease diagnosis and number of other autoimmune conditions reported ($r(675) = -.045$, $p < .238$). Another autoimmune condition was diagnosed on average 2.17 (±16.519) years later than coeliac disease.

Conclusion

In this study, prevalence of co-occurring coeliac disease and a secondary autoimmune disorder is higher in females. This reflects previous literature and prevalence of coeliac disease itself(3). This could be due to genetics(5) or poor health care attendance of males (6, 7) and in turn poor diagnosis of autoimmune conditions in males. Although co-occurrence of coeliac disease and other autoimmune disorders increase with age in this population, results are not strong enough to suggest age impacts the link between coeliac disease and other autoimmune conditions. More research is needed to investigate this.

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ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

What about the siblings? Self-regulation, agency, and quality of life in siblings of children with Celiac Disease

Submitted by: Portuguese Celiac Association - Gabriela Figueiredo[1], Pedro Rosário[1] and Paula Magalhães[1]
1 - Psychology Research Center, School of Psychology, University of Minho, Portugal

Introduction

Over the past 25 years, there has been an increasing prevalence of celiac disease [1]. This is a chronic, multiple-organ, autoimmune disease in genetically predisposed individuals, precipitated by the ingestion of gluten. There is no cure for celiac disease; only strict adherence to a gluten-free diet can prevent both short and long-term consequences [2]. However, associated food-related restrictions, and its implications, can have a serious impact on the individual's dietary consumption, social interactions, family's dynamics, and economic costs [3]. Confronted with this life-long situation and close monitoring requirement, impact of the celiac disease is not circumscribed to the individual with the diagnosis, but also to caregivers and extended family [4,5]. Little attention has been given to the impact of celiac disease on siblings, who share common genetic and the same within-family environment [5,6]. Particularly in case of children, during key developmental periods of childhood, detrimental consequences can be more serious on emotional and behavioral issues [4,6].

Method

The main goal of this project is to evaluate the role of self-regulation and agency processes in the quality of life and school achievement of siblings of children with celiac disease. Thus, a book chapter, a systematic review, and two empirical studies (qualitative and quantitative) will be performed.

Analysis and results

Results from the chapter and systematic review show that how life-style restrictions affect quality-of-life and emotion regulation of siblings vary across individuals depending on how effectively they use self-regulation strategies. Self-regulation comprises processes that allow individuals to control personal, behavioral, and environmental influences that affect human actions [7]. Research shows that individuals can be taught how to self-regulate their behavior and improve their confidence in successfully self-managing their behaviors to achieve a desired outcome [8]. Children who self-regulate their behavior have low likelihood of displaying externalizing and internalizing problems; tend to be high achievers academically and reach higher education qualification later in life; and tend to have a low likelihood of long-term unemployment in adulthood [9]. Recent studies suggest a better compliance to a gluten-free diet when self-regulation strategies are combined with agency, i.e., the ability to influence one's functioning and the course of events by one's actions [10,11].

Conclusion

Next steps of this project involve the development of a qualitative study with semi-structured interviews to the sibling, parents, and the child with celiac disease, aged 12-19 years, to explore the functioning, structure, and autonomy in Portuguese families that live with celiac disease, as well as the relationships between siblings and parents and their use of self-regulation strategies. Additionally, a quantitative study will be conducted online to assess the relationships between variables that mediate quality-of-life, emotional self-regulation, and school achievement, with the possibility of extending this study to other countries. Results will provide in-depth knowledge that will contribute to the development of effective guidance for families and health professionals. This project also aims to raise awareness to this topic, reinforcing the key role of psychology advocacy in improving the disease management and relationships of all involved.

Acknowledgements

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ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Evaluation of the nutrition menu for children with celiac disease in educational institutions of the Republic of Belarus

Submitted by: Sycheuskaya N.[1], Bashun N.[1], Lipnitskaya E.[2], Mikhalchuk L.[1]
1 - Yanka Kupala State University of Grodno; 2 - Harmony without gluten

Introduction

According to the data of the scientific-methodical institution «National Institute of Education» of the Ministry of Education of the Republic of Belarus, 220 children were registered, with the officially confirmed diagnosis of celiac disease, aged from 1 to 18 years among students of pre-school and general secondary schools of the Republic of Belarus. These children receive dietary (therapeutic and preventive) nutrition appropriate to their age and the duration of their stay. Nutrition is provided according to the approximate two-week diets developed on the basis of established norms of physiological needs for nutrients and energy, differentiated by age of students (1-4 years, 4-7 years, 7-14 years, 14-18 years) with taking into account seasonality (summer-autumn, winter-spring), duration of stay in the educational institution (from 2 to 7 hours, 10.5 hours, 12 hours and 24 hours), variety and combination of food products, laboriousness of cooking, established nutritional standards and money spending on food. On the basis of an approximate two-week diet, daily diets are prepared taking into account the commodity, local and other characteristics. Daily requirements for proteins, fats and carbohydrates as well as energy are established by Regulation of the Ministry of Health of the Republic of Belarus No.180 “On approval of the Sanitary Norms and Rules “Requirements for nutrition of the population: norms of physiological needs in energy and food substances for various groups of the population of the Republic of Belarus” dated November 20, 2012. For children with celiac disease, daily needs are also reflected in the Order of the Ministry of Health of the Republic of Belarus dated July 13, 2012 No. 801.

