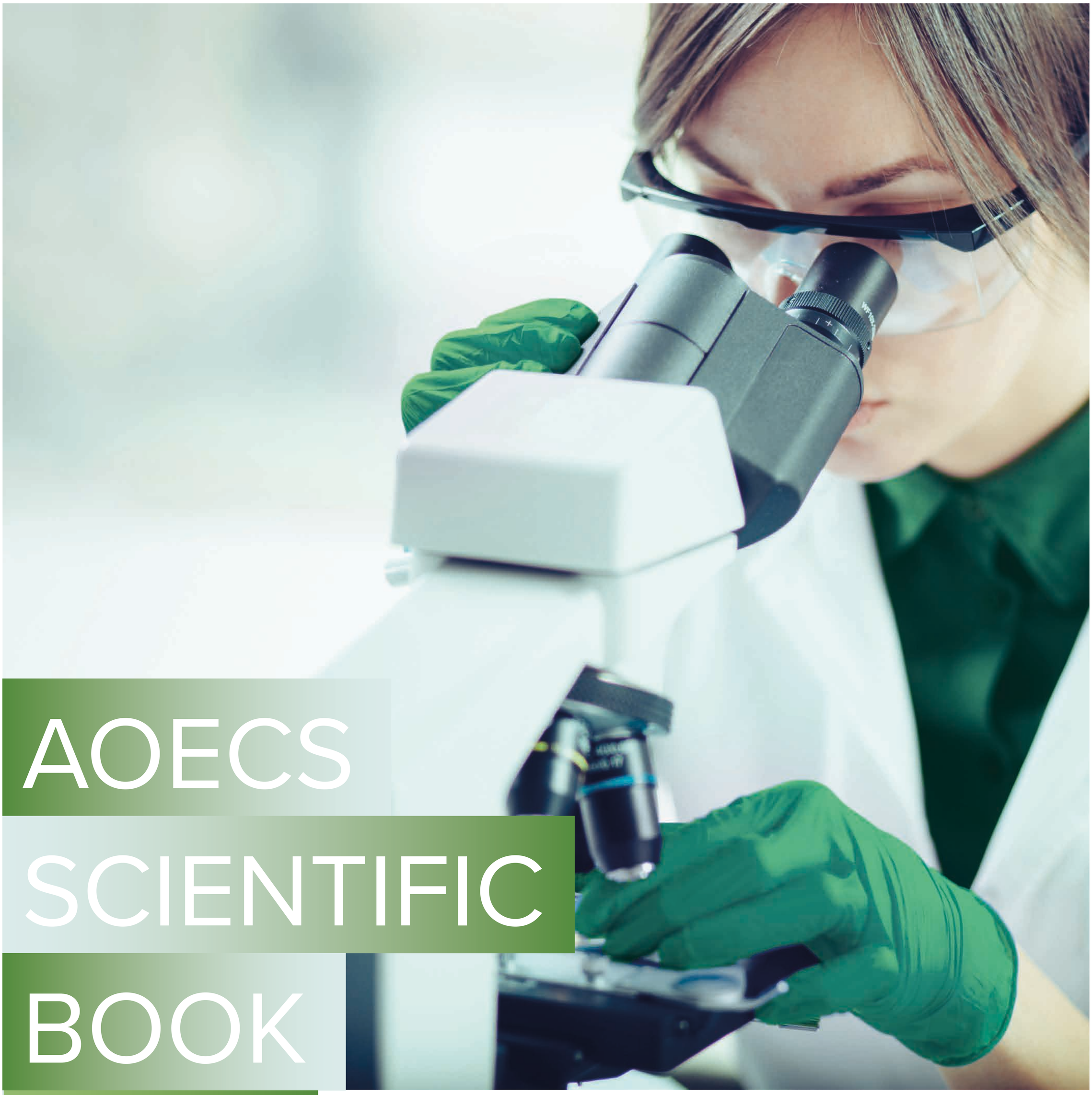
AOECS

Association of European Coeliac Societies



AOECS SCIENTIFIC BOOK

2023

Uniting and empowering coeliac societies in Europe and beyond

AOECS Scientific Book 2023

AOECS

Association of European Coeliac Societies

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. Today, the only available treatment 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 second collection of scientific posters to the public, which were displayed during the 35th AOECS General Assembly held in November 2023, in Athens, Greece.

With this poster's exhibition and the subsequent e-book, AOECS aims to spread the word and incentivize research and innovation related to coeliac disease. We want to acknowledge the work developed with the support of our member societies in different countries, as well as encourage researchers to continue working in this field.

For this second edition of 2023, AOECS received 15 scientific abstracts and posters which we are delighted to make available to the public in this e-book.

The posters come from different countries with the support of our member societies, and they cover a diverse range of scientific research and innovation topics such as:

new possible markers of mucosal permeability or about mRNA non-invasive biomarkers with potential future applications; edible packaging for gluten-free food from alternative biobased materials to plastic; food testing improvements for gluten-free products, a comparison about their nutritional values; an evaluation of the final prize of gluten-free products in a concrete market; results from different surveys about patients perceptions; improvements in clinical management or expectations about alternatives to the gluten-free diet and also some epidemiological approaches in different countries.

AOECS has submitted all received posters to an independent evaluation conducted by two experts in the field, members of the International Society for the Study of Celiac Disease (ISSCD).

ISSCD is a non-profit organisation of professionals working in the field of coeliac disease and other gluten-mediated disorders, with whom AOECS works closely.

We want to warmly thank ISSCD for their contribution to this project as well as to each and every author that has submitted their posters to this second edition 2023. Their contributions to enhance intelligence and awareness around coeliac disease are priceless, and we invite them to continue their passionate work in this field.

Veronica Rubio
Secretary General, AOECS

ACKNOWLEDGEMENT

COUNTRY & SUPPORTING COELIAC ORGANISATION	TITLE	AUTHORS
Uzbekistan - Page 7 Independent	**Gluten-free products - should we trust the labels: the experience of Uzbekistan.**	Geller SI, Kamilova AT, Abdullaeva DA, Umarnazarova ZE, Shamsutdinova MA, Raxmatov MX
Uzbekistan - Page 8 Independent	**The values of antimicrobial peptides in pediatric newly diagnosed celiac disease.**	Kamilova AT, Geller SI, Umarnazarova ZE, Abdullaeva DA, Azizova GK, Azimova ND, Usmanova KSh
Spain - Page 9 Catalan Coeliac Association (SMAP)	**CD association membership overtime, the Madrid experience.**	Juan I. Serrano-Vela
Germany - Page 10 German Coeliac Society (DZG)	**First in human trial of IMU-856, an orally available epigenetic modulator of barrier regeneration for the treatment of celiac disease.**	Buriánek F, Mihajlović M, Pröbstl D, Peelen E, Fonseca J, Schreieck A, Wirth M, Kehler I, Vitt D, Kohlhof H, Muehler A
Italy - Page 11 Italian Coeliac Association (AIC)	**Circulating microRNAs as novel non-invasive biomarkers of paediatric celiac disease and adherence to gluten-free diet.**	Felli C, Baldassarre A, Uva P, Alisi A, Cangelosi D, Ancinelli M, Caruso M, Paolini A, Montano A, Silano M, Vincentini O, Catassi C, Lionetti E, Gatti S, Ferretti F, Masotti A
Ireland - Page 12 Coeliac Society of Ireland	**An Investigation into the Family Prevalence of Coeliac Disease in Ireland**	Shkrabalyuk Y, Kiernan S, Keogh S, Kennedy A
Ireland - Page 13 Coeliac Society of Ireland	**Nutritional and Cost Comparison of Gluten Free and Gluten Containing Products on an Irish Market**	Kiernan S, Keogh S, Burrowes L
Belarus - Page 14 Harmony without gluten	**Gluten-Free edible packaging for food products**	Ekaterina Lipnitskaja, Tatsiana Savitskaya, Iryna Kimlenka, Dzmitry Hrynshpan

ACKNOWLEDGEMENT

COUNTRY & SUPPORTING COELIAC ORGANISATION	TITLE	AUTHORS
United Kingdom / USA - Page 15 Celiac Disease Foundation	**Physician Management of Celiac Disease: A Comparison of Disease Knowledge, Diagnosis, and Patient Management between Gastroenterologists and Primary Care Physicians in Germany, Italy, Spain, and the United States – Findings from a Real-World Survey**	Niamh Harvey, Hannah Knight, Rachael Meadows, Grace O'Neill, Fatima Dawod, Rina Lukanova, Julia McBeth, Marilyn Geller
United Kingdom / USA - Page 16 Celiac Disease Foundation	**Diagnosing Celiac Disease in the United States of America, Germany, Italy and Spain: Findings from a Real-World Survey**	Fatima Dawod, Hannah Knight, Sophie Barlow, Niamh Harvey, Grace O'Neill, Rina Lukanova, Marilyn Geller
Italy - Page 17 Italian Coeliac Association (AIC)	**Potential treatments alternative to the GFD: patients' expectations**	Susanna Neuhold, Giovanni Bartolone
Italy - Page 18 Italian Coeliac Association (AIC)	**Gluten-free beer from barley malt and wheat: an In vitro study for potential toxicity**	Olimpia Vincentini, Valentina Prota, Francesca De Battistis, Susanna Neuhold, Marco Silano
USA - Page 19 Celiac Disease Foundation	**The Virtual Celiac Symptoms Study: reported symptoms over 12 weeks in adults**	Lisa M. Meckley, Mariel Arvizu, Jessica R. Marden, Sakshi Sethi, Sanjana Sundaresan, Marilyn Geller, Dawn Adams, Edwin Liu, Daniel A. Leffler
USA - Page 20 Celiac Disease Foundation	**The Virtual Celiac Symptoms Study: reported symptoms over 12 weeks in adolescents**	Dawn Adams, Lisa M. Meckley, Mariel Arvizu, Jessica R. Marden, Sakshi Sethi, Elyse Swallow, Marilyn Geller, Edwin Liu, Daniel A. Leffler
Jordan - Page 21 Celiac Care Providers Society	**Assessment of Quality of Life Among Children with Celiac Disease in Jordan**	Laith M. Haj-Ahmad, Abida Alqaisi, Eyad Altamimi

EVALUATION PANEL

This year AOECS wanted to provide authors with additional feedback and words of encouragement from experts in research.

In partnership with the International Society for the Study of Celiac Disease (ISSCD), the AOECS has worked closely with two experts that could evaluate the work received with particular attention to:

- Clarity and accessibility of the information
- Degree of Innovation
- The impact of the projects on the quality of life of coeliac patients

ISSCD is a non-profit organisation of professionals working in the field of coeliac disease and other gluten-mediated disorders. The high level of skills, knowledge, and expertise of the evaluation panel, makes its recommendations particularly valuable for the authors.

All the authors have received a certificate of participation as well as a brief comment from the evaluation panel.

We want to warmly thank the ISSCD experts for their contribution to the AOECS posters evaluation panel, to encourage authors to continue with their research and innovation activity, which is precious for coeliacs and their families.

The scientific papers on display at the 35th Annual Conference in Athens, Greece.

EVALUATION PANEL

MEMBERS OF THE AOECS POSTER EVALUATION PANEL

Robert (Bob) Anderson, MB ChB PhD

Dr. Anderson's research in patients with coeliac disease has helped to cement the role of gluten-reactive T-cells as the fundamental drivers of coeliac disease. His work was the first to show that T-cells specific for gluten circulate in coeliac disease patients' blood confirming coeliac disease is a systemic disease not limited to the gut. His team used these insights to produce the first comprehensive T-cell epitope map of gluten to guide the future development of highly specific food tests, diagnostics, therapies, and "non-toxic" cereals.
Subsequently, Dr. Anderson designed and led the supporting research and clinical development of the first specific T-cell-directed immunotherapy for coeliac disease. Insights from this program revealed the immunological basis for clinical reactions to gluten and provided new opportunities for biopsy-free diagnosis, monitoring, and accelerating drug development for coeliac disease.
Dr. Anderson completed undergraduate medicine and a PhD in New Zealand, and then trained in gastroenterology in Melbourne Australia. His career in coeliac disease combining vaccinology and T-cell immunology began as a post-doctoral scientist at Oxford University in Professor Adrian Hill's and Derek Jewell's labs.
Dr. Anderson returned to Melbourne and established the coeliac disease research program at the Walter and Eliza Hall Institute based on a strong partnership with Coeliac Australia. Dr Anderson transitioned from academic to commercial roles in Australia and then in the United States while developing experimental immunotherapy for coeliac disease. Dr. Anderson is now in clinical practice at Mackay Base Hospital and continues the development of T-cell diagnostics and novel therapies as co-founder and director of Novoviah Pharmaceuticals in Queensland Australia. Dr. Anderson is the current President of the International Society for the Study of Coeliac Disease.

Fabiana Zingone, Associate Professor

Dr. Zingone is an Associate Professor in the Gastroenterology Unit at Azienda Ospedale Università Padova, Italy, specializing in immune-mediated gastrointestinal disorders, with a focus on celiac disease.
After completing her residency at the "Federico II" University of Naples in 2012, she was awarded a Clinical Research Training Fellowship in Gastrointestinal Epidemiology at the University of Nottingham, during which she obtained a Master of Science in Applied Epidemiology. From 2013 to 2017, she conducted various research projects on celiac disease and inflammatory bowel disease at the University of Salerno.
In December 2015, she completed her PhD on the epidemiology of celiac disease.
In June 2017, she was appointed as an Assistant Professor at the Department of Surgery, Oncology, and Gastroenterology at the University of Padua. Dr. Zingone has extensive international collaborations with leading figures in celiac disease research and has received multiple awards for her work in the field.
She currently serves on the boards of the International Society for the Study of Celiac Disease (ISSCD) and the Italian Society of Gastroenterology and Digestive Endoscopy (SIGE).

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Gluten-free products - should we trust the labels: the experience of Uzbekistan

Submitted by: Geller SI [1], Kamilova AT [1], Abdullaeva DA [1], Umarnazarova ZE [1], Shamsutdinova MA [2] , Raxmatov MX [2]

[1]Republican specialized scientific practical medical Center of Pediatrics of Ministry of Health of Republic of Uzbekistan
[2]Sanitary-epidemiological welfare and public health service of Ministry of Health of Republic of Uzbekistan

Introduction

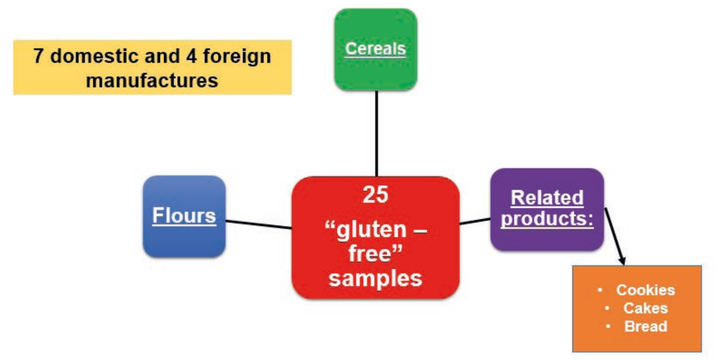
In Uzbekistan, there has been a significant increase in companies supplying products claiming to be gluten-free. Some companies label their products as “gluten-free” despite the absence of accredited laboratories for certification in our country.

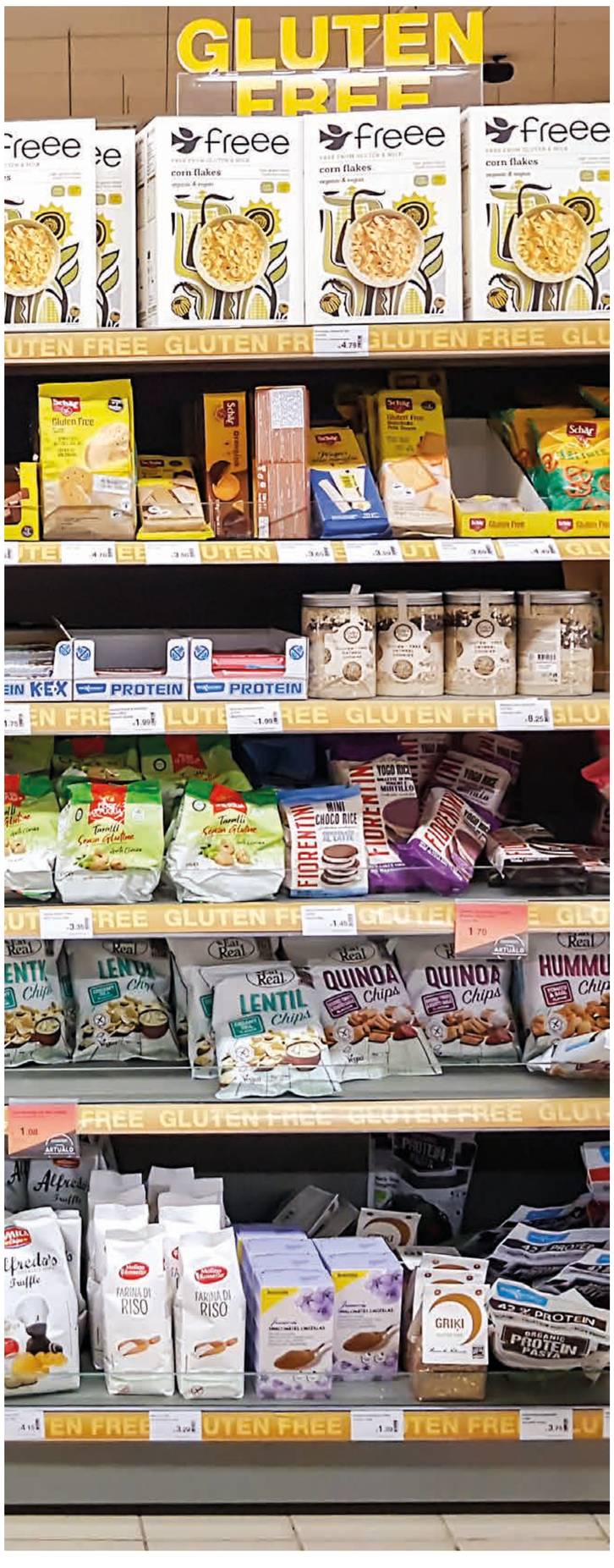
Our aim is to detect the presence of hidden gluten in products produced both in Uzbekistan and abroad.

Method

A total of 25 samples were chosen, as shown in Figure 1. These products were analyzed in duplicate using the ELISA kit RIDASCREEN® Gliadin R7001. All samples were extracted by the patented Cocktail method (R7006/R7016, official method R5-Mendez). A sample was considered gluten-free when the gluten concentration was below 20 mg/kg.

Figure 1





Results

Figure 2

Results of determining the presence of hidden gluten in products that were labeled “gluten-free”

Of 3 positive samples, the gluten content exceeded the threshold

- by fourfold in two samples (rice flour and corn flour), produced in Uzbekistan and labeled as “Gluten-free”
- by 0.94mg in one sample (buckwheat flour), produced in Russia with an indication of potential traces of gluten.

Retest of the rice flour with a different release date, the result was negative, suggesting the possibility of wheat contamination depending on the batch, and highlighting the need for batch-specific testing.

Figure 3

Assessing of manufacturers and the availability of product information on packaging

Out of the eleven manufacturers 45.4% conducted their sales primarily through social networks without an official point of sale. Moreover, 56.5% of their products lacked information about the series and batch numbers, and 36.0% were missing packaging including information about the manufacturer, production date, and batch number.

Conclusion

1. It is crucial to implement a mandatory quality control system for gluten-free products in Uzbekistan.
2. It is necessary to issue an official certificate taking into account international experience.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

The values of antimicrobial peptides in pediatric newly diagnosed celiac disease

Submitted by: Kamilova AT, Geller SI, Umarnazarova ZE, Abdullaeva DA, Azizova GK, Azimova ND, Usmanova KSh.

Republican Specialized Scientific Practice Medical Center of Pediatrics Ministry of health of Uzbekistan

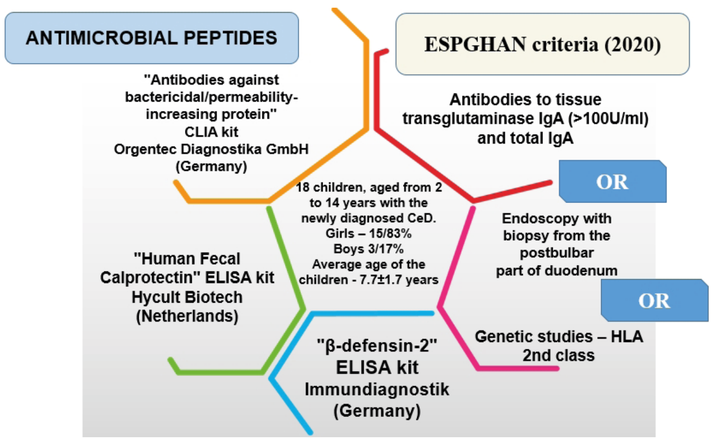
Introduction

Celiac disease (CeD) is an autoimmune disease characterized by certain serological and histological changes caused by the ingestion of gluten in genetically susceptible individuals.[1]

Our aim is to determine antimicrobial peptides - fecal β-defensin-2, fecal calprotectin (FC) and antibodies against bactericidal/permeability increasing protein (anti-BPI) and their relation with intestinal permeability of children with CeD.

