April 2021 Alert

Items 1-159

1. **The Underlying Effects of Celiac Disease and Subsequent Implications on Deployment in the United States Army**


Authors

Grayson Seidel 1, Halle Kotchman 2, Erin Milner 1 3, Kevin J O'Donovan 1

Affiliations

- 1 Department of Chemistry and Life Science, United States Military Academy, West Point, NY 10996, USA.
- 2 Case Western Reserve University School of Medicine, Cleveland, OH 44106, USA.
- 3 Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA.

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DOI: 10.1093/milmed/usab177
Abstract

Introduction: The purpose of this review is to provide an overview of the etiology, pathology, and treatments for celiac disease (CD), as well as to provide context as to how CD impacts the U.S. military.

Materials and methods: To conduct this review, the authors surveyed recent epidemiology and immunology literature in order to provide a detailed summary of the current understanding of CD, its diagnosis, and the real-world impacts within the Department of Defense (DoD).

Results: We described the gluten proteins and both the immune response in CD. We further describe the underlying genetic risk factors and diagnosis and pathogenesis of the disease and conclude the review with a discussion of how current DoD regulations impact U.S. military readiness.

Conclusion: Celiac disease (CD) is an autoimmune disorder that results in damage to the small intestine. Ingestion of gluten in a CD patient is usually followed by villous atrophy in the small intestine, often along with other gastrointestinal symptoms. Around 1% of patients diagnosed with CD can experience complications if gluten-free diet is not followed, including intestinal lymphoma and hyposplenism. Therefore, a patient showing possible symptoms should discuss the diagnostic process with their healthcare providers to ensure adequate understanding of serological and genetic tests along with the histological examination of intestinal biopsy. Patients should seek consults with registered dietitians to structure their diets appropriately. Considering the prevalence and incidence of CD and gluten intolerances are increasing, the military should consider providing gluten-free Meals Ready-to-Eat as an option for all service members. Given the retention of service members with CD, subsequent admission of personnel with mild CD that does not affect the duties will allow the DoD access to a growing population of fully capable service members with critical technical skills who are eager to serve the USA.

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Authors

Andrea Costantino 1 2, Leda Roncoroni 1 2 3, Daniele Noviello 4, Nicoletta Nandi 4, Vincenza Lombardo 1 2, Alice Scricciolo 1 2, Lucia Scaramella 1 2, Maurizio Vecchi 1 2 4, Luca Elli 1 2

Affiliations

1 Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
2 Center for Prevention and Diagnosis of Celiac Disease, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
3 Department of Biomedical, Surgical and Dental Sciences, Università degli Studi di Milano, Milan, Italy.
4 Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy.

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Abstract

Background and Aims: Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, telemedicine has been supporting many patients with chronic diseases worldwide. However, data on celiac disease (CeD) nutritional and gastroenterological remote monitoring are scanty. The aims of our study
were to verify patients' trust in telemedicine and to evaluate the feasibility of telemedicine in nutritional monitoring. **Material and Methods:** We used telemedicine in place of the scheduled but not provided follow-up visits during the first lockdown of the COVID-19 pandemic. Patients received a phone call, and televisits were conducted for CeD patients with mild or moderate symptoms and/or with blood alterations. The patient's adherence to the gluten-free diet (GFD) was evaluated according to the Celiac Dietary Adherence Test (CDAT). When gluten contamination was suspected, a point-of-care gluten detection test was prescribed. The patient's trust in telemedicine was assessed, through an adapted version of the Patient Trust Assessment Tool (PATAT) questionnaire, as the percentage of patients giving a score of at least 4 out of 5 on a Likert scale for three selected key statements: "I can trust televisit," "I can trust that possible problems with the telemedicine service will be solved properly," and "I feel at ease when working with this website." **Results:** One hundred and twelve CeD patients were phone called; among symptomatic patients, 39 out of the 42 scheduled (92.9%) televisits were performed. Among the 39 visits, 34 (87.2%) questionnaires were compiled. The patients included in the study obtained a CDAT score from 7 to 13 (11 ± 2). Gluten detection tests were prescribed to 11 patients, resulting positive in 2. Trust in the telemedicine service was achieved in 94.1, 88.2, and 97.1% for the three selected key statements of the PATAT questionnaire. **Conclusion:** During the COVID-19 pandemic, telemedicine showed to be feasible and the majority of patients trusted the combined gastroenterological and nutritional televisits. Gluten detection tests demonstrated to be useful tools for the patient and for the caregiver to confirm adherence to the GFD remotely.

**Keywords:** COVID-19; celiac disease; gluten detection test; gluten free diet; nutrition; telehealth; telemedicine; televisits.

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**Conflict of interest statement**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Comprehensive Analysis of CDR3 Sequences in Gluten-Specific T-Cell Receptors Reveals a Dominant R-Motif and Several New Minor Motifs


Authors

Shiva Dahal-Koirala 1 2, Louise Fremgaard Risnes 1 2, Ralf Stefan Neumann 1, Asbjørn Christophersen 1 2, Knut E A Lundin 1 2 3, Geir Kjetil Sandve 4, Shuo-Wang Qiao 1 2, Ludvig M Sollid 1 2

Affiliations

1 K.G. Jebsen Coeliac Disease Research Centre, Department of Immunology, University of Oslo, Oslo, Norway.
2 Department of Immunology, University of Oslo and Oslo University Hospital-Rikshospitalet, Oslo, Norway.
3 Department of Gastroenterology, Oslo University Hospital-Rikshospitalet, Oslo, Norway.
4 Biomedical Informatics, Department of Informatics, University of Oslo, Oslo, Norway.

Abstract

Gluten-specific CD4+ T cells are drivers of celiac disease (CeD). Previous studies of gluten-specific T-cell receptor (TCR) repertoires have found public TCRs shared across multiple individuals, biased usage of particular V-genes and conserved CDR3 motifs. The CDR3 motifs within the gluten-specific TCR repertoire, however, have not been systematically investigated. In the current study, we analyzed the largest TCR database of gluten-specific CD4+ T cells
studied so far consisting of TCRs of 3122 clonotypes from 63 CeD patients. We established a TCR database from CD4+ T cells isolated with a mix of HLA-DQ2.5:gluten tetramers representing four immunodominant gluten epitopes. In an unbiased fashion we searched by hierarchical clustering for common CDR3 motifs among 2764 clonotypes. We identified multiple CDR3α, CDR3β, and paired CDR3α:CDR3β motif candidates. Among these, a previously known conserved CDR3β R-motif used by TRAV26-1/TRBV7-2 TCRs specific for the DQ2.5-glia-α2 epitope was the most prominent motif. Furthermore, we identified the epitope specificity of altogether 16 new CDR3α:CDR3β motifs by comparing with TCR sequences of 231 T-cell clones with known specificity and TCR sequences of cells sorted with single HLA-DQ2.5:gluten tetramers. We identified 325 public TCRα and TCRβ sequences of which 145, 102 and 78 belonged to TCRα, TCRβ and paired TCRαβ sequences, respectively. While the number of public sequences was depended on the number of clonotypes in each patient, we found that the proportion of public clonotypes from the gluten-specific TCR repertoire of given CeD patients appeared to be stable (median 37%). Taken together, we here demonstrate that the TCR repertoire of CD4+ T cells specific to immunodominant gluten epitopes in CeD is diverse, yet there is clearly biased V-gene usage, presence of public TCRs and existence of conserved motifs of which R-motif is the most prominent.

**Keywords:** CDR3 motifs; R-motif; T-cell receptors; celiac disease; gluten-specific T-cell receptors; public T-cell receptors.

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**Conflict of interest statement**

SD-K, LR, RN, AC, KL, S-WQ, GS and LS are holders of a patent application entitled "Method of diagnosing celiac disease" (US20210010077A1) on the use of the gluten-specific T cell receptor sequences described in the current work for diagnosis of celiac disease.

4. **Potential impact of celiac disease genetic risk factors on T cell receptor signaling in gluten-specific CD4+ T cells**

Authors

Olivier B Bakker # 1, Aarón D Ramírez-Sánchez # 1, Zuzanna A Borek # 1, Niek de Klein # 1, Yang Li # 1, Rutger Modderman 1, Yvonne Kooy-Winkelaar 2, Marie K Johannesen 3 4, Filomena Matarese 5, Joost H A Martens 5, Vinod Kumar 1 6 7, Jeroen van Bergen 2, Shuo-Wang Qiao 3 4, Knut E A Lundin 3 8, Ludvig M Sollid 3 4, Frits Koning 2, Cisca Wijmenga 1 3, Sebo Withoff 1, Iris H Jonkers 9

Affiliations

1 Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
2 Department of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands.
3 K.G. Jebsen Coeliac Disease Research Centre, Institute of Clinical Medicine, University of Oslo, Oslo, Norway.
4 Department of Immunology, Oslo University Hospital, Rikshospitalet, Oslo, Norway.
5 Department of Molecular Biology, Nijmegen Centre for Molecular Life Sciences, Radboud University, Nijmegen, The Netherlands.
6 Department of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, The Netherlands.
7 Nitte (Deemed to be University), Division of Infectious Diseases, Nitte University Centre for Science Education and Research (NUCSER), Paneer Campus, Deralakatte, Mangaluru, 575018, India.
8 Department of Gastroenterology, Oslo University Hospital, Rikshospitalet, Oslo, Norway.
9 Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. i.h.jonkers@umcg.nl

# Contributed equally.

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- DOI: 10.1038/s41598-021-86612-5
Abstract

Celiac disease is an auto-immune disease in which an immune response to dietary gluten leads to inflammation and subsequent atrophy of small intestinal villi, causing severe bowel discomfort and malabsorption of nutrients. The major instigating factor for the immune response in celiac disease is the activation of gluten-specific CD4+ T cells expressing T cell receptors that recognize gluten peptides presented in the context of HLA-DQ2 and DQ8. Here we provide an in-depth characterization of 28 gluten-specific T cell clones. We assess their transcriptional and epigenetic response to T cell receptor stimulation and link this to genetic factors associated with celiac disease. Gluten-specific T cells have a distinct transcriptional profile that mostly resembles that of Th1 cells but also express cytokines characteristic of other types of T-helper cells. This transcriptional response appears not to be regulated by changes in chromatin state, but rather by early upregulation of transcription factors and non-coding RNAs that likely orchestrate the subsequent activation of genes that play a role in immune pathways. Finally, integration of chromatin and transcription factor binding profiles suggest that genes activated by T cell receptor stimulation of gluten-specific T cells may be impacted by genetic variation at several genetic loci associated with celiac disease.

- 82 references

5. **Psyllium Improves the Quality and Shelf Life of Gluten-Free Bread**


Authors

Camilly Fratelli 1, Fernanda Garcia Santos 1, Denise Garcia Muniz 1, Sascha Habu 1 2, Anna Rafaela Cavalcante Braga 1 3, Vanessa Dias Capriles 1

Affiliations

- 1 Department of Biosciences, Institute of Health and Society (Campus Baixada Santista), Federal University of São Paulo, Rua Silva Jardim, 136, Santos CEP 11015-020, Brazil.
Psyllium husk powder was investigated for its ability to improve the quality and shelf life of gluten-free bread. Gluten-free bread formulations containing 2.86%, 7.14%, and 17.14% psyllium by flour weight basis were compared to the control gluten-free bread and wheat bread in terms of performance. The effect of time on crumb moisture and firmness, microbial safety, and sensory acceptability using a 10-cm scale was assessed at 0, 24, 48, and 72 h postproduction. Crumb firming was observed during the storage time, especially for the control gluten-free bread, which had a crumb firmness 8-fold higher than that of the wheat bread. Psyllium addition decreased the crumb firmness values by 65-75% compared to those of the control gluten-free bread during 72 h of storage. The longest delay in bread staling was observed with a 17.14% psyllium addition. The psyllium-enriched gluten-free bread was well accepted during 72 h of storage, and the acceptability scores for aroma, texture, and flavor ranged from 6.8 to 8.3, which resembled those of wheat bread. The results showed that the addition of 17.14% psyllium to the formulation improved the structure, appearance, texture, and acceptability of gluten-free bread and delayed bread staling, resembling physical and sensory properties of wheat bread samples during 72 h of storage. Therefore, according to the obtained results, this approach seems to be promising to overcome some of the limitations of gluten-free breadmaking.

**Keywords:** acceptability; bread quality; gluten-free; multiple factor analysis; staling process.
Oral Mucosa as a Potential Site for Diagnosis and Treatment of Allergic and Autoimmune Diseases


Authors

Cristina Gomez-Casado, Javier Sanchez-Solares, Elena Izquierdo, Araceli Díaz-Perales, Domingo Barber, María M Escribese

Affiliations

1 Institute of Applied Molecular Medicine, Department of Basic Medical Sciences, Faculty of Medicine, San Pablo CEU University, 28003 Madrid, Spain.
2 Center of Plant Biotechnology and Genomics, Technical University of Madrid, 28040 Madrid, Spain.

PMID: 33925074
DOI: 10.3390/foods10050970

Abstract

Most prevalent food allergies during early childhood are caused by foods with a high allergenic protein content, such as milk, egg, nuts, or fish. In older subjects, some respiratory allergies progressively lead to food-induced allergic reactions, which can be severe, such as urticaria or asthma. Oral mucosa remodeling has been recently proven to be a feature of severe allergic phenotypes and autoimmune diseases. This remodeling process includes epithelial barrier disruption and the release of inflammatory signals. Although little is known about the immune processes taking place in the oral mucosa, there are a few reports describing the oral mucosa-associated immune system. In this review, we will provide an overview of the recent knowledge about the role of the oral mucosa in food-induced allergic reactions, as well as in severe respiratory allergies or food-induced autoimmune diseases, such as celiac disease.
Keywords: autoimmune disease; celiac disease; desensitization; diagnosis; food allergy; inflammatory disease; oral mucosa; systemic disease; treatment.

Ancient and Modern Cereals as Ingredients of the Gluten-Free Diet: Are They Safe Enough for Celiac Consumers?


Authors

Francesca Colombo 1, Chiara Di Lorenzo 1, Simone Biella 1, Corinne Bani 1, Patrizia Restani 1

Affiliation

1 Department of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, 20133 Milan, Italy.

PMID: 33924221
DOI: 10.3390/foods10040906

Abstract

Celiac disease is an autoimmune disorder that occurs in genetically predisposed individuals after consuming prolamins from some cereals. Although the products available for celiac subjects have increased significantly in quality and quantity over the last few decades, research still focuses on identifying new ingredients to improve the nutritional, sensorial and functional qualities of gluten-free products. In terms of toxicity for people with celiac disease, there is a wide variability between ancient and modern grains. The most contradictory results are related to the role of oats in the gluten-free diet. In order to clarify the role of minor cereals (such as oat) and ancient grains in the diets of celiac patients, this review discusses recent in vitro and in vivo studies performed on those cereals for which the toxicity for celiac subjects is still controversial. According to in vivo studies, selected oat varieties could be tolerated by celiac patients. On the other hands, although some wheat-ancient grains (Triticum monococcum, Triticum aestivum ssp. spelta and Kamut®) showed a reduced in vitro toxicity, to date, these grains
are still considered toxic for celiac patients. Contradictory results underline the importance of studying the safety of "unusual" cereals in more detail.

**Keywords:** Avena sativa; Triticum aestivum ssp. spelta; Triticum monococcum; Triticum turgidum; celiac disease; gluten-free diet.

8. **Stiff Person Syndrome and Gluten Sensitivity**


**Authors**

Marios Hadjivassiliou ¹, Panagiotis Zis ¹, David S Sanders ², Nigel Hoggard ³, Ptolemaios G Sarrigiannis ¹

**Affiliations**

- ¹ Academic Department of Neurosciences, Sheffield Teaching Hospitals NHS Trust, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK.
- ² Academic Department of Gastroenterology, Sheffield Teaching Hospitals NHS Trust, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK.
- ³ Department of Infection, Immunity & Cardiovascular Disease, University of Sheffield, Sheffield S10 2JF, UK.

- PMID: 33923904
- DOI: 10.3390/nu13041373

**Abstract**

Stiff person syndrome (SPS) is a rare autoimmune disease characterised by axial stiffness and episodic painful spasms. It is associated with additional autoimmune diseases and cerebellar ataxia. Most patients with SPS have high levels of glutamic acid decarboxylase (GAD) antibodies. The aetiology of SPS remains unclear but autoimmunity is thought to play a major part. We have previously demonstrated overlap between anti-GAD ataxia and gluten sensitivity. We have also demonstrated the beneficial effect of a gluten-free...
diet (GFD) in patients with anti-GAD ataxia. Here, we describe our experience in the management of 20 patients with SPS. The mean age at symptom onset was 52 years. Additional autoimmune diseases were seen in 15/20. Nineteen of the 20 patients had serological evidence of gluten sensitivity and 6 had coeliac disease. Fourteen of the 15 patients who had brain imaging had evidence of cerebellar involvement. Twelve patients improved on GFD and in seven GFD alone was the only treatment required long term. Twelve patients had immunosuppression but only three remained on such medication. Gluten sensitivity plays an important part in the pathogenesis of SPS and GFD is an effective therapeutic intervention.

**Keywords:** anti-GAD antibodies; cerebellar ataxia; coeliac disease; gluten free diet; gluten sensitivity; stiff person syndrome.

9. **Emerging Roles of Gut Virome in Pediatric Diseases**


**Authors**

Valerio Fulci 1, Laura Stronati 1, Salvatore Cucchiara 2, Ilaria Laudadio 1, Claudia Carissimi 1

**Affiliations**

- 1 Department of Molecular Medicine, Sapienza University of Rome, 00161 Rome, Italy.
- 2 Department of Women's and Children's Health, Sapienza University of Rome, 00161 Rome, Italy.