Method

The aim of the study is to analyze the quality of nutrition for children with celiac disease provided in educational institutions. The object of the study is the nutrition of children with celiac disease, namely daily rations provided in educational institutions in the Brest region (Brest) and the Minsk region (Minsk). The provided nutrition includes three meals - breakfast, lunch and afternoon tea, while the caloric content of the diet must be at least 70% of the child’s daily physiological needs.

Results

During the study of the nutrition of celiac children provided in the Brest region (Brest), the daily diet for the 6-10 age group was analyzed. When evaluating the two-week diets for children with celiac disease provided in the Brest region, the following values were obtained: proteins - 45.52±0.57 g, fats - 43.67±1.49 g, carbohydrates - 146.35±4.11 g, the energy value of the diet - 1125.05 ± 17.45 kcal, potassium - 1907.85 ± 14.25 mg, calcium - 359.99 ± 9.71 mg, magnesium - 223.635±10.285 mg, phosphorus - 702.0.95±4.255 mg, iron - 8.56±0.97 mg, vitamin A - 0.19±0.05 mg, β-carotene - 3.305±0.245 mg, vitamin B1 - 0.495±0.015 mg, B2 - 0.61± 0.05 mg, B3 (PP) - 8.29±0.62 mg, vitamin C - 42.115±7.805 mg, vitamin D - 0.46±0.01 µg, vitamin E - 5.12±0.07 mg , vitamin K - 3.43±0.09 mg. According to the data obtained, the dietary content of fats, carbohydrates and energy values are below the norm in the range from 18 to 30%. There is a significant lack of Ca, and fat-soluble vitamins D and K. Also found insufficient content of vitamins B1, B2, PP. The content of potassium is exceeded by 3 times.

During the study of the nutrition of children with celiac disease provided in the Minsk region (Minsk), the daily diets of three age groups (6-11, 11-14 and 14-17 years old) were analysed. When evaluating two-week diets for children aged 6-11 years, the following values were obtained: proteins - 41.365±0.155 g, fats - 37.355±2.215 g, carbohydrates - 133.485±10.655 g, energy value of the diet - 1028.8±22.9 kcal, potassium - 1513.85±50.45 mg, calcium - 353.925±0.775 mg, magnesium - 195.915±6.155 mg, phosphorus - 549.005±1.815 mg, iron - 9.68±1.67 mg, vitamin A - 0.42±0.19 mg, β-carotene - 1.945±0.175 mg, vitamin B1 - 0.44±0.03 mg, B2 - 0.66±0.03 mg, B3 (PP) - 6.615±0.025 mg, vitamin C - 35.605±4.745 mg, vitamin D - 0.44±0.32 µg, vitamin E - 5.41±0.59 mg, vitamin K - 7.44±0.98 µg. When evaluating the two-week diets of children aged 11-14 years, the following values were obtained: proteins - 48.3±0.8 g, fats - 45.59±1.27 g, carbohydrates - 149.86±10.8 g, energy value diet - 1191.45±35.05 kcal, potassium - 1759.05±61.65 mg, calcium - 383.695±1.085 mg, magnesium - 231.59±2.02 mg, phosphorus - 628.475±8.945 mg, iron - 10.715±1.715 mg, vitamin A - 0.45±0.2 mg, β-carotene - 2.38±0.14 mg, vitamin B1 - 0.525±0.045 mg, B2 - 0.735±0.025 mg, B3 (PP) - 8.335 ± 0.365 mg, vitamin C - 41.625 ± 5.365 mg, vitamin D - 0.475 ± 0.315 µg, vitamin E - 6.605 ± 0.605 mg, vitamin K - 9.855 ± 0.255 µg. In the nutrition of children with celiac disease 6-11 years old and 11-14 years old in the Minsk region, the content of fats, carbohydrates in the diet and the energy value are below the norm in the range from 26 to 41%. There is a significant lack of fat-soluble vitamins D and K. Also found to be insufficient in Ca, vitamins B1 and PP. The content of potassium is exceeded by almost 2 times.

When evaluating the two-week diets in the Minsk region (Minsk) of children aged 14-17 years, the following values were obtained: proteins - 48.88±1.08 g, fats - 47.06±0.7 g, carbohydrates - 151.1±12.54 g, energy value of the diet - 1215.8±48.3 kcal, potassium - 1819.1±97.8 mg, calcium - 390.095±1.445 mg, magnesium - 243.135±11.775 mg, phosphorus - 640.42±2 .66 mg, iron - 10.89±1.82 mg, vitamin A - 0.45±0.2 mg, β-carotene - 2.545±0.065 mg, vitamin B1 - 0.535±0.045 mg, B2 - 0.755±0.015 mg , B3 (PP) - 8.52±0.24 mg, vitamin C - 45.385±6.265 mg, vitamin D - 0.485±0.305 µg, vitamin E - 6.92±0.43 mg, vitamin K - 12.015±0.485 µg. According to the data obtained, the dietary content of fats, carbohydrates and energy values are below the norm in the range from 32 to 49%. There is a significant lack of fat-soluble vitamins D and K. Also found to be insufficient in Ca, vitamins B1 and PP.