Method

We examined 18 children, aged from 2 to 14 years with the newly diagnosed celiac disease. The control group consisted of 20 healthy children of the appropriate age.



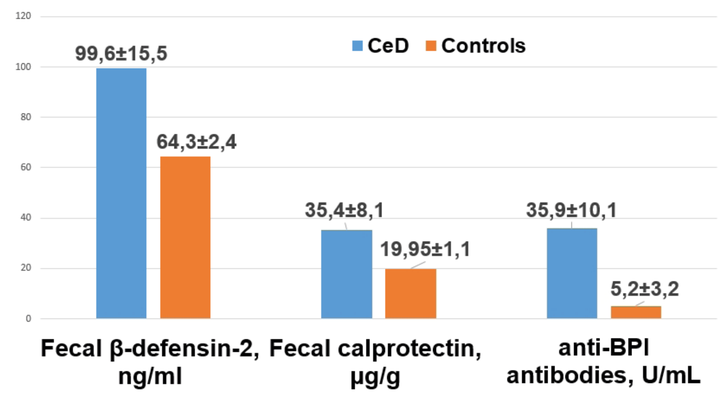
Results

In celiac disease, the integrity of the intestinal barrier was negative (-0.1±0.004 o.u.) compared with the control group (0.3±0.02 o.u, $p<0.05$). According to Fig.1, in patients with celiac disease:

- β-defensin-2 level increased 1.5-fold in coprofiltrates compared to the control ($p<0.05$).
- fecal calprotectin level was 1.7 times higher than the control levels ($p<0.05$).
- The concentration of anti-BPI antibodies in the CeD exceeded 7 times to the norm ($p<0.001$).

Figure 1

Level of antimicro-bial peptides in children with celiac disease.

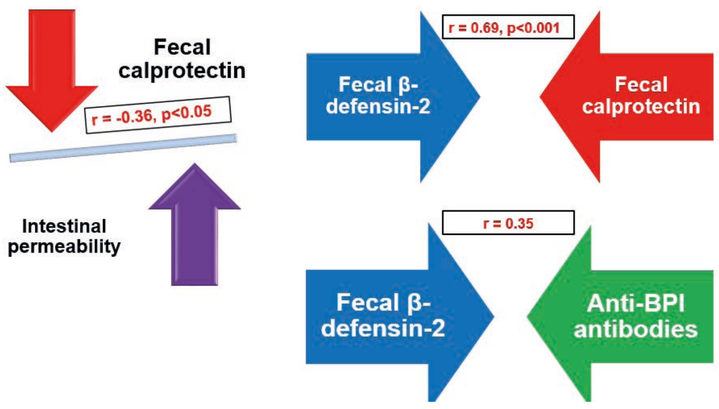


In children with CeD:

- Fecal calprotectin was inversely correlated with intestinal permeability ($r = -0.36$, $p<0.05$).
- Noteworthy is the direct correlation between the values of fecal β-defensin-2 and fecal calprotectin ($r = 0.69$, $p<0.001$).

Figure 2

Correlation relationships of antimicrobial peptides.



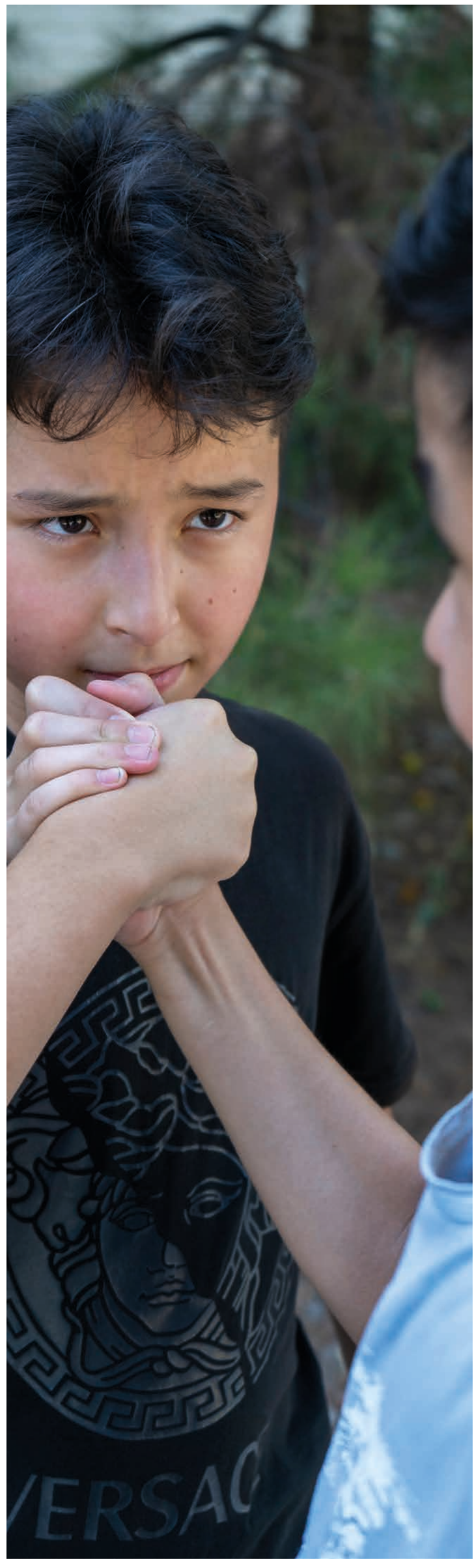
There was direct, but weak relationship between fecal β-defensin-2 and anti-BPI antibodies ($r = 0.35$).

Conclusion

1. Significant elevations in fecal calprotectin and β-defensin-2 were observed in children with celiac disease. These findings showed a negative effect of increased fecal calprotectin on heightened intestinal permeability.
2. A highly reliable direct correlation was found between fecal calprotectin and β-defensin-2 values, emphasizing the important role of the innate intestinal immune system in recognizing inflammation and heightened intestinal permeability in children with celiac disease

References

1. Fasano A, Catassi C. Celiac disease. N Engl J Med. 2012; 367: 2419-26



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

CD association membership overtime, the Madrid experience

Submitted by: Juan I. Serrano-Vela

Coeliac Disease & Gluten Sensitivity Association Madrid

Introduction

The only treatment for coeliac disease (CD) is a strict long-life gluten free diet (GFD). Periodical medical supervision and the role of CD associations are essential for the well-being of patients[1].

A national official registry of patients with CD does not exist in Spain. Results from different worldwide epidemiological studies conclude that the prevalence of CD has increased over the last four decades to 1-2% and is more frequent in females (2:1); nearly 70% of cases remain undetected. Both children and adults may develop the condition and more cases are diagnosed over than below 20 years old today[1].

In Spain, a study conducted in Catalonia estimated a prevalence of 1/71 in children and 1/357 in adults, with a female to male ratio of 2.5:1[2], and the Spanish Registry of Pediatric CD (REPAC) reported 61% of females[3]. Previous REPAC results had found the highest incidence in Europe: 7.9 new cases in 100,000 subjects per year (4).

Objective

The objective of the present work is to describe the evolution of membership to the Coeliac Disease & Gluten Sensitivity Association Madrid (CDAM) since 1990 to 2022 an discuss the trends observed compared to the epidemiological data available.

Method and materials

Observational study based on membership registry of CDAM since January 1990 to December 2022 including the age at diagnosis, date of membership and sex of 18,446 consecutive cases. Number of new members and cumulative active members per year was extracted. Sex and age ratios, and the timeframe from diagnosis to membership, were calculated. Pediatric ages were defined below 15 years old.

Results

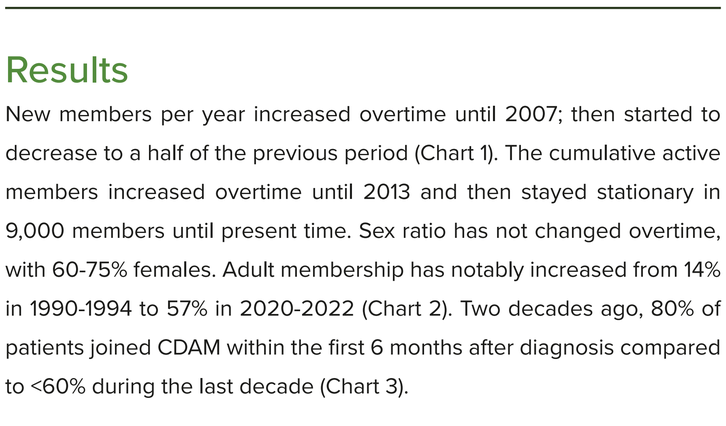
New members per year increased overtime until 2007; then started to decrease to a half of the previous period (Chart 1). The cumulative active members increased overtime until 2013 and then stayed stationary in 9,000 members until present time. Sex ratio has not changed overtime, with 60-75% females. Adult membership has notably increased from 14% in 1990-1994 to 57% in 2020-2022 (Chart 2). Two decades ago, 80% of patients joined CDAM within the first 6 months after diagnosis compared to <60% during the last decade (Chart 3).

Discussion/Conclusion

Sex ratio and age at diagnosis observed among CDAM members overtime reflect the trends shown by epidemiological studies. However, CDAM membership does not parallel the increasing trend in CD diagnosis. This prompt the necessity to discuss the role of CD associations and the reasons why newly diagnosed patients rely less and less on these support groups.

Chart 1

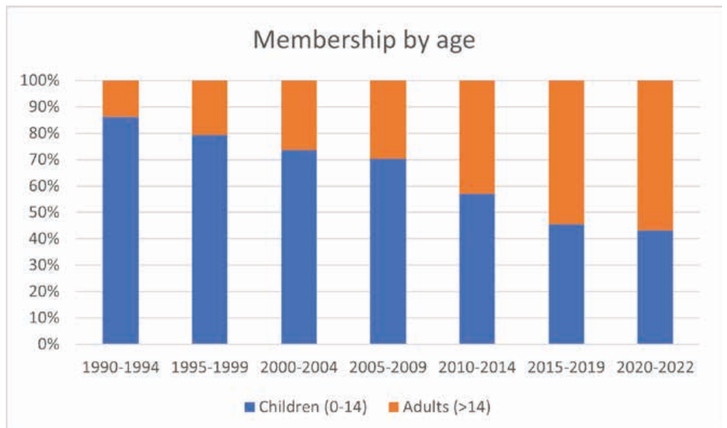
New members per year



Number of patients registered in the Coeliac Disease & Gluten Sensitivity Association Madrid (Spain) every year from 1990 to 2022

Chart 2

Membership by age at diagnosis



Proportion of pediatric (0-14 years old) vs. adult (>14 years old) patients registered in the Coeliac Disease & Gluten Sensitivity Association Madrid since 1990 to 2022.

Chart 3

Membership delay (1990-2022)

Acknowledgements

I would like to thank SMAP – Celiacs Catalunya for the supporting letter for this poster and specially Esther Roger and Cristóbal Pérez for their comments and suggestions.

References

1. Catassi C, Verdu EF, Bai JC, Lionetti E. Lancet. 2022; 399(10344):2413-26.
2. Mariné M, Farre C, Alsina M, Vilar P, Cortijo M, Salas A, et al. Aliment Pharmacol Ther. 2011; 33(4):477-86.
3. Pérez Solís D, Cilleruelo Pascual ML, Ochoa Sangrador C, García Burriel JI, Sánchez-Valverde Visus F, Eizaguirre Arocena FJ, et al. J Pediatr Gastroenterol Nutr. 2022; 74(6):805-11.
4. Cilleruelo ML, Roman-Riechmann E, Sanchez-Valverde F, Donat E, Manuel-Ramos J, Martín-Orte E, et al. J Pediatr Gastroenterol Nutr. 2014; 59(4):522-6.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

First in human trial of IMU-856, an orally available epigenetic modulator of barrier regeneration for the treatment of celiac disease

Submitted by: Buriánek F [1], Mihajlović M [2], Pröbstl D [1], Peelen E [1], Fonseca J [1], Schreieck A[1], Wirth M [1], Kehler I [1], Vitt D [1], Kohlhof H [1], Muehler A[1]

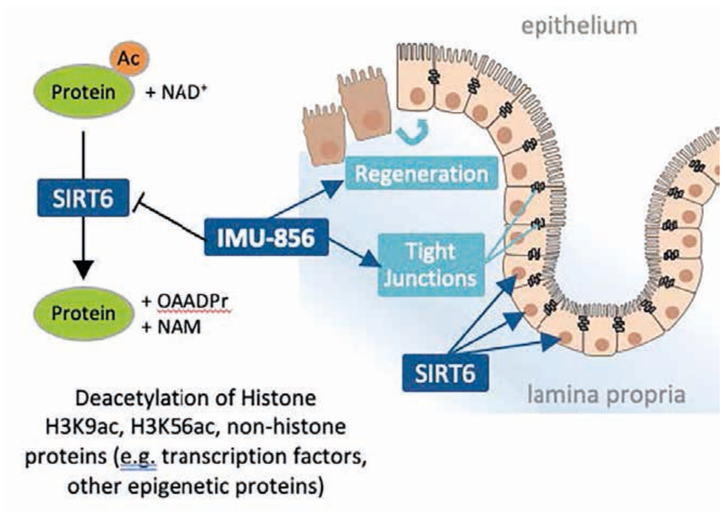
[1]Immunic AG, Germany, [2]Formerly Immunic AG, Germany

Introduction

IMU-856 is an orally available, systemically acting and highly selective small molecule modulator that targets SIRT6 (Sirtuin 6), a protein which serves as a transcriptional regulator of intestinal barrier function and regeneration of bowel epithelium. Furthermore, in preclinical studies, the mechanism of IMU-856 has been shown to not affect the status of immune cells. IMU-856´s mechanism of action may present a new approach to treat celiac disease and other intestinal barrier function-associated diseases.

Figure 1

SIRT6 is a NAD+-dependent histone/nonhistone protein deacetylase and ADP-ribosyltransferase. IMU-856 improves regeneration and appropriate function of the gut lining by supporting self-renewal and differentiation processes.

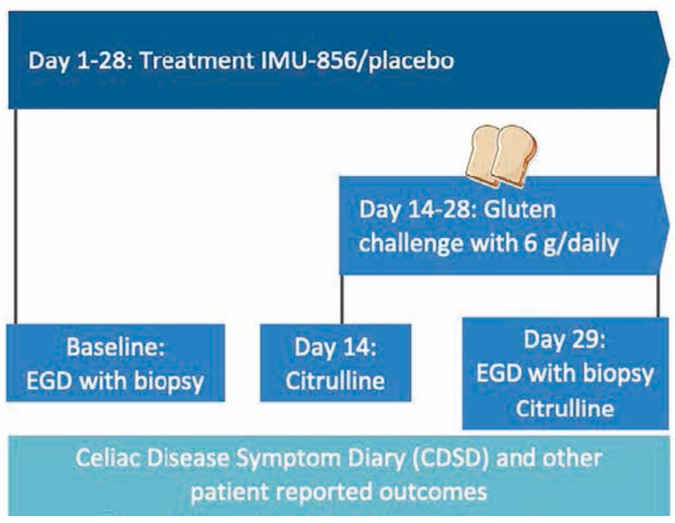


Method

This was a first-in-human, double-blind, randomized, placebo-controlled clinical trial of IMU-856 in healthy volunteers and patients with celiac disease. In the single and multiple ascending dose part of this clinical trial, healthy human subjects were randomized to either placebo or active treatment with different dose levels of IMU-856 or placebo.

Figure 2

Flow chart of IMU-856 Phase 1b trial in patients with celiac disease. N enrolled/completed = 43/35 patients (IMU-856: N=29/24).



Phase 1b was designed to assess the safety and tolerability of 28-days of dosing of IMU-856 at two different dose levels (80mg + 160mg once daily) in patients with celiac disease during periods of gluten-free diet and a 15-days gluten challenge (6g gluten/daily). Secondary objectives included pharmacokinetics as well as histology, symptoms, and noninvasive biomarkers.

Results

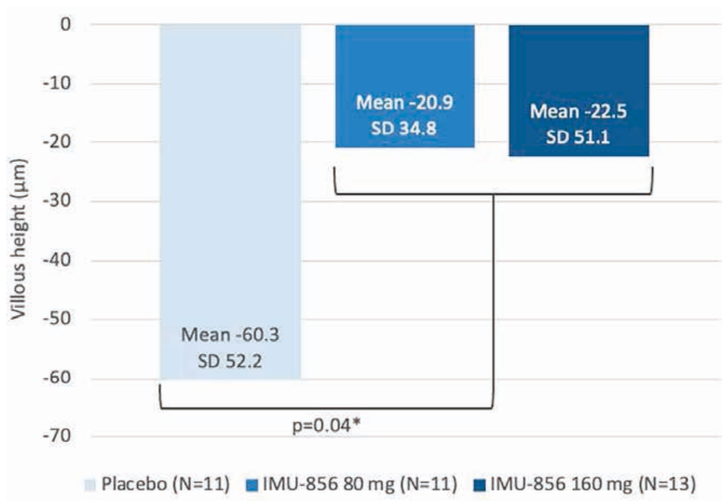
IMU-856 was safe and well-tolerated with a benign adverse event profile and with pharmacokinetics that allow once-daily dosing.

Treatment with IMU-856 showed positive effects in the four main dimensions of clinical outcome in celiac disease patients:

- Protection against gluten induced intestinal damage.
- Improved enterocyte health and function.
- Enhanced nutrient absorption.
- Reduction of gluten-induced increase in symptom severity.

Figure 3

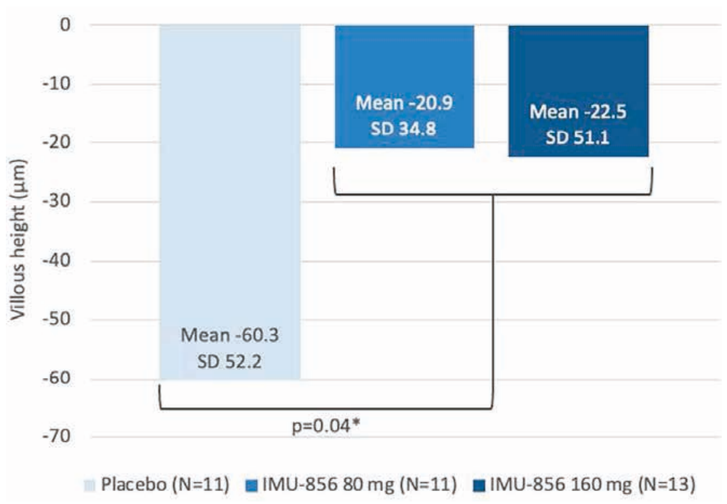
IMU-856 protected against gluten-induced intestinal epithelial damage by significantly reducing the decrease in villous height as compared to placebo.



Wilcoxon Two-Sample Test comparison between pooled IMU-856 groups and placebo, performed as post-hoc exploratory statistical analysis.

Figure 4

IMU-856 improved plasma citrulline levels (biomarker for enterocyte health) already within the first 2 weeks prior to gluten challenge. This improvement was further maintained throughout the trial including a 15-day gluten challenge.



Number of Patients: Placebo: N=13 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 80 mg: N=14 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 160 mg: N=13 for Mean Change Baseline to Day 14, N=13 for Mean Change Baseline to Day 29.

Figure 5

IMU-856 showed enhanced nutrient absorption as exemplified by Vitamin B12 levels.