- PMID: 33923593
- DOI: 10.3390/ijms22084127

**Abstract**

In the last decade, the widespread application of shotgun metagenomics provided extensive characterization of the bacterial "dark matter" of the gut microbiome, propelling the development of dedicated, standardized bioinformatic pipelines and the systematic collection of metagenomic data
into comprehensive databases. The advent of next-generation sequencing also unravels a previously underestimated viral population (virome) present in the human gut. Despite extensive efforts to characterize the human gut virome, to date, little is known about the childhood gut virome. However, alterations of the gut virome in children have been linked to pathological conditions such as inflammatory bowel disease, type 1 diabetes, malnutrition, diarrhea and celiac disease.

**Keywords:** celiac disease; children; diarrhea; inflammatory bowel disease; malnutrition; metagenomics; type 1 diabetes; virome.

10. **Mycotoxin Occurrence and Risk Assessment in Gluten-Free Pasta through UHPLC-Q-Exactive Orbitrap MS**


**Authors**

Josefa Tolosa 1, Yelko Rodríguez-Carrasco 1, Giulia Graziani 2, Anna Gaspari 2, Emilia Ferrer 1, Jordi Mañes 1, Alberto Ritieni 2 3

**Affiliations**

- 1 Department of Food Chemistry and Toxicology, University of Valencia, Av. Vicent A. Estellés, s/n, Burjassot, 46100 Valencia, Spain.
- 2 Department of Pharmacy, Università di Napoli Federico II, Via D. Montesano, 80131 Napoli, Italy.
- 3 UNESCO Chair of Health Education and Sustainable Development at University of Naples, 80131 Napoli, Italy.

- PMID: [33923097](https://www.ncbi.nlm.nih.gov/pubmed/33923097)
- DOI: [10.3390/toxins13050305](https://doi.org/10.3390/toxins13050305)

**Abstract**

Celiac disease (CD) is a genetic-based autoimmune disorder which is characterized by inflammation in the small intestinal mucosa due to the intolerance to gluten. Celiac people should consume products without gluten,
which are elaborated mainly with maize or other cereals. Contamination of cereals with mycotoxins, such as fumonisins (FBs) and aflatoxins (AFs) is frequently reported worldwide. Therefore, food ingestion is the main source of mycotoxin exposure. A new analytical method was developed and validated for simultaneous analysis of 21 mycotoxins in gluten-free pasta, commonly consumed by celiac population as an alternative to conventional pasta. Ultrahigh-performance liquid chromatography coupled to quadrupole Orbitrap high-resolution mass spectrometry (UHPLC-Q-Exactive Orbitrap MS) was used for analyte separation and detection. The mycotoxins included in this work were those widely reported to occur in cereal samples, namely, ochratoxin-A (OTA), aflatoxins (AFB1, AFB2, AFG1 and AFG2), zearalenone (ZON), deoxynivalenol (DON), 3-acetyl-deoxynivalenol and 15-acetyl-deoxynivalenol (3-AcDON and 15-AcDON, respectively), nivalenol (NIV), neosolaniol (NEO), fusarenone-X, (FUS-X), T-2 toxin (T-2) and HT-2 toxin (HT-2), fumonisin B1 and B2 (FB1 and FB2, respectively), enniatins (ENN A, ENN A1, ENN B and ENN B1) and beauvericin (BEA). The validated method was successfully applied to 84 gluten-free pasta samples collected from several local markets of Campania region (Italy) during September to November 2020 to monitor the occurrence of mycotoxins and to assess the exposure to these food contaminants. A significant number of samples (95%) showed mycotoxin contamination, being Fusarium mycotoxins (FB1, ZON and DON) the most commonly detected ones. Regarding the risk assessment, the higher exposures were obtained for NIV, DON and FB1 for children and teenagers age group which can be explained due to their lower body weight.

**Keywords:** HRMS-Orbitrap; exposure; gluten-free pasta; liquid-chromatography; multiresidue method; mycotoxins.

11. **Small Bowel Epithelial Precursor Lesions: A Focus on Molecular Alterations**


**Authors**

Alessandro Vanoli ¹, Federica Grillo ², Daniela Furlan ³, Giovanni Arpa ¹, Oneda Grami ¹, Camilla Guerini ¹, Roberta Riboni ¹, Luca Mastracci ², Antonio Di Sabatino ⁴
Abstract

The wider use of gastrointestinal endoscopic procedures has led to an increased detection of small intestinal preneoplastic and neoplastic epithelial lesions, most of which are identified in the duodenum and ampullary region. Like their malignant counterparts, small intestinal glandular precursor lesions, which include adenomas and hamartomas, may arise sporadically or be associated with hereditary tumor syndromes, such as familial adenomatous polyposis, MUTYH-associated polyposis, Lynch syndrome, Peutz-Jeghers syndrome, juvenile polyposis syndrome, and Cowden syndrome. In addition, dysplastic, preinvasive lesions have been observed adjacent to small bowel adenocarcinomas complicating immune-related disorders, such as celiac or Crohn's disease. Adenomatous lesions may exhibit an intestinal-type, gastric-type, or, very rarely, serrated differentiation, related to different molecular pathogenetic mechanisms. Finally, in the background of multiple endocrine neoplasia 1 syndrome, precursor neuroendocrine growths have been described. In this review we offer a comprehensive description on the histomolecular features of the main histotypes of small bowel epithelial precursors lesions, including: (i) sporadic adenomas (intestinal-type and gastric-type; non-ampullary and ampullary); (ii) syndromic adenomas; (iii) small bowel dysplasia in celiac and Crohn's disease; (iv) serrated lesions; (v) hamartomatous lesions; and (vi) neuroendocrine precursor lesions.
Keywords: APC; Crohn’s disease; GNAS; adenoma; ampulla; celiac disease; hamartoma; neuroendocrine; polyposis; small intestine.


Authors

Paola Conte ¹, Simone Pulina ¹, Alessandra Del Caro ¹, Costantino Fadda ¹, Pietro Paolo Urgeghe ¹, Alessandra De Bruno ², Graziana Difonzo ³, Francesco Caponio ³, Rosa Romeo ², Antonio Piga ¹

Affiliations

¹ Department of Agricultural Sciences, Università degli Studi di Sassari, Viale Italia 39/A, 07100 Sassari, Italy.
² Department of Agraria, University Mediterranea of Reggio Calabria, 89124 Reggio Calabria, Italy.
³ Department of Soil Plant and Food Sciences, University of Bari Aldo Moro, Via Amendola 165/A, 70126 Bari, Italy.

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DOI: 10.3390/foods10050923

Abstract

Nowadays, food processing by-products, which have long raised serious environmental concerns, are recognized to be a cheap source of valuable compounds. In the present study, incorporation of phenolic-rich extracts (500 and 1000 mg kg⁻¹) from olive leaves (OL) and olive mill wastewater (OMW) into conventional gluten-free formulations has been exploited as a potential strategy for developing nutritious and healthy breadsticks with extended shelf-life. To this end, moisture, water activity (a_w), visual and textural properties, the composition of biologically active compounds (soluble, insoluble, and bio-accessible polyphenols), antioxidant activity, oxidation stability, and consumer preference of the resulting breadsticks were
investigated. Fortified breadsticks had higher moisture and $a_{w}$, lower hardness, and similar color in comparison to the control, especially in the case of OL extract supplementation. All enriched formulations significantly affected the phenolic composition, as evidenced by the decrease in insoluble/soluble polyphenols ratio (from 7 in the control up to 3.1 and 4.5 in OL and OMW, respectively), and a concomitant increase in polyphenol bio-accessibility (OL: 14.5-23% and OMW: 10.4-15% rise) and antioxidant activity (OL: 20-36% and OMW: 11-16% rise). Moreover, a significant shelf-life extension was observed in all fortified breadsticks (especially in case of OMW supplementation). Sensory evaluation evidenced that 61% of the assessors showed a marked, but not significant, tendency to consider the sample supplemented with high levels of OL as a more palatable choice.

**Keywords:** antioxidants; breadsticks; gluten-free; olive oil by-products; oxidation stability.

13. **Technological, Nutritional and Sensory Properties of an Innovative Gluten-Free Double-Layered Flat Bread Enriched with Amaranth Flour**


**Authors**

Antonio Piga ¹, Paola Conte ¹, Simonetta Fois ², Pasquale Catzeddu ², Alessandra Del Caro ¹, Anna Maria Sanguinetti ¹, Costantino Fadda ¹

**Affiliations**

- ¹ Dipartimento di Agraria, Università degli Studi di Sassari, Viale Italia 39/A, 07100 Sassari, Italy.
- ² Porto Conte Ricerche Srl, Località Tramariglio, 07041 Alghero, Italy.

**PMID:** [33922117](https://www.ncbi.nlm.nih.gov/pubmed/33922117)

**DOI:** [10.3390/foods10050920](https://doi.org/10.3390/foods10050920)
Abstract

Celiac disease is increasing all over the world. In this context, most recent research in this area is addressing and attempting to improve the nutritional value and sensory characteristics of gluten-free (GF) food products and to enhance their technological properties. Here, amaranth flour was studied as a potential healthy ingredient for the development of an innovative GF flat bread. Starting from two different basic formulations (rice flour:corn starch and rice flour:tapioca starch, 50:50), the impact of partially replacing rice flour (6%) and starch (6%) with amaranth on the nutritional characteristics, polyphenol composition, textural, and sensory properties of the resulting GF flat breads was explored. The substitution with amaranth led to detrimental effects on the doughs' viscometric properties, especially in the case of tapioca starch, but significantly improved the doughs' textural properties. All the amaranth-enriched flat breads showed a better color and a significant increase in all polyphenols fractions but lower antioxidant activity. During bread storage for three days, a detrimental effect on both starch retrogradation, toughness, and extensibility properties were observed, especially when tapioca starch was used. Check-all-that-apply (CATA) sensory test results showed that the incorporation of amaranth increased yeast odor and yeast flavor perception and decreased the softness in mouth-only in tapioca-based samples. A better compromise among technological, nutritional, and sensory properties was achieved when amaranth flour was added to the basic rice and corn formulation.

Keywords: gluten-free flat bread; sensory analysis; shelf life; starch; texture.

14. Distal Pancreatectomy with Celiac Axis Resection: Systematic Review and Meta-Analysis


Authors

Giuseppe Nigri ¹, Niccolò Petrucciani ¹, Elena Belloni ¹, Alessio Lucarini ¹, Paolo Aurello ¹, Francesco D'Angelo ¹, Salomone di Saverio ², Alessandro Fancellu ³, Giovanni Ramacciato ¹
Affiliations

1 Department of Medical and Surgical Sciences and Translational Medicine, Sapienza University of Rome, Sant'Andrea Hospital, 00189 Rome, Italy.
2 Department of Surgery, Cambridge University Hospitals NHS Foundation Trust, Cambridge CB2 0QQ, UK.
3 Department of Medical, Surgical and Experimental Sciences, University of Sassari, 07100 Sassari, Italy.

PMID: 33921838
DOI: 10.3390/cancers13081967

Abstract

Background: Major vascular invasion represents one of the most frequent reasons to consider pancreatic adenocarcinomas unresectable, although in the last decades, demolitive surgeries such as distal pancreatectomy with celiac axis resection (DP-CAR) have become a therapeutical option.

Methods: A meta-analysis of studies comparing DP-CAR and standard DP in patients with pancreatic adenocarcinoma was conducted. Moreover, a systematic review of studies analyzing oncological, postoperative and survival outcomes of DP-CAR was conducted.

Results: Twenty-four articles were selected for the systematic review, whereas eleven were selected for the meta-analysis, for a total of 1077 patients. Survival outcomes between the two groups were similar in terms of 1 year overall survival (OS) (odds ratio (OR) 0.67, 95% confidence interval (CI) 0.34 to 1.31, p = 0.24). Patients who received DP-CAR were more likely to have T4 tumors (OR 28.45, 95% CI 10.46 to 77.37, p < 0.00001) and positive margins (R+) (OR 2.28, 95% CI 1.24 to 4.17, p = 0.008). Overall complications (OR, 1.72, 95% CI, 1.15 to 2.58, p = 0.008) were more frequent in the DP-CAR group, whereas rates of pancreatic fistula (OR 1.16, 95% CI 0.81 to 1.65, p = 0.41) were similar.

Conclusions: DP-CAR was not associated with higher mortality compared to standard DP; however, overall morbidity was higher. Celiac axis involvement should no longer be considered a strict contraindication to surgery in patients
with locally advanced pancreatic adenocarcinoma. Considering the different baseline tumor characteristics, DP-CAR may need to be compared with palliative therapies instead of standard DP.

**Keywords:** borderline resectable; pancreatic cancer; vascular reconstruction.

15. **Non-Celiac Gluten/Wheat Sensitivity: Clinical Characteristics and Microbiota and Mycobiota Composition by Response to the Gluten Challenge Test**


**Authors**

Valentina Ponzo ¹, Ilario Ferrocino ², Ilaria Goitre ¹, Marianna Pellegrini ¹, Mauro Bruno ³, Marco Astegiano ³, Gianni Cadario ⁴, Eleonora Castellana ⁵, Fabio Bioletto ¹, Maria Rita Corvaglia ², Patrizia Malfa ⁶, Luca Cocolin ², Ezio Ghigo ¹, Simona Bo ¹

**Affiliations**

- ¹ Department of Medical Sciences, University of Torino, 10126 Torino, Italy.
- ² Department of Agricultural, Forestry and Food Science, University of Torino, 10095 Torino, Italy.
- ³ Gastroenterology and Digestive Endoscopy Unit, "Città della Salute e della Scienza" Hospital, 10126 Torino, Italy.
- ⁴ Allergology and Clinical Immunology Unit, "Città della Salute e della Scienza" Hospital, 10126 Torino, Italy.
- ⁵ Hospital Pharmacy, "Città della Salute e della Scienza" Hospital, 10126 Torino, Italy.
- ⁶ Proge Farm, 28100 Novara, Italy.

**PMID:** 33921293

**DOI:** 10.3390/nu13041260
Abstract

The aims of this observational "proof-of-concept" study were to analyze the clinical/psychological characteristics and gut microbiota/mycobiota composition of individuals with suspected non-celiac gluten/wheat sensitivity (NCGS/WS) according to responses to the double-blind-placebo-controlled (DBPC) crossover gluten challenge test. Fifty individuals with suspected NCGS/WS were subjected to the DBPC challenge test; anthropometric measurements, psychometric questionnaires, and fecal samples were collected. Twenty-seven (54%) participants were gluten responsive (NCGS), and 23 were placebo responsive, with an order effect. NCGS individuals displayed a significantly lower risk of eating disorders and a higher mental health score when compared to placebo-responsive participants, confirmed by multiple logistic regression analyses (OR = 0.87; 95% CI 0.76-0.98, \( p = 0.021 \), and \( OR = 1.30; 95\% CI 1.06-1.59, \ p = 0.009, \) respectively). Principal coordinate analyses based on microbiota composition showed a separation by the DBPC response \( ( p = 0.039 ) \). For \textit{Bacteroides} \( ( p = 0.05 ) \) and \textit{Parabacteroides} \( ( p = 0.007 ) \), the frequency of amplicon sequence variants was lower, and that for \textit{Blautia} \( ( p = 0.009 ) \) and \textit{Streptococcus} \( ( p = 0.004 ) \) was higher in NCGS individuals at multiple regression analyses. No difference in the mycobiota composition was detected between the groups. In conclusion, almost half of the individuals with suspected gluten sensitivity reported symptoms with placebo; they showed lower mental health scores, increased risk for eating disorders, and a different gut microbiota composition.

\textbf{Keywords}: gluten sensitivity; gut microbiota; gut mycobiota; mental status.

16. \textbf{High-Fat Foods and FODMAPs Containing Gluten Foods Primarily Contribute to Symptoms of Irritable Bowel Syndrome in Korean Adults}


\textbf{Authors}

\textit{Woori Na}, \textit{Yeji Lee}, \textit{Hyeji Kim}, \textit{Yong Sung Kim}, \textit{Cheongmin Sohn}
Abstract

Dietary control plays an important role in the treatment of irritable bowel syndrome (IBS). However, few studies have examined the relationship between dietary intake and symptoms of IBS in Koreans. The current cross-sectional study aimed to examine the diet in food consumption and nutrient intake in Korean adults aged 20 to 40 with IBS. The data collected were completed by 857 subjects using a community-based web survey. The questionnaire covered functional bowel disorders based on Rome III, the semi-quantitative Food Frequency Questionnaire (SQ-FFQ), and the food items causing symptoms. In total, 186 of 857 subjects (21.7%) were diagnosed with IBS. The non-IBS group had a fat intake of 76.9 ± 47.9 g/day, while the IBS group had a fat intake of 86.6 ± 55.1 g/day (p = 0.014). The non-IBS group had a total fermentable oligosaccharide, disaccharide, monosaccharide, and polyol (FODMAP) intake of 12.6 ± 9.7 g/day, whereas the IBS group had a total FODMAP intake of 13.9 ± 9.9 g/day (p = 0.030). Foods that contributed to the onset of symptoms in the IBS group were instant noodles (70.8%), Chinese noodles with vegetables and seafood (68.7%), pizza (67.2%), and black bean sauce noodles (66.3%) which are mostly classified as high fat and high gluten foods. The dietary intake of IBS patients differs from that of non-IBS subjects. Increased intake of gluten-containing or high-fat foods due to the westernized diet caused more IBS symptoms than high FODMAPs and dairy products in Korean adults in their 20 s to 40 s.