Conclusion

Based on an analysis of the diets provided, it can be argued that it is necessary to develop separate diets for all age groups and to use special programs and services to produce more individualized daily menu in educational institutions. It is also important to offer a wider range of different dishes, including flour confectionery products to prevent violations of protein-free and gluten-free diets by children.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Features of the intestinal microbiome in patient with gluten-sensitive diseases who are on an agliadin diet

Submitted by: Prof. Olena Gubska, MD, PhD, Olga Naumova, MD, PhD, Andrii Kuzminets, MD, PhD, Oleg Denesyuk, MD, Oleksandr Kolyada, PhD, Vladislav Moseyko, Oleksii Dolko, MD.

Introduction

Gastrointestinal bacteria are crucial for human health. They form an intestinal microbiome (IM) - a set of microorganisms that live on the surface and inside the human host. Its disturbance - intestinal dysbiosis - is associated with a violation of both quantitative and qualitative composition of the IM and accompanies different gastrointestinal disorders, including functional digestive disorders, organic diseases, and special conditions, such as NCGS and CD.

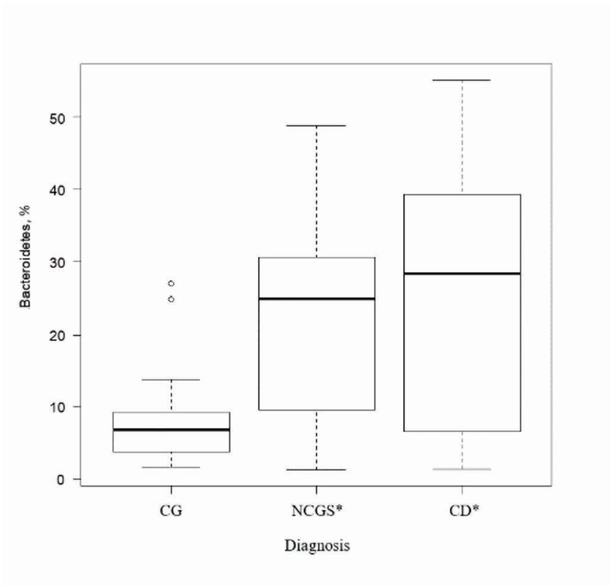
Methods

The study included 25 adults, 14 (56%) with CD and 11 (44%) - with NCGS. The control group (CG) included 24 people without clinical or anamnestic signs of gluten-sensitive pathology or diseases of the gastrointestinal tract. We used the real-time PCR method and studied the faecal content of the Bacteroidetes, Firmicutes, Actinobacteria phylae, other representatives of the IM ("other" indicator, which reflects the total percentage of all bacterial DNA, except for the mentioned above), and calculated the ratio Firmicutes/Bacteroidetes.

Results

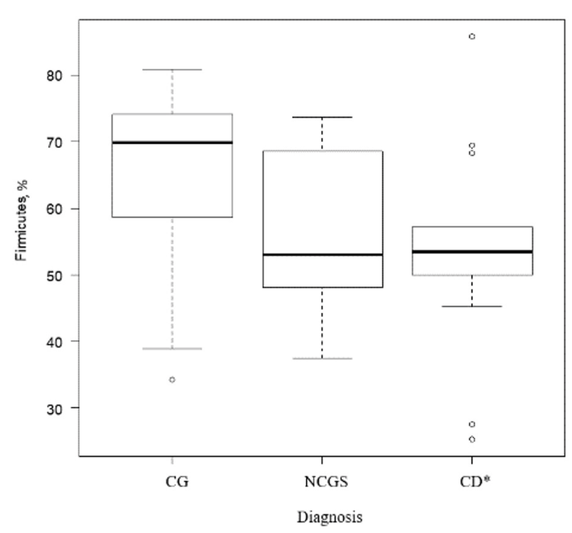
The medians of the agliadin diet duration (DD) were 9 (IQR 6-12) years in the CD group and 4 (IQR 3-5) years in the NCGS group (p = 0.087). DD and the patients' age were correlated with faecal content of Bacteroidetes, Firmicutes, their ratio (F/B), and Actinobacteria and did not correlate with the content of "other" types.

The Bacteroidetes content was 28.4 (IQR 6.58-39.28) % in CD patients, 24.98 (IQR 8.83-31.04) in NCGS patients (p>0.1 with CD), and 6.83 (IQR 3.69-9.22) in the CG (p<0.05 with GRDs). There was a positive correlation of average strength with age (ρ = 0.47, p <0.001) and the DD (ρ = 0.398, p = 0.006).