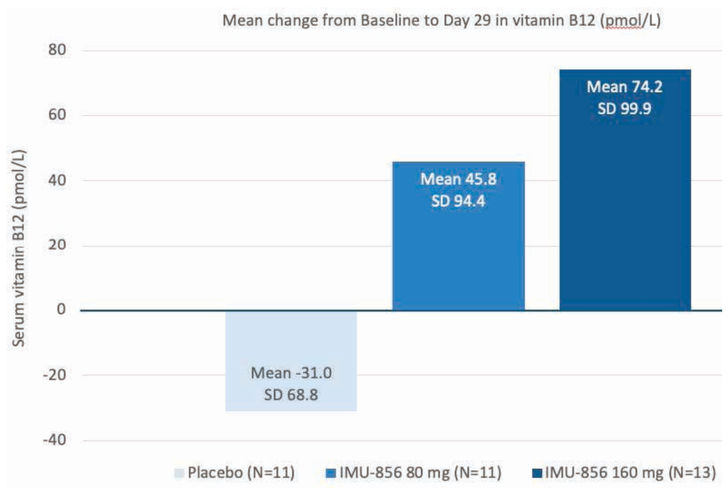
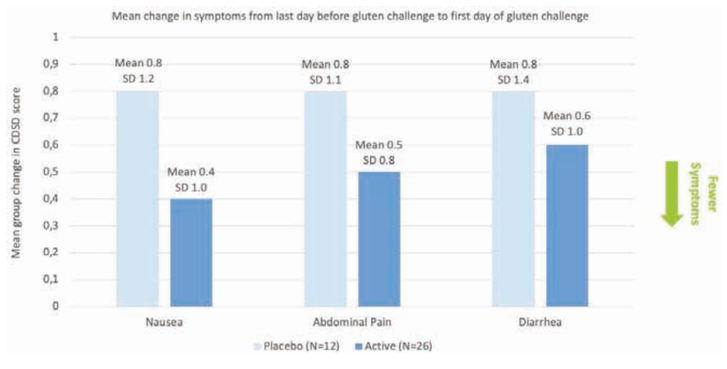


Figure 6

IMU-856 reduced gluteninduced acute symptoms (from left to right: nausea, abdominal pain, diarrhea) as assessed by Celiac Disease Symptom Diary (CDSD). Light blue: Placebo. Medium blue: pooled active.



Conclusion

IMU-856 is a highly selective and potent epigenetic modulator, showing first signals of improving the intestinal barrier integrity in patients with celiac disease undergoing a gluten challenge. IMU-856 was safe and well-tolerated with a benign adverse event profile and with pharmacokinetics that allow once-daily dosing. Phase 1b provided proof of concept data for IMU-856 in patients with celiac disease during periods of gluten-free diet and 15-days gluten challenge, setting stage for a potential first-in-class oral celiac disease therapy.

IMU-856 may offer extensive potential beyond celiac disease in other diseases, both intestinal and systemic, with compromised intestinal barrier integrity.

Abbreviations

- *EGD: esophagogastroduodenoscopy*
- *SD: standard deviation*
- *IMP: investigational medicinal product*

Acknowledgments

All authors are/were employed by Immunic AG.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Circulating microRNAs as novel non-invasive biomarkers of paediatric celiac disease and adherence to gluten-free diet

Submitted by: Fondazione Celiachia Onlus, and Andrea Masotti [1]

[1]*Bambino Gesù Children's Hospital, IRCCS, Research Laboratories, Rome, Italy*

Introduction

The gold standard for the diagnosis of paediatric CD is a combination of serological tests and duodenal biopsy. In 2012 and in 2020, the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines suggested the possibility to avoid the biopsy only in adolescents and children who present HLA-DQ2/DQ8 haplotype, positivity to EMA-IgA, and levels of TGA-IgA ten-fold upper the limit of normal (ULN)[1, 2]. Thus, a diagnostic test that totally excludes an invasive approach has not been discovered so far and the discovery of novel biological markers would represent an undoubted advantage for the diagnosis of CD (especially in doubt cases) and prognostic evaluation. MiRNAs are highly stable and tissue-specific and their expression profile may constitute a specific signature of disease[3]. Circulating miRNAs are highly stable, resistant to RNases digestion, extreme pH, high temperatures, extended storage, and multiple freeze–thaw cycles. Their presence in biological fluids (i.e., serum, plasma, saliva, urine) provides the opportunity to employ circulating miRNAs as new non-invasive biomarkers.

Circulating miRNAs can represent also a valid method for effectively monitoring the response to GFD in celiac disease patients.

In this context, the Celiac Foundation funded a project entitled "Circulating MicroRNA signatures for the identification of new potential diagnostic biomarkers of Celiac Disease and the response to gluten-free diet".

The aim of this project was to find novel biomarkers for the diagnosis of Celiac Disease and to monitor the adherence to a gluten-free diet.

Method

In our prospective observational study, we examined the expression of circulating miRNAs in a cohort of CD patients (both at diagnosis and on gluten-free diet, respectively referred as CD and GFD) compared to healthy controls. By small RNA-Seq we discovered a set of circulating miRNAs that were further validated by qPCR with specific assays.

Study participants

This study was an observational prospective cohort study with a control group. A total number of 120 subjects ranging from 3 to 15 years belonging to three groups: CD (n=40), CD on GFD for more than six months (n=40), and CTRL (n=40) that were consecutively recruited at the Bambino Gesù Children's Hospital of Rome at the Hepatology, Gastroenterology and Nutrition Department from January 2014 to December 2018.

Discovery and validation of circulating miRNAs by RNA Sequencing and qPCR

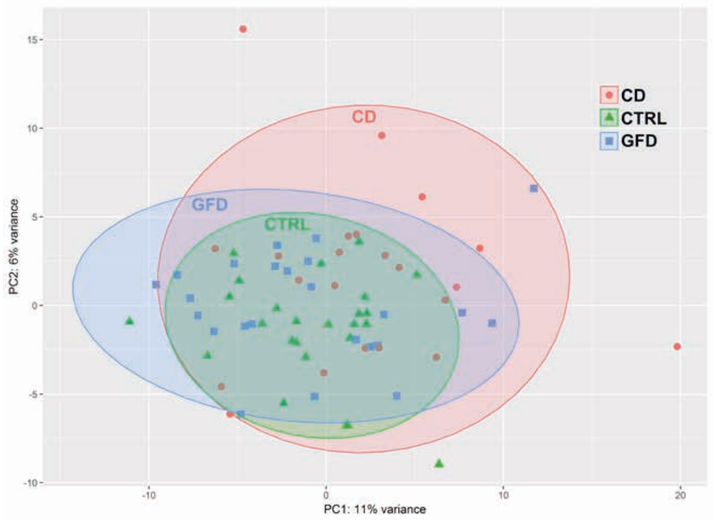
Circulating miRNAs were sequenced by using a small RNA sequencing protocol. Deregulated miRNAs detected by RNA sequencing were validated in the independent set by qPCR.

Analysis

All variables were expressed as mean ± standard deviation (SD), whereas qualitative data as percentage. Comparison of the mean among the groups was performed using ANOVA or non-parametric tests or chi-square (contingency tables). ANOVA has been applied for data (i.e., age) passing normality test (D'Agostino-Pearson $p>0.05$). Where normality was not verified (i.e., BMI and IgA) the non-parametric Kruskal-Wallis test has been applied. Post-hoc analysis was carried out by Tukey method. Receiver operating characteristic (ROC) and area under the curve (AUC) was determined to establish sensitivity and specificity of the relevant miRNAs.

Chart 1

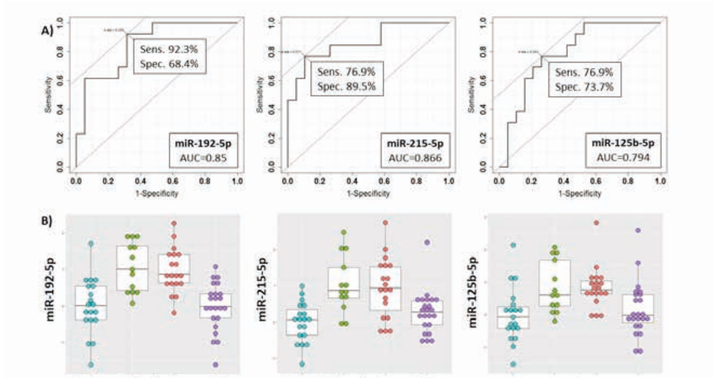
Principal component analysis (PCA)



Principal component analysis (PCA) of RNA-Seq data for CTRL, CD and GFD groups. The colored regions represent the distribution of data for each category, whereas each symbol represents a patient.

Chart 2

ROC curves and DotPlots



ROC curves for the discrimination of borderline CD patients (CD-bord) compared to CTRL (A) and DotPlots (B) of miR-192-5p, miR-215-5p and miR-125b-5p for the four groups of patients (CTRL, CD-bord, CD and GFD). The asterisk indicates a significant difference ($p<0.001$). ROC curves of the model obtained by using the three miRNAs (i.e., miR-192-5p, miR-215-5p and miR-125b-5p) and the two-fold cross-validation for the diagnosis of CD patients compared to controls.

Results

From qPCR data we obtained two lists of 30 significantly ($p<0.05$) dysregulated circulating miRNAs in CD patients compared to CTRL and 30 miRNAs when compared to GFD. To obtain a list of relevant miRNAs, we extracted only those miRNAs circulating in CD patients and modulated either compared to CTRL or to GFD patients. A total number of 13 miRNAs were shared between these two groups, eight miRNAs were upregulated (i.e., miR-486-5p, miR-194-5p, miR-885-5p, miR-99a-5p, miR-215-5p, miR-363-3p, miR-125b-5p, miR-192-5p) and five were donwregulated (i.e., miR-30c-5p, miR-326, miR-339-5p, miR-151a-5p and miR-103a-3p). We found that out of the 13 miRNAs able to discriminate the three groups (i.e., CD, GFD and controls), three of them, namely miR-192-5p, miR-215-5p and miR-125b-5p (alone or in combination), were able to discriminate these three groups with high accuracy and specificity. In particular, miR-192-5p reached a sensitivity of 62.5% and a specificity of 94.7% (AUC=0.854), miR-215-5p a sensitivity of 71.9% and a specificity of 89.5% (AUC=0.842) and miR-125b-5p a sensitivity of 78.1% and a specificity of 78.9% (AUC=0.803). As a further investigation, we assessed if these three miRNAs are useful also to predict CD in those cases with an uncertain diagnosis (i.e., patients with levels of TGA-IgA below 10 times the limit of normal). We found that miR-192-5p reached a sensitivity of 92.3% and a specificity of 68.4% (AUC=0.85), miR-215-5p a sensitivity of 76.9% and a specificity of 89.5% (AUC=0.866) and miR-125b-5p a sensitivity of 76.9% and a specificity of 73.7% (AUC=0.794).

Conclusion

Our data strongly support the use of circulating miRNAs as a supplementary tool for the diagnosis of celiac disease without recurring to intestinal biopsy, a procedure that, especially for children, may result quite invasive and not very tolerated.

We have identified three valuable novel non-invasive biomarkers that alone or in combination may be employed successfully in the clinical practice for the diagnosis and follow-up of pediatric CD patients.

References

1. Husby, S., Koletzko, S., Korponay-Szabo, I.R., Mearin, M.L., Phillips, A., Shamir, R., Troncone, R., et al. (2012). European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J. Pediatr. Gastroenterol. Nutr. 54, 136-160
2. Husby, S., Koletzko, S., Korponay-Szabo, I., Kurppa, K., Mearin, M.L., Ribes-Koninckx, C., Shamir, R., et al. (2020). European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. J. Pediatr. Gastroenterol. Nutr. 70, 141-156
3. Mitchell, P.S., Parkin, R.K., Kroh, E.M., Fritz, B.R., Wyman, S.K., Pogosova-Agadjanyan, E.L., Peterson, A., et al. (2008). Circulating microRNAs as stable blood-based markers for cancer detection. Proc. Natl. Acad. Sci. U. S. A. 105, 10513-10518

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

An Investigation into the Family Prevalence of Coeliac Disease in Ireland

Submitted by: Shkrabalyuk Y [1,2], Kiernan S [3], Keogh S [3], Kennedy A [1]

[1]Technological University Dublin, [2]Trinity College Dublin, [3]Coeliac Society of Ireland

Introduction

Around 1-2% of the global population, and 0.5-1% of Ireland's population[1] are diagnosed with coeliac disease, but many remain undiagnosed.

International and Irish clinical guidelines recommend that "high-risk" populations, such as first-degree relatives and those with co-occurring conditions are screened for coeliac disease[2,3].

The objective of this study was to determine the rate of testing and diagnosis of coeliac disease (CD) amongst first-degree relatives (FDRs) of individuals with CD in Ireland, and hence adherence to clinical guidelines, and investigate the percentage of FDRs with conditions related to CD.

Method

2.952 active adult members of the Coeliac Society of Ireland were invited to participate in an online anonymous survey investigating how many of their FDRs were tested and/or diagnosed with CD.

Data was collected over two weeks and analysed using Microsoft Excel and IBM SPSS.

Analysis

Demographic data and testing and/or diagnosis of CD data or a co-occurring condition in FDRs was analysed using descriptive statistics. Differences were assessed using chi-square tests.

Chart 1

Coeliac Disease Screening and Diagnosis Rates Among First-Degree

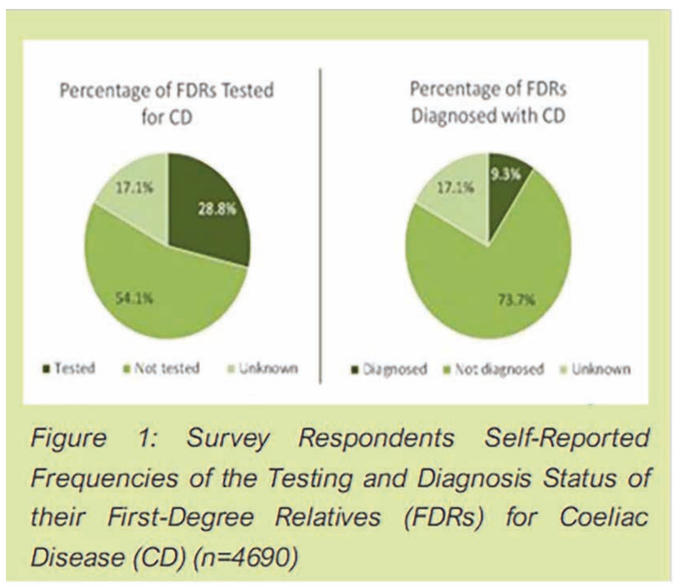


Figure 1: Survey Respondents Self-Reported Frequencies of the Testing and Diagnosis Status of their First-Degree Relatives (FDRs) for Coeliac Disease (CD) (n=4690)

Chart 2

Co-occurring Conditions in First-Degree Relatives (n=4.690)

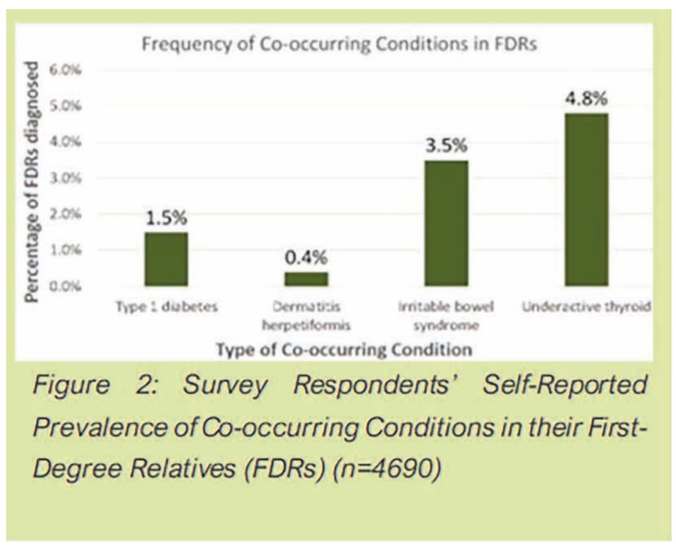


Figure 2: Survey Respondents' Self-Reported Prevalence of Co-occurring Conditions in their First-Degree Relatives (FDRs) (n=4690)

Results

Amongst 709 respondents, 81% (n=574) were 35-74 years of age and 77% (n=543) were female. On average, 28.8% (n=1353) of FDRs were tested and 9.3% (n=435) were diagnosed with CD.

On average, 28.8% (n=1353) of FDRs were tested and 9.3% (n=435) were diagnosed with CD.

Children were the most likely group of FDRs to be tested and/or diagnosed compared to other FDRs.

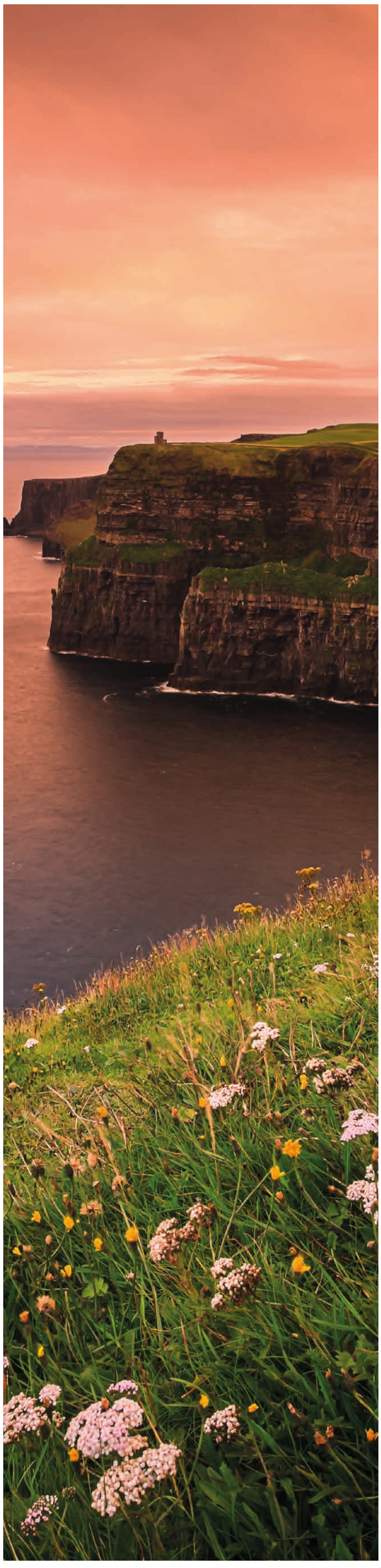
A significant positive association was found between female respondents and the chance that a FDR was tested (P=0.012). Underactive thyroid was the most reported co-occurring condition in FDRs (4.8%; n=227).

Conclusion

- Many FDRs of an individual with CD are not currently tested for CD in Ireland.
- The rate of diagnosis of CD is higher amongst FDRs than the general population[4,5] through the HLA-DQ2/DQ8 alleles, which can be passed on genetically[6].
- However, many cases may still be undiagnosed due to the lack of implementation of the current guidance around testing FDRs, many cases may still be undiagnosed due to the lack of implementation of the current guidance around testing FDRs.

References

1. Singh P, Arora A, Strand TA, Leffler DA, CatassiC, Green PH, et al. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. Clinical Gastroenterology and Hepatology. 2018;16(6):823-36.e2.
2. Russel A, Shanahan E, Quigley E. Diagnosis and Management of Adult Coeliac Disease [Internet]. ICGP Quality in Practice Committee; 2015 [cited 2021 Nov 4]. Available from: https://www.icgp.ie/speck/properties/asset/asset.cfm?type=LibraryAsset&id=B06470E0-E7BD-1996-2FB2139E0E0F1F20&property=asset&revision=tip&disposition=attachment&app=icgp&filename=ICGP_QRG_Coeliac_Disease.pdf
3. National Institute for Health and Clinical Excellence. Coeliac Disease: recognition, assessment and management [Internet]. [London]: NICE; 2015 [cited 2021 Nov 4]. Available from: https://www.nice.org.uk/guidance/ng20/resources/coeliac-disease-recognition-assessment-and-management-pdf-1837325178565
4. Lopes LHC, Muniz JG, Oliveira RP, Sdepanian VL. Celiac Disease in Brazilian Firstdegree Relatives: The Odds Are Five Times Greater for HLA DQ2 Homozygous. J Pediatr Gastroenterol Nutr. 2019;68(5):e77-e80.
5. Shahraki T, Hill I. Prevalence of celiac disease in first-degree relative of children in Sistan and Baluchestan province (Iran). Journal of Digestive Diseases. 2016;17(10):685-91
6. Cecilio LA, Bonatto MW. THE PREVALENCE OF HLA DQ2 AND DQ8 IN PATIENTS WITH CELIAC DISEASE, IN FAMILY AND IN GENERAL POPULATION. ABCD Arquivos Brasileiros de Cirurgia Digestiva (São Paulo). 2015;28(3):183-5.



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Nutritional and Cost Comparison of Gluten Free and Gluten Containing Products on an Irish Market

Submitted by: Kiernan S, Keogh S, Burrowes L

Coeliac Society of Ireland

Introduction

Coeliac disease is an autoimmune condition which requires people to follow a lifelong gluten free diet.

Gluten is found in wheat and other commonly used cereals which are seen in most staple food products such as bread, pasta, breakfast cereals, crackers, and bread mixes.

Gluten-free products are becoming more available but are more expensive[1] than gluten-containing products. Several reports suggest gluten-free products may be nutritionally inferior to gluten-containing products [2-4].

The aim of this study is to compare cost and nutrient content of GF and GC foods on the Irish market.

Method

Cost and nutritional label data for GF and GC foods was collected in five Irish supermarkets with largest market share.

Staple foods were selected: bread, pasta, ready-to-eat breakfast cereals, bread mixes and crackers.

Fat, saturates, carbohydrate, sugar, fibre, protein, salt, and cost were compared per 100g between GF and GC.