Keywords: FODMAP; Korea; dietary assessment; glutens; high fat; irritable bowel syndrome.
Effect of Octenyl Succinic Anhydride (OSA) Modified Starches on the Rheological Properties of Dough and Characteristic of the Gluten-Free Bread


Authors

Jarosław Korus, Rafal Ziobro, Teresa Witczak, Kamila Kapusniak Jochym, Lesław Juszczak

Affiliations

1 Department of Carbohydrate Technology, Faculty of Food Technology, University of Agriculture in Krakow, 30-149 Kraków, Poland.
2 Department of Engineering and Machinery for Food Industry, Faculty of Food Technology, University of Agriculture in Krakow, 30-149 Kraków, Poland.
3 Department of Biochemistry, Biotechnology and Ecotoxicology, Faculty of Science and Technology, Jan Długosz University in Częstochowa, 42-200 Częstochowa, Poland.
4 Department of Food Analysis and Evaluation of Food Quality, Faculty of Food Technology, University of Agriculture in Krakow, 30-149 Kraków, Poland.

PMID: 33920373  
DOI: 10.3390/molecules26082197

Abstract

The study focused on the influence of starch modified by octenyl succinic anhydride (OSA) on the rheological and thermal properties of gluten-free dough containing corn and potato starch with the addition of pectin and guar gum as structure-forming substances. The starch blend used in the original dough recipe was partially (5% to 15%) replaced with OSA starch. The rheological properties of dough samples were determined, and the properties...
of the resulting bread were analyzed. It was found that the dough samples behaved as weak gels, and the values of storage and loss moduli (G' and G'', respectively) significantly depended on angular frequency. Various shares of OSA starch in recipes modified dough in different ways, causing changes in its rheological characteristics. The introduction of OSA starch preparations resulted in changes in the bread volume and physical characteristics of the crumb. All the applied preparations caused an increase in bread porosity and the number of pores larger than 5 mm, and there was a parallel decrease in pore density. The presence of OSA starch preparations modified bread texture depending on the amount and type of the applied preparation. The introduction of OSA starches in gluten-free bread formulation caused a significant drop in the enthalpy of retrograded amylopectin decomposition, indicating a beneficial influence of such type of additive on staling retardation in gluten-free bread.

**Keywords:** OSA starch; gluten-free bread; rheology; staling; texture.

18. **Small and Large Intestine (I): Malabsorption of Nutrients**


**Authors**

Miguel A Montoro-Huguet ¹ ² ³, Blanca Belloc ² ³, Manuel Domínguez-Cajal ² ³

**Affiliations**

- ¹ Departamento de Medicina, Psiquiatría y Dermatología, Facultad de Ciencias de la Salud y del Deporte, University of Zaragoza, 50009 Zaragoza, Spain.
- ² Unidad de Gastroenterología, Hepatología y Nutrición, Hospital Universitario San Jorge de Huesca, 22004 Huesca, Spain.
- ³ Aragonese Institute of Health Sciences (IACS), 50009 Zaragoza, Spain.

- PMID: 33920345
- DOI: 10.3390/nu13041254
Abstract

Numerous disorders can alter the physiological mechanisms that guarantee proper digestion and absorption of nutrients (macro- and micronutrients), leading to a wide variety of symptoms and nutritional consequences. Malabsorption can be caused by many diseases of the small intestine, as well as by diseases of the pancreas, liver, biliary tract, and stomach. This article provides an overview of pathophysiologic mechanisms that lead to symptoms or complications of maldigestion (defined as the defective intraluminal hydrolysis of nutrients) or malabsorption (defined as defective mucosal absorption), as well as its clinical consequences, including both gastrointestinal symptoms and extraintestinal manifestations and/or laboratory abnormalities. The normal uptake of nutrients, vitamins, and minerals by the gastrointestinal tract (GI) requires several steps, each of which can be compromised in disease. This article will first describe the mechanisms that lead to poor assimilation of nutrients, and secondly discuss the symptoms and nutritional consequences of each specific disorder. The clinician must be aware that many malabsorptive disorders are manifested by subtle disorders, even without gastrointestinal symptoms (for example, anemia, osteoporosis, or infertility in celiac disease), so the index of suspicion must be high to recognize the underlying diseases in time.

**Keywords:** malabsorption; maldigestion; micronutrients.

19. **Involvement of Smad7 in Inflammatory Diseases of the Gut and Colon Cancer**


**Authors**

Edoardo Troncone 1, Irene Marafini 1, Carmine Stolfi 1, Giovanni Monteleone 1

**Affiliation**

1 Department of Systems Medicine, University of Rome "Tor Vergata", 00133 Rome, Italy.

PMID: 33920230
Abstract

In physiological conditions, the human intestinal mucosa is massively infiltrated with various subsets of immune cells, the activity of which is tightly regulated by several counter-regulatory factors. One of these factors is transforming growth factor-β1 (TGF-β1), a cytokine produced by multiple cell types and targeting virtually all the intestinal mucosal cells. Binding of TGF-β1 to its receptors triggers Smad2/3 signaling, thus culminating in the attenuation/suppression of immune-inflammatory responses. In patients with Crohn's disease and patients with ulcerative colitis, the major human inflammatory bowel diseases (IBD), and in mice with IBD-like colitis, there is defective TGF-β1/Smad signaling due to high levels of the intracellular inhibitor Smad7. Pharmacological inhibition of Smad7 restores TGF-β1 function, thereby reducing inflammatory pathways in patients with IBD and colitic mice. On the other hand, transgenic over-expression of Smad7 in T cells exacerbates colitis in various mouse models of IBD. Smad7 is also over-expressed in other inflammatory disorders of the gut, such as refractory celiac disease, necrotizing enterocolitis and cytomegalovirus-induced colitis, even though evidence is still scarce and mainly descriptive. Furthermore, Smad7 has been involved in colon carcinogenesis through complex and heterogeneous mechanisms, and Smad7 polymorphisms could influence cancer prognosis. In this article, we review the data about the expression and role of Smad7 in intestinal inflammation and cancer.

Keywords: Crohn’s disease; TGF-beta; inflammatory bowel diseases; ulcerative colitis.

20. Electrochemical DNA Biosensor That Detects Early Celiac Disease Autoantibodies


Authors
Abstract

Although it is estimated that more than one million Americans have celiac disease (CD), it remains challenging to diagnose. CD, an autoimmune and inflammatory response following the ingestion of gluten-containing foods, has symptoms overlapping with other diseases and requires invasive diagnostics. The gold standard for CD diagnosis involves serologic blood tests followed by invasive confirmatory biopsies. Here, we propose a less invasive method using an electrochemical DNA (E-DNA) biosensor for CD-specific autoantibodies (AABs) circulating in blood. In our approach, CD-specific AABs bind a synthetic neoepitope, causing a conformational change in the biosensor, as well as a change in the environment of an attached redox reporter, producing a measurable current reduction. We assessed the biosensor's ability to detect CD-specific patient-derived AABs in physiological buffer as well as buffer supplemented with bovine serum. Our biosensor was able to detect AABs in a dose-dependent manner; increased signal change correlated with increased AAB concentration with an apparent dissociation constant of 0.09 ± 0.03 units/mL of AABs. Furthermore, we found our biosensor to be target-specific, with minimal off-target binding of multiple unrelated biomarkers. Future efforts aimed at increasing sensitivity in complex media may build upon the biosensor design presented here to further improve CD AAB detection and CD diagnostic tools.
Keywords: E-DNA-based biosensors; biosensor; celiac disease; celiac disease autoantibodies; celiac disease autoantibody epitope; celiac disease diagnostics.

21. **Mobile Application for Promoting Gluten-Free Diet Self-Management in Adolescents with Celiac Disease: Proof-of-Concept Study**


Authors

Sonya Meyer 1, Gali Naveh 2

Affiliations

- 1 Department of Occupational Therapy, Ariel University, Ariel 40700, Israel.
- 2 Department of Industrial Engineering and Management, Shamoon College of Engineering, Beer-Sheva 8410802, Israel.

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DOI: 10.3390/nu13051401

Abstract

Celiac disease (CD) is a chronic disease treated by maintaining and managing a lifelong restrictive gluten-free diet. The purpose of this study was to develop a mobile application, Plan My C-Day, to promote self-management skills among youth with CD during adolescence—a time when decreased adherence often occurs—and examine its usability among adolescents with CD. Plan My C-Day contains three simulations of activities involving eating out and actions to take when preparing for these events. It was developed and pilot tested by 13 adolescents with CD. Application use and user perception data were collected and analyzed. Participants chose 160 actions within the simulations. For over 75% of participants, the time to complete the simulation decreased from the first to the third (last) simulation by an average of 50%. The average reported
usability perception was 3.71 on a scale of 1 to 5, with system ease of use and ease of learning obtaining the highest scores. This study demonstrated that the Plan My C-Day mobile application's self-management content, features, and functions operated well and that the simulations were easy to understand and complete. Further development will include the option to add self-created activities and adaptation to different languages and cultures.

**Keywords:** celiac; mobile application; self-management; system usability; user satisfaction.

22. **Chickpea and Chestnut Flours as Non-Gluten Alternatives in Cookies**


**Authors**

Marta Torra 1, Mayara Belorio 1, Manuel Ayuso 2, Marcio Carocho 2, Isabel C F R Ferreira 2, Lillian Barros 2, Manuel Gómez 1

**Affiliations**

- 1 Food Technology Area, College of Agricultural Engineering, University of Valladolid, 34071 Palencia, Spain.
- 2 Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal.

**PMID:** 33919256  
**DOI:** 10.3390/foods10050911

**Abstract**

This study proposes the use of a mix composed of chickpea flour and chestnut flour in cookies, aiming to improve their acceptability. Cookie properties and nutritional value were also analysed. The gluten-free cookies were made by using different mixes of chickpea and chestnut flours (0:100, 25:75, 50:50, 75:25, 100:0). Dough rheology and cookie dimensions, texture, external colour and acceptability were evaluated. The presence of the chestnut flour increased the values of G' and G", but reduced the loss factor (tan δ) when
compared with the doughs made with chickpea flour. Chestnut flour also
decreased the diameter and the spread ratio of the cookies, while increasing
the hardness and darkening of the cookies. Furthermore, adding chestnut to
the flour mixture increased the nutritional quality of the cookies by adding
unsaturated fatty acids and fibre. The use of reduced percentages of chestnut
flour (25%) resulted in masking the off-flavour of the chickpea flour, which
improved the cookie's acceptability without significantly changing the dough
rheology, cookie dimensions, hardness, or lightness.

**Keywords:** acceptability; chestnut; chickpea; cookie; nutritional quality.

23. **Potential Application of Resistant Starch Sorghum in Gluten-Free Pasta: Nutritional, Structural and Sensory Evaluations**


**Authors**

Mariasole Cervini ¹, Alice Gruppi ², Andrea Bassani ², Giorgia Spigno ², Gianluca Giuberti ²

**Affiliations**

- ¹ Department of Biotechnology, University of Verona, Strada Le Grazie
  15, 37134 Verona, Italy.
- ² Department for Sustainable Food Process (DiSTAS), Università
  Cattolica del Sacro Cuore, via Emilia Parmense 84, 29122 Piacenza, Italy.

- PMID: [33919201](https://www.ncbi.nlm.nih.gov/pubmed/33919201)
- DOI: [10.3390/foods10050908](https://doi.org/10.3390/foods10050908)

**Abstract**

Gluten-free (GF) pasta samples containing rice flour replaced with 0, 5, 10, 15
 g/100 g (w/w) of a resistant starch ingredient from annealed sorghum starch
(annRS) were formulated. The highest total dietary fiber and RS contents ($p <
0.05$) were measured in uncooked pasta with 15 g/100 g of annRS addition
(15-annRS). After cooking, the 15-annRS pasta was characterized by an RS
content of 5.8 g/100 g dry matter, confirming the thermal resistance of annRS.
The use of annRS positively influenced the optimal cooking time, the cooking loss, the firmness, and the stickiness of the cooked samples, with not remarkably change in color after cooking. The starch hydrolysis index values decreased as the level of annRS increased. Despite a significant decrease in the overall sensory with increasing levels of annRS, all samples were characterized by a value > 5, which is considered the limit of acceptability. The use of annRS in GF pasta up to 15 g/100 g can contribute to creating GF products with high total dietary fiber content, slowly digestible starch properties, and without drastically compromising the sensory attributes.

**Keywords:** annealing; dietary fibre; hydrolysis index; pasta; resistant starch.


**Authors**

Urszula Krupa-Kozak ¹, Natalia Drabińska ¹, Natalia Bačzek ¹, Kristýna Šimková ¹, Małgorzata Starowicz ¹, Tomasz Jeliński ¹

**Affiliation**

¹ Institute of Animal Reproduction and Food Research, Polish Academy of Sciences, Tuwima 10 Str., 10-748 Olsztyn, Poland.

**PMID:** 33918917  
**DOI:** 10.3390/foods10040819

**Abstract**

In comparison to conventional bread, gluten-free bread (GF) shows many post-baking defects and a lower nutritional and functional value. Although broccoli leaves are perceived as waste products, they are characterised by a high content of nutrients and bioactive compounds. The present study
evaluated the nutritional value, technological quality, antioxidant properties, and inhibitory activity against the formation of advanced glycation end-products (AGEs) of GF enriched with broccoli leaf powder (BLP). Compared to the control, gluten-free bread with BLP (GFB) was characterised by a significantly ($p < 0.05$) higher content of nutrients (proteins and minerals), as well as improved specific volume and bake loss. However, what needs to be emphasised is that BLP significantly ($p < 0.05$) improved the antioxidant potential and anti-AGE activity of GFB. The obtained results indicate that BLP can be successfully used as a component of gluten-free baked products. In conclusion, the newly developed GFB with improved technological and functional properties is an added-value bakery product that could provide health benefits to subjects on a gluten-free diet.

**Keywords:** Brassica; anti-ages; antioxidant activity; coeliac disease; gluten-free diet; technological properties; texture parameters; vegetable by-product.

25. **Fecal Calprotectin and Eosinophil-Derived Neurotoxin in Children with Non-IgE-Mediated Cow's Milk Protein Allergy**


**Authors**

María Roca 1, Ester Donat 1 2, Ana Rodriguez Varela 3, Eva Carvajal 4, Francisco Cano 3, Ana Armisen 3, Helena Ekoff 5, Antonio José Cañada-Martínez 6, Niclas Rydell 5, Carmen Ribes-Konincx 1 2

**Affiliations**

- 1 Celiac Disease and Digestive Immunopathology Unit, Instituto de Investigación Sanitaria La Fe, 46026 Valencia, Spain.
- 2 Pediatric Gastrohepatology Unit, Hospital Universitario y Politécnico La Fe, 46026 Valencia, Spain.
- 3 Pediatrics, Primary Health Care Center of Betera, 46117 Valencia, Spain.
- 4 Department of Paediatrics, Hospital Casa de Salud, 46021 Valencia, Spain.
Abstract

Our aim is to assess the efficacy of fecal calprotectin (fCP) and fecal eosinophil-derived neurotoxin (fEDN) as diagnostic markers of cow's milk protein allergy (CMPA) and for monitoring the infants' response to a non-IgE mediated cow's milk protein (CMP)-free diet. We prospectively recruited infants aged 0 to 9 months. Stool samples were taken from 30 infants with CMPA, 19 with mild functional gastrointestinal disorders, 28 healthy infants, and 28 children who presented mild infections. Despite the fact that levels of fCP and fEDN in CMPA infants were higher than in healthy infants at month 0, differences for both parameters did not reach statistical significance (p-value 0.119 and 0.506). After 1 month of an elimination diet, no statistically significant differences in fCP with basal levels were found (p-values 0.184) in the CMPA group. We found a high variability in the fCP and fEDN levels of young infants, and discrepancies in individual behavior of these markers after a CMP-free diet was started. It seems that neither fCP nor fEDN levels are helpful to discriminate between healthy infants and those with signs or symptoms related to non-IgE-mediated CMPA. Additionally, it is debatable if on an individual basis, fCP or fEDN levels could be used for clinical follow-up and dietary compliance monitoring. However, prospective studies with larger populations are needed to draw robust conclusions.

Keywords: eosinophil-derived neurotoxin; fecal calprotectin; non-IgE-mediated cow’s milk protein allergy.

The Level of Processing, Nutritional Composition and Prices of Canadian Packaged Foods and Beverages with and without Gluten-Free Claims

Authors

Laura Vergeer 1, Beatriz Franco-Arellano 1 2, Gabriel B Tjong 1, Jodi T Bernstein 1, Mary R L’Abbé 1

Affiliations

1 Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, ON M5S 1A8, Canada.
2 Faculty of Health Sciences, Ontario Tech University, Oshawa, ON L1G 0C5, Canada.