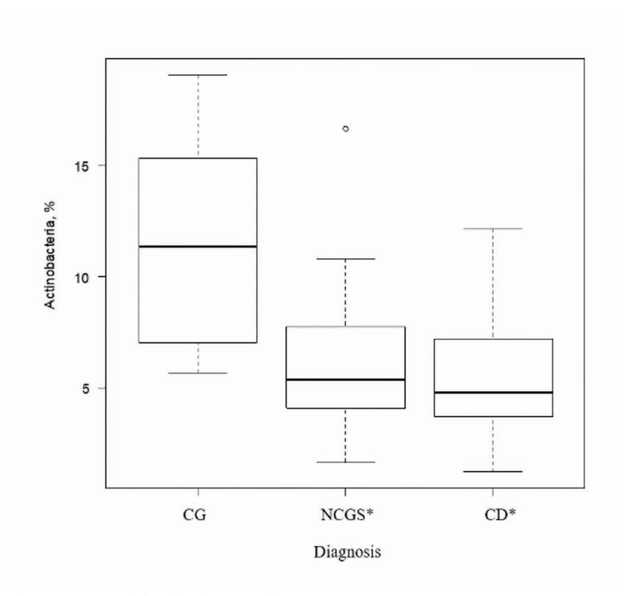
Faecal content of Bacteroidetes, %

Firmicutes content was 53.47 (IQR 49.98-57.21) % in CD patients (p<0,05 with CG), 53.0 (IQR 47.13-71.95) % in NCGS patients (p>0.1 with other groups) and 69.89 (IQR 58.58- 74.1) % of CG. Negative correlations of medium strength of Firmicutes bacteria were revealed with age (ρ = -0.42, p = 0.003,) and a weak correlation with the DD (ρ = -0.36, p = 0.015).



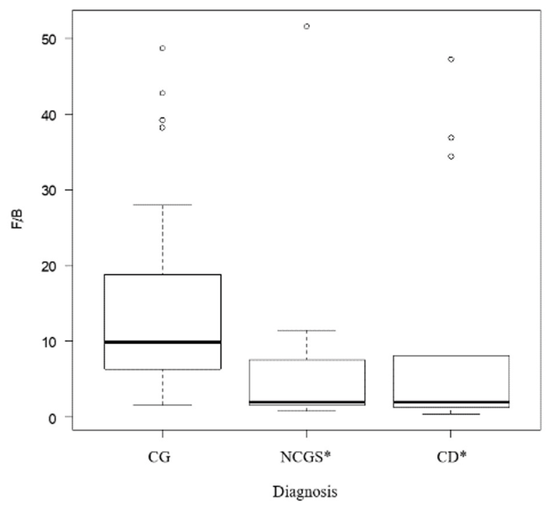
Faecal content of Firmicutis,%

The Actinobacteria content was 4.8 (IQR 3.73 - 7.2) % in CD patients, 5.37 (IQR 3.89-8.56) % in NCGS patients (p>0.1 with CD), and 11.36 (IQR 7.07-15.34) in the CG (p<0.01 with GRDs). There was a negative correlation of average strength with age (ρ = -0.53, p <0.001) and the DD (ρ = -0.5, p <0.001).



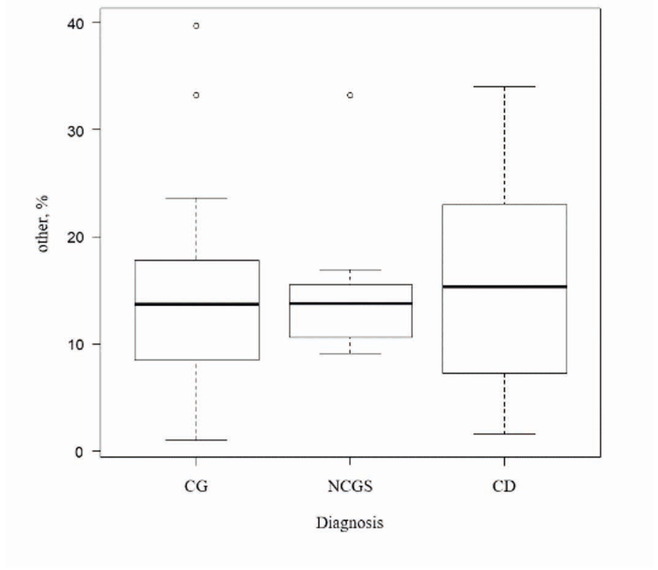
Faecal content of Actinobacteria

The F/B ratio was 1,996 (IQR 1.27-8.15) in CD patients, 2.0 (IQR 1.63-8.25) in NCGS patients (p>0.1 with CD), and 9.986 (IQR 6.37-18.80) in CG (p<0.05 with GRDs). Negative correlations of medium strength with age (ρ = -0.46, p <0.001) and with the DD (ρ = -0.38, p = 0.009) were revealed.



Faecal F/B ratio

The content of "other" types of IM was 15.39 (IQR 7.25-23.06) in CD patients, 13.78 (IQR 9.48-16.05) in NCGS patients, and 13.66 (IQR 8.43-17.78) in CG. This indicator had no significant difference (p> 0.99) between all three groups. No correlation was found between the content of "other" types of intestinal microflora with age or the DD (p> 0.7).