Chart 1

Cost Difference Between Gluten and GF Foods

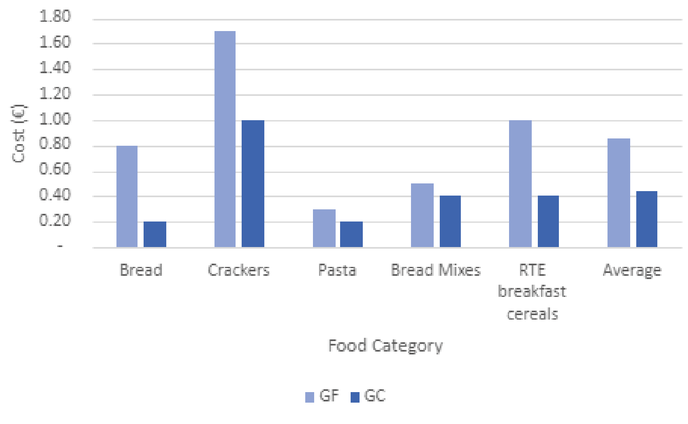


Chart 2

Energy Difference Between Gluten and GF Foods

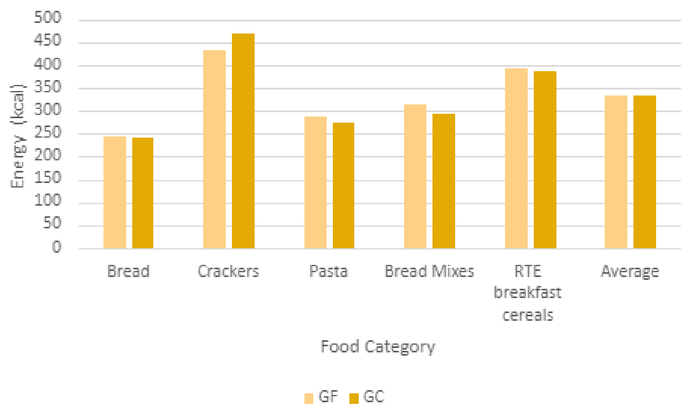
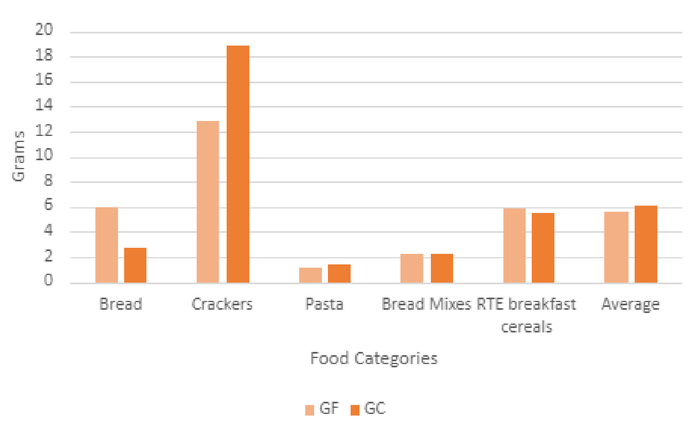


Chart 3

Fat Difference Between Gluten and GF Foods



Results

On average, GF products cost €0.42 more than GC products per 100g.

GF bread was €0.60 more expensive than GC bread per 100g. GF oats were 79% more expensive than GC oats.

Little difference in nutrient value between GF and GC products was found when comparing averages of all products combined.

Nutritional disparities were found when nutrient contents were compared within categories.

GF brown bread had 23% more kilocalories than GC bread. Saturates were 39% higher in GF breads.

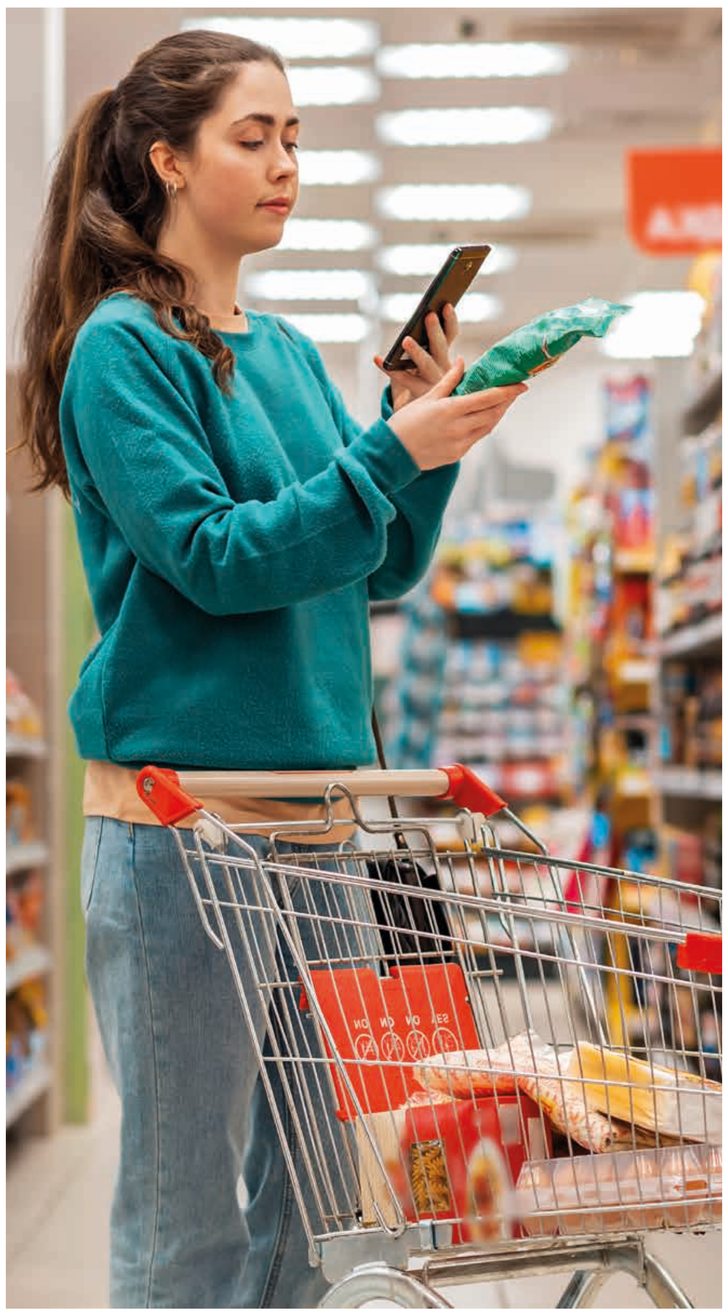
Nutritional discrepancies are further highlighted in subcategories e.g., GF crackers had 48% more fat than GC and flavoured crackers GF had 148% more fat than GC.

Conclusion

- There is a clear increase in cost for GF staple foods which may impact patients with CD on lower incomes.
- Although nutrient contents of GF foods are on average similar to GC foods, large differences within categories exist which may have implications for patients with coeliac disease who have restricted diets.
- There is no nutritional advantage to following a gluten free diet over a gluten containing diet, unless deemed necessary for medical reasons.
- Cost may be a hindrance in choice and adherence to the gluten free diet. This needs to be addressed to optimise adherence to the diet and overall health.

References

1. Hopkins S, Soon JM. Nutritional quality, cost, and availability of gluten-free food in England. British Food Journal. 2019;121(11):2867-82.
2. Kulai T, Rashid M. Assessment of Nutritional Adequacy of Packaged Gluten-free Food Products. (1486-3847 (Print)).
3. Fry L, Madden AA-O, Fallaize RA-O. An investigation into the nutritional composition and cost of gluten-free versus regular food products in the UK. (1365-277X (Electronic)).
4. Miranda J, Lasa A Fau - Bustamante MA, Bustamante Ma Fau - Churruca I, Churruca I Fau - Simon E, Simon E. Nutritional differences between a gluten-free diet and a diet containing equivalent products with gluten. (1573-9104 (Electronic)).



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Gluten-Free edible packaging for food products

Submitted by: Ekaterina Lipnitskaja [1], Tatsiana Savitskaya [2], Dzmitry Hrynshpan [2], Iryna Kimlenka [2], Sviatlana Makarevich [2], Nadegda Tsygankova [2]

[1] Presenting author, [2] Belarusian State University

Introduction

Packaging waste is a leading threat to the environment today. The problem is exacerbated by the fact that the responsible synthetic polymers are not subject to physical, chemical and biological degradation. Landfill treatment and incineration remain the most popular path in treating polymer waste leaving recycling with its high economic cost behind. These conventional methods of disposing plastic waste have irreversible impacts for people and ecosystem.

We have not yet come up with the cost-effective way of turning polymer waste into biogas. We are not able to convert disposable plates into reusable ones, and the produce made from the recycled materials falls short of superior quality.

Today, we cannot afford to solely rely on biodegradable polymer materials, made, for instance, using cellulose and its derivatives, chitin, chitosan, polyvinyl alcohol, etc. This is not just because they are more expensive than polyethylene, but just because their production process is significant detriment to the environment.

Biodegradable composite plastic consisting of synthetic and natural polymers sounds like a good idea but so far it hasn't been a very successful one. It is rather danger because of microplastic (less than 5 microns pieces of synthetic polymers with long life).

Method

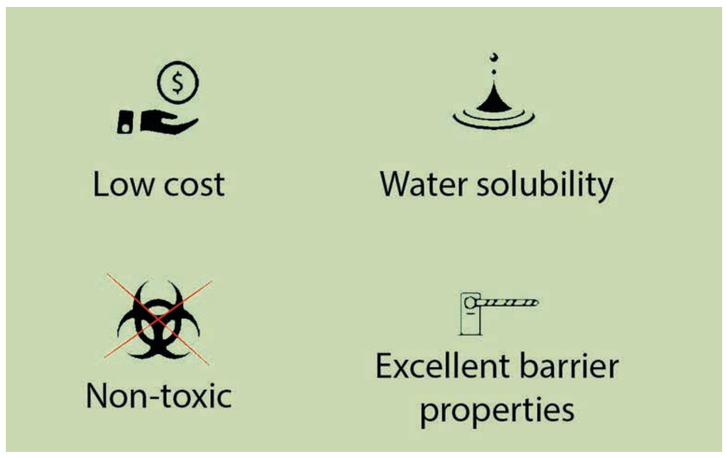
We believe that one of the best option to satisfy the customers' interests and at the same time comply with the EU Directives is to establish a full-scale production of a new type of packaging - edible films and coatings that are completely degradable by the human and animal body.

Edible films and coatings are the only kind of biodegradable polymer packaging that does not require individual collection and certain conditions for recycling.

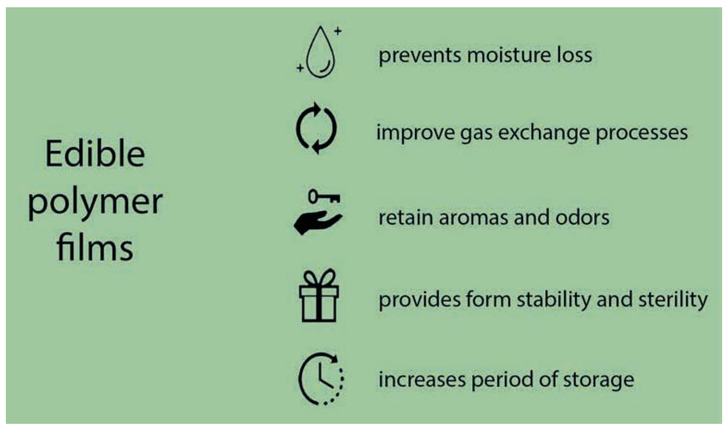
Edible packaging is a polymer material biodegradable at the molecular l evel that is disintegrated by oxidation and hydrolysis conducted by intracellular and extracellular ferments (endo- and exoenzymes) present in the digestive system of the human and animal body. It is a candidate to replace the microbial breakdown process that utilizes bacteria and fungi.

Analysis

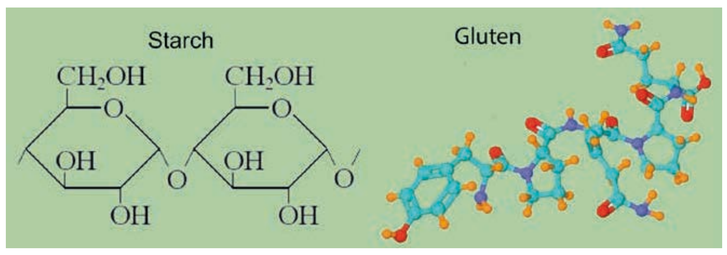
Starch, on the basis of which biodegradable films are created, being a natural polysaccharide, has a number of unique properties.



Edible films can also be obtained from various other polymers, including gluten. But some (1 % of the world's population) have gluten intolerance - coeliac disease. People with diagnosed coeliac disease require a lifelong strictly GF diet. In addition to coeliac disease patients, it has been hypothesized that a substantial proportion of the population may be gluten intolerant (non-coeliac gluten sensitivity), and could benefit from reducing gluten in their diet.



To solve this problem, we can offer edible films based on corn, not wheat. There is no gluten in the protein composition of corn starch. So, corn starch is the optimal polymer for the development of the casting solutions recipes suitable for producing packaging films. The development of gluten-free edible films and coatings can become one of the effective methods for increasing the shelf life of packaged gluten-free food. Edible packaging is a polymer material biodegradable at the molecular level that is disintegrated by oxidation and hydrolysis conducted by intracellular and extracellular ferments present in the digestive system of the human and animal body. It is a candidate to replace the microbial breakdown process that utilizes bacteria and fungi.



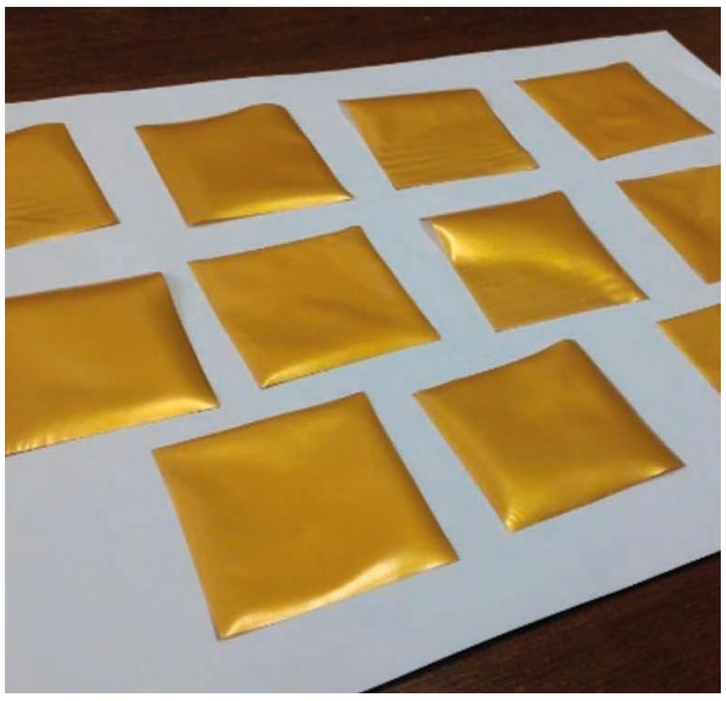
Results and Conclusion

Edible films and coatings based on corn starch have been developed at the Belarusian State University. The marine polymers, plant and fruit extracts with antioxidant and antimicrobial properties are the ingredients of edible packaging as well. The technology has laboratory and pilot level.

We proposed edible films for sticky candy (toffee, souffe, Turkish delight, etc.) wrapping, portion packaging for honey, tartlets for baking cakes, cupcakes, spices, for frying meet and fish, etc. Thin oral strips quickly dissolve in the mouth and contains vitamins, minerals, bioactive substances. These films allow to provide a new way of introducing the active ingredient into the human and animal body - transmucosal, which differs from oral in speed, convenience and efficiency, allows to reduce the dose of the target component. Complete replacement of synthetic packaging is impossible, but its use may be limited through the development of edible films and coatings for certain commodity groups.

Acknowledgements

The investigation has been carried out in the frame of the Belarusian Republican Foundation for Fundamental Research project N1J X228-005



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Physician Management of Coeliac Disease: A Comparison of Disease Knowledge, Diagnosis, and Patient Management between Gastroenterologists and Primary Care Physicians in Germany, Italy, Spain, and the United States – Findings from a Real-World Survey

Submitted by: Niamh Harvey [1], Hannah Knight [1], Rachael Meadows [1], Grace O'Neill [1], Fatima Dawod [1], Rina Lukanova [1], Julia McBeth [2], Marilyn Geller [2]

[1] Adelphi Real World, Bollington, Manchester, United Kingdom; [2] Celiac Disease Foundation, Woodland Hills, CA, USA

Introduction

Gastroenterologists (GIs) and primary care physicians (PCPs) are both involved in the diagnosis and management of coeliac disease (CeD). However, little is known about the differences in disease knowledge and approaches to diagnosing and managing patients with CeD between these physician groups.

We aimed to explore these differences between GIs and PCPs.

Method

Data were extracted from the Adelphi CeD Disease Specific Programme™,[1] a cross-sectional survey of GIs and PCPs involved in the management of patients with CeD conducted in Germany, Italy, Spain, and the United States of America (USA) from July 2021-January 2022. Physicians completed an attitudinal survey pertaining to their treatment practices; diagnostic and CeD monitoring practices; factors determining disease progression, severity, and remission; villus atrophy; and gluten intake.

Analysis

Data were split into GI and PCP responses and compared using t-test, Fisher's exact and Chi-squared tests, as appropriate; p-values <0.05 were considered statistically significant.

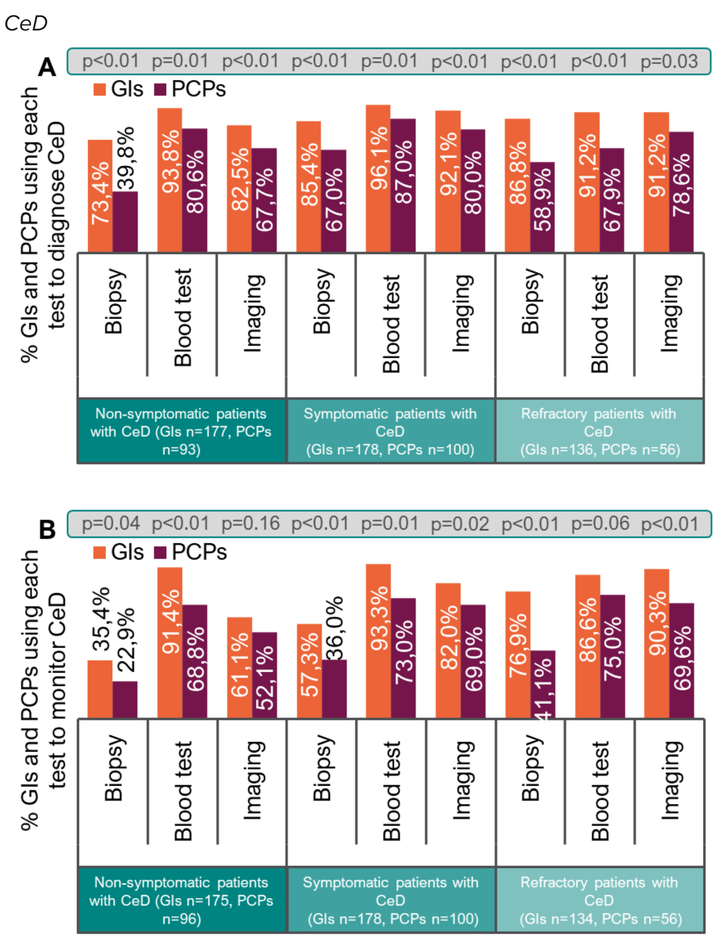
Results

In total 278 physicians (Germany, 61; Italy, 60; Spain, 60; USA, 97), comprised of 178 GIs and 100 PCPs were included.

GIs reported higher use of biopsies, blood tests, and imaging tests than PCPs for diagnosis (p<0.05), with similar trends observed for monitoring tests (Figure 1).

Figure 1

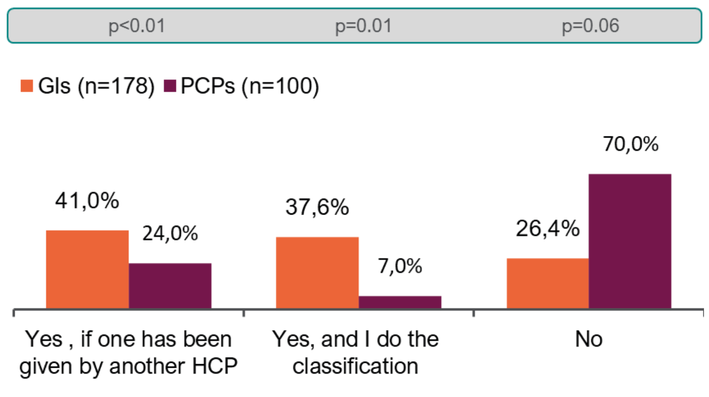
Tests used by GIs and PCPs to (A) diagnose and (B) monitor patients with CeD



Marsh classification use was low among PCPs; 70% stated they do not use it, compared to 26% of GIs (p<0.01) (Figure 2).