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DOI: 10.3390/nu13041183

Abstract

Little is known about the healthfulness and cost of gluten-free (GF) foods, relative to non-GF alternatives, in Canada. This study compared the extent of processing, nutritional composition and prices of Canadian products with and without GF claims. Data were sourced from the University of Toronto Food Label Information Program (FLIP) 2013 (n = 15,285) and 2017 (n = 17,337) databases. Logistic regression models examined the association of NOVA processing category with GF claims. Calorie/nutrient contents per 100 g (or mL) were compared between GF and non-GF products. Generalized linear models compared adjusted mean prices per 100 g (or mL) of products with and without GF claims. The prevalence of GF claims increased from 7.1% in 2013 to 15.0% in 2017. GF claims appeared on 17.0% of ultra-processed foods, which were more likely to bear GF claims products than less-processed categories. Median calories and sodium were significantly higher in GF products; no significant differences were observed for saturated fat or sugars. Compared to non-GF products, adjusted mean prices of GF products were higher for 10 food categories, lower for six categories and not significantly different for six categories. Overall, GF claims are becoming increasingly prevalent in Canada; however, they are often less healthful and more expensive than non-GF alternatives, disadvantaging consumers following GF diets.
Abstract

Polyphenols are classified as an organic chemical with phenolic units that display an array of biological functions. However, polyphenols have very low bioavailability and stability, which make polyphenols a less bioactive compound. Many researchers have indicated that several factors might affect the efficiency and the metabolism (biotransformation) of various polyphenols, which include the gut microbiota, structure, and physical properties as well as its interactions with other dietary nutrients (macromolecules). Hence, this mini-review covers the two-way interaction between polyphenols and gut microbiota (interplay) and how polyphenols are metabolized (biotransformation) to produce various polyphenolic metabolites. Moreover,
the protective effects of numerous polyphenols and their metabolites against various gastrointestinal disorders/diseases including gastritis, gastric cancer, colorectal cancer, inflammatory bowel disease (IBD) like ulcerative colitis (UC), Crohn's disease (CD), and irritable bowel syndrome (IBS) like celiac disease (CED) are discussed. For this review, the authors chose only a few popular polyphenols (green tea polyphenol, curcumin, resveratrol, quercetin), and a discussion of their proposed mechanism underpinning the gastroprotection was elaborated with a special focus on clinical evidence. Overall, this contribution would help the general population and science community to identify a potent polyphenol with strong antioxidant, anti-inflammatory, anti-cancer, prebiotic, and immunomodulatory properties to combat various gut-related diseases or disorders (complementary therapy) along with modified lifestyle pattern and standard gastroprotective drugs. However, the data from clinical trials are much limited and hence many large-scale clinical trials should be performed (with different form/metabolites and dose) to confirm the gastroprotective activity of the above-mentioned polyphenols and their metabolites before recommendation.

**Keywords:** biotransformation; curcumin; gastrointestinal diseases; gastroprotective; polyphenols; resveratrol.

28. [Comparison of the In Vitro Bioavailability of Selected Minerals from Gluten-Free Breads Enriched with Grains and Synthetic Organic and Non-Organic Compounds](https://www.mdpi.com/2672-2779/26/7/2085)


**Authors**

[Anna Rogaska](#)¹, [Julita Reguła](#)¹, [Joanna Suliburska](#)¹, [Zbigniew Krejpcio](#)¹

**Affiliation**

- ¹ Department of Human Nutrition and Dietetics, Poznan University of Life Sciences, Wojska Polskiego St. 31, 60-624 Poznan, Poland.

**PMID:** [33917296](https://www.ncbi.nlm.nih.gov/pubmed/33917296)
Abstract

**Introduction:** Despite the constant efforts of scientists to improve the texture, sensory properties, and nutritional value of gluten-free bread, obtaining high bioavailability of minerals is still a huge challenge. Gluten-free bakery products are characterized by a low bioavailability of minerals. The aim of this study was to design gluten-free bread with high bioavailability of minerals commonly found in deficiencies in people struggling with gluten intolerance.

**Material and methods:** The material consisted of gluten-free breads designed to obtain the highest possible content of minerals in the bread while maintaining a good structure and taste.

**Results:** Higher contents of all the analyzed minerals were obtained in breads with natural and synthetic additives, both in rice and buckwheat bread, compared to basic bread. There was also a higher content of the analyzed minerals in buckwheat bread in comparison to rice bread for each type of additive. Higher bioavailability of iron, copper, calcium, and magnesium was noted in rice bread, while the bioavailability of zinc was higher in buckwheat bread.

**Conclusion:** The additives used increased the bioavailability of the analyzed minerals from the gluten-free breads. The use of various variants of flour (rice, buckwheat) influenced the bioavailability of iron, zinc, copper, calcium, and magnesium. The release of minerals from gluten-free bread depends on the element and added components (seeds or synthetic additives).

**Keywords:** bioavailability; calcium; copper; gluten-free breads; in vitro; iron; magnesium; zinc.

29. [Probiotics Supplements Reduce ER Stress and Gut Inflammation Associated with Gliadin Intake in a Mouse Model of Gluten Sensitivity](https://doi.org/10.3390/nu13041221)

Authors

Eleonora Ferrari ¹ ² , Romina Monzani ¹ ² , Valentina Saverio ¹ ² , Mara Gagliardi ¹ ²
, Elżbieta Pańczyszyn ¹ ² , Valeria Raia ³ ⁴ , Valeria Rachela Villella ⁴ , Gianni Bona ⁵ , Marco
Pane ⁶ , Angela Amoruso ⁶ , Marco Corazzari ¹ ² ⁷

Affiliations

¹ Department of Health Science, University of Piemonte Orientale, 28100 Novara, Italy.
² Center for Translational Research on Autoimmune and Allergic Disease (CAAD), University of Piemonte Orientale, 28100 Novara, Italy.
³ Regional Cystic Fibrosis Center, Pediatric Unit, Department of Translational Medical Sciences, Federico II University Naples, 80134 Naples, Italy.
⁴ European Institute for Research in Cystic Fibrosis (IERFC-Onlus), San Raffaele Scientific Institute, 20132 Milan, Italy.
⁵ Division of Pediatrics, Department of Health Science, University of Piemonte Orientale, 28100 Novara, Italy.
⁶ Probiotical Research Srl, 28100 Novara, Italy.
⁷ Interdisciplinary Research Center of Autoimmune Diseases (IRCAD), University of Piemonte Orientale, 28100 Novara, Italy.

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Abstract

Exposure to gluten, a protein present in wheat rye and barley, is the major inducer for human Celiac Disease (CD), a chronic autoimmune enteropathy. CD occurs in about 1% worldwide population, in genetically predisposed individuals bearing human leukocyte antigen (HLA) DQ2/DQ8. Gut epithelial cell stress and the innate immune activation are responsible for the breaking oral tolerance to gliadin, a gluten component. To date, the only treatment available for CD is a long-term gluten-free diet. Several studies have shown that an altered composition of the intestinal microbiota (dysbiosis) could play a key role in the pathogenesis of CD through the modulation of intestinal permeability and the regulation of the immune system. Here, we show that gliadin induces a chronic endoplasmic reticulum (ER) stress condition in the
small intestine of a gluten-sensitive mouse model and that the coadministration of probiotics efficiently attenuates both the unfolded protein response (UPR) and gut inflammation. Moreover, the composition of probiotics formulations might differ in their activity at molecular level, especially toward the three axes of the UPR. Therefore, probiotics administration might potentially represent a new valuable strategy to treat gluten-sensitive patients, such as those affected by CD.

Keywords: CD; CFTR; TG2; UPR; probiotics.

30. **GLP-1 and Intestinal Diseases**


Authors

Jenna Elizabeth Hunt 1, Jens Juul Holst 1 2, Palle Bekker Jeppesen 3, Hannelouise Kissow 1 2

Affiliations

- 1 Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark.
- 2 Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark.
- 3 Department of Medical Gastroenterology and Hepatology, Rigshospitalet, 2200 Copenhagen, Denmark.

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Abstract

Accumulating evidence implicates glucagon-like peptide-1 (GLP-1) to have, beyond glucose maintenance, a beneficial role in the gastrointestinal tract. Here, we review emerging data investigating GLP-1 as a novel treatment for intestinal diseases, including inflammatory bowel diseases, short-bowel syndrome, intestinal toxicities and coeliac disease. Possible beneficial mechanisms for these diseases include GLP-1's influence on gastric emptying, its anti-inflammatory properties and its intestinotrophic effect. The current
knowledge basis derives from the available GLP-1 agonist treatments in experimental animals and small clinical trials. However, new novel strategies including dual GLP-1/GLP-2 agonists are also in development for the treatment of intestinal diseases.

**Keywords:** GLP-1; coeliac disease; inflammatory bowel disease (IBD); intestinal disease; mucositis; short-bowel syndrome (SBS).

31. **Characterizing the Rheological and Bread-Making Properties of Wheat Flour Treated by "Gluten Friendly™" Technology**


**Authors**

Carmela Lamacchia¹, Loretta Landriscina¹, Carla Severini¹, Rossella Caporizzi¹, Antonio Derossi¹

**Affiliation**

- ¹ Department of Agriculture, Food, Natural resources and Engineering (DAFNE), University of Foggia, 71122 Foggia, Italy.

**Abstract**

After discovering an innovative technology for the reshaping of gluten proteins-the "Gluten Friendly™" system—that confers to wheat flour some unprecedented characteristics, such as reduced epitope antigenicity and a positive modulation of the gut microbiota, its effects on the production and quality of bread have been studied. Mainly, we have investigated the chemical, rheological and pasting properties of Gluten Friendly Flour (GFF) and of control flour (CF) with the aim of analyzing and interpreting potential differences. Furthermore, the bread made from GFF and CF was evaluated in terms of microstructure properties and sensory quality. The experiments demonstrated that GFF became soluble in aqueous solution, making it
unfeasible to isolate using the Glutomatic apparatus. Although the water absorption of GFF increased by 10% compared to CF, dough elasticity was reduced, and dough stability decreased from 5 to 2 min. A significant increase in the alveograph index (P/L) from 0.63 to 6.31 was detected, whereas pasting properties did not change from the control flour. Despite these profound modifications in the rheological properties, GFF exhibited a high ability to shape dough and to produce bread with high quality and negligible differences from the control bread in terms of appearance, taste, aroma, color and texture.

**Keywords:** Gluten FriendlyTM technology; gluten friendly bread; microwaves; pasting properties; rheological properties; sensorial evaluation.

32. **ATP8B1, ABCB11, and ABCB4 Genes Defects: Novel Mutations associated with cholestasis with Different phenotypes and Outcomes**


**Authors**

Abdulrahman Al-Hussaini ¹, Khurram Lone ², Muhammed Salman Bashir ³, Sami Alrashidi ², Mosa Fagih ⁴, Alanoud Alanazi ², Salem Alyaseen ², Abdulaziz Almayouf ², Muhanad Alruwaithi ², Ali Asery ²

**Affiliations**

1. Division of Pediatric Gastroenterology, Children's Specialized Hospital, King Fahad Medical City; College of Medicine, Alfaisal University; Prince Abdullah bin Khalid Celiac Disease Research Chair, Department of Pediatrics, Faculty of Medicine, King Saud University Riyadh, Kingdom of Saudi Arabia. Electronic address: aa_alhussaini@yahoo.com.
2. Division of Pediatric Gastroenterology, Children's Specialized Hospital, King Fahad Medical City.
Abstract

Objectives: To characterize the clinical, laboratory, histological, molecular features and outcome of gene-confirmed progressive familial intrahepatic cholestasis (PFIC) 1-3 among Arabs and to evaluate for "genotype-phenotype correlations."

Study design: We retrospectively reviewed charts of 65 children (ATP8B1 defect = 5, ABCB11 = 35, ABCB4 = 25) who presented between 2008 and 2019 with cholestasis. The clinical phenotype of a disease was categorized based on response of cholestasis and itching to ursodeoxycholic acid (UDCA) and ultimate outcome, into mild (complete response), intermediate (partial response, non-progressive), and severe (progression to end-stage liver disease).

Results: Overall, 27 different mutations were identified [ATP8B1, n= 5; ABCB11, n=11; ABCB4, n=11], comprising 10 novel ones. Six patients with heterozygous missense mutations (ATP8B1, n=2; ABCB11, n=4) had transient cholestasis. Of the remaining 3 PFIC1 patients, 2 developed severe phenotype (splicing and frameshift mutations). Of the remaining 31 PFIC2 patients, 25 developed severe disease (15 due to frameshift and splicing mutations). Of 25 PFIC3 patients, 10 developed severe phenotype (1 splicing and 3 frameshift mutations; 6 missense). Patients with PFIC2 had significantly shorter survival time and more rapid disease progression than Patients with PFIC3 (P < .001). Patients with frameshift mutations in ABCB11 gene (p.Thr127Hisfs*6) and ABCB4 gene (p.Phe210Serfs*5) had significantly shorter survival time than missense mutations (P = 0.011; P = .0039, respectively).

Conclusion: We identified genotype-phenotype correlations among mutations in ABCB11 and ABCB4 genes, which underscore the prognostic value of early
genetic diagnosis. The disease course in PFIC3 patients could be favorably modified by UDCA therapy.

**Keywords:** Cholestasis; PFIC; Saudi Arabia.

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**Full text links**

**Cancer Risk in Patients with Autoimmune Hepatitis: A Nationwide Population-Based Cohort Study with Histopathology**


**Authors**

Rajani Sharma ¹ ², Elizabeth C Verna ¹ ², Tracey G Simon ³, Jonas Söderling ⁴, Hannes Hagström ⁵ ⁶, Peter H R Green ² ⁷, Jonas F Ludvigsson ² ⁴ ⁸ ⁹

**Affiliations**

- ¹ Center for Liver Disease and Transplantation, Division of Digestive and Liver Diseases, Columbia University Irving Medical Center, New York, New York, USA.
- ² Division of Digestive and Liver Diseases, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, USA.
- ³ Transplant Hepatology, Division of Gastroenterology, Massachusetts General Hospital, Boston, Massachusetts, USA.
- ⁴ Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
- ⁵ Unit of Hepatology, Center for Digestive Diseases, Karolinska University Hospital, Stockholm, Sweden.
Abstract

We aimed to determine the risk of incident cancer in autoimmune hepatitis (AIH) compared to the general population and siblings. AIH was defined by the presence of a medical diagnosis of AIH and a liver biopsy in a nationwide Swedish population-based cohort study. We identified 5,268 adults with AIH diagnosed 1969-2016 and 22,996 matched general population reference individuals and 4,170 sibling comparators. Using Cox regression, hazard ratios (HRs) were determined for any incident cancer and sub-types determined from the Swedish Cancer Register. During follow-up, a cancer diagnosis was made in 1,119 individuals with AIH (17.2/1000 person-years) and 4,450 reference individuals (12.0/1000 person-years). This corresponded to an HR of 1.53 (95%CI: 1.42,1.66). Cancer risk was highest in those with cirrhosis. There was a 29.18-fold increased risk of hepatocellular carcinoma (HCC) (95%CI, 17.52,48.61). The annual incidence risk of HCC in individuals with AIH who had cirrhosis was 1.1% per year. AIH was also linked to non-melanoma skin cancer (HR=2.69) and lymphoma (HR=1.89). Sibling analyses yielded similar risk estimates for any cancer (HR=1.84) and HCC (HR=23.10). AIH is associated with an increased risk of any cancer, in particular, HCC and extra-hepatic malignancies. The highest risk for cancer, especially HCC, is in patients with cirrhosis.

Keywords: Cirrhosis; Hepatitis; Hepatocellular Carcinoma; Histopathology; Malignancy; Population-based.
Segmental Arterial Mediolysis (SAM) Leading to Chronic Renal Insufficiency


Authors

John-Paul O'Shea 1, Sarah Gordon 2, Richard Horak 3, J Matthew Meadows 3

Affiliations

1 Department of Medicine, Tripler Army Medical Center, Honolulu, HI, 96859, USA.
2 Department of Nephrology, Walter Reed National Military Medical Center, Bethesda, MD, 20889, USA.
3 Department of Radiology, Tripler Army Medical Center, Honolulu, HI, 96859, USA.

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Free PMC article

Abstract

Background: Segmental arterial mediolysis (SAM) is a rare self-limiting non-atherosclerotic, non-inflammatory vasculopathy. SAM typically affects the visceral arteries of the abdomen to include the celiac, mesenteric, and renal arteries. SAM has a favorable prognosis in most cases with an asymptomatic course but can have mortality rates as high as 50% due to acute aneurysmal
rupture. Very few cases of adverse long-term sequelae involving SAM have been described, and this report of chronic kidney disease represents a sentinel case illustrating that chronic disease can and does occur as a result of SAM and should be investigated for at follow-up.

**Case presentation:** In this case report, we describe a case of a 45-year-old male with erectile dysfunction but without any readily identifiable risk factors for chronic kidney disease (CKD) or vasculopathy, who presented with bilateral renal infarction and parenchymal infarcts due to SAM and who subsequently developed CKD at follow-up. We conduct a mini-literature review that discusses the pathogenesis of SAM in the context of vasospastic diseases, as well as compares the outcomes of observation-only, versus medical-management, versus endovascular-interventions in patients with SAM.

**Conclusion:** This is the first case to our knowledge of CKD occurring as an outcome of SAM without any preceding significant comorbidity, highlighting that whereas SAM is of itself rare and typically resolves, chronic disease can linger and should be evaluated for on follow-up. Further, we argue that radiological evidence of precursor vasospastic disease may exist in several locations apart from the index lesion and thus warrants wider whole-body radiographic exploration for lesions as an opportunity to prevent chronic sequelae as illustrated in this case report from occurring. Finally, a review of published case-series suggests that disease progression is less likely to occur after endovascular-intervention compared to observation-only or medical management and the risk of intervention vs conservative management should therefore be discussed with the patient.

**Keywords:** erectile dysfunction; vasculopathy; vasospastic.

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**Conflict of interest statement**

The authors declare that they have no conflicts of interest.