Faecal content of "other" types of IM

Conclusion

We found significant IM changes in patients with celiac disease and non-celiac gluten sensitivity, which was expressed in an increase of the Bacteroidetes content with a parallel decrease in the content of Firmicutes and Actinobacteria. The most significant were changes in Actinobacteria content, a little less significant - the Firmicutes/Bacteroidetes ratio. The detected intestinal microbiome changes are most likely to be a consequence of dietary features of such patients, namely the side effect of maintaining an agliadin diet.

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ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Disease Burden and Quality of Life Impacts in Patients With Celiac Disease on a Gluten-Free Diet: An Analysis of the iCureCeliac Registry

Submitted by: Takeda Pharmaceutical Company Limited, Cambridge, MA; Celiac Disease Foundation, Woodland Hills, CA; Analysis Group, Inc., Boston, MA

Background

Celiac disease (CeD) is an immune-mediated disorder. CeD symptoms and other clinical manifestations are triggered by exposure to dietary gluten, which over time and with poor management can result in long-term health complications.

A gluten-free diet (GFD) is the only management option currently available to patients with CeD, and there is substantial heterogeneity in the clinical manifestations of CeD and in patients' response to a GFD.

Study Objective

To identify patient subgroups with distinct CeD symptom burden profiles and describe corresponding clinical characteristics, as well as the impact of CeD on quality of life (QoL), health status and work productivity, and the effectiveness of a GFD across subgroups.

Methods

Data source

The iCureCeliac® patient registry, hosted by the Celiac Disease Foundation, is the largest geographically diverse registry of US patients diagnosed with CeD and treated in CeD referral centers and community practices.

The registry contains data collected online from 2015 to present. Data collected during the period December 2015 to October 2019 are analyzed here.

Study design

This study was a cross-sectional analysis of iCureCeliac® patient registry data.

Patients were included in the analysis if they reported a biopsy-confirmed diagnosis of CeD and had complete Patient-Reported Outcomes Measurement Information System-Gastrointestinal Symptom (PROMIS-GI) and Celiac Symptom Index (CSI) questionnaire data.

Subgroup identification

Patient subgroups with distinct CeD-related symptom burden profiles (as measured by multiple domains in the PROMIS-GI and CSI questionnaires) were identified using latent class analysis (LCA).

LCA is a model-based clustering method that uses observed indicator variables to identify distinct unobserved patient clusters (i.e. latent classes) in a heterogeneous population, such that the resulting patient clusters are internally homogeneous with regard to their clinical profile and disease experience (e.g. CeD-related symptom burden profile), but distinct from other identified clusters.

The following indicator variables were included in the LCA model.

- ***Eight PROMIS-GI4 domains:*** belly pain, bowel incontinence, constipation, diarrhea, disrupted swallowing, gas and bloating, nausea and vomiting, and reflux – categorized into quintiles assigned values of 1 to 5 (higher values corresponding to higher severity).
- ***Categorical CSI5 score:*** total scores (range: 16–80) were assigned values of 1 to 3, where '1' indicates a low symptom burden (CSI score ≤ 30), '2' indicates a moderate symptom burden (31 ≤ CSI score ≤ 44) and '3' indicates a high symptom burden (CSI score ≥ 45).

Statistical analysis

Latent class analysis

The preliminary number of LCA-defined subgroups was determined using the Bayesian Information Criterion (BIC). The interpretability and meaningfulness of preliminary subgroups identified using this data-driven approach were evaluated, allowing determination of the optimal number of LCA-defined subgroups.

The LCA approach was then re-implemented using the same list of indicator variables, with the optimal number of LCA-defined subgroups pre-specified.

Description of variables

Variables of interest (e.g. demographics, clinical characteristics, QoL as measured by the Celiac Disease Quality Of Life Survey [CD-QOL],6 health status as measured by the RAND 36-item Short-Form Health Survey [SF-36]7 and self-reported adherence to a GFD) were described for the overall population and compared between LCA-defined subgroups.

Continuous variables were described using means and standard deviations (SDs), with analysis of variance (ANOVA) tests for comparisons between LCA-defined subgroups; categorical variables were described using frequencies and proportions, with chi-square tests for comparisons between patient subgroups.

Results

- Of 5,690 patients in the iCureCeliac® registry, 3,699 patients reported a biopsy-confirmed diagnosis of CeD. Of those 3,699 patients, 711 had complete PROMIS-GI data, and 1,351 patients had complete CSI data.
- In total, 376 patients had complete data for both scales and were included in this analysis.
- The LCA identified two distinct subgroups.
- Patients in subgroup 1 (52.4%) had lower PROMIS-GI domain and CSI scores, indicating a lower CeD symptom burden profile.
- Patients in subgroup 2 (47.6%) had higher PROMIS-GI domain and CSI scores, indicating a higher CeD symptom burden profile.
- Descriptive statistics for the indicator variables used in the LCA model are presented in Table 1.
- In the overall population (N = 376; Table 2), most patients were female (82.4%), mean (SD) age at CeD diagnosis was 35.7 (17.2) years and duration of CeD was 5.1 (6.9) years.
- Most patients (93.1%) reported always maintaining a strict GFD, despite almost half (47.3%) reporting CeD symptoms even with adherence to a strict GFD.
- In general, patient demographics were similar between LCA subgroups, and there were no differences in self-reported adherence to a GFD (p = 0.71; Table 2).
- Patients with higher CeD symptom burden generally had a shorter time to onset of symptoms after exposure to gluten (Table 2).