Figure 2

GIs- and PCPs-reported use of Marsh classification



GIs – Gastroenterologists; PCPs – Primary care physicians; HCP – Health care professional

Regardless of villus atrophy level, more PCPs than GIs stated they don't know whether villus atrophy is reversible for patients with CeD (p<0.01) (Table 1).

Table 1

GIs and PCPs perception of reversibility of villus atrophy

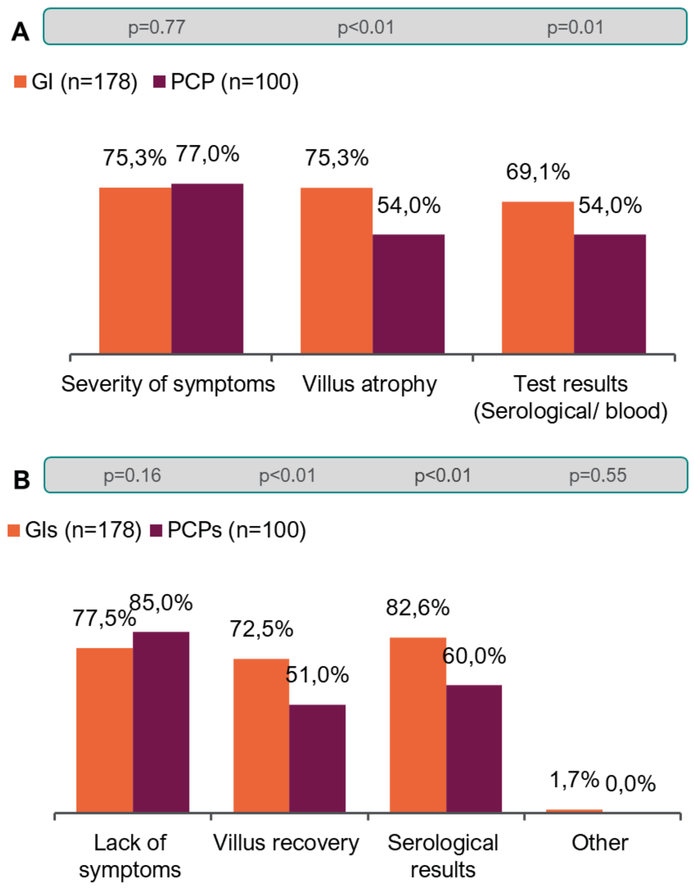
In what percentage of patient's with CeD is the villus atrophy…		GIs (n=178)	PCPs (n=100)	p-values
Mild villus atrophy	Reversible, mean (SD)	74.1 (31.3)	48.1 (40.4)	<0.01
	Nonreversible, mean (SD)	13.0 (17.4)	13.9 (19.7)	0.70
	Don't know, mean (SD)	12.9 (30.3)	38.1 (46.5)	<0.01
Marked villus	Reversible, mean (SD)	59.4 (31.1)	33.8 (31.6)	<0.01
	Nonreversible, mean (SD)	26.1 (24.2)	25.7 (25.8)	0.89
	Don't know, mean (SD)	14.5 (31.0)	40.6 (45.5)	<0.01
Complete villus	Reversible, mean (SD)	43.3 (32.7)	17.6 (24.1)	<0.01
	Nonreversible, mean (SD)	37.5 (31.6)	33.9 (36.3)	0.38
	Don't know, mean (SD)	19.2 (34.2)	48.6 (46.5)	<0.01

GIs – Gastroenterologists; PCPs – Primary care physicians; SD – Standard deviation

GIs were more likely to take villus atrophy into account when determining disease progression (GI 75%, PCP 47%), disease severity (GI 75%, PCP 54%), and remission status (GI 72%, PCP 51%; all p<0.01) (Figure 3).

Figure 3

Top three factors GIs and PCPs used to (A) determine CeD severity and (B) determine if a patient is in remission



GIs – Gastroenterologists; PCPs – Primary care physicians; CeD – Celiac disease

Differences were seen in the perceived safe level of gluten intake for patients with CeD; 58% of GIs stated there is no safe level, compared to 35% of PCPs. In addition, 17% of PCPs stated they don't know if gluten intake is acceptable for non-symptomatic patients (vs 8% of GIs, p=0.02) (Table 2).

Table 2

GIs- and PCPs-reported patient diagnosis and management practices.

a. How do you measure disease progression? n (%)	GIs (n=178)	PCPs (n=100)	p-values
Test results (serological/ blood)	137 (77.0)	61 (61.0)	0.01
Villus atrophy/ degree of villus loss or regression	134 (75.3)	47 (47.0)	<0.01
How the patient is feeling/ quality of life	113 (63.5)	75 (75.0)	0.06
Persistence of symptoms	112 (62.9)	68 (68.0)	0.43
Progressive constitutional symptoms	86 (48.3)	51 (51.0)	0.71
Imaging tests (endoscopy)	84 (47.2)	43 (43.0)	0.53
Other	1 (0.6)	0 (0.0)	1.00

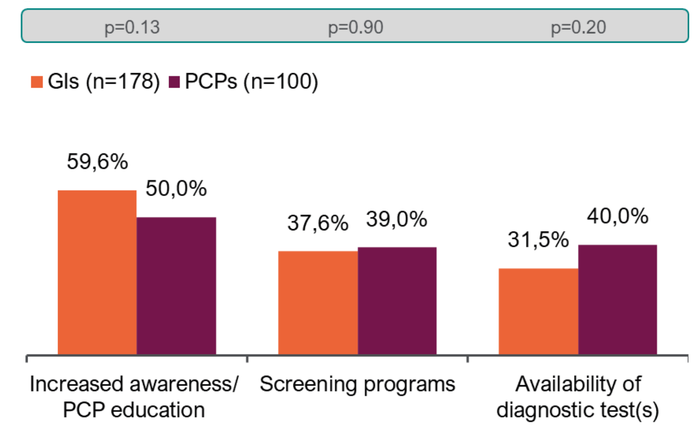
b. Is there a safe level of gluten intake for patients with CeD to ingest? n (%)	GIs (n=160) [a]	PCPs (n=79) [a]	p-values
Yes, patients can safely intake a level of gluten	8 (5.0)	8 (10.1)	<0.01
Varies between type of CeD	15 (9.4)	16 (20.3)	
Depends on the patient	45 (28.1)	27 (34.2)	
No safe level	92 (57.5)	28 (35.4)	
c. If the patient is non-symptomatic, is gluten intake acceptable? [b] n (%)	**GIs (n=164) [b]**	**PCPs (n=83) [b]**	**p-values**
Yes	30 (18.3)	18 (21.7)	0.61
No	134 (81.7)	65 (78.3)	

GIs – Gastroenterologists; PCPs – Primary care physicians; SD – Standard deviation; CeD – Celiac disease; aPhysicians not selecting 'don't know'; bWhen phrasing this question to physicians, no distinction was made between products with levels of gluten ≤20 parts per million and products free of all gluten. Note: (b) n=18 and n=21 GIs and PCPs, respectively, responded don't know (p=0.02) (c) n=14 and n=17 GIs and PCPs, respectively, responded don't know (p=0.03)

Despite the disparities, 60% of GIs and 50% of PCPs stated increased awareness and education of PCPs is the main attribute that would help facilitate early diagnosis of CeD (Figure 4).

Figure 4

Top three attributes GIs and PCPs believe would help facilitate the early diagnosis of patients with CeD



GIs – Gastroenterologists; PCPs – Primary care physicians; CeD – Celiac disease

Conclusion

This study showed key differences in CeD diagnosis and management between GIs and PCPs and an irrefutable knowledge gap observed among PCPs. This highlights a need for further education to improve the consistency of care for patients with CeD.

References

1. Norstrom F, et al., BMC Gastroenterol. 2011;7;11:118

Affiliations

Adelphi Real World, Bollington, Manchester, United Kingdom

Celiac Disease Foundation, Woodland Hills, California, United States

Disclosures

JM and MG are employees of Celiac Disease Foundation

NH, HK, RM, GO, FD and RL are employees of Adelphi Real World.

The DSP and all associated data are wholly owned by Adelphi Real World.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Diagnosing Coeliac Disease In The United States Of America, Germany, Italy And Spain: Findings From A Real-World Survey

Submitted by: Fatima Dawod [1], Hannah Knight [1], Sophie Barlow [1], Niamh Harvey [1], Grace O'Neill [1], Rina Lukanova [1], Marilyn Geller [2]

[1] Adelphi Real World, Bollington, United Kingdom; [2] Celiac Disease Foundation, Woodland Hills, CA, USA

Introduction

Late diagnosis of coeliac disease (CeD) can lead to long-term health complications and other autoimmune disorders, which may be prevented if managed sooner[1].

Differences in the diagnosis of CeD across countries have not been widely researched.

We aimed to assess diagnosis patterns in the United States of America (US) and three European countries.

Objective

To identify differences in the diagnosis of CeD within the US, Germany (DE), Italy (IT) and Spain (ES).

Method

Data were drawn from the Adelphi Real World CeD Disease Specific Programme (DSP)™, a cross-sectional survey with retrospective data collection of physicians and their patients with CeD, conducted in the US, Germany, Italy and Spain between July 2021 and January 2022. The DSP methodology has been previously published and validated[2-4].

Gastroenterologists (GIs) and primary care physicians (PCPs) were recruited to complete patient record forms for their next eight consulting adult CeD patients who were symptomatic in the last 12 months.

Physicians reported time to diagnosis, reasons for delayed diagnosis, events leading to diagnosis and tests used to diagnose. The same patients were invited to complete a voluntary patient self-completion form which captured consultation history and awareness of CeD prior to diagnosis.

Analysis

Pairwise analysis was used to compare outcomes between countries using Bonferroni corrected t-tests and Fisher's exact test, performed using Stata 175.

Significance was observed at α=0.0083 (0.05/6) to adjust for multiple testing.

Superscript letters (UDIE) indicate pairwise significant differences between countries amongst outcomes with Bonferroni corrections (p<0.0083).

Results

Overall, 278 physicians (178 GIs, 100 PCPs) reported data on 2,244 patients with CeD in the US, Germany, Italy, and Spain, described in Table 1.

Table 1

Patient demographics

	US	DE	IT	ES
n	**792**	**488**	**483**	**481**
Age, Years, mean (SD)	39.8 (14.6)	33.7 (11.0)	35.0 (13.4)	36.3 (13.9)
Sex, n (%)				
Female	499 (63.0)	289 (59.2)	304 (62.9)	307 (63.8)
BMI, mean (SD)	25.6 (4.6)	22.9 (3.1)	24.8 (34.0)	23.3 (3.2)
Smoking status, n (%)				
Current smoker	54 (6.8)	79 (16.2)	107 (22.2)	65 (13.5)
Employment status*, n (%)				
Full-time	478 (60.4)	319 (63.5)	243 (50.3)	224 (46.6)
Student	106 (13.4)	84 (17.2)	129 (26.7)	104 (21.6)
Part-time	96 (12.1)	48 (9.8)	41 (8.5)	42 (8.7)

*Top three. SD, standard deviation; BMI, Body Mass Index; US, United States of America; DE, Germany; IT, Italy, ES, Spain.

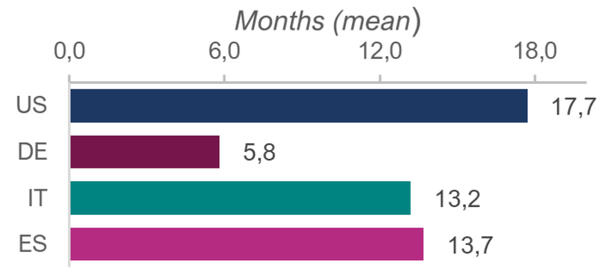
Patient self-reported data was collected from 289 (US), 266 (DE), 135 (IT) and 251 (ES) patients.

Patients waited a mean [SD] of 17.7 [43.9] (US), 5.8 [9.3] (DE), 13.2 [26.4] (IT) and 13.7 [21.8] (ES) months before seeing a physician after symptom onset, significantly lowest in Germany (Fig 1a).

Figure 1

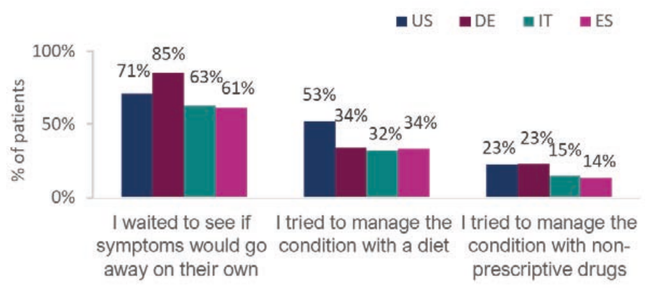
Patient-reported symptom onset to initial consultation.

1a. Mean time from symptom onset to initial consultation (months)



The main reason for this delay was patients waiting to see if their symptoms would subside, most commonly observed in Germany. This was followed by patients trying to manage their condition with a diet, which was significantly more common in the US (Fig 1b).

1b. Top three reasons for delay from symptom onset to initial consultation.



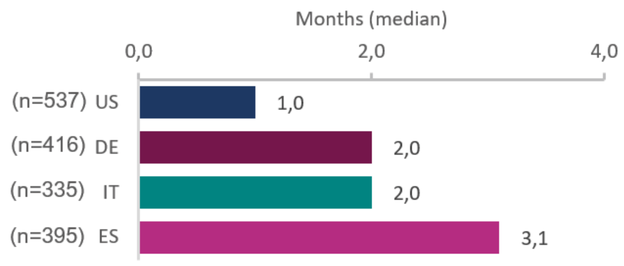
Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; UDIESuperscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083

Patients experienced a further delay of 1-3 months from initial consultation to diagnosis (Fig 2a), most commonly due to waiting for tests to be performed in the US, Italy and Spain and waiting for specialist referral in Germany (Fig 2b).

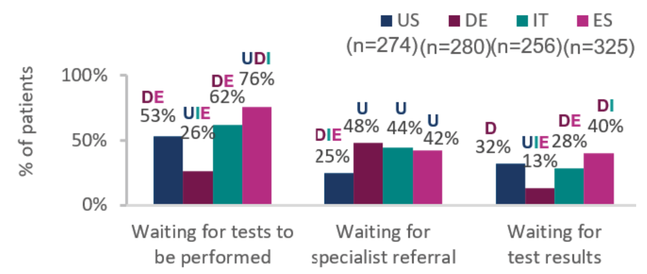
Figure 2

Physician-reported initial consultation to diagnosis.

2a. Mean time from consultation to diagnosis (months)[a]



2b. Top three reasons for delay between initial consultation and diagnosis[b]



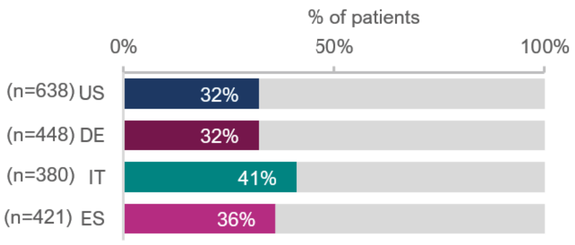
[a]Patients with known diagnosis date. [b]Patients who experienced a delay between consultation and diagnosis. US, United States of America; DE, Germany; IT, Italy; ES, Spain; UDIESuperscript letters indicate pairwise significant differences between countries with Bonferroni corrections

Over a third of patients were initially misdiagnosed, significantly higher in Italy compared to the US; the most common misdiagnosis was irritable bowel syndrome, significantly higher in the US compared to the other countries (Fig 3).

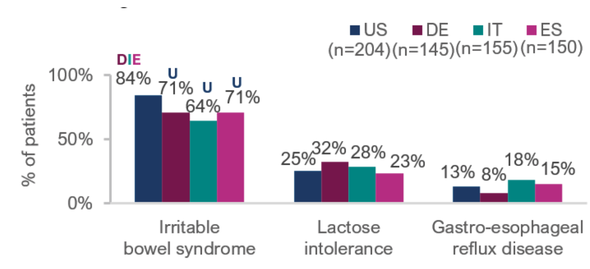
Figure 3

Physician-reported misdiagnosis.

3a. Proportion of patients initially misdiagnosed.



3b. Top three misdiagnoses of those initially misdiagnosed.

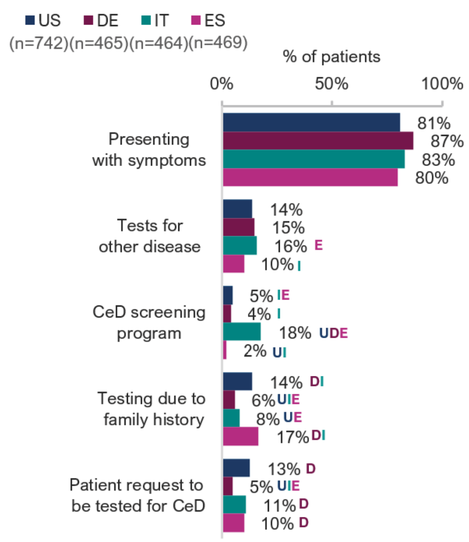


Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; UDIESuperscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Circumstances leading to diagnosis varied across countries: symptom presentation was most prevalent overall. CeD screening programme was higher in Italy compared to all other countries (Fig 4).

Figure 4

Physician-reported events leading to diagnosis..



Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; UDIESuperscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Patient request to be tested was lower in Germany, likely due to the low patient awareness of CeD prior to diagnosis (Table 2).

Table 2

Patient-reported awareness of CeD prior to diagnosis-reported events leading to diagnosis..

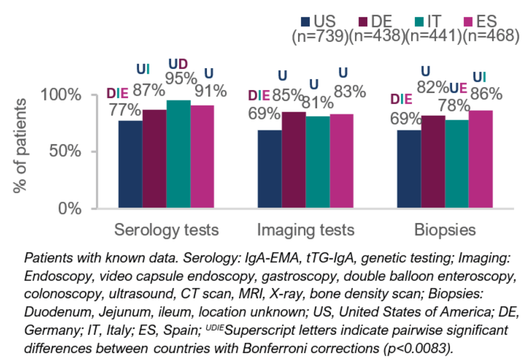
	US	DE	IT	ES
n	**287**	**263**	**133**	**251**
Patients aware of CeD prior to diagnosis, n (%)	136 (47.4)[D]	36 (13.7)[UIE]	75 (56.4)[D]	140 (55.8)[D]

CeD, celiac disease; US, United States of America; DE, Germany; IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

All diagnostic tests were used significantly less in the US compared to all other countries (Fig 5).

Figure 5

Physician-reported tests used to diagnose.



Patients with known data. Serology: IgA-EMA, tTG-IgA, genetic testing; Imaging: Endoscopy, video capsule endoscopy, gastroscopy, double balloon enteroscopy, colonoscopy, ultrasound, CT scan, MRI, X-ray, bone density scan; Biopsies: Duodenum, Jejunum, ileum, location unknown; US, United States of America; DE, Germany; IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Conclusion

We found that patients in the US, Germany, Italy and Spain experienced long delays in their diagnosis of CeD and were frequently misdiagnosed, with the greatest disparity observed between the US and Germany.

Future research is needed to determine the impact of delayed diagnosis on further health complications and patient outcomes in CeD.

References

1. Norstrom F, et al., BMC Gastroenterol. 2011;7;11:118
2. Anderson P, et al., Cur Med Res Opin. 2008;24(11):3063-72
3. Babineaux SM, et al., BMJ Open. 2016;6(8):e010352
4. Higgins V, et al., Diabetes Metab Syndr Obes. 2016;1(9):371-380
5. StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp

Disclosures

Fatima Dawod, Hannah Knight, Sophie Barlow, Niamh Harvey, Grace O'Neill & Rina Lukanova are employees of Adelphi Real World. Marilyn Geller is an employee of Celiac Disease Foundation.

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Potential treatments alternative to the GFD: patients' expectations

Submitted by: Susanna Neuhold [1], Giovanni Bartolone [1,2]

[1]AIC, Italian Celiac Association, [2]University of Catania, Di3a - Department Agricolture Nutrition Environment

Introduction

Thanks to the Gluten Free Diet (GFD), celiacs, if diagnosed in time, can recover and stay healthy[1]. Yet, the management and psychological, social and economic burdens of the GFD have a great impact on celiacs and adherence to therapy is not easy[2]. Finding alternatives to the diet, therefore, could have benefits for celiacs, increasing their Quality of Life (QoL). Nevertheless, not all new therapies could be appreciated or accepted by patients.

With this work, we aimed to understand what the Italian celiac patients really want and would accept better and which factors can help the scientific community to have a possible effective and good therapy been accepted by celiacs, guaranteeing adherence to it.