- [26 references](#)
- [2 figures](#)

**Full text links**
Evaluation of parameters associated with growth retardation in children with coeliac disease


Authors

Didem G Taskin 1, Alihan Sursal 2, Ali E Dogan 3, Fatih Ozdener 4

Affiliations

1 Department of Pediatric Gastroenterology, Adana City Training and Research Hospital, Adana, Turkey.
2 Department of Neuroscience, Bahcesehir University, School of Medicine, Istanbul, Turkey.
3 Medical Department, Nutricia, Advanced Medical Nutrition, Istanbul, Turkey.
4 Department of Pharmacology, Bahcesehir University, School of Medicine, Istanbul, Turkey.

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DOI: 10.1111/jpc.15525

Abstract

Aims: Coeliac disease (CD) is an autoimmune disorder with a prevalence ≤2% that causes an immune reaction to gluten. Growth retardation (GR) generally accompanies CD due to gastrointestinal complications and should be treated as early as possible along with initiation of a gluten-free diet. The aim of this study was to determine the indicators of GR in patients with CD.

Methods: This single-centre retrospective study included paediatric outpatients with CD. All patients were diagnosed with CD via serological analysis and upper gastrointestinal endoscopy if necessary. Patient records
were obtained from Adana City Training and Research Hospital. Patients that were diagnosed with GR accompanying CD were given oral nutritional supplements and followed-up every 3-6 months. Statistical relationships between demographics, and anthropometric measurements, duration of breastfeeding, gluten contact time, diet duration, presenting complaints and serological findings were evaluated.

**Results:** This study included 169 paediatric outpatients between ages 1 and 18. Longer symptom duration and shorter breastfeeding duration were significantly correlated with GR accompanying CD (P = 0.007 and P = 0.029, respectively). Vomiting was the only symptom that was correlated with the presence of GR (P = 0.010). Helicobacter pylori infection was not correlated with the presence of GR (P = 0.277).

**Conclusions:** GR should be treated as early as possible to reduce the severity of CD and a 6 months sole breastfeeding followed by solid foods accompanied by breastfeeding for 2 years is crucial for preventing GR. Moreover, vomiting as a presenting complaint in patients with CD might be indicative of the presence of GR.

**Keywords:** breastfeeding; coeliac disease; growth retardation; paediatrics.

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- [31 references](#)

**Full text links**

36. **Technical Aspects of Intensive Care Unit Management: A Single-Center Experience at a Tertiary Academic Hospital**

Abstract

**Purpose:** Special technical issues associated with the function and maintenance of medical devices arise in intensive care units (ICUs). This study explored the level of comfort of ICU staff in dealing with selected equipment, the factors that are associated with the staff's ease of adaptation to new technologies, and the role of technical support staff.

**Patients and methods:** This is a single-center cross-sectional questionnaire-based survey that was conducted in February 2018 and targeted nurses working in the ICUs of King Saud University Medical City in Riyadh, Saudi Arabia.
Results: Among the 297 nurses who completed the survey, almost all of the respondents (99.3%) were aware of the ICU equipment preventive maintenance program. Most of the nurses had received training on how to use infusion pumps (96.2%), cardiac monitoring systems (78.0%), and cardiac defibrillation devices (73.9%). Sixty nurses (20.2%) indicated that at least one super user was available for at least one device. About half of the staff reported one device whose user manual was available. Most nurses reported having no resources regarding updates on medical devices.

Conclusion: Our findings revealed an alarming need to address technical issues related to medical devices used in the ICU and to design a framework for the safe operation of medical devices based on international practices. It is necessary to empower the role of the super user and medical device clinical educator as well as to optimize communication between the national regulatory body of medical devices and healthcare providers, especially those working in acute care areas.

Keywords: ICU; biomedical; medical devices; safety.

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Conflict of interest statement

The authors report no conflicts of interest in this work.

- [11 references]

Full text links

37. The Evolving Landscape of Biomarkers in Celiac Disease: Leading the Way to Clinical Development

Celiac disease is a common immune-mediated disease characterized by abnormal T-cell responses to gluten. For many patients, symptoms and intestinal damage can be controlled by a gluten-free diet, but, for some, this approach is not enough, and celiac disease progresses, with serious medical consequences. Multiple therapies are now under development, increasing the need for biomarkers that allow identification of specific patient populations and monitoring of therapeutic activity and durability. The advantage of identifying biomarkers in celiac disease is that the underlying pathways driving disease are well characterized and the histological, cellular, and serological changes with gluten response have been defined in gluten challenge studies. However, there is room for improvement. Biomarkers that measure histological changes require duodenal biopsies and are invasive. Less invasive peripheral blood cell and cytokine biomarkers are transient and dependent upon gluten challenge. Here, we discuss established biomarkers and new approaches for biomarkers that may overcome current limitations.

**Keywords:** biomarkers; celiac disease; clinical development; diagnosis; disease monitoring; patient populations.
Conflict of interest statement

The authors declare that this study was funded by Takeda Pharmaceutical Company Ltd. All authors were employees of Takeda Pharmaceuticals Inc. Co., and were responsible for the content, collection, analysis, interpretation of data, preparation of this article and the decision to submit it for publication.

- 61 references

Full text links

38. Chemometric approach-based characterization and screening of gluten free flours for development of Indian unleavened flatbread


Authors

Sonal Patil 1 2, Sachin K Sonawane 2, S S Arya 1

Affiliations

- 1 Food Engineering and Technology Department, Institute of Chemical Technology, Nathalal Parekh Marg, Matunga, Mumbai, Maharashtra 400019 India.
- 2 Food Science and Technology, School of Biotechnology and Bioinformatics, D. Y. Patil University, Level 5, Plot No. 50, CBD Belapur, Navi Mumbai, 400614 India.

- PMID: 33897019
- PMCID: PMC8021619 (available on 2022-05-01)
Abstract

The objective of the study was to screen amongst various gluten free flours to prepare Indian unleavened flatbread using principal component analysis (PCA) and hierarchical cluster analysis (HCA) as a mathematical tool. Gluten free flours studied in this work were, rice, sorghum, moong, amaranth, sama, ragi, water chestnut, buckwheat, soy, tamatind kernel, chickpea, black gram and unripe banana flour. The characteristics of sorghum: rice flatbread was analyzed such as dough making ability, subjective rollability, puffing and acceptability with respect to wheat. Interrelationship between the parameters analyzed and the different gluten free flours were investigated by using PCA and HCA. PCA revealed that the first two components represented 92.56% of the total variability in flatbread making characteristics. HCA classified samples into 6 clusters on the basis of measured flatbread making characteristics. From the results, moong, water chestnut and unripe banana flour in addition to mixture sorghum: rice (30:70) flour were chosen as ingredients for the preparation of Indian unleavened flatbread.

Keywords: Chemometrics; Flatbread; Gluten free; HCA; PCA.

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Conflict of interest statement

Conflict of interest All authors in the manuscript do not have any conflict of interest.

Eye disorders in patients with celiac disease and inflammatory bowel disease: A study using clinical data warehouse


Authors
Abstract

**Background and aim:** To analyze the prevalence of ophthalmic manifestations in patients with celiac disease, Crohn's disease and ulcerative colitis in Munich/Germany.

**Methods:** A total of 272,873 patients of Ludwig Maximilians Universitat Ophthalmological Hospital with eye disease were evaluated between 2003 and 2019. The International Classification of Diseases, 10th revision (ICD-10) of celiac disease Crohn's disease, ulcerative colitis, and all medical records which had the diagnosis of these diseases were analyzed.

**Results:** A total of 272,873 patients were analyzed, with a mean age of 53 years, with approximately 48% female patients, and 51% male patients. We selected 72 patients with celiac disease (68% women and 32% men), with a minimum age of 8 years, maximum of 103 years, and an average of 52 years. The most common diagnoses were dry eye (32%) and cataract (12%). The mean intraocular pressure of patients with celiac disease was 15 mmHg.
During the same study period, 103 patients with Crohn's disease were analyzed, with an average intraocular pressure of 14 mmHg. The minimum age of the patients was 12 years and a maximum of 93 years with an average age of 55 years, with 57% of females and 43% of males. The most common diagnoses were cataract (22%) and dry eye (19%). During the same study period, 99 patients with ulcerative colitis were analyzed, with an average intraocular pressure of 14 mmHg. The minimum age of the patients was 6 years and a maximum of 96 years, with an average age of 61 years, with 36% of females and 64% of males. The most common diagnoses were cataract (29.2%) and dry eye (12%).

Conclusions: The main ophthalmological manifestations of patients requiring eye follow-up were dry eye and cataract for all the diseases analyzed, which can be considered as coincident complications. None of the three diseases had increased intraocular pressure. Thus, celiac disease presented a profile of ophthalmological manifestation similar to the other intestinal inflammatory diseases studied.

Keywords: Celiac disease; Crohn’s disease; eye; eye manifestations; inflammatory bowel disease; ocular complications; ulcerative colitis.

Full text links

40. Adherence to dietary treatment and clinical factors associated with anti-transglutaminase antibodies in celiac disease during the follow-up


Authors

Marta Miró 1, Manuel Alonso-Garrido 1, Manuel Lozano 1,2, Juanjo Peiró 3, Lara Manyes 1
Introduction: In clinical practice, celiac disease (CD) is monitored through anti-transglutaminase (TGA-IgA) antibody levels. The normalization of serum levels in successive periodic measurements indicates good response and adherence to dietary treatment.

Objectives: To evaluate the factors associated with the evolution of TGA-IgA antibodies and their association with dietary non-compliance and diseases related to CD.

Methods: This prospective observational study was carried out in 254 participants, who were recruited from patients from a hospital in southern Spain. Information about sex, age, serological test results, HLA DQ2/DQ8 haplotypes, mucosal atrophy, gastrointestinal and extra-intestinal symptoms, as well as diagnosis of diseases related to CD, was collected.

Results: Clinical manifestations, such as diarrhoea, abdominal pain and weight loss, showed differences according to sex and age. Children under 18 years of age presented a degree of total or severe atrophy of the intestinal villi. TGA-IgA antibodies concentrations were directly associated with the number of digestive disorders manifested by the patient and the record of dietary non-compliance and inversely related to the number of extra-digestive disorders.
Conclusions: Adolescents between 12 and 18 years old were the least monitored as well as the group with more extra-intestinal symptoms reported. Therefore, it is necessary to develop strategies in clinical practice aimed at this population group and continuous monitoring should be implemented to improve life quality and reduce complications that may arise in the long term.

Keywords: Celiac disease; Diet; Dietary non-compliance; TGA-IgA antibodies.

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Conflict of interest statement

The authors declare no conflict of interest.

- 64 references
- 1 figure

Full text links

41. A case of subcapsular renal hematoma status post celiac artery thrombectomy


Author

Peter Iskander

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- PMCID: PMC8041721
- DOI: 10.1016/j.ijscr.2021.105798

Free PMC article
Abstract

**Introduction:** 30 year old male with no significant past medical history presenting to the hospital with significant left-sided abdominal pain.

**Case presentation:** Patient was found to have a thrombus within the celiac artery for which he underwent a catheter assisted thrombolysis procedure. Hypercoagulable work-up revealed evidence of a JAK 2 V617F mutation which is indicative of Polycythemia Vera. The patient returned the following day with considerable left-sided flank pain associated with shortness of breath, nausea, and vomiting. CT performed showed evidence of an expanding left renal subcapsular hematoma. Patient was treated conservatively with IV fluids and pain medication before he was discharged hemodynamically stable after a few days.

**Discussion/conclusion:** Accessory renal vessels can be a rare finding coming of the celiac artery and so, care must be taken to evaluate vascular anatomy to avoid iatrogenic injuries; a bleed from one of these vessels could lead to the development of a hematomas, as seen with this patient.

**Keywords:** Catheter assisted thrombolysis; Celiac artery thrombus; Ekosonic Endovascular System (EKOS) catheter; Hypercoagulability; JAK2 mutations; Myeloproliferative disorders; Polycythemia vera; Renal subcapsular hematoma.

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- 12 references
- 3 figures

**Full text links**

42. **Laparoscopic treatment of median arcuate ligament syndrome without**
ganglionectomy of the celiac plexus in the hybrid operating room: Report of a case


Authors

Hiroto Kayashima 1, Ryosuke Minagawa 2, Shoichi Inokuchi 2, Tadashi Koga 2, Nobutoshi Miura 3, Kiyoshi Kajiyama 2

Affiliations

1 Department of Surgery, Iizuka Hospital, 3-83 Yoshio-machi, Iizuka, Fukuoka, 820-8505, Japan. Electronic address: hirotokayashima@gmail.com.
2 Department of Surgery, Iizuka Hospital, 3-83 Yoshio-machi, Iizuka, Fukuoka, 820-8505, Japan.
3 Department of Radiology, Iizuka Hospital, 3-83 Yoshio-machi, Iizuka, Fukuoka, 820-8505, Japan.

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• PMCID: PMC8044698
• DOI: 10.1016/j.ijscr.2021.105840

Free PMC article

Abstract

Introduction: Median arcuate ligament syndrome (MALS) is a rare condition in which the median arcuate ligament (MAL) causes compression of the celiac artery (CA) and plexus. Although 13-50 % of healthy population exhibit radiologic evidence of the CA compression, the majority remains asymptomatic. With or without symptoms, MALS have a risk of developing collateral circulation that leads to pancreaticoduodenal artery (PDA) aneurysms that have high risk of rupture. The treatment of MALS is the surgical release of the MAL. However, the necessity of ganglionectomy of the celiac plexus is still unclear.
Presentation of case: A 60-year-old man with a ruptured PDA aneurysm caused by MALS was admitted to our hospital for an emergency. After treatment for the ruptured PDA aneurysm by transcatheater arterial coil embolization, he underwent elective laparoscopic MAL release in the hybrid operation room to check blood flow of the CA intraoperatively. The angiography of the CA immediately after MAL release without ganglionectomy of the celiac plexus showed the antegrade blood flow to the proper hepatic artery instead of the retrograde flow via the pancreaticoduodenal arcade. The postoperative course was uneventful and the follow-up computed tomography revealed no residual CA stenosis.

Discussion: Unlike symptomatic MALS, it might be enough to just release the MAL without ganglionectomy of the celiac plexus for asymptomatic MALS, especially that with the treated PDA aneurysm.

Conclusion: Laparoscopic treatment of MALS in hybrid operating room could allow for adequate MAL release without ganglionectomy of the celiac plexus using the intraoperative angiography of the CA.

Keywords: Celiac plexus; Hybrid operating room; Intraoperative angiography; Laparoscopy; Median arcuate ligament syndrome.

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- 20 references
- 4 figures

Full text links

43. Larazotide acetate induces recovery of ischemia-injured porcine jejenum via repair of tight junctions

Intestinal ischemia results in mucosal injury, including paracellular barrier loss due to disruption of tight junctions. Larazotide acetate (LA), a small peptide studied in Phase III clinical trials for treatment of celiac disease, regulates tight junctions (TJs). We hypothesized that LA would dose-dependently hasten recovery of intestinal ischemic injury via modulation of TJs. Ischemia-injured tissue from 6-8-week-old pigs was recovered in Ussing chambers for 240 minutes in the presence of LA. LA (1 μM but not 0.1 μM or 10 μM) significantly enhanced transepithelial electrical resistance (TER) above ischemic injured controls and significantly reduced serosal-to-mucosal flux LPS (P<0.05). LA (1 μM) enhanced localization of the sealing tight junction protein claudin-4 in repairing epithelium. To assess for the possibility of fragmentation of LA, an in vitro enzyme degradation assay using the brush border enzyme aminopeptidase M, revealed generation of peptide fragments. Western blot analysis of total protein isolated from uninjured and ischemia-injured porcine intestine showed aminopeptidase M enzyme presence in both tissue types, and mass spectrometry analysis of samples collected during ex vivo analysis confirmed formation of LA fragments. Treatment of tissues with LA fragments had no effect alone, but treatment with a fragment missing both aminoterminus glycines inhibited barrier recovery stimulated by 1 μM LA. To reduce potential LA inhibition by fragments, a D-amino acid analog of larazotide
Analog #6, resulted in a significant recovery response at a 10-fold lower dose (0.1 μM) similar in magnitude to that of 1 μM LA. We conclude that LA stimulates repair of ischemic-injured epithelium at the level of the tight junctions, at an optimal dose of 1 μM LA. Higher doses were less effective because of inhibition by LA fragments, which could be subverted by chirally-modifying the molecule, or microdosing LA.

Conflict of interest statement

Anthony Blikslager and Zachary Slifer were funded, in part, by Innovate Pharmaceuticals to perform this work. Anthony Blikslager consulted for Innovate Biopharmaceuticals Inc and 9 Meters Biopharma. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

Full text links

44. Increased Fecal Bile Acid Excretion in a Significant Subset of Patients with Other Inflammatory Diarrheal Diseases


Authors

Priya Vijayvargiya ¹, Daniel Gonzalez Izundegui ¹, Gerardo Calderon ¹, Sarah Tawfic ², Sarah Batbold ², Hiba Saifuddin ², Patrick Duggan ², Valeria Melo ², Taylor Thomas ², Megan Heeney ², Adrian Beyde ², James Miller Jr ², Kenneth Valles ², Kafayat Oyemade ², Joseph F Brant ², Jessica Atieh ¹, Leslie J Donato ³, Michael Camilleri ⁴

Affiliations

- ¹ Clinical Enteric Neuroscience Translational and Epidemiological Research (CENTER), Division of Gastroenterology and Hepatology, Mayo Clinic, 200 First St. S.W. Charlton Bldg., Rm. 8-110, Rochester, MN, 55905, USA.
Abstract

**Background:** Increased fecal bile acid excretion (IBAX) occurs in a third of patients with functional diarrhea.

**Aims:** To assess the prevalence of IBAX in benign inflammatory intestinal and colonic diseases presenting with chronic diarrhea.