Table 1 –

Descriptive statistics for indicator variables used in the LCA model.

Table 1. Descriptive statistics for indicator variables used in the LCA model.

	Overall N = 376	Lower CeD symptom burden n = 197	Higher CeD symptom burden n = 179	*p* value
PROMIS-GI				
Domain score, mean (SD)				
Belly pain[a]	50.7 (10.8)	43.6 (6.5)	58.5 (9.1)	< 0.001
Bowel incontinence[b]	4.7 (1.8)	4.2 (0.9)	5.3 (2.4)	< 0.001
Constipation[a]	49.3 (8.0)	46.4 (7.4)	52.5 (7.4)	< 0.001
Diarrhea[a]	49.7 (8.9)	45.0 (6.1)	54.8 (8.7)	< 0.001
Disrupted swallowing[a]	45.4 (7.0)	42.5 (4.4)	48.7 (8.0)	< 0.001
Gas and bloating[a]	52.9 (8.7)	47.5 (6.6)	58.9 (6.4)	< 0.001
Nausea and vomiting[a]	48.6 (7.5)	45.3 (4.7)	52.3 (8.2)	< 0.001
Reflux[a]	45.1 (7.9)	41.0 (5.8)	49.5 (7.6)	< 0.001
CSI[c]				
Total score, mean (SD)	36.9 (10.3)	30.4 (6.9)	44.0 (8.6)	< 0.001
Categorical score, n (%)				
Low burden (16 < CSI ≤ 30)	111 (29.5)	106 (53.8)	5 (2.8)	< 0.001
Moderate burden (31 ≤ CSI ≤ 44)	180 (47.9)	86 (43.7)	94 (52.5)	
High burden (45 ≤ CSI < 80)	85 (22.6)	5 (2.5)	80 (44.7)	

[a]T-score: mean (SD) of 50 (10) for the US general population (higher scores correspond to more of the concept being measured [i.e. higher severity]); [b]Summed score: score range 4–20 (higher scores correspond to more of the concept being measured [i.e. higher severity]); [c]CSI score range: 16–80 (higher scores denote more severe symptoms).
CeD, celiac disease; CSI, Celiac Symptom Index; LCA, latent class analysis; PROMIS-GI, Patient-Reported Outcomes Measurement Information System-Gastrointestinal Symptom; SD, standard deviation.

Compared with patients with a lower symptom burden, patients with a higher symptom burden:

- had a higher mean number of days per year absent from school or work owing to CeD ($p < 0.05$; Figure 1)
- were more likely to report CeD symptoms despite self-reported adherence to a GFD ($p < 0.001$) and were less likely to report a GFD as very effective for treating their most significant CeD symptoms ($p < 0.001$; Table 3)
- had a worse mean (SD) CD-QOL score – lower versus higher CeD symptom burden subgroups, 52.2 (13.4) versus 64.6 (14.5), respectively, $p < 0.001$ (overall, 58.1 [15.2]; lower scores correspond to better QoL)
- had a higher prevalence of CeD-related health conditions ($p < 0.05$ in all save one condition [seizure: $p = 0.477$; Figure 2]) and vitamin and mineral deficiencies (all $p < 0.01$; Figure 3)
- and had worse general health status as measured by the SF-36 ($p < 0.001$ in all domains; Figure 4).

Table 2 –

Patient demographic and CeD characteristics for the overall study population and LCA subgroups.

Table 2. Patient demographic and CeD characteristics for the overall study population and LCA subgroups.

Characteristic	Overall N = 376	Lower CeD symptom burden n = 197	Higher CeD symptom burden n = 179	*p* value
Age, mean (SD), years				
At survey	40.9 (17.9)	40.0 (18.7)	41.9 (17.0)	0.301
At diagnosis	35.7 (17.2)	34.8 (18.3)	36.8 (15.9)	0.268
Gender, n (%)				
Female	310 (82.4)	154 (78.2)	156 (87.2)	0.067
Male	64 (17.0)	42 (21.3)	22 (12.3)	
Other/unknown	2 (0.5)	1 (0.5)	1 (0.6)	
Race, n (%)				
White	334 (88.8)	184 (93.4)	150 (83.8)	< 0.01
Hispanic	13 (3.5)	7 (3.6)	6 (3.4)	
Other	29 (7.7)	6 (3.0)	23 (12.8)	
Duration of disease, mean (SD), years	5.1 (6.9)	5.5 (7.9)	4.7 (5.5)	0.28
Time between self-reported exposure to gluten and symptom onset, n (%)				
< 2 hours	114 (30.3)	46 (23.4)	68 (38.0)	< 0.001
2–24 hours	143 (38.0)	79 (40.1)	64 (35.8)	
> 24 hours	20 (5.3)	10 (5.1)	10 (5.6)	
Unknown	44 (11.7)	23 (11.7)	21 (11.7)	
Does not develop symptoms	30 (8.0)	25 (12.7)	5 (2.8)	
Missing	25 (6.6)	14 (7.1)	11 (6.1)	
Keeps a strict GFD (self-reported adherence), n (%)				
Never	3 (0.8)	1 (0.5)	2 (1.1)	0.71
Sometimes	4 (1.1)	2 (1.0)	2 (1.1)	
Often	17 (4.5)	7 (3.6)	10 (5.6)	
Always	350 (93.1)	186 (94.4)	164 (91.6)	
Missing	2 (0.5)	1 (0.5)	1 (0.6)	