Method and materials

An online survey made through Google Forms was shared by the Italian Celiac Association (AIC) among Italian celiacs trough social media and newsletters for 2 months (end July – end September 2022). The survey was completely anonymous and celiacs were informed that data would be elaborated in aggregated form so that respondents were able to feel free to express themselves without feeling any judgment.

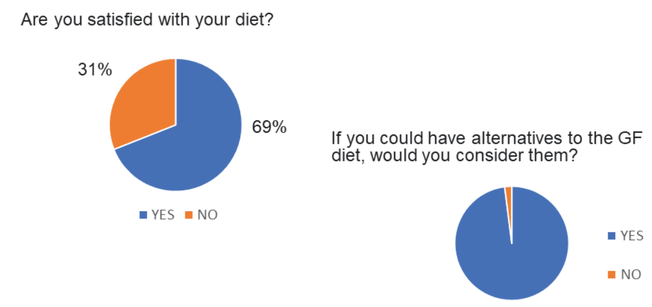
The survey was made up of 40 questions focused on the top 4 main research fields (Vaccine therapies, Genetic editing, Enzymatic therapies, Technological processes). A brief and simple explanation of these topics was given in the most neutral way, and it was clarified that all therapies are still under development, at different stages, and there are still no conclusive results, applicable in the clinic on the general population, nor is it possible now to make predictions on outcomes and timings.

Results

7.808 participants joined the survey. Even if the majority (69%) declared to be satisfied with the GFD, almost all respondents declared that, if they could have alternatives to the GF diet, would consider them.

Chart 1

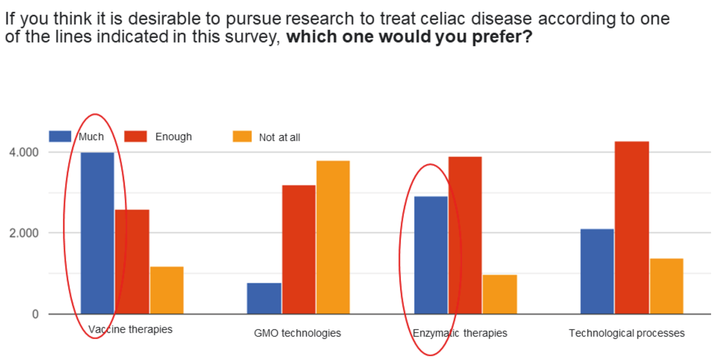
GFD satisfaction and attitude towards new therapies



Among the top 4 topics explored, the most preferred was the vaccine therapies, followed by the enzymatic ones.

Chart 2

Preferences

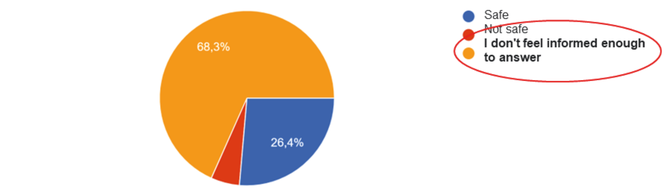


Conclusion

These research fields were presented in the most neutral way possible, yet it was not easy to explain in a simple and accessible way their mechanism. So, one of the main factors that can influence attitudes of patients towards specific therapies and, in case, help compliance is the access to clear information.

Chart 3

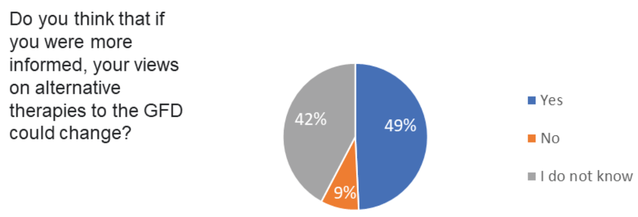
Information about effectiveness and safety



At the question "How would you evaluate safety/efficacy of…?" replies were often "I don't feel informed enough to answer".

Chart 4 –

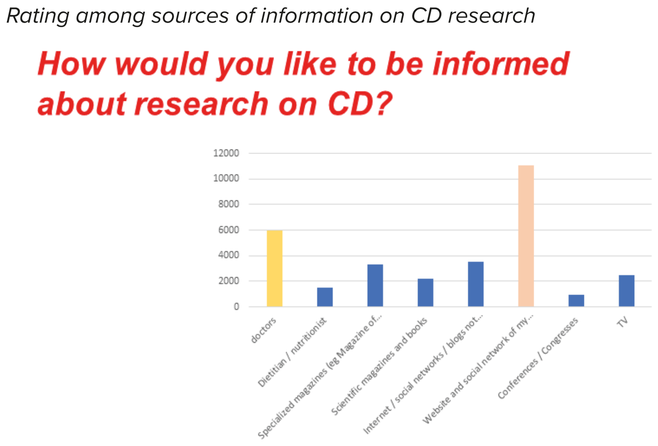
Information and attitude towards new therapies



Almost half of the respondents declared that they likely would change their opinion on new therapies if more information was available and, when they were asked on how they would like to be informed about research on CD, ***patients associations and doctors were the most rated****.*

Chart 5

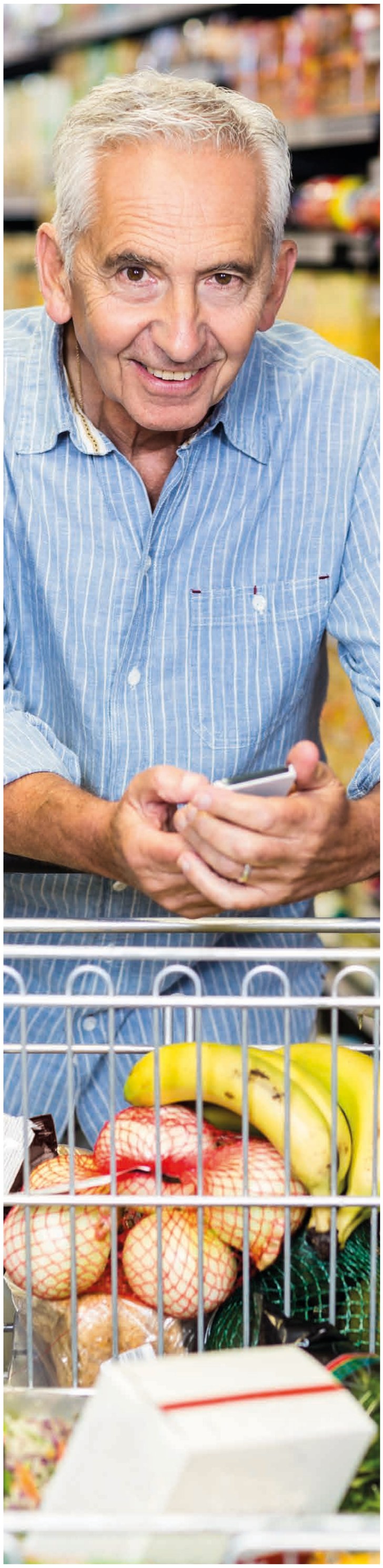
Rating among sources of information on CD research



In conclusion, a clear information on possible new therapies, explained by doctors together with the relevant Patient Association could be the key point to guarantee compliance to any new therapy for CD.

References

1. Caio G., Volta U., Sapone A., Leffler D.A., De Giorgio R., Catassi C., Fasano A. Celiac disease: A comprehensive current review. BMC Med. 2019;17:142.
2. Aljada B., Zohni A., El-Matary W.: The gluten-free diet for celiac disease and beyond. Nutrients. 2021; 13:3993.



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Gluten-free beer from barley malt and wheat: an In vitro study for potential toxicity

Submitted by: Olimpia Vincentini [1], Valentina Prota [1], Francesca De Battistis [1], Susanna Neuhold [2] and Marco Silano [3]

[1]Department of Food Safety and Nutrition and Veterinary Public Health, Italian National Institute of Health, [2]AIC, Italian Celiac Association, [3]Department of Cardiovascular, Endocrine-metabolic Diseases and Aging, Italian National Institute of Health

Introduction

Gluten free beers are obtained from ingredients that naturally do not contain gluten, or from gluten containing grains in which the gluten content is chemically or physically reduced in order to comply with the gluten-free EU law (20 ppm or less of gluten).

The Food and Drug Administration (U.S.) does not allow the label “gluten free” for fermented foods produced from a gluten containing ingredient that have undergone technological treatments, since it states that there is not any suitable method for the detection and quantification of gluten in fermented or hydrolyzed food.

In contrast, in the EU such beers are currently allowed to bear a gluten-free label. This is a topic of much debate at the moment, because of these divergent opinions.

Method

Analysis: 3 different batches of 10 labeled gluten-free (GFB) and 10 barley (gluten) containing beer (GCB) samples were analyzed by both R5 competitive and R5 sandwich ELISA.

Evaluation of potential toxicity: Caco-2 cells were exposed to GFB and GCB for 24 hours (dil 1:10 V/V) and analyzed for IL-8 and TNF-alfa cytokines release. Moreover, agglutination assay on K562(S) cells was performed by exposing the cells for 15 minutes to GFB and GCB.

Results

R5 Elisa competitive and sandwich assays verified the absence of gluten (values less than 10 ppm) and high repeatability between samples from the same and different batches in the GFB. In contrast, the gluten content detected in GCB showed high variability among different brands, evidencing the toxicity of these beers for CD patients.

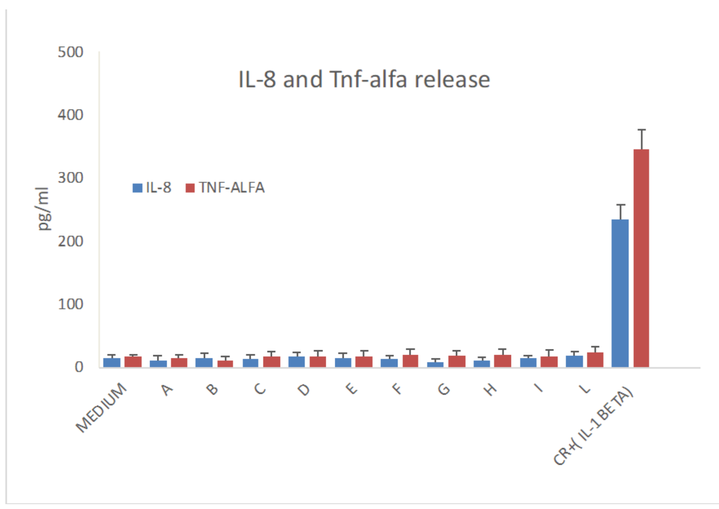
Chart 1

R5 analysis for gluten content

Gluten-free Beers (GFB)				Gluten Containing -Beers (GCB)			
Sample	Batch	R5 Competitive	R5 Sandwich	Sample	Batch	R5 Competitive	R5 Sandwich
GFB-A	A1	< 10.00	<5.00	GCB-M	M1	54,7	5,4
	A2	< 10.00	<5.00		M2	62,7	5,86
	A3	< 10.00	<5.00		M3	54,9	5,26
GFB-B	B1	< 10.00	<5.00	GCB-N	N1	129,84	10,05
	B2	< 10.00	<5.00		N2	128,31	10,73
	B3	< 10.00	<5.00		N3	136,68	10,31
GFB-C	C1	< 10.00	<5.00	GCB-O	O1	67,25	23,15
	C2	< 10.00	<5.00		O2	64,31	24,02
	C3	< 10.00	<5.00		O3	66,09	23,59
GFB-D	D1	< 10.00	<5.00	GCB-P	P1	10,02	5,34
	D2	< 10.00	<5.00		P2	10	6,04
	D3	< 10.00	<5.00		P3	11,02	5,55
GFB-E	E1	< 10.00	<5.00	GCB-Q	Q1	< 10.00	<5.00
	E2	< 10.00	<5.00		Q2	< 10.00	<5.00
	E3	< 10.00	<5.00		Q3	< 10.00	<5.00
GFB-F	F1	< 10.00	<5.00	GCB-R	R1	< 10.00	<5.00
	F2	< 10.00	<5.00		R2	< 10.00	<5.00
	F3	< 10.00	<5.00		R3	< 10.00	<5.00
GFB-G	G1	< 10.00	<5.00	GCB-S	S1	50,89	6,02
	G2	< 10.00	<5.00		S2	52,15	5,86
	G3	< 10.00	<5.00		S3	49,89	6,27
GFB-H	H1	< 10.00	<5.00	GCB-T	T1	34,78	5,01
	H2	< 10.00	<5.00		T2	33,41	5,68
	H3	< 10.00	<5.00		T3	31,84	5,87
GFB-I	I1	< 10.00	<5.00	GCB-U	W1	37,71	5,9
	I2	< 10.00	<5.00		W2	39,69	5,12
	I3	< 10.00	<5.00		W3	37,45	5,62
GFB-L	L1	< 10.00	<5.00	GCB-V	X1	22,55	5,44
	L2	< 10.00	<5.00		X2	22,89	5,72
	L3	< 10.00	<5.00		X3	23,04	5,21

Chart 2

IL-8 and TNF-alfa release

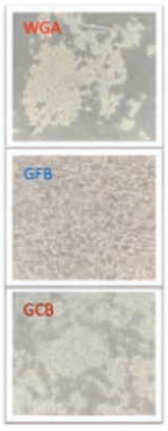


No inflammatory effect has been observed in Caco-2 cells for GFB.

Chart 1

Agglutination assay

Beer	% Agglutinated cells
Wheat gliadin	95
GFB-A	6
GFB-B	8
GFB-C	5
GFB-D	4
GFB-E	3
GFB-F	8
GFB-G	6
GFBH	7
GFB-I	10
GFB-L	6
GCB-M	45
GCB-N	38



No agglutinating activity was observed for GFB in K562 cells.

Conclusion

Competitive and Sandwich R5 Elisa were used to assess the presence of any non-hydrolyzed gluten residues, since the fermentation process is not standardized for all products. The competitive R5 was confirmed to be the most sensitive analysis for fermented products.

Interestingly some of the GCB reported gluten content values below the threshold limit.

Although LC-MS/MS is more sensitive than the R5 ELISA, it has not yet been validated to reliably quantify the amount of gluten in beer so it is not an approved method of analyzing gluten, moreover is too expensive and too demanding in terms of time and skill for the manufacturers.

Apart from detection methods, potential immunogenicity and inflammatory effect of the detected fragment can only be evaluated by clinical studies. Hence, in this study it was adopted an in vitro approach to assess potential toxicity of GFB from barley and/or wheat malt.

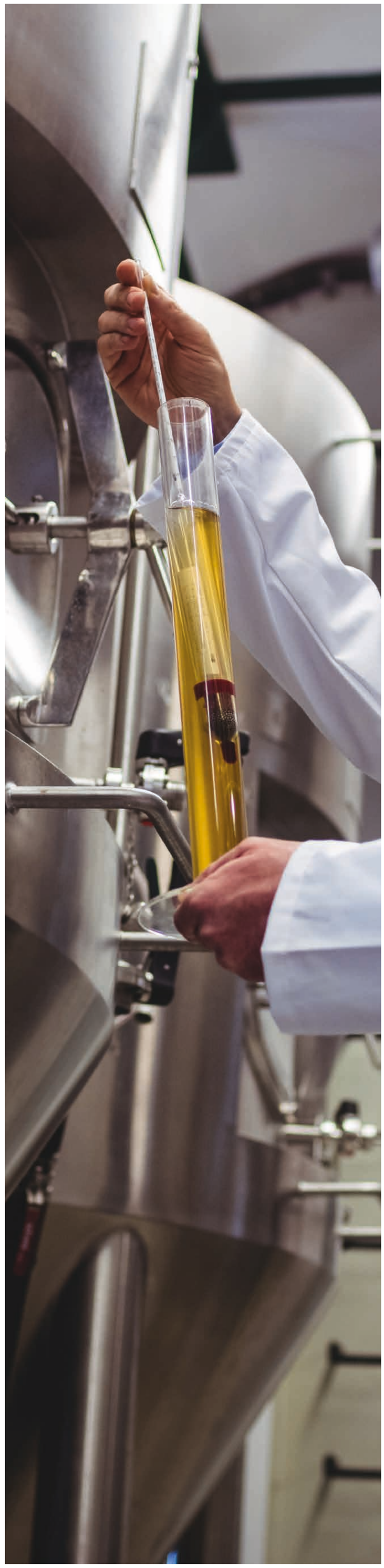
Overall, the results obtained suggest that GFB analyzed in the present in vitro study did not trigger an inflammatory effect in in vitro cellular models.

References

1. Real A, Comino I, Moreno M de L, López-Casado, M Á, Lorite, P, Torres M I, Cebolla Á, and Sousa C. (2014). Identification and In Vitro Reactivity of Celiac Immunoactive Peptides in an Apparent Gluten-Free Beer. PLoS ONE, 9(6), e100917.
2. Spada V, Di Stasio L, Picascia, S, Messina B, Gianfrani C, Mamone G, and Picariello G. (2020). Immunogenic Potential of Beer Types Brewed With Hordeum andTriticum spp. Malt Disclosed by Proteomics. Frontiers in Nutrition, 7
3. Scherf KA, Catassi C, Chirdo FG, Ciclitira PJ, Feighery CF, Gianfrani C, Koning F, Lundin KEA, Masci S, Schuppan D, Smulders MJM, Tranquet O, Troncone R and Koehler P (2021) Statement of the Prolamin Working Group on the Determination of Gluten in Fermented Foods Containing Partially Hydrolyzed Gluten. Front. Nutr. 7:626712.

Acknowledgment

This project has been funded by the Italian Celiac Association



ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

The Virtual Celiac Symptoms Study: reported symptoms over 12 weeks in adults

Submitted by: Lisa M. Meckley [1], Mariel Arvizu [1], Jessica R. Marden [2], Sakshi Sethi [2], Sanjana Sundaresan [2], Marilyn Geller [3], Dawn Adams [4], Edwin Liu [5], Daniel A. Leffler [1]

[1] Takeda Development Center Americas, Inc., Cambridge, MA, USA; [2] Analysis Group, Inc., Boston, MA, USA; [3] Celiac Disease Foundation and presenting author, Woodland Hills, CA, USA; [4] Vanderbilt University Medical Center, Nashville, TN, USA; [5] Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA

Introduction

Coeliac disease (CeD) is an autoimmune condition triggered by gluten consumption and characterized by autoantibodies and inflammation of the small intestine.[1,2]

CeD is estimated to affect approximately 1% of people worldwide.[3]

The only management option for CeD is strict adherence to a gluten-free diet (GFD), but this has major limitations and many individuals may still experience symptoms and/or intestinal damage owing to inadvertent gluten ingestion or barriers to sufficient adherence such as food availability, financial constraints or patient perceptions.[4–7]

Symptoms are an important metric in CeD and have a significant impact on patient lives.[2]

The Virtual Celiac Symptoms Study (VCSS) is the first prospective observational study to assess daily symptom patterns and impacts of CeD in US adults and adolescents following a GFD.

The baseline disease characteristics of the adult population of this study were previously described.[8]

Objectives

To assess GFD experience and CeD-related symptoms in the adult population of the VCSS over 12 weeks.

Methods

Study design

- An observational prospective study (VCSS; NCT05309330) was conducted in US adults and adolescents with CeD.
- Participants self-reported information via a smartphone app regarding:
  - CeD diagnosis, demographics and clinical characteristics
  - occurrence and severity of daily symptoms over 12 weeks (via the Celiac Disease Symptom Diary 2.1; CDSD 2.1©),[9] which included questions regarding the severity of diarrhea, abdominal pain, bloating, nausea and tiredness, and the frequency of vomiting and diarrhea
  - known and suspected inadvertent gluten exposure over 12 weeks
- Participants were recruited by the Celiac Disease Foundation via digital advertisements (email, social media channels, app push notifications, website advertisements and a study microsite).
- Data collection began on July 25, 2022, and completed on March 4, 2023.

Inclusion Criteria

- English-speaking, aged ≥ 18 years (for the adult cohort) and residing in the USA.
- Diagnosis of CeD for ≥ 1 year, confirmed via self-reported biopsy and serology.
- Adherence to a GFD for ≥ 6 months.
- CeD-related symptoms (patient-reported) within the past 3 months.
- Daily access to a smartphone and Internet/Wi-Fi/cellular data.

Exclusion Criteria

- Planned or current involvement in any clinical study with an investigationaldrug, or surgical procedure or gluten challenge during the 3-month observation period.

Data analysis

- The number of days with core CeD symptoms during the 12-week study period was recorded and a weighted mean number of days with each symptom was determined to account for any days with missing data (weighted mean was calculated as the mean proportion of days with reported symptom(s) across participants weighted by the total study period of 84 days).
- Prevalence of core CeD symptoms during the 12-week study period was stratified by self-reported level of GFD adherence at study initiation and by irritable bowel syndrome (IBS) status of participants.
  - An assessment of the symptom prevalence in participants with and without IBS was of interest because a significant proportion (> 20%) of participants reported IBS as a comorbidity.
- Participants were included in these analyses if they experienced any symptom at least once during the 12-week study period.
- All measures were analyzed using descriptive statistics with R version 4.0.4. The *p* values were generated using a χ^2 test for categorical variables (or Fisher's exact test when expected value < 5) and analysis of variance (ANOVA) for continuous variables.