**Methods:** All patients with known inflammatory diseases or resections who underwent 48 h fecal fat and BA testing for chronic diarrhea at a single center were included. Quiescent disease was based on clinical evaluation and serum, endoscopic and imaging studies. IBAX was defined by: > 2337 µmol total BA/48 h; or primary fecal BAs > 10%; or > 4% primary BA plus > 1000 µmol total BA /48 h. Demographics, fecal weight, fecal fat, stool frequency and consistency were collected. Nonparametric statistical analyses were used for group comparisons.

**Results:** Sixty patients had celiac disease (51 quiescent, 9 active), 66 microscopic colitis (MC: 34 collagenous, 32 lymphocytic), 18 ulcerative colitis (UC), and 47 Crohn’s disease (CD). Overall, fecal fat, 48 h stool weight, frequency and consistency were not different among subgroups except for inflammatory bowel disease (IBD) based on disease location. Almost 50% patients with celiac disease and MC had IBAX, with a greater proportion with increased primary fecal BA. Among UC patients, rates of IBAX were higher with pancolonic disease. A high proportion of patients with ileal resection or CD affecting ileum or colon had IBAX. IBAX was present even with quiescent inflammation in UC or CD.
**Conclusions:** A significant subset of patients with MC, quiescent celiac disease and IBD had increased fecal BA excretion, a potential additional therapeutic target for persistent diarrhea.

**Keywords:** Celiac; Colitis; Collagenous; Crohn's; Lymphocytic; Microscopic; Ulcerative.

- 24 references

**Full text links**

45. **High-resolution genotyping of HLA class I loci in children with type 1 diabetes and celiac disease**


**Authors**

Shehab Alshiekh ¹ ², Daniel E Geraghty ³, Daniel Agardh ¹

**Affiliations**

- ¹ Department of Clinical Sciences, Lund University/CRC, Malmö, Sweden.
- ² Department of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.
- ³ Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, United States.

- PMID: 33885207
- DOI: 10.1111/tan.14280

**Abstract**

**Objectives:** HLA-DQ2 and DQ8 contribute to the strongest risk haplotypes for type 1 diabetes (T1D) and celiac disease (CD). The variation in genetic risk
association is likely linked to different HLA class II loci susceptibility, but association studies of HLA class I alleles are scarce. The aim was to investigate HLA class I A, B, and C alleles polymorphisms in children with only T1D, CD, and a subgroup with both T1D and CD (T1D w/CD).

**Materials and methods:** HLA class I A, B, and C genes were genotyped using next-generation targeted sequencing (NGTS). A conditional analysis was performed on 68 children with T1D, 219 children with CD and seven children with T1D w/CD enrolled from a birth cohort study at high genetic risk children from the South of Sweden.

**Results:** Among 1764 HLA class I allele variants, A*29:02:01 in T1D w/CD was associated with both T1D (OR=21.42 (1.05, 1322.4), P=0.0231) and CD (OR=35 (2.36, 529.12), P=0.0051) along with C*05:01:01 with both T1D (OR=5.54 (1.06, 24.8), P=0.02) and CD (OR=6.84 (1.46, 26.01), P=0.0077). No independent effects of HLA-B allele associations were observed in T1D w/CD.

**Conclusion:** Although the distribution of HLA class I alleles differs between children with T1D and CD, the A*29:02:01 and C*05:01:01 alleles showed shared risk association of both diseases. This article is protected by copyright. All rights reserved.

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46. **Pancreatic Cancer-Associated Pain Management**


**Authors**

AndrewL Coveler ¹, Jonathan Mizrahi ², Bory Eastman ³, Smith Jim Apisarnthanarax ², Shalini Dalal ⁴, Terry McNearney ⁵, Shubham Pant ², Precision Promise Consortium
Affiliations

1 Departments of Medical Oncology, University of Washington, Seattle, Washington, USA.
2 Departments of Radiation Oncology, University of Washington, Seattle, Washington, USA.
3 Department of Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, USA.
4 Department of Palliative, Rehabilitation, and Integrative Medicine, University of Texas MD Anderson Cancer Center, Houston, Texas, USA.
5 Pancreatic Cancer Action Network.

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DOI: 10.1002/onco.13796

Free article

Abstract

Pain is highly prevalent in patients with pancreatic cancer and contributes to the morbidity of the disease. Pain may be due to pancreatic enzyme insufficiency, obstruction, and/or a direct mass effect on nerves in the celiac plexus. Proper supportive care to decrease pain is an important aspect of the overall management of these patients. There are limited data specific to the management of pain caused by pancreatic cancer. Here we review the literature and offer recommendations regarding multiple modalities available to treat pain in these patients. The dissemination and adoption of these best supportive care practices can improve quantity and quality of life for patients with pancreatic cancer. IMPLICATIONS FOR PRACTICE: Pain management is important to improve the quality of life and survival of a patient with cancer. The pathophysiology of pain in pancreatic cancer is complex and multifactorial. Despite tumor response to chemotherapy, a sizeable percentage of patients are at risk for ongoing cancer-related pain and its comorbid consequences. Accordingly, the management of pain in patients with pancreatic cancer can be challenging and often requires a multifaceted approach.

Keywords: Pain management; Palliative care; Pancreatic neoplasms.
Abdominal pain is a very common presentation in the accident and emergency department. However, vasculitis is not the usual first differential diagnosis. This paper discusses a case of polyarteritis nodosa presenting with acute abdominal pain alone. Common surgical conditions were obviously considered, but they were not found to cause the patient's problems. We describe how investigations led to this diagnosis discussed in detail in this paper. It is important to remember that prompt recognition of unusual life-threatening conditions can lead to timely intervention.

**Keywords:** gastrointestinal surgery; vasculitis.
Conflict of interest statement

Competing interests: None declared.

Full text links

48. Larazotide Acetate: A Pharmacological Peptide Approach to Tight Junction Regulation


Authors

Zachary M Slifer 1, B Radha Krishnan 2, Jay Madan 3, Anthony T Blikslager 1

Affiliations

1 Clinical Sciences, North Carolina State University, United States.
2 Research and Development, Innovate Biopharmaceuticals, Inc, United States.

PMID: 33881350
DOI: 10.1152/ajpgi.00386.2020

Abstract

Larazotide acetate (LA) is a single-chain peptide of eight amino acids that acts as a tight junction regulator to restore intestinal barrier function. LA is currently being studied in phase 3 clinical trials and is orally administered to adult patients with celiac disease as an adjunct therapeutic to enhance intestinal barrier function that has been disrupted by gliadin-induced immune
reactivity. Mechanistically, LA is thought to act as a zonulin antagonist to reduce zonulin-induced increases in barrier permeability and has been associated with the redistribution and rearrangement of tight junction proteins and actin filaments to restore intestinal barrier function. More recently, LA has been linked to inhibition of myosin light chain kinase, which likely reduces tension on actin filaments, thereby facilitating tight junction closure. Small (rodent) and large (porcine) animal studies have been conducted that demonstrate the importance of LA as a tight junction regulatory peptide in conditions other than celiac disease, including collagen-induced arthritis in mice and intestinal ischemic injury in pigs.

**Keywords:** Tight junction; barrier function; celiac disease.

**Full text links**

49. **Unravelling the effects of procyanidin on gliadin digestion and immunogenicity**


**Authors**

Dias Ricardo 1, Francisco Telmo 1, Bessa Pereira Catarina 1, Mateus Nuno 1, de Freitas Victor 1, Pérez-Gregorio Rosa 1

**Affiliation**

1 LAQV-REQUIMTE Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade do Porto, Rua do Campo Alegre 687, 4169-007 Porto, Portugal. maria.gregorio@fc.up.pt.

- PMID: 33881102
- DOI: 10.1039/d1fo00382h
Abstract

The effect of procyanidin dimer B3, a common food tannin, on the digestion of gliadin proteins was investigated by monitoring the changes in the immunogenic peptides produced during in vitro digestion and immunoreactivity. Interaction studies between procyanidin dimer B3, gluten proteins and/or digestive enzymes were performed by SDS-PAGE. The effect of procyanidin B3 on the enzymatic activity of trypsin, chymotrypsin and pancreatin was evaluated. The differences in the number and nature of immunogenic peptides released during digestion were identified by mass spectrometry. Briefly, the enzymatic activity of gastrointestinal enzymes was only slightly affected but a significant decrease in the immunological properties of the peptides produced during digestion was observed. Overall, although further studies are needed, the interaction between polyphenols and gluten proteins clearly influences gluten protein digestion and immunogenicity, thus suggesting that the consumption of dietary polyphenols can significantly affect the degree of celiac disease downstream immune reactions.

Full text links

50. Nutri-epigenetics: the effect of maternal diet and early nutrition on the pathogenesis of autoimmune diseases


Authors

Dhinoth K Bangarusamy 1, Arun P Lakshmanan 1, Sara Al-Zaidan 1, Shaikha Alabduljabbar 1, Annalisa Terranegra 2

Affiliations
Abstract

Autoimmune diseases comprise a wide group of diseases involving a self-response of the immune system against the host. The etiopathogenesis is very complex involving disease-specific factors but also environmental factors, among which the diet. Maternal diet during pregnancy as well as early nutrition recently attracted the interest of the scientists as contributing to the immune programming. In this paper, we reviewed the most recent literature on the effect of maternal diet and early nutrition in modulating the immune system in a selected subset of autoimmune diseases: type 1 diabetes, celiac disease, inflammatory bowel disease, juvenile idiopathic arthritis and rheumatoid arthritis. Particularly, we focused our narrative on the role of maternal and perinatal nutrition in the epigenetic mechanisms underlying the auto-immune response. Maternal diet during pregnancy as well as breastfeeding and early nutrition play a big role in many epigenetic mechanisms. Most of the nutrients consumed by the mother and the infant are known exerting epigenetic functions, such as folate, methionine, zinc, vitamins B12 and D, fibers, casein and gliadin, and they were linked to gene expression changes in the immune pathways. Despite the common role of maternal diet, breastfeeding and early nutrition in almost all the autoimmune diseases, each disease seems to have specific diet-driver epigenetic mechanisms that require further investigations. The research in this field is opening new routes to establishing a precision nutrition approach to the autoimmune diseases.

Full text links
Intestinal lymphoma, although rare, is the second most common extra-nodal site of lymphoma, following stomach. It is usually secondary to systemic involvement and is predominantly of non-Hodgkin's subtype. In addition to the risk factors for lymphomas occurring elsewhere, certain risk factors are specific for intestinal lymphoma. These include enteropathies such as celiac disease and inflammatory bowel disease. Imaging is the cornerstone in the management of intestinal lymphoma. Contrast-enhanced computed tomography or positron emission tomography-computed tomography are the preferred modalities for diagnosis, staging, monitoring response to treatment, and for follow-up evaluation. Bowel lymphomas can have various morphological patterns on imaging; however, certain characteristic features, if present, may prove invaluable in its diagnosis. Hence, it is imperative to be acquainted with the myriad of imaging findings in bowel lymphoma and its complications which may not only help in vivo distinction from other commoner bowel lesions but alter the management accordingly.
Keywords: Aneurysmal dilatation; Bowel obstruction; Entero-enteric fistula; Intestinal lymphoma; Lymphoma.

- 29 references

Full text links

52. **Assessment of price and nutritional quality of gluten-free products versus their analogues with gluten through the algorithm of the nutri-score front-of-package labeling system**


Authors

Sara De Las Heras-Delgado¹, Adoración de Las Nieves Alías-Guerrero¹, Esther Cendra-Duarte¹, Jordi Salas-Salvadó², Elisenda Vilchez³, Esther Roger³, Pablo Hernández-Alonso⁴, Nancy Babio²

Affiliations

- ¹ Universitat Rovira i Virgili, Departament de Bioquímica i Biotecnologia, Unitat de Nutrició Humana. Hospital Universitari San Joan de Reus, Reus, Spain. nancy.babio@urv.cat pablo.hernandez@fimabis.org
- ² Universitat Rovira i Virgili, Departament de Bioquímica i Biotecnologia, Unitat de Nutrició Humana. Hospital Universitari San Joan de Reus, Reus, Spain. nancy.babio@urv.cat pablo.hernandez@fimabis.org and Consorcio CIBER, M.P. Fisiopatología de la Obesidad y Nutrición (CIBEROObn), Instituto de Salud Carlos III (ISCI), Madrid, Spain and Institut d'Investigació Pere Virgili (IISPV), Reus, Spain.
- ³ Celiac Association of Catalonia. Nutrition Department, Barcelona, Spain.
Abstract

Evidence has shown that the nutritional quality of gluten-free products (GFPs) is lower than that of non-GFPs. Our main objective was to compare the nutritional quality through nutritional profiles of foods underlying the Nutri-Score front-of-pack and the price of GFPs with respect to non-GFPs, and to evaluate whether there is a correlation between both parameters. Nutritional information of all products was obtained from the CELIACBASE database and the price through Spanish supermarkets websites. Global quality using the Nutri-Score algorithm and the price were compared between both types of products. GFPs do not always have poorer quality than their counterparts. A better quality of gluten-free pasta was correlated with the higher price but also a worse quality of gluten-free muesli was correlated with the higher price. The price of GFPs compared to non-GFPs was higher up to 391.5%. However, for ham and cheese pizza, ham pizza, Marie biscuits, and baby biscuits, the difference was not statistically significant. Generally, the price of GFPs did not correlate with better nutritional quality. Nutri-Score would ease the nutritional quality identification, empowering consumers and could also influence manufacturers to improve the nutritional quality of GFPs. Nowadays, given that many GFPs have poor nutritional quality, they should be included only occasionally in a balanced gluten-free diet.
Diagnostic and Predictive Contribution of Autoantibodies Screening in a Large Series of Patients With Primary Immunodeficiencies


Authors

Azzeddine Tahiat 1, Abdelghani Yagoubi 2, Mohamed Samir Ladj 3, Reda Belbouab 3, Samira Aggoune 4, Laziz Atek 4, Djamila Bouziane 5, Souhila Melzi 6, Chahinez Boubidi 7, Warda Drali 8, Chafa Bendahmane 9, Hamza Iguerguesdaoune 1, Shem Taguemount 1, Asma Soufane 1, Asma Oukil 1, Abdalbasset Kefi 10, Hassen Messaoudi 11, Nadia Boukhenfouf 12, Mohamed Amine Ifri 13, Tahar Bencharif Madani 14, Hayet Belhadi 15, Keltoum Nafissa Benhala 16, Mokhtar Kharri 16, Naceria Cherif 17, Leila Smati 18, Zakia Arada 8, Zoulikha Zeroual 7, Zair Bouzerar 6, Ouardia Ibsaine 5, Hachemi Maouche 4, Rachida Boukari 3, Kamel Djenouhat 1

Affiliations

1 Department of Medical Biology, Rouiba Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
2 Pediatric Gastroenterology, Centre Algérois de Pédiatrie, Algiers, Algeria.
3 Department of Pediatrics, Mustapha University Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
4 Department of Pediatrics, El-Harrach Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
5 Department of Pediatrics, Ain Taya Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
6 Department of Pediatrics, Bab El-Oued University Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
7 Department of Pediatrics A, Hussein Dey University Hospital, Algiers Faculty of Medicine, University of Algiers 1, Algiers, Algeria.
Abstract

Objectives: To evaluate the diagnostic and predictive contribution of autoantibodies screening in patients with primary immunodeficiencies (PIDs).

Methods: In the present study, PID patients and healthy controls have been screened for 54 different autoantibodies. The results of autoantibodies screening in PID patients were correlated to the presence of autoimmune diseases.

Results: A total of 299 PID patients were included in this study with a predominance of antibody deficiencies (27.8%) followed by immunodeficiencies affecting cellular and humoral immunity (26.1%) and complement deficiencies (22.7%). Autoimmune manifestations were present in 82 (27.4%) patients. Autoimmune cytopenia (10.4%) was the most common
autoimmune disease followed by gastrointestinal disorders (10.0%), rheumatologic diseases (3.7%), and endocrine disorders (3.3%). Autoantibodies were found in 32.4% of PID patients and 15.8% of healthy controls \((P < 0.0005)\). Anti-nuclear antibodies (ANA) (10.0%), transglutaminase antibody (TGA) (8.4%), RBC antibodies (6.7%), anti-smooth muscle antibody (ASMA) (5.4%), and ASCA (5.0%) were the most common autoantibodies in our series. Sixty-seven out of the 82 patients with autoimmune manifestations (81.7%) were positive for one or more autoantibodies. Eleven out of the 14 patients (78.6%) with immune thrombocytopenia had positive platelet-bound IgM. The frequencies of ASCA and ANCA among patients with IBD were 47.4% and 21.0% respectively. All patients with celiac disease had TGA-IgA, while six out of the 11 patients with rheumatologic diseases had ANA (54.5%). Almost one third of patients (30/97) with positive autoantibodies had no autoimmune manifestations. ANA, rheumatoid factor, ASMA, anti-phospholipid antibodies and ANCA were often detected while specific AID was absent. Despite the low positive predictive value of TGA-IgA and ASCA for celiac disease and inflammatory bowel disease respectively, screening for these antibodies identified undiagnosed disease in four patients with positive TGA-IgA and two others with positive ASCA.