CeD, celiac disease; GFD, gluten-free diet; LCA, latent class analysis; SD, standard deviation.

Table 3 –

Patient perception of GFD effectiveness in overall symptom management.

Table 3. Patient perception of GFD effectiveness in overall symptom management.

n (%)	Overall N = 376	Lower CeD symptom burden n = 197	Higher CeD symptom burden n = 179	*p* value
CeD symptoms despite adherence to a strict GFD				
Yes	172 (47.3)	56 (29.3)	116 (67.1)	< 0.001
No	131 (36.0)	99 (51.8)	32 (18.5)	
Unknown	61 (16.8)	36 (18.8)	25 (14.5)	
GFD treats the most significant symptoms				
Not at all	9 (2.4)	4 (2.0)	5 (2.8)	< 0.001
Moderately[a]	62 (16.5)	10 (5.1)	52 (29.1)	
Very much[b]	248 (66.0)	147 (74.6)	101 (56.4)	
Unknown	17 (4.5)	8 (4.1)	9 (5.0)	
Missing	40 (10.6)	28 (14.2)	12 (6.7)	

[a]'Moderately' includes the responses 'A little bit' and 'Somewhat'. [b]'Very much' includes the responses 'Quite a bit' and 'Very much'
CeD, celiac disease; GFD, gluten-free diet.

Figure 1 – Absenteeism due to CeD.

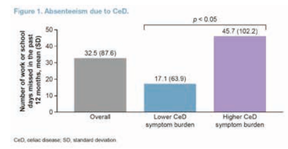


Figure 2 – Prevalence of CeD-related health conditions.

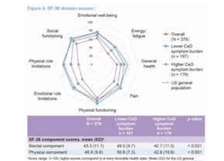
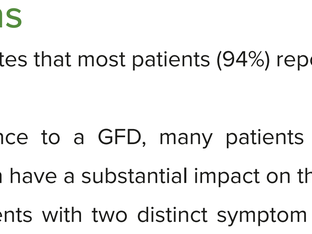


Figure 3 – Prevalence of CeD-related vitamin and mineral deficiencies.



Limitations

- The registry contains US patient data only, which may not be representative of other countries.
- Patients who are willing to fill out the survey may differ from the general CeD population.
- Of the patients included in the registry, only a small proportion had complete data for both the CSI and PROMIS-GI questionnaires.
- Information on clinical metrics (e.g. biomarkers of enteropathy, laboratory measures) that may aid in distinguishing symptom burden profiles was not available.

Figure 4 – SF-36 domain scores.

Conclusions

- This study indicates that most patients (94%) report always adhering to a strict GFD.
- Despite adherence to a GFD, many patients still experience CeD symptoms, which have a substantial impact on their day-to-day lives.
- Using LCA, patients with two distinct symptom burden profiles were identified, as captured by the PROMIS-GI and CSI questionnaires.
- Higher CeD symptom burden was associated with decreased QoL, increased CeD-related health conditions and nutritional deficiencies, and increased absenteeism (lending to the high level of absenteeism in theoverall population, with patients reporting an average of approximately 33 days of work or school missed in the preceding year).
- Patients with lower symptom burden were less likely to report many CeD-related health conditions or vitamin deficiencies and are more likely to believe that a GFD treats their symptoms.
- These data underscore the heterogeneity of CeD and the need for therapeutic options beyond a GFD to mitigate disease burden in patients with CeD.

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Disclosures

K. Chen was an employee of Takeda Pharmaceutical Company Limited at the time of the research. M. Geller is an employee of Celiac Disease Foundation, a nonprofit organization that received funding from Takeda to conduct this study. D. Leffler and L Meckley are employees of Takeda Pharmaceutical Company Limited. F. Mu, K. Kponee-Shovein and E Swallow are employees of Analysis Group, Inc., a consultancy that received funding from Takeda to conduct this study.