Results

Demographics and clinical characteristics

- Adults (≥ 18 years at enrollment) comprised 338 (70.4%) of the 480 enrolled participants **(Table 1)**.
  - The mean (standard deviation; SD) age was 37.9 (12.5) years, 87.9% self-identified as female, 98.5% reported to be of White race and 66.0% had a college or graduate (master's or doctorate) degree.
  - The majority (71.0%) of adult participants self-reported moderate (38.5%) or severe (32.5%) symptoms at baseline.
- At study initiation, severity of symptoms was unrelated to adult participant demographics, clinical characteristics and time since diagnosis of CeD
- The most common self-reported comorbidities at baseline were anxiety (56.8%) and depression (42.3%) **(Table 1).**
- Although 90.0% of adult participants reported at least one comorbidity, only IBS and anemia were related to severity of symptoms at study initiation.

Baseline symptoms

- At study entry, 58.3% of participants reported symptoms in the past week, 31.1% in the past month and 10.7% in the past 3 months **(Table 2)**.
- At study initiation, participants reported that symptoms following gluten exposure were "extremely likely" (63.0%) and the likelihood was greater in those with severe symptoms than in those with mild symptoms (89.1% versus 10.5%) **(Table 2)**.

Frequency of gluten exposure over the 12-week study period

- The mean (SD) number of days with reported gluten exposure was 7.1 (9.3) **(Table 3)**.

Frequency and prevalence of symptoms over the 12-week study period

The mean (SD) number of days of reported symptoms was 60.3 (20.0) **(Table 3)**.

- Tiredness, bloating and abdominal pain were the most frequently experienced symptoms during the 12 weeks of the study **(Figure 1)**.
- All adult participants reported at least one core CeD symptom.
  - Each GI symptom, with the exception of nausea (in participants whoreported adhering to a GFD and "never eating gluten accidentally or on purpose") and vomiting, occurred at least once in over 90.0% of adult participants **(Figure 2)**.
  - Participants experienced symptoms regardless of their level of GFD adherence (self-reported at baseline) or diagnosis of IBS **(Figure 2)**.

Key messages

- Despite adherence to a gluten-free diet, ongoing gastrointestinal (GI) symptoms are common in adult patients with coeliac disease (CeD).
- This observational study highlights the need for continued monitoring of patients with CeD and that GI symptoms may be appropriate for inclusion as endpoints in clinical trials of potential CeD therapies.

Table 1

Participant baseline demographics and clinical disease characteristics across categories of self-reported symptom severity

	Overall	Severity of self-reported symptoms at baseline				
		Mild	Moderate	Severe	Varies widely	*p* value
Number of participants, n (%)	338 (100)	19 (5.6)	130 (38.5)	110 (32.5)	79 (23.4)	–
Age, years, mean (SD)	37.9 (12.5)	40.7 (11.7)	37.4 (12.1)	37.9 (13.6)	38.1 (11.9)	0.75
White race, n (%)	333 (98.5)	18 (94.7)	129 (99.2)	107 (97.3)	79 (100)	0.14
BMI, kg/m², mean (SD)	27.3 (7.4)	26.4 (5.3)	27.5 (6.9)	26.4 (7.7)	28.1 (8.2)	0.42
Sex, n (%)						
Female	297 (87.9)	15 (79.0)	115 (88.5)	97 (88.2)	70 (88.6)	0.65
Male	41 (12.1)	4 (21.1)	15 (11.5)	13 (11.8)	9 (11.4)	–
Education, n (%)						
High school graduate or lower	23 (6.8)	1 (5.3)	10 (7.7)	5 (4.5)	7 (8.9)	0.83
Some college	92 (27.2)	4 (21.1)	31 (23.9)	39 (35.5)	18 (22.8)	0.13
College/graduate degree	223 (66.0)	14 (73.7)	89 (68.5)	66 (60.0)	54 (68.4)	0.47
Time since CeD diagnosis, years, mean (SD)	7.3 (5.3)	5.4 (5.6)	6.8 (4.6)	7.8 (5.9)	7.8 (5.2)	0.13
Comorbidities,[a] n (%)						
At least one comorbidity	304 (89.9)	17 (89.5)	117 (90.0)	101 (91.8)	69 (87.3)	0.76
Anxiety	192 (56.8)	10 (52.6)	70 (53.9)	63 (57.3)	49 (62.0)	0.69
Depression	143 (42.3)	9 (47.4)	46 (35.4)	50 (45.5)	38 (48.1)	0.23
GERD	86 (25.4)	6 (31.6)	28 (21.5)	32 (29.1)	20 (25.3)	0.51
IBS	70 (20.7)	0 (0.0)	19 (14.6)	28 (25.5)	23 (29.1)	0.003
Thyroid disease	70 (20.7)	5 (26.3)	27 (20.8)	26 (23.6)	12 (15.2)	0.46
Anemia	68 (20.1)	3 (15.8)	19 (14.6)	33 (30.0)	13 (16.5)	0.02
Dermatitis herpetiformis	44 (13.0)	3 (15.8)	10 (7.7)	19 (17.3)	12 (15.2)	0.10
Osteoporosis/osteopenia	31 (9.2)	4 (21.1)	9 (6.9)	12 (10.9)	6 (7.6)	0.20
SIBO	18 (5.3)	1 (5.3)	4 (3.1)	7 (6.4)	6 (7.6)	0.41
IBD[b]	8 (2.4)	0 (0.0)	3 (2.3)	2 (1.8)	3 (3.8)	0.84
Type 1 diabetes	6 (1.8)	2 (10.5)	1 (0.8)	2 (1.8)	1 (1.3)	0.07

[a]Disorders that participants had in addition to CeD. Listed are current medical problems, diagnosed by a doctor or other healthcare professional, for which participants are currently or were receiving treatment within the past 12 months. Participants were allowed to select all that apply. [b]Includes ulcerative colitis and Crohn's disease. CeD, coeliac disease; GERD, gastroesophageal reflux disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; SD, standard deviation; SIBO, small intestine bacterial overgrowth.

Table 2

Symptom occurrence at study initiation among adult participants with CeD across categories of baseline disease severity

	Overall	Severity of self-reported symptoms at baseline				
		Mild	Moderate	Severe	Varies widely	*p* value
Number of participants, n (%)	338 (100)	19 (5.6)	130 (38.5)	110 (32.5)	79 (23.4)	–
Most recent CeD symptoms experienced at study initiation, n (%)						
In the past week	197 (58.3)	8 (42.1)	82 (63.1)	62 (56.4)	45 (57.0)	0.32
In the past month	105 (31.1)	11 (57.9)	34 (26.2)	34 (30.9)	26 (32.9)	0.05
In the past 3 months	36 (10.7)	0 (0.0)	14 (10.8)	14 (12.7)	8 (10.1)	0.48
Likelihood of symptoms after gluten exposure, self-reported at study initiation, n (%)						
Extremely likely	213 (63.0)	2 (10.5)	58 (44.6)	98 (89.1)	55 (69.6)	< 0.0001
Likely	71 (21.0)	4 (21.1)	46 (35.4)	6 (5.5)	15 (19.0)	< 0.0001
Somewhat likely	39 (11.5)	8 (42.1)	22 (16.9)	4 (3.6)	5 (6.3)	< 0.0001
Unlikely	8 (2.4)	5 (25.3)	1 (0.8)	0 (0.0)	2 (2.5)	< 0.0001
Extremely unlikely	7 (2.1)	0 (0.0)	3 (2.3)	2 (1.8)	2 (2.5)	1.00
Level of GFD adherence[a], self-reported at study initiation, n (%)						
I eat a GFD and rarely eat gluten on purpose	26 (7.7)	1 (5.3)	10 (7.7)	7 (6.4)	8 (10.1)	0.83
I eat a GFD and rarely eat gluten accidentally	241 (71.3)	16 (84.2)	93 (71.5)	76 (69.1)	56 (70.9)	0.61
I eat a GFD and never eat gluten accidentally or on purpose	71 (21.0)	2 (10.5)	27 (20.8)	27 (24.6)	15 (19.0)	0.56

[a]None of the participants reported "eating gluten-free diet sometimes" or "eating gluten-containing foods regularly".CeD, coeliac disease; GFD, gluten-free diet; SD, standard deviation.

Table 3

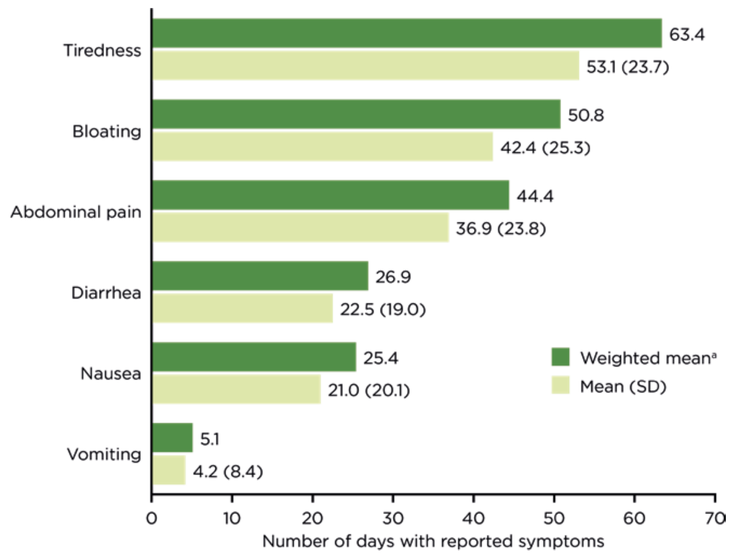
Frequency of reported symptoms and gluten exposure among adult participants with CeD across categories of baseline disease severity during the 12-week study period

	Overall	Severity of self-reported symptoms at baseline				
		Mild	Moderate	Severe	Varies widely	*p* value
Number of participants, n (%)	338 (100)	19 (5.6)	130 (38.5)	110 (32.5)	79 (23.4)	–
Frequency of symptoms/gluten exposure, mean (SD) number of days during 12-week study period						
Symptoms reported	60.3 (20.0)	61.5 (17.8)	58.7 (20.7)	60.0 (21.4)	63.1 (17.3)	0.49
Gluten exposure (known or suspected)	7.1 (9.3)	8.5 (14.2)	7.1 (8.2)	7.4 (10.9)	6.2 (6.0)	0.78

CeD, coeliac disease; SD, standard deviation.

Figure 1

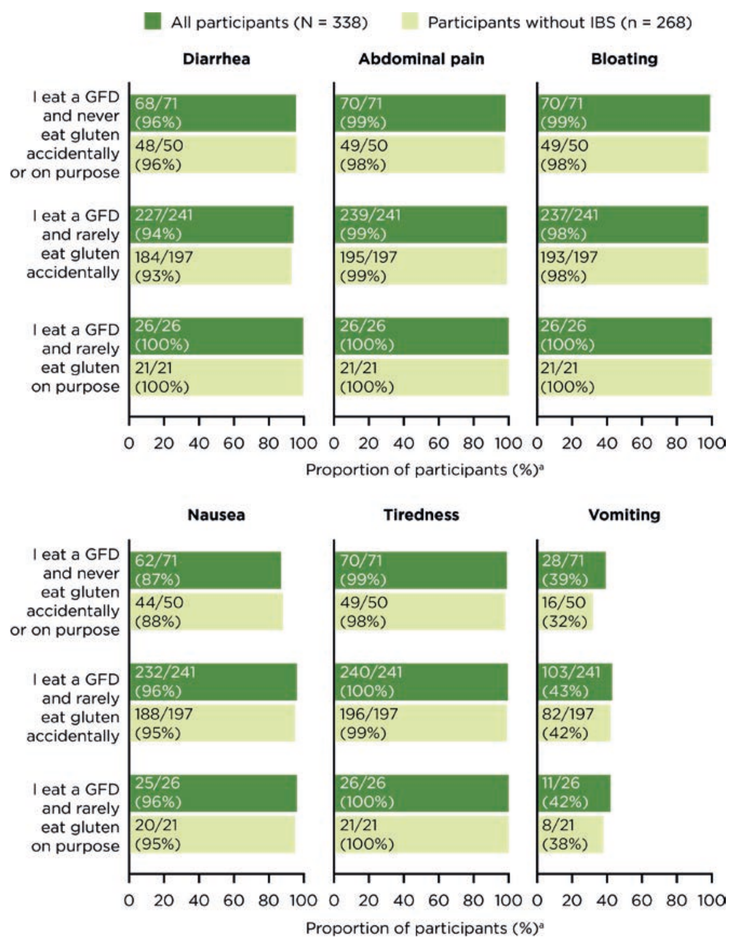
Number of days with core CeD symptoms during the 12-week study period among adult participants (N = 338) who experienced each symptom



Symptoms were assessed using CDSD 2.1 and included diarrhea, abdominal pain, bloating, nausea, tiredness and vomiting. All participants (N = 338) with available data on ≥ 1 day were included in this analysis. [a]The weighted mean was calculated as the mean proportion of days with reported symptom(s) across participants weighted by the total study period days (84 days). CDSD, Celiac Disease Symptom Diary; CeD, coeliac disease; SD, standard deviation.

Figure 2

CeD core symptoms during the 12-week study period stratified by level of adherence to GFD and IBS diagnosis reported at baseline



[a]None of the participants reported "eating gluten-free diet sometimes" or "eating gluten-containing foods regularly".CeD, coeliac disease; GFD, gluten-free diet; SD, standard deviation.

Limitations

- There is currently no classification of symptom severity for CeD, thus participant self-assessment was used for this study.
- The self-reporting of daily symptoms and dietary intake are subject to inherent biases.10 Furthermore, daily reporting could increase awareness of GFD adherence, which may lead to changes in participants' dietary choices during the course of the study.
- There may be misclassification of CeD status by participants.
- Generalizability of these results might be limited because the participants of this study were US adults who were mostly White, highly educated and recruited from a patient advocacy group.

Conclusions

- Adult participants reported frequent CeD symptoms during the 12-week study period, regardless of level of adherence to a GFD (self-reported at baseline) or IBS diagnosis.
- This study further highlights the unmet need for additional treatments for patients with CeD beyond management with a GFD.
- GI symptoms such as diarrhea, nausea, bloating and abdominal pain may be relevant co-endpoints for assessment of treatment effects in clinical trials of potential CeD therapies.
- Further CeD populations should be assessed to explore regional variations in these outcomes.

References

1. Caio G et al. BMC Med 2019;17:142.
2. Leffler DA et al. Value Health 2017;20:637–43.
3. Singh P et al. Clin Gastroenterol Hepatol 2018;16:823–36.
4. Hall NJ et al. Appetite 2013;68:56–62.
5. Rubio-Tapia A et al. Am J Gastroenterol 2023;118:59–76.
6. Leffler DA et al. Dig Dis Sci 2008;53:1573–81.
7. Singh J et al. J Hum Nutr Diet 2011;24:479–86.
8. Meckley LM et al. Gastroenterology 2023;164:S–1037.
9. Mapi Research Trust. Available from: https://eprovide.mapi-trust.org. (Accessed September 2023)
10. Silvester JA et al. Aliment Pharmacol Ther 2020;52:1469–79.

Acknowledgements

The authors would like to acknowledge Lin Zou and Allison Quintana for analytical support, Elyse Swallow and James Signorovitch for consulting services, and Julia McBeth and Marissa Mahoney for study logistics support.

Funding

This study was sponsored by Takeda Development Center Americas, Inc. Medical writing support was provided by Christina Nikolakopoulou, PhD, of Oxford PharmaGenesis, Oxford, UK and was funded by Takeda Pharmaceuticals.

Disclosures

Data first presented at the United European Gastroenterology Week, October 14–17, 2023, Copenhagen, Denmark. **LMM** was an employee of Takeda Development Center Americas, Inc. at the time of this study and holds Takeda stock. **MA** and **DAL** are employees of Takeda Development Center Americas, Inc. and receive stock or stock options. **JRM**, **SSe** and **SSu** are employees of Analysis Group, Inc., which received research support from Takeda Development Center Americas, Inc. **MG** is an employee of the Celiac Disease Foundation, which received financial support from Takeda Development Center Americas, Inc. **DA** and **EL** serve as consultants for Takeda Pharmaceuticals.

Presented at 35th Association of European Coeliac Societies General Assembly Conference, November 2–5, 2023, Athens, Greece
Corresponding author: daniel.leffler@takeda.com

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

The Virtual Celiac Symptoms Study: reported symptoms over 12 weeks in adolescents

Submitted by: Dawn Adams [1], Lisa M. Meckley [2], Mariel Arvizu [2], Jessica R. Marden [3], Sakshi Sethi [3], Elyse Swallow [3], Marilyn Geller [4], Edwin Liu [5], Daniel A. Leffler [2]

[1] Vanderbilt University Medical Center, Nashville, TN, USA; [2] Takeda Development Center Americas, Inc., Cambridge, MA, USA; [3] Analysis Group, Inc., Boston, MA, USA; [4] Celiac Disease Foundation and presenting author, Woodland Hills, CA, USA; [5] Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO, USA

Introduction

- Coeliac disease (CeD) is an autoimmune condition triggered by gluten exposure.[1]
- CeD symptoms are an important metric in disease activity and significantly affect patients' lives.[2]
- The only management option for CeD is a gluten-free diet (GFD), which has major limitations, and patients following a GFD may continue to experience symptoms due to inadvertent gluten ingestion.[3–7]
- Challenges with adherence to a GFD are common among adolescents.[8]
- An increased understanding of GFD adherence and distinct symptom patterns of different patient populations could help to better inform the management of CeD.
- The Virtual Celiac Symptoms Study (VCSS) is the first observational study to assess daily symptom patterns and impacts of CeD in US adults and adolescents adhering to a GFD.

Objective

To assess GFD experience and CeD-related symptoms in the adolescent population of the VCSS over 12 weeks.

Methods

Study design

- An observational prospective study (VCSS; NCT05309330) was conducted in US adults and adolescents with CeD.
- Participants self-reported information via a smartphone app regarding:
  - CeD diagnosis, demographics and clinical characteristics
  - occurrence and severity of daily symptoms over 12 weeks (via the Celiac Disease Symptom Diary 2.1; CDSD 2.1©),[9] which included questions regarding the severity of diarrhea, abdominal pain, bloating, nausea and tiredness, and the frequency of vomiting and diarrhea
  - known and suspected inadvertent gluten exposure over 12 weeks
- Participants were recruited by the Celiac Disease Foundation via digital advertisements (email, social media channels, app push notifications, website advertisements and a study microsite).
- Data collection began on July 25, 2022, and completed on March 4, 2023.

Inclusion Criteria

- English-speaking, aged 12 to < 18 years at baseline (for the adolescent cohort) and residing in the USA.
- Diagnosis of CeD for ≥ 1 year (self-reported positive biopsy and/or serology).
- Adherence to a GFD for ≥ 6 months.
- CeD-related symptoms (patient-reported) within the past 3 months.
- Daily access to a smartphone and Internet/Wi-Fi/cellular data.

Exclusion Criteria

- Planned or current involvement in any clinical study with an investigational drug, or surgical procedure or gluten challenge during the 3-month observation period.

Data analysis

- The number of days with core CeD symptoms during the 12-week study period were recorded and a weighted mean number of days with each symptom was determined to account for any days with missing data (weighted mean was calculated as the mean proportion of days with reported symptom(s) across participants weighted by the total study period of 84 days).
- Prevalence of core CeD symptoms during the 12-week study period was stratified by self-reported level of GFD adherence and by irritable bowel syndrome (IBS) status of participants at study initiation.
  - An assessment of the symptom prevalence in participants with and without IBS was of interest because the symptoms of IBS and CeD overlap.
- Participants were included in these analyses if they experienced any symptom at least once during the 12-week study period.
- All measures were analyzed using descriptive statistics with R version 4.0.4. The *p* values were generated using a χ^2 test for categorical variables (or Fisher's exact test when expected value < 5) and analysis of variance (ANOVA) for continuous variables.

Key messages

- Despite adhering to a gluten-free diet (GFD), adolescent patients with coeliac disease (CeD) continued to experience gastrointestinal (GI) symptoms over a 12-week observation period.
- This study emphasizes the unmet need for the development of therapies for adolescent patients with CeD on a GFD.
- GI symptoms may be appropriate endpoints in future research of CeD therapies.

Results

Baseline demographics/clinical characteristics

- Adolescents (12 to < 18 years at enrollment) comprised 142 (29.6%) of the 480 enrolled participants **(Table 1)**.
  - The mean (standard deviation; SD) age was 14.5 (1.7) years, mean (SD) time since CeD diagnosis was 5.4 (3.4) years, 66.9% of participants self-identified as female and 97.9% reported to be of White race.
- In total, 16 participants (11.3%) reported having a hospitalization or emergency room visit due to CeD symptoms in the past 12 months, most of whom reported adhering to a GFD and "*rarely eating gluten accidentally*" **(Table 1)**.
- The most common self-reported comorbidities at baseline were anxiety (39.4%) and depression (21.1%) **(Table 1)**.

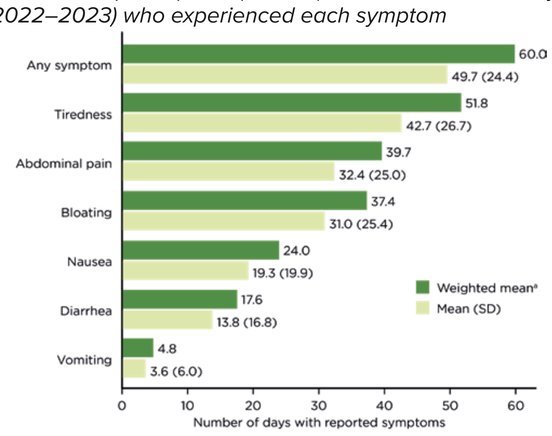
Frequency of gluten exposure over the 12-week study period

- The mean (SD) number of days with reported gluten exposure was 7.1 (9.3) **(Table 2)**.

Frequency and prevalence of symptoms over the 12-week study period

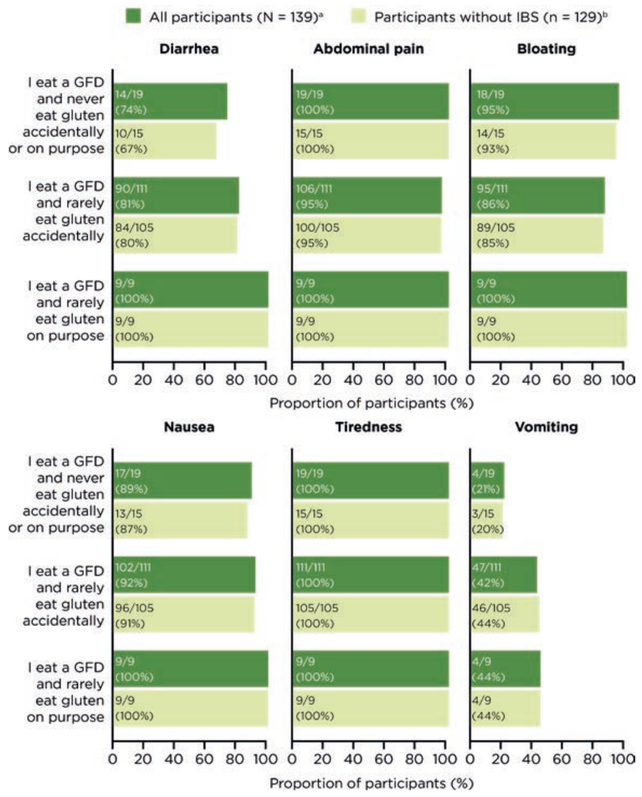
- The mean (SD) number of days of reported symptoms was 49.7 (24.4) (**Figure 1**).
  - Of the 65 participants reporting moderate, severe or very severe symptoms, the mean (SD) number of days with these symptoms was 55.4 (22.4); weighted mean 67.7.
- Among the core CeD symptoms experienced by adolescent participants during the 12 weeks of the study, tiredness, abdominal pain and bloating had the highest number of days with symptom occurrence (Figure 1).
- All adolescent participants reported at least one core CeD symptom.
  - Each GI symptom occurred at least once in > 80% of adolescent participants (with the exception of diarrhea in participants who reported adhering to a GFD and "never eating gluten accidentally or on purpose" and vomiting; (**Figure 2**).
  - Adolescent participants experienced symptoms regardless of level of adherence to a GFD (self-reported at baseline) or IBS diagnosis (**Figure 2**).

Figure 1
Number of days with core CeD symptoms during the 12-week study period among adolescent participants (N = 142) of the Virtual Celiac Symptoms Study (2022–2023) who experienced each symptom



[a]*Disorders that participants had in addition to CeD. Listed are current medical problems, diagnosed by a doctor or other healthcare professional, for which participants are currently or were receiving treatment within the past 12 months. Participants were allowed to select all that apply.* [b]*Includes ulcerative colitis and Crohn's disease. CeD, coeliac disease; GERD, gastroesophageal reflux disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; SD, standard deviation; SIBO, small intestine bacterial overgrowth.*

Figure 2
CeD core symptoms experienced by adolescent participants during the 12-week study period stratified by level of adherence to a GFD self-reported at baseline



[a]*Total number of adolescent participants was 139 because none of the participants reported "eating gluten-free diet sometimes" and participants who reported "eating gluten-containing foods regularly" (n = 3) were not included in this analysis.*
[b]*Total number of adolescent participants was 129 because participants who reported "eating gluten-containing foods regularly" (n = 2) were not included in this analysis.*
CeD, coeliac disease; GFD, gluten-free diet; IBS, irritable bowel syndrome. Data inside bars represent n/N (%).

Limitations

- There is currently no classification of symptom severity for CeD, thus participant self-assessment was used for this study.
- The self-reporting of daily symptoms and dietary intake are subject to inherent biases. Furthermore, daily reporting could increase awareness of GFD adherence, which may lead to changes in participants' dietary choices during the course of the study.
- There may be misclassification of CeD status by participants.
- The experience among adolescent patients with CeD in countries other than the USA may differ.

Conclusions

- Despite self-reported adherence to a GFD, all adolescent participants reported at least one GI symptom
- The findings from this study emphasize the need to better delineate between symptoms perceived to be related to gluten exposure and those that are not, and to develop therapies for the treatment and management of CeD among adolescent patients on a GFD.
- Symptom patterns identified in this study indicate that specific GI symptoms could be explored as relevant endpoints in future research of potential CeD medications.

Table 1. *Baseline demographics and clinical disease characteristics of adolescent participants of the Virtual Celiac Symptoms Study (2022–2023) stratified by level of adherence to a GFD.*

	Overall	Self-reported level of adherence to a GFD at baseline				
		I eat gluten-containing foods regularly	I eat a GFD and rarely eat gluten on purpose	I eat a GFD and rarely eat gluten accidentally	I eat a GFD and never eat gluten accidentally or on purpose	*p* value
Number of participants, n (%)	142 (100)	3 (2.1)	9 (6.3)	111 (78.2)	19 (13.4)	–
Age, years, mean (SD)	14.5 (1.7)	14.3 (2.1)	14.2 (1.9)	14.4 (1.7)	15.2 (1.7)	0.26
White race, n (%)	139 (97.9)	3 (100)	8 (88.9)	109 (98.2)	19 (100)	0.28
BMI, kg/m², mean (SD)	20.9 (4.3)	23.1 (0.4)	21.7 (5.4)	20.8 (4.4)	21.0 (3.4)	0.83
Sex, n (%)						
Female	95 (67.0)	3 (100)	7 (77.8)	72 (64.9)	13 (68.4)	0.75
Male	47 (33.1)	0 (0.0)	2 (22.2)	39 (35.1)	6 (31.6)	–
Education, n (%)						
Some HS/HS graduate/some college	79 (55.6)	2 (66.7)	5 (55.6)	60 (54.1)	12 (63.2)	0.91
Elementary/middle school	63 (44.4)	1 (33.3)	4 (44.4)	51 (46.0)	7 (36.8)	–
Time since CeD diagnosis, years, mean (SD)	5.4 (3.4)	2.2 (1.6)	3.5 (1.6)	5.8 (3.4)	4.8 (3.6)	0.05
Time spent following a GFD, years, mean (SD)	5.3 (3.4)	2.5 (2.2)	2.8 (1.4)	5.6 (3.4)	4.7 (3.5)	0.03
Comorbidities, n (%)						
At least one comorbidity	102 (71.8)	3 (100)	8 (88.9)	76 (68.5)	15 (79.0)	0.43
Anxiety	56 (39.4)	2 (66.7)	4 (44.4)	40 (36.0)	10 (52.6)	0.37
Depression	30 (21.1)	1 (33.3)	4 (44.4)	20 (18.0)	5 (26.3)	0.15
ADHD	24 (17.0)	1 (33.3)	2 (22.2)	17 (15.3)	4 (21.1)	0.52
Anemia	13 (9.2)	0 (0.0)	2 (22.2)	8 (7.2)	3 (15.8)	0.22
GERD	13 (9.2)	1 (33.3)	2 (22.2)	8 (7.2)	2 (10.5)	0.11
IBS	11 (7.8)	1 (33.3)	0 (0.0)	6 (5.4)	4 (21.1)	0.04
Thyroid disease	8 (5.6)	0 (0.0)	0 (0.0)	8 (7.2)	0 (0.0)	0.81
Type I diabetes	3 (2.1)	0 (0.0)	1 (11.1)	2 (1.8)	0 (0.0)	0.28
Failure to thrive as a child or difficulty gaining weight, n (%)	51 (35.9)	1 (33.3)	3 (33.3)	40 (36.0)	7 (36.8)	1.00
Hospitalization or ER visit due to CeD symptoms in the past 12 months, n (%)	16 (11.3)	0 (0.0)	5 (55.6)	10 (9.0)	1 (5.3)	0.004

ADHD, attention-deficit/hyperactivity disorder; BMI, body mass index; CeD, coeliac disease; ER, emergency room; GERD, gastroesophageal reflux disease; GFD, gluten-free diet; HS, high school; IBS, irritable bowel syndrome; SD, standard deviation.

Table 2. *Frequency of gluten exposure among adolescent participants of the Virtual Celiac Symptoms Study (2022–2023) during the 12-week study period stratified by level of adherence to a GFD at baseline.*

	Overall	Self-reported level of adherence to a GFD at baseline				
		I eat gluten-containing foods regularly	I eat a GFD and rarely eat gluten on purpose	I eat a GFD and rarely eat gluten accidentally	I eat a GFD and never eat gluten accidentally or on purpose	*p* value
Number of participants, n (%)	142 (100)	3 (2.1)	9 (6.3)	111 (78.2)	19 (13.4)	–
Number of participants with known or suspected gluten exposure, n (%)	103 (72.5)	2 (66.7)	9 (100)	80 (72.1)	12 (63.2)	–
Frequency of gluten exposure (known or suspected), mean (SD) number of days during the 12-week study period	6.7 (8.7)	37.5 (38.9)	14.9 (7.0)	5.3 (6.1)	4.8 (4.5)	< 0.0001

GFD, gluten-free diet; SD, standard deviation.

References

1. Caio G et al. BMC Med 2019;17:142.
2. Leffler DA et al. Value Health 2017;20:637–43.
3. Rubio-Tapia A et al. Am J Gastroenterol 2023;118:59–76.
4. Hall NJ et al. Appetite 2013;68:56–62.
5. Leffler DA et al. Dig Dis Sci 2008;53:1573–81.
6. Singh J et al. J Hum Nutr Diet 2011;24:479–86.
7. Syage JA et al. Am J Clin Nutr 2018;107:201–7.
8. Chang D et al. Aliment Pharmacol Ther 2022; 56 Suppl 1:s73–85.
9. Mapi Research Trust. Available from: https://eprovide.mapi-trust.org. (Accessed September 2023).

Acknowledgements

The authors would like to acknowledge Lin Zou and Allison Quintana for analytical support, Sanjana Sundaresan and James Signorovitch for consulting services, and Julia McBeth and Marissa Mahoney for study logistics support.

Funding

This study was sponsored by Takeda Development Center Americas, Inc. Medical writing support was provided by Christina Nikolakopoulou, PhD, of Oxford PharmaGenesis, Oxford, UK and was funded by Takeda Pharmaceuticals.

Disclosures

Data first presented at the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Annual Meeting, October 4–7, 2023, San Diego, **CA**. **DA** and **EL** serve as consultants for Takeda Pharmaceuticals. **LMM** was an employee of Takeda Development Center Americas, Inc. at the time of this study and holds Takeda stock. **MA** and **DAL** are employees of Takeda Development Center Americas, Inc. and receive stock or stock options. **JRM**, **SS** and **ES** are employees of Analysis Group, Inc., which received research support from Takeda Development Center Americas, Inc. **MG** is an employee of the Celiac Disease Foundation, which received financial support from Takeda Development Center Americas, Inc.

Presented at 35th Association of European Coeliac Societies General Assembly Conference, November 2–5, 2023, Athens, Greece.

Corresponding author: daniel.leffler@takeda.com

ABSTRACT OF ORIGINAL RESEARCH ON COELIAC DISEASE

Assessment of Quality of Life Among Children with Celiac Disease in Jordan

Submitted by: Celiac Care Providers Society, Laith M. Haj-Ahmad [1], Abida Alqaisi [2], Eyad Altamimi [3]

[1]Faculty of Medicine, University of Jordan, Amman, Jordan, [2]Celiac Care Providers Society, Amman, Jordan, [3]Pediatric and Neonatal Department, Jordan University of Science and Technology, Irbid, Jordan

Introduction

Celiac disease has a profound impact on the daily lives of patients who are diagnosed with this chronic autoimmune enteropathy and affected by its myriad of clinical implications.

Thus, health-related quality of life (Hrqol) surveys proved invaluable in assessing children with this condition. We aimed to assess Hrqol of children with celiac disease in Jordan.

Method

After applying our inclusion criteria to 400 children registered with the Celiac Care Providers Society (CCPS), we conducted a cross-sectional study that yielded 126 patients for analysis using the Kidscreen-52 questionnaire.

Data was analyzed using descriptive statistics and average T-scores across 10 health domains. The sample was divided into four cohorts based on concomitant disorders, disease duration, adherence to gluten free diet (GFD), and growth issues.

Independent sample t-tests, p-values, and Cohen's ds were determined for each cohort.

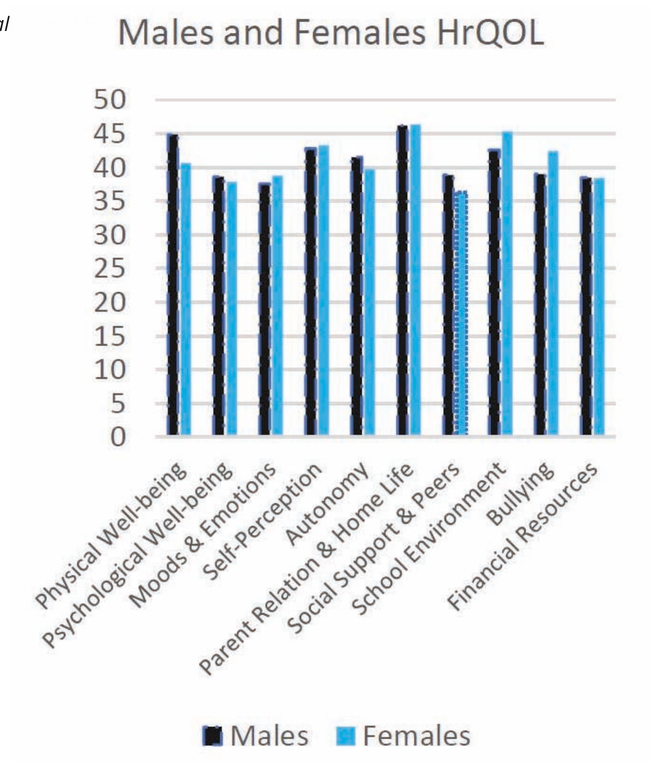
Table 1

Characteristics	Number, (%)
Average Age (Years) ±SD	13.4±2.49
Sex	
Male	56 (44.4)
Female	70 (55.6)
Subgroup analysis	
Average duration since diagnosis (Years) ±SD	4.27±3.09
Patients strictly following Gluten-Free Diet	77 (61.1)
Have a comorbid chronic illness(es)	85 (67.5)
Having growth problems:	43 (34.1)
- Weight <-2SD	9 (7.1)
- Height < -2SD	13 (10.3)
- Both weight and Height < -2SD	21 (16.7)

Table 1. Patient demographics

Chart 1

Mal



Results

Male celiac patients performed worse in six health domains compared to the general population: moods and emotions, self-perception, bullying, psychological well-being, social support, and financial resources. The last three of which showed poorer performance in female celiacs too. Moods and emotions and self-perception were significantly worse in males with chronic disease and without GFD adherence. Females with growth issues performed worse in school environment and financial resources. Refer to table (1) for relevant demographics and chart (1) for Hrqol among males and females.

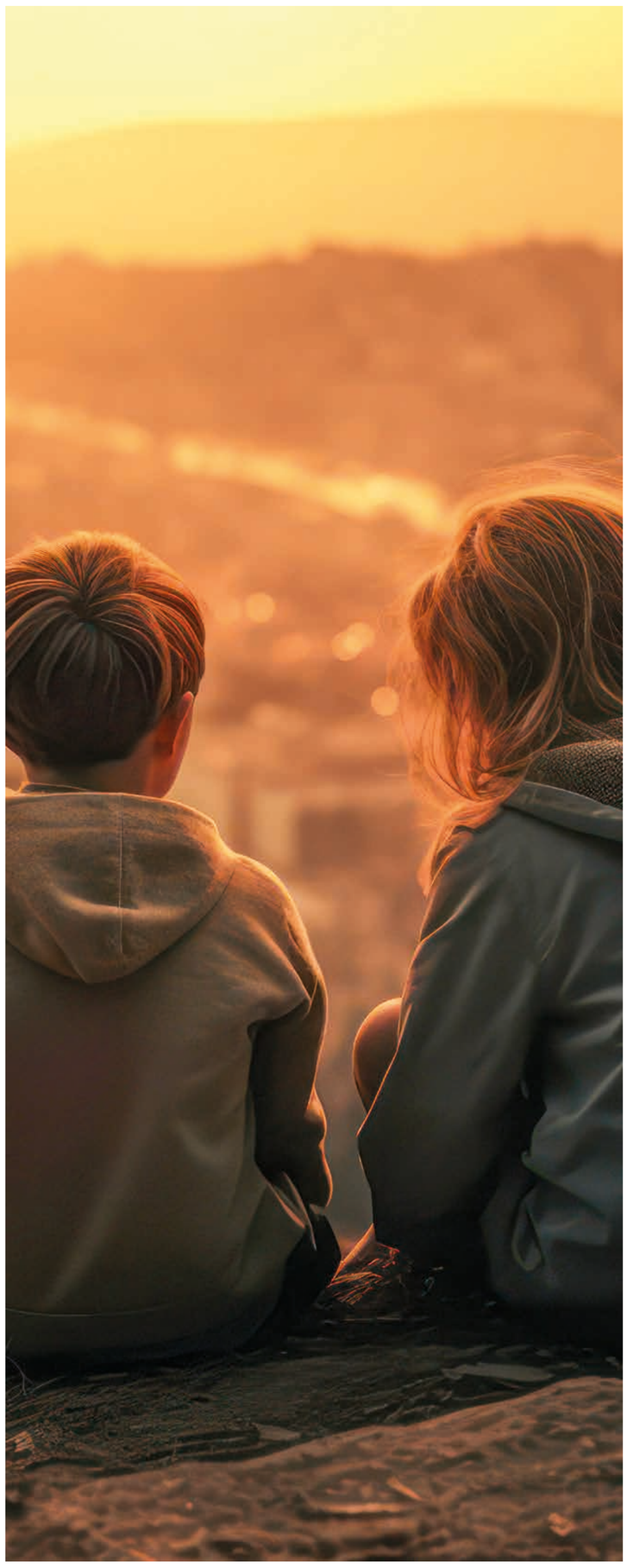
Conclusion

Our data strongly support the use of circulating miRNAs as a supplementary tool for the diagnosis of celiac disease without recurring to intestinal biopsy, a procedure that, especially for children, may result quite invasive and not very tolerated.

We have identified three valuable novel non-invasive biomarkers that alone or in combination may be employed successfully in the clinical practice for the diagnosis and follow-up of pediatric CD patients.

References

1. Therrien, Amelie, 'Celiac Disease: Extraintestinal Manifestations and Associated Conditions.', Journal of Clinical Gastroenterology, 54.1 (2020), 8–21.
2. Ravens-Sieberer U, Herdman M, Devine J, et al. The European KIDSCREEN approach to measure quality of life and well-being in children: development, current application, and future advances. Qual Life Res. 2014;23(3):791-803.



CONTACT

If you have any questions regarding the content in this brochure, please contact us at **helpdesk@aoecs.org**, or visit our webpage **www.aoecs.org**

AOECS
Association of European Coeliac Societies

This brochure was created in Nov. 2023 by the Association of European Coeliac Societies (AOECS). The AOECS is an international non-profit association, registered in Belgium. Registered number: BE0460502154. Registered Office: 4, Rue de la Presse, B-1000 Brussels, Belgium