**Conclusion:** The present study provides valuable information about the frequency and the diagnostic/predictive value of a large panel of autoantibodies in PIDs. Given the frequent association of some AIDs with certain PIDs, screening for corresponding autoantibodies would be recommended. However, positivity for autoantibodies should be interpreted with caution in patients with PIDs due to their low positive predictive value.

**Keywords:** autoantibody; autoimmune cytopenia; celiac disease; platelet-bound IgM; primary immunodeficiencies; screening; transglutaminase antibody.

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**Conflict of interest statement**
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- 34 references
- 1 figure

**Full text links**

54. **Barley**

Review  
In: Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–.  
2021 Apr 19.

- PMID: [30000887](#)
- Bookshelf ID: [NBK501827](#)

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**Excerpt**

Barley (*Hordeum vulgare*) contains starch, dietary fiber such as beta-glucan, and the enzyme diastase. Barley is a purported galactogogue and is used by mothers in many cultures to increase their milk supply.[1-5] Some animal evidence indicates that a polysaccharide in barley can increase serum prolactin,[5-7] and one human study supports some galactogogue activity of barley malt and lemon balm in mothers of preterm infants.[8] Galactogogues should never replace evaluation and counseling on modifiable factors that affect milk production.[9,10] No data exist on the excretion of any components of barley into breastmilk or on the safety and efficacy of barley in nursing mothers or infants. Barley is safe to be consumed during breastfeeding, except by persons with celiac disease. Allergy to barley occurs rarely.

Dietary supplements do not require extensive pre-marketing approval from the U.S. Food and Drug Administration. Manufacturers are responsible to ensure the safety, but do not need to prove the safety and effectiveness of
dietary supplements before they are marketed. Dietary supplements may
contain multiple ingredients, and differences are often found between labeled
and actual ingredients or their amounts. A manufacturer may contract with an
independent organization to verify the quality of a product or its ingredients,
but that does not certify the safety or effectiveness of a product. Because of
the above issues, clinical testing results on one product may not be applicable
to other products. More detailed information about dietary supplements is
available elsewhere on the LactMed Web site.

- 10 references

Full text links

55. **Pyruvate kinase M2 in chronic inflammations: a potpourri of crucial protein-protein interactions**


Authors

Sagarkumar Patel # 1, Anwesha Das # 1, Payal Meshram 1, Ayushi Sharma 1, Arnab Chowdhury 1, Heena Jariyal 2, Aishika Datta 3, Deepaneeta Sarmah 3, Lakshmi Vineela Nalla 3, Bichismita Sahu 1, Amit Khairnar 3, Pallab Bhattacharya 3, Akshay Srivastava 4, Amit Shard 5

Affiliations

- 1 Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research, Ahmedabad, Opposite Air Force Station, Gandhinagar, Gujarat, 382355, India.
Abstract

Chronic inflammation (CI) is a primary contributing factor involved in multiple diseases like cancer, stroke, diabetes, Alzheimer's disease, allergy, asthma, autoimmune diseases, coeliac disease, glomerulonephritis, sepsis, hepatitis, inflammatory bowel disease, reperfusion injury, and transplant rejections. Despite several expansions in our understanding of inflammatory disorders and their mediators, it seems clear that numerous proteins participate in the onset of CI. One crucial protein pyruvate kinase M2 (PKM2) much studied in cancer is also found to be inextricably woven in the onset of several CI's. It has been found that PKM2 plays a significant role in several disorders using a network of proteins that interact in multiple ways. For instance, PKM2 forms a close association with epidermal growth factor receptors (EGFRs) for uncontrolled growth and proliferation of tumor cells. In neurodegeneration, PKM2 interacts with apurinic/apyrimidinic endodeoxyribonuclease 1 (APE1) to onset Alzheimer's disease pathogenesis. The cross-talk of protein tyrosine phosphatase 1B (PTP1B) and PKM2 acts as stepping stones for the commencement of diabetes. Perhaps PKM2 stores the potential to unlock the pathophysiology of several diseases. Here we provide an overview of the notoriously convoluted biology of CI's and PKM2. The cross-talk of PKM2 with several proteins involved in stroke, Alzheimer's, cancer, and other diseases has
also been discussed. We believe that considering the importance of PKM2 in inflammation-related diseases, new options for treating various disorders with the development of more selective agents targeting PKM2 may appear.

**Keywords:** Cancer; Chronic inflammation; Protein–protein interactions; Pyruvate kinase M2 (PKM2).

- **198 references**

**Full text links**

Response To Celiac Plexus Block Confirms Neurogenic Etiology of Median Arcuate Ligament Syndrome


**Authors**

Dennis A Barbon, Richard Hsu, Josef Noga, Bryan Lazzara, Todd Miller, Brian F Stainken

- **PMID:** [33862195](https://www.ncbi.nlm.nih.gov/pubmed/33862195)
- **DOI:** [10.1016/j.jvir.2021.04.003](https://doi.org/10.1016/j.jvir.2021.04.003)

**Abstract**

**Purpose:** To evaluate the response of Median Arcuate Ligament Syndrome (MALS) symptoms, including postprandial pain, nausea, and vomiting to celiac plexus block (CPB) and to correlate response with arterial anatomy.

**Materials and methods:** In a single-institution, retrospective cohort of clinically diagnosed MALS patients, 96 patients (75 female, 21 male, mean age 27 years) underwent 103 CT-guided percutaneous CPB procedures. Imaging, procedural, and clinical reports were reviewed. Primary outcomes evaluated
were technical success, change in self-reported pain score, and change in nausea and vomiting.

**Results:** Preprocedural computed tomography (CT) imaging was available in 81/96 patients, demonstrating findings of celiac artery compression in 22/81 (27%) patients. Technical success was achieved in 102/103 cases. No major adverse events and one moderate adverse event were reported. Postprandial pain score decreased in 86 patients (84%), and mean score decreased from 6.3 to 0.9 points (p < .001). Prevalence of postprandial nausea decreased from 37.9% to 11.6% (p < .001), and vomiting decreased from 15.5% to 4.9% (p = .019). There were no differences in post-CPB pain relief between patients with and without celiac artery compression (p = .745).

**Conclusions:** In patients with a clinical diagnosis of MALS, a large majority reported pain relief and decreased gastrointestinal symptoms after CPB. Pain relief did not correlate with presence of celiac arterial abnormalities. This supports neuropathy as the primary etiology of MALS, and suggests that absence of celiac stenosis should not be used as an exclusion criterion.

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**Full text links**

57. Efficient implementation of the 'non-biopsy approach' for the diagnosis of childhood celiac disease in the Netherlands: a national prospective evaluation 2010-2013


**Authors**

Caroline R Meijer ¹, Joachim J Schweizer ², Anne Peeters ², Hein Putter ³, M Luisa Mearin ²
Abstract

The aim of this study was (1) to prospectively evaluate the nationwide implementation of the ESPGHAN-guidelines for the diagnosis of celiac disease (CD), (2) to investigate the incidence and clinical presentation of diagnosed childhood CD (0-14 years) in the Netherlands, and (3) to compare the findings with national survey data from 1975 to 1990 and 1993 to 2000 using the same approach. From 2010 to 2013, all practicing paediatricians were invited to report new celiac diagnoses to the Dutch Pediatric Surveillance Unit. Data were collected via questionnaires. A total of 1107 children with newly diagnosed CD were reported (mean age, 5.8 years; range, 10 months-14.9 years; 60.5% female). After the introduction of the non-biopsy approach in 2012, 75% of the diagnoses were made according to the guideline with a significant decrease of 46.3% in biopsies. The use of EMA and HLA-typing significantly increased with 25.8% and 62.1%, respectively. The overall incidence rate of childhood CD was 8.8-fold higher than in 1975-1990 and 2.0-fold higher than in 1993-2000. During the study period, the prevalence of diagnosed CD was 0.14%, far below 0.7% of CD identified via screening in the general Dutch paediatric population. Clinical presentation has shifted towards less severe and extra-intestinal symptoms. Conclusion: ESPGHAN guidelines for CD diagnosis in children were effectively and rapidly implemented in the Netherlands. Incidence of diagnosed CD among children is still significantly rising with a continuous changing clinical presentation. Despite the increasing incidence of diagnoses, significant underdiagnosis still remains. What is Known: • Since 2000 the incidence of diagnosed childhood CD in the
Netherlands has shown a steady rise. • The rise in incidence has been accompanied by a changing clinical presentation at diagnosis. What is New: • The ESPGHAN guidelines 2012 for CD diagnosis were effectively and rapidly implemented in the Netherlands. • The incidence of diagnosed childhood CD in the Netherlands has continued to rise significantly during the reported period.

**Keywords:** Childhood celiac disease; Clinical presentation; Guideline; Implementation; Incidence.

- 40 references

**Full text links**

58. **Intraoperative Celiac Plexus Block with Pre-peritoneal Infusion Reduces Opioid Usage in Major Hepato-pancreato-biliary Surgery: A Pilot Study**


**Authors**

Zhe Hao T Teo 1, Boon Lim J Tey, Chek Wun Foo, Wan Yi Wong, Jee Keem Low

**Affiliation**

- 1 Department of Hepatopancreatobiliary Surgery, Tan Tock Seng Hospital, Singapore Department of Anesthesiology, Woodlands Health Campus, Singapore Department of Anesthesiology, Tan Tock Seng Hospital, Singapore.

- PMID: 33856374
- DOI: 10.1097/SLA.0000000000004883
Abstract

Objective: Given the role of celiac plexus block (CPB) in the management of chronic pain, we sought to investigate the utility of CPB in the control of post-operative pain in major hepato-pancreato-biliary surgeries.

Summary background data: CPB has been in practice for decades for the management of upper abdominal visceral pain, especially in cancer patients. Typically, in this group of patients with chronic pain, a neurolytic agent is injected to cause irreversible neural damage to achieve pain control. We aim to apply this concept to post-operative pain control by injecting bupivacaine to the celiac plexus instead of a neurolytic agent. We aim to investigate if this novel technique decreases post-operative opioid usage, offers better pain relief and leads to earlier ambulation.

Methods: A retrospective, single institution study comparing consecutive patients who received intraoperative CPB and pre-peritoneal infusion (PPI) with patients who received only PPI in open hepato-pancreato-biliary surgery between the year 2016 to 2019 by a single surgeon. Patients with incomplete data on PCA usage and post-operative ambulation information were excluded.

Results: Patients with CBP used 31% less morphine on POD1 compared to patient without CBP and 42% less morphine on POD2. Overall average morphine usage was significantly lower in patients with CBP. Duration of PCA was shorter for patient with CBP compared with patient without CBP. The dynamic visual analogue score was marginally better in patients with CBP. Time to ambulation was similar in both groups.

Conclusions: CPB can be considered a part of the multimodal approach for post-operative pain management in open hepato-pancreato-biliary surgeries.

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Conflict of interest statement

Conflict of Interest: Authors declare no Conflict of Interest for this article.

Full text links
Medication use and microscopic colitis: a multicentre retrospective cohort study


Authors

Haley M Zylberberg 1, Amrit K Kamboj 2, Nicole De Cuir 3, Conor M Lane 4, Sahil Khanna 2, Darrell S Pardi 2, Benjamin Lebwohl 3

Affiliations

1 Division of Internal Medicine, Icahn School of Medicine at Mount Sinai, New York City, NY, USA.
2 Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA.
3 Division of Digestive and Liver Diseases, Department of Medicine, Columbia University College of Physicians and Surgeons, New York City, NY, USA.
4 Department of Internal Medicine, Mayo Clinic, Rochester, MN, USA.

PMID: 33852749
DOI: 10.1111/apt.16363

Abstract

Background: Medication use has been implicated in the development of microscopic colitis (MC). However, studies have demonstrated inconsistent findings and there exist variations in design.

Aim: To measure the association between medication use and MC.

Methods: Patients who underwent a colonoscopy over a 10-year period at two academic medical centres (Columbia University Medical Centre and Mayo Clinic) were identified. Cases were patients with biopsy-proven MC and controls were patients who underwent colonoscopy for evaluation of diarrhoea with biopsies negative for MC. Cases were matched by age, gender and calendar period with up to two controls. Demographics, medication use,
smoking history and coeliac disease status were collected. Conditional logistic regression was used with and without adjustment for smoking.

**Results:** A total of 344 patients with MC were matched to 668 controls. After adjusting for smoking, there was an inverse association between MC and use of proton pump inhibitors (PPIs) (OR 0.64; 95% CI 0.47-0.87), H2 blockers (OR 0.46; 95% CI 0.24-0.88) and oral diabetes medications (OR 0.47; 95% CI 0.27-0.81). There was a positive association with nonsteroidal anti-inflammatory drug (NSAID) use and MC (OR 1.63; 95% CI 1.12-2.38).

**Conclusions:** NSAID use was associated with MC, while use of PPIs, H2 blockers and oral diabetes medications were inversely related to MC. Our use of a control group with diarrhoea, as opposed to healthy controls, may have contributed to these inverse associations. Future studies of drug-induced microscopic colitis should include control groups with diarrhoea, and not only healthy controls.

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- [30 references](#)

**Full text links**

60. [Vaccination in adult patients: shingles vaccines and vaccination in case of anatomical or functional asplenia](Rev Med Suisse. 2021 Apr 14;17(734):744-749. [Article in French])

**Authors**

Aline Munting ¹, Pierre Alex Crisinel ²

**Affiliations**
Abstract

Shingles vaccination and pneumococcal vaccination of patients with celiac disease are among the most recent updates for the vaccination of vulnerable adults, in Switzerland. Shingles and especially post-herpes zoster pain remain an unresolved public health issue. The only vaccine available in Switzerland is very little administered because it is not reimbursed by health insurance companies. A second shingles vaccine is announced for 2022 and should help to reduce the burden of this disease. It has been known for many years that celiac disease is accompanied by hyposplenism in adults. The resulting increased risk of invasive pneumococcal infections justifies, since 2020, a recommendation for vaccination against these encapsulated bacteria.

La vaccination contre le zona et la vaccination contre les pneumocoques des patients souffrant de maladie cœliaque font partie des mises à jour les plus récentes pour la vaccination de l’adulte vulnérable, en Suisse. Le zona et surtout les douleurs postzostériennes restent un problème de santé publique non résolu. Le seul vaccin disponible en Suisse est très peu administré en raison de son non-remboursement par les caisses-maladie. Un deuxième vaccin contre le zona est annoncé pour 2022 et devrait contribuer à alléger le fardeau de cette maladie. On sait depuis de nombreuses années que la maladie cœliaque s’accompagne d’un hyposplénisme chez l’adulte. Le risque accru d’infections invasives à pneumocoques qui en découle justifie, depuis 2020, une recommandation de vaccination contre ces bactéries encapsulées.

Conflict of interest statement

Les auteurs n’ont déclaré aucun conflit d’intérêts en relation avec cet article.
Association Between Celiac Disease and Autism Spectrum Disorder: A Systematic Review


Authors

Joshua Quan 1 2, Nicola Panaccione 1, Jocelyn Jeong 2 3, Fox E Underwood 1, Stephanie Coward 2, Joseph W Windsor 1 2, Paul E Ronksley 2, Dominica Gidrewicz 3, Jennifer deBruyn 2 3, Justine M Turner 4, Benjamin Lebwohl 5 6, Gilaad G Kaplan 1 2, James A King 2 7 8

Affiliations

1 Department of Medicine.
2 Department of Community Health Sciences.
3 Department of Pediatrics, University of Calgary, Calgary.
4 Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada.
5 Department of Medicine, Celiac Disease Center, Columbia University College of Physicians and Surgeons.
6 Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY.
7 Alberta SPOR Support Unit Data Platform, Alberta Health Services.
8 Centre for Health Informatics, University of Calgary, Calgary, Alberta, Canada.

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DOI: 10.1097/MPG.0000000000003051

Abstract

Objective: The aim of the study was to perform a systematic review assessing the research investigating the association between celiac disease (CD) and autism spectrum disorder (ASD).
**Methods:** A literature search of MEDLINE and EMBASE was performed without limits placed on year or language. Observational studies reporting on the occurrence of CD among patients with ASD and/or the occurrence of ASD among patients with CD were included. Study design, characteristics, diagnostic criteria for ASD and CD, and the frequency of positive cases in the studied sample were recorded. Study quality was assessed using an adapted Newcastle-Ottawa Quality Assessment Scale. Due to substantial heterogeneity between studies, a meta-analysis was not performed.

**Results:** Of the 298 unique citations identified within our search strategy, 17 articles evaluating the association between CD and ASD were included. Of those articles, 13 observed samples of patients with ASD, and 6 observed samples of patients with CD. Overall, most studies had small sample sizes and reported no evidence for an association between the 2 conditions. However, a limited number of population-based studies of higher quality suggested a potential association between CD and ASD.

**Conclusions:** Most studies assessing an association between CD and ASD are at risk for systematic and/or random error. A potential link has, however, been shown in a handful of high-quality studies, and, therefore, this comorbidity cannot be ruled out. Future studies should recruit larger sample sizes, include precise definitions of CD and ASD, and exclude patients with ASD on a gluten-free diet.

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**Conflict of interest statement**

G.G.K. is a CIHR Embedded Clinician Research Chair. The remaining authors report no conflicts of interest.

- 46 references

**Full text links**

[Open Full Text](http://www.wolterskluwer.com)
Anaemia in Dermatitis Herpetiformis: Prevalence and Associated Factors at Diagnosis and One-year Follow-up


Authors

Anna Alakoski, Camilla Pasternack, Timo Reunala, Katri Kaukinen, Heini Huhtala, Eriika Mansikka, Juha Jernman, Kaisa Hervonen, Teea Salmi

Affiliation

1 Department of Dermatology, Tampere University Hospital, FIN-33521 Tampere, Finland.

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DOI: 10.2340/00015555-3795

Free article

Abstract

Dermatitis herpetiformis is a cutaneous manifestation of coeliac disease. Anaemia is a common finding in patients with untreated coeliac disease, but little is known about the occurrence of anaemia in those with dermatitis herpetiformis. This study investigated the prevalence of anaemia and factors associated with anaemia in 250 patients with dermatitis herpetiformis, at diagnosis and one year after diagnosis. As controls, 139 patients with coeliac disease were included. Patient records were reviewed to gather baseline clinical, histological, and laboratory data. Follow-up data for patients with dermatitis herpetiformis were collected from patient records and via questionnaires or at follow-up visits. The prevalence of anaemia was 12% in patients with dermatitis herpetiformis and 17% in patients with coeliac disease at diagnosis (p = 0.257). Anaemia in patients with dermatitis herpetiformis was not associated with the severity of skin symptoms or small
bowl damage. The prevalence of anaemia at a 1-year follow-up had increased to 19%, but it was associated mainly with dapsone treatment.

**Keywords:** dapsone; gluten-free diet; villous atrophy; coeliac disease.

**Full text links**

63. [Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions?](https://doi.org/10.1038/s41577-021-00538-7)


**Author**

Cezmi A Akdis 1 2

**Affiliations**

- 1 Swiss Institute of Allergy and Asthma Research (SIAF), University Zurich, Davos, Switzerland. akdisac@siaf.uzh.ch.
- 2 Christine Kühne-Center for Allergy Research and Education, Davos, Switzerland. akdisac@siaf.uzh.ch.

- PMID: [33846604](https://pubmed.ncbi.nlm.nih.gov/33846604/)
- DOI: [10.1038/s41577-021-00538-7](https://doi.org/10.1038/s41577-021-00538-7)

**Abstract**

There has been a steep increase in allergic and autoimmune diseases, reaching epidemic proportions and now affecting more than one billion people worldwide. These diseases are more common in industrialized countries, and their prevalence continues to rise in developing countries in parallel to urbanization and industrialization. Intact skin and mucosal barriers are crucial
for the maintenance of tissue homeostasis as they protect host tissues from infections, environmental toxins, pollutants and allergens. A defective epithelial barrier has been demonstrated in allergic and autoimmune conditions such as asthma, atopic dermatitis, allergic rhinitis, chronic rhinosinusitis, eosinophilic esophagitis, coeliac disease and inflammatory bowel disease. In addition, leakiness of the gut epithelium is also implicated in systemic autoimmune and metabolic conditions such as diabetes, obesity, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and autoimmune hepatitis. Finally, distant inflammatory responses due to a 'leaky gut' and microbiome changes are suspected in Alzheimer disease, Parkinson disease, chronic depression and autism spectrum disorders. This article introduces an extended 'epithelial barrier hypothesis', which proposes that the increase in epithelial barrier-damaging agents linked to industrialization, urbanization and modern life underlies the rise in allergic, autoimmune and other chronic conditions. Furthermore, it discusses how the immune responses to dysbiotic microbiota that cross the damaged barrier may be involved in the development of these diseases.

- 203 references

Full text links

64. **Can Coupling Multiple Complementary Methods Improve the Spectroscopic Based Diagnosis of Gastrointestinal Illnesses? A Proof of Principle *Ex Vivo* Study Using Celiac Disease as the Model Illness**


Authors

Sara J Fraser-Miller 1, Jeremy S Rooney 1, Michael Lau 2, Keith C Gordon 1, Michael Schultz 3 4 5
Affiliations

- 1 Dodd-Walls Centre for Photonic and Quantum Technologies, Department of Chemistry, University of Otago, Dunedin 9054, New Zealand.
- 2 Southern Community Laboratories, Dunedin 9016, New Zealand.
- 3 Gastroenterology Research Unit, Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin 9054, New Zealand.
- 4 Mercy Hospital, Dunedin 9010, New Zealand.
- 5 Gastroenterology Department, Southern District Health Board, Dunedin 9016, New Zealand.

PMID: 33844904
DOI: 10.1021/acs.analchem.0c04963

Abstract

Spectroscopic methods are a promising approach for providing a point-of-care diagnostic method for gastrointestinal mucosa associated illnesses. Such a tool is desired to aid immediate decision making and to provide a faster pathway to appropriate treatment. In this pilot study, Raman, near-infrared, low frequency Raman, and autofluorescence spectroscopic methods were explored alone and in combination for the diagnosis of celiac disease. Duodenal biopsies (n = 72) from 24 participants were measured ex vivo using the full suite of studied spectroscopic methods. Exploratory principal component analysis (PCA) highlighted the origin of spectral differences between celiac and normal tissue with celiac biopsies tending to have higher protein relative to lipid signals and lower carotenoid spectral signals than the samples with normal histology. Classification of the samples based on the histology and overall diagnosis was carried out for all combinations of spectroscopic methods. Diagnosis based classification (majority rule of class per participant) yielded sensitivities of 0.31 to 0.77 for individual techniques, which was increased up to 0.85 when coupling multiple techniques together. Likewise, specificities of 0.50 to 0.67 were obtained for individual techniques, which was increased up to 0.78 when coupling multiple techniques together. It was noted that the use of antidepressants contributed to false positives, which is believed to be associated with increased serotonin levels observed in the gut mucosa in both celiac disease and the use of selective serotonin reuptake inhibitors (SSRIs); however, future work with greater numbers is required to
confirm this observation. Inclusion of two additional spectroscopic methods could improve the accuracy of diagnosis (0.78) by 7% over Raman alone (0.73). This demonstrates the potential for further exploration and development of a multispectroscopic system for disease diagnosis.

Full text links

65. **In vivo assessment of a delayed release formulation of larazotide acetate indicated for celiac disease using a porcine model**


Authors

Hiroko Enomoto ¹, James Yeatts ¹, Liliana Carbajal ¹, B Radha Krishnan ², Jay P Madan ², Sandeep Laumas ², Anthony T Blikslager ¹, Kristen M Messenger ¹

Affiliations

- ¹ Comparative Medicine Institute, North Carolina State University, Raleigh, NC, United States of America.
- ² Innovate Biopharmaceuticals Inc., Raleigh, NC, United States of America.

PMID: 33844694
PMCID: PMC8041193
DOI: 10.1371/journal.pone.0249179

Abstract

There is no FDA approved therapy for the treatment of celiac disease (CeD), aside from avoidance of dietary gluten. Larazotide acetate (LA) is a first in class oral peptide developed as a tight junction regulator, which is a lead candidate
for management of CeD. A delayed release formulation was tested in vitro and predicted release in the mid duodenum and jejunum, the target site of CeD. The aim of this study was to follow the concentration versus time profile of orally administered LA in the small intestine using a porcine model. A sensitive liquid chromatography/tandem mass spectrometry method was developed to quantify LA concentrations in porcine intestinal fluid samples. Oral dosing of LA (1 mg total) in overnight fasted pigs resulted in time dependent appearance of LA in the distal duodenum and proximal jejunum. Peak LA concentrations (0.32-1.76 μM) occurred at 1 hour in the duodenum and in proximal jejunum following oral dosing, with the continued presence of LA (0.02-0.47 μM) in the distal duodenum and in proximal jejunum (0.00-0.43 μM) from 2 to 4 hours following oral dosing. The data shows that LA is available in detectable concentrations at the site of CeD.

Conflict of interest statement

The authors have read the journal’s policy and have the following competing interests: AB and KM’s institution has received funding from Innovate Biopharmaceuticals, now 9meters Biopharm. KM has received speaking honoraria, travel compensation, or research support from Zoetis, Bayer, Ellevet, Piedmont Animal Health, Scullion Strategy, Jurox, Mallinckrodt, and RxActuator. AB has consulted for Innovate Biopharma and 9-meters Biopharma. He has also received honoraria from Kemin. RK, JM and SL are currently employees or consultants of or own stock in 9Meters Biopharm. This does not alter our adherence to PLOS ONE policies on sharing data and materials. There are no patents, products in development or marketed products associated with this research to declare.

- 44 references
- 6 figures

Full text links

Navigating celiac disease and the gluten-free diet in China

Authors

Qianhui Zhang, Randi L Wolf, Anne R Lee, Carlo Catassi, Patricia Zybert, Peter Hr Green, Benjamin Lebwohl

Affiliations

1 Program in Nutrition, Department of Health and Behavioral Studies, Teachers College, Columbia University, USA.
2 Celiac Disease Center, 21611Columbia University Irving Medical Center, USA.
3 Department of Pediatrics, 9294Polytechnic University of Marche, Italy.
4 Mailman School of Public Health, Columbia University, USA.

PMID: 33843325
DOI: 10.1177/0260106021990254

Abstract

Background: Little is known about celiac disease (CeD) diagnosis and management in China.

Aim: This pilot aimed to be the first study to describe, quantitatively and qualitatively, how individuals living in China navigate CeD and the gluten-free diet (GFD).

Methods: Participants were 13 adults and four parents of children with reported CeD, recruited from 11 mainland China cities via an online GFD support group. CeD-specific quality of life (CD-QOL and CD-PQOL) and diet adherence (CDAT) were assessed. In-depth interviews addressed experiences with CeD and the GFD.

Results: Six of 17 participants reported biopsy- or serology-confirmed CeD. The mean (SD) adult CDAT score was 15.2 (3.6), > 13 indicating inadequate GFD adherence. The mean adult CD-QOL score was 62.1 (24.1) out of 100, in the "medium" to "good" range. Results were similar in children. Major interview themes included: (1) a challenging journey to obtain diagnosis; (2)
social and structural barriers to maintaining the GFD; and (3) reliance on self in management of CeD.

**Conclusion:** Obtaining a diagnosis, maintaining a GFD, and living with CeD can be extremely challenging in mainland China. Results suggest an urgent need for CeD-specific education and Asian-adapted GFD guidance for both healthcare practitioners and patients.

**Keywords:** Celiac disease; China; gluten-free diet; interview; quality of life.

**Full text links**

67. **Diagnostic Value of Persistently Low Positive TGA-IgA Titers in Symptomatic Children With Suspected Celiac Disease**


**Authors**

Chiara Marja Trovato 1, Monica Montuori 1, Annalisa Morelli 1, Danilo Alunni Fegatelli 2, Annarita Vestri 2, Carla Giordano 3, Salvatore Cucchiara 1, Giacomo Caio 4, Salvatore Oliva 1

**Affiliations**

- 1 Pediatric Gastroenterology and Liver Unit, Maternal and Child Health Department.
- 2 Department of Statistical Science.
- 3 Department of Radiological, Oncological and Pathological Sciences, Sapienza University of Rome, Rome.
- 4 Department of Medical Sciences, University of Ferrara, Ferrara, Italy.

- PMID: 33843181
- DOI: 10.1097/MPG.0000000000003047
Abstract

Objectives: While the algorithm to diagnose celiac disease (CD) in children with elevated anti-transglutaminase IgA (TGA-IgA) titers (>10 times upper limit of normal, ULN) is well defined, the management of children with low TGA-IgA values represents a clinical challenge. We aimed to identify the diagnostic value of persistently low positive TGA-IgA titers in predicting CD in children.

Methods: We retrospectively analyzed children with symptoms or signs of CD, not eligible for a no-biopsy approach. We included children with at least 2 TGA-IgA measurements, endomysial antibody (EMA) assessment and esophagagastroduodenoscopy with biopsies. TGA-IgA values were provided as multiples of ULN. Patients were classified in groups according to median TGA-IgA values: A (TGA-IgA > 1 ≤ 5 × ULN; defined as "low-positive"), B (TGA-IgA > 5 < 10 × ULN; "moderate-positive"), and C (controls).

Results: Data of 281 children were analyzed. Of 162 children in group A, CD was diagnosed in 142 (87.7%), whereas normal duodenal mucosa was found in 20. In group B, all 62 children (100%) received a CD diagnosis. Group C included 57 controls. EMA were undetectable in 31 (15%) of mucosal atrophy cases. On the receiver-operating characteristic curve (area under the curve = 0.910), a mean value of 1.7 ULN showed a sensitivity of 81.4% and specificity of 81.8% to predict mucosal damage.

Conclusions: Repeated low or moderate TGA-IgA values (<5 ULN or <10 ULN) are good predictors of a CD diagnosis. Symptomatic children with persistently low positive TGA-IgA titers should undergo esophagagastroduodenoscopy regardless of their EMA status.

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Conflict of interest statement

The authors report no conflicts of interest.

- 34 references
Single-Center Review of Celiac Plexus/Retrocrural Splanchnic Nerve Block for Non-Cancer Related Pain


Authors

Harris Liou 1, Min J Kong 2, Sadeer J Alzubaidi 2, M-Grace Knutinen 2, Indravadan J Patel 2, J Scott Kriegshauser 3

Affiliations

1 Alix School of Medicine, Mayo Clinic, Scottsdale, AZ, 85259.
2 Department of Radiology, Mayo Clinic, 5779 E Mayo Blvd, Phoenix, AZ, 85054.
3 Department of Radiology, Mayo Clinic, 5779 E Mayo Blvd, Phoenix, AZ, 85054. Electronic address: skriegshauser@mayo.edu.

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DOI: 10.1016/j.acra.2021.03.005

Abstract

Rationale and objectives: Celiac plexus and retrocrural splanchnic nerve (CP/RSN) blocks are widely used for cancer-related abdominal pain, but there is limited literature on their efficacy for non-cancer related pain. Our aim was to determine the indications and effectiveness of CT-guided CP/RSN blocks performed on patients with abdominal pain from non-cancer related sources.

Materials and methods: CT-guided CP/RSN blocks for non-cancer related abdominal pain from 2011-2020 were retrospectively reviewed for patient demographics, procedure details, duration of pain relief, and complications.
Effective blocks were defined as patient-reported pain relief or decrease in opioid use lasting 2 or more days for temporary blocks and 14 or more days for permanent blocks.

**Results:** Of 72 CT-guided CP/RSN blocks for non-cancer related abdominal pain, 48 (67%) were effective for a mean of 51 days (median 14, range 2-700). Of the 18 permanent blocks, 9 (50%) were effective for a mean of 111 days (median 90, range 14-390). Of the 54 temporary blocks, 39 (72%) were effective for a mean of 37 days (median 9, range 2-700). Indications included postural orthostatic tachycardia syndrome/dysautonomia (77% effective, 20/26), pancreatitis (86% effective, 12/14), postsurgical pain (62% effective, 8/13), median arcuate ligament syndrome (70% effective, 7/10), chronic pain syndrome (20% effective, 1/5), gastroparesis (80% effective, 4/5), and renal cystic disease (33% effective, 1/3). For postural orthostatic tachycardia syndrome /dysautonomia, pancreatitis, post-surgical pain, and MALS, there were no statistically significant differences in effectiveness between celiac vs. splanchnic blocks in groups matched by indication and intended duration (temporary/permanent).

**Conclusions:** CT-guided CP/RSN blocks can effectively manage non-cancer related abdominal pain, though there is discrepancy in efficacy between temporary and permanent blocks.

**Keywords:** CT-guided; abdominal pain; benign pain; celiac plexus block; splanchnic nerve block.

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**Conflict of interest statement**

DECLARATION OF COMPETING INTEREST None

**Full text links**
Gluten-degrading bacteria: availability and applications


Authors

Viia Kõiv 1, Tanel Tenson 2

Affiliations

1 Institute of Technology, University of Tartu, Tartu, Estonia. viia.koiv@ut.ee.
2 Institute of Technology, University of Tartu, Tartu, Estonia.

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PMCID: PMC8053163
DOI: 10.1007/s00253-021-11263-5

Free PMC article

Abstract

Gluten is a mixture of storage proteins in wheat and occurs in smaller amounts in other cereal grains. It provides favorable structure to bakery products but unfortunately causes disease conditions with increasing prevalence. In the human gastrointestinal tract, gluten is cleaved into proline and gluten rich peptides that are not degraded further. These peptides trigger immune responses that might lead to celiac disease, wheat allergy, and non-celiac gluten sensitivity. The main treatment option is a gluten-free diet. Alternatively, using enzymes or microorganisms with gluten-degrading properties might alleviate the disease. These components can be used during food production or could be introduced into the digestive tract as food supplements. In addition, natural food from the environment is known to enrich the microbial communities in gut and natural environmental microbial communities have high potential to degrade gluten. It remains to be investigated if food and environment-induced changes in the gut microbiome could contribute to the triggering of gluten-related diseases. KEY POINTS: •
Wheat proteins, gluten, are incompletely digested in human digestive tract leading to gluten intolerance. • The only efficient treatment of gluten intolerance is life-long gluten-free diet. • Environmental bacteria acquired together with food could be source of gluten-degrading bacteria detoxifying undigested gluten peptides.

**Keywords:** Celiac disease; Environment; Food; Peptidases.

**Conflict of interest statement**

The authors declare no competing interests.

- **136 references**
- **2 figures**

**Full text links**

**70. Is mass screening for coeliac disease a wise use of resources? A health economic evaluation**


**Authors**

Fredrik Norström ¹, Anna Myléus ², Katrina Nordyke ³, Annelie Carlsson ⁴, Lotta Högberg ⁵, Olof Sandström ³ ⁶, Lars Stenhammar ⁵, Anneli Ivarsson ³, Lars Lindholm ³

**Affiliations**

- ¹