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ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

The Prevalence of Other Autoimmune Conditions Alongside Coeliac Disease

Submitted by: Sarah Kiernan from the Coeliac society of Ireland

Introduction

Autoimmune conditions, such as coeliac disease, cause an inappropriate immune response, resulting in damage to the body's own cells(1, 2). Individuals with an autoimmune condition have an increased risk of developing secondary autoimmune conditions(3). Prevalence of other autoimmune conditions alongside coeliac disease is estimated to be 10-30-fold higher than that of the general population(4-7). However, a clearer understanding of the prevalence of this association is needed. Type one diabetes mellitus and thyroid diseases such as Hashimoto and Grave's disease, are the most common autoimmune conditions seen alongside coeliac disease(4, 6, 8). Other autoimmune conditions have been associated with coeliac disease but research on them is limited(4, 6, 8). The aim of this study is to evaluate the prevalence of other autoimmune conditions in a coeliac population.

Method

A survey was designed in survey monkey and circulated to the 3,381 active members of the Coeliac Society of Ireland over a 2-week period.

Participants

Only adults were included in this study. Although the coeliac society comprises of gluten intolerant members, only those with coeliac disease and dermatitis herpetiformis were included.

Survey Questions

Questions asked, members their sex, year of birth and if they had another autoimmune condition. If they had another autoimmune condition they could choose which condition from a drop down list and if the condition was not on the list they could name it in other. Year of both coeliac disease diagnosis and year of other autoimmune condition diagnosis was also asked.

Analysis

Responses were analysed with SPSS version 27.0 software. Categorical variables were summarized by descriptive statistics, including total numbers, averages and percentages. Names of new autoimmune conditions were recorded and checked with an external health care professional that thew were indeed autoimmune.

Chart 1 –
Proportion of coeliac disease population reporting autoimmune condition

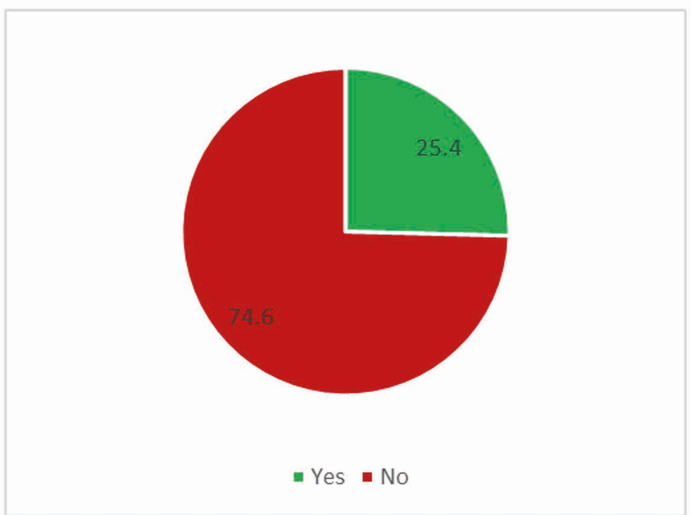

Chart 1; chart represents in percentages, the proportion of individuals to said "yes" or "no" to being diagnosed with another autoimmune condition.

Chart 2 –
Proportion of each autoimmune condition reported alongside coeliac disease

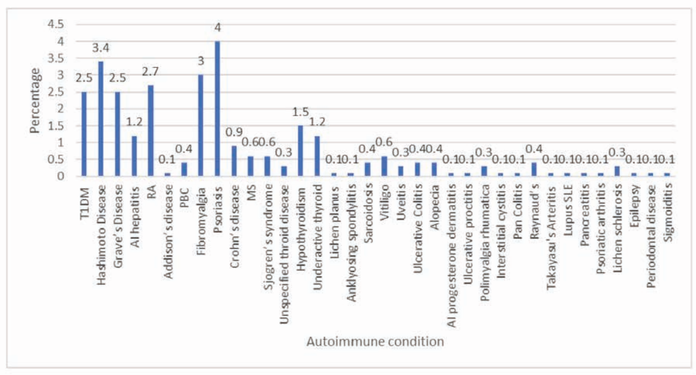

Chart 2; chart represents in percentages, the proportion of each condition reported by the total population.

Results

25.4% of 677 responders reported diagnosis of another autoimmune condition alongside coeliac disease. Psoriasis was the most common autoimmune condition (4% of the population). Hashimoto Disease (3.4% of the population), fibromyalgia (3% of the population) and rheumatoid arthritis (2.7% of the population) were the second, third and fourth most common condition. Those with Graves' disease and type one Diabetes comprised of 2.5% of the total population. A total of 36 different autoimmune conditions were reported alongside coeliac disease. A secondary autoimmune condition was diagnosed on average 2.17 (±16.519) years later than coeliac disease.

Conclusion

Prevalence of other autoimmune conditions alongside coeliac disease in this study falls in the upper range of prevalence found in previous research which is 15-30%(4, 8, 9). Unlike other studies(4, 6, 8), psoriasis and not type one diabetes or thyroid conditions are the most common autoimmune condition reported in this coeliac population. This study summarizes the largest list of autoimmune conditions to occur alongside coeliac disease to date. This study suggests, overall other autoimmune conditions that co-occur alongside coeliac disease are diagnosed before coeliac disease. This suggests that those with other autoimmune conditions could possibly have and should be checked for coeliac disease.

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CONTACT

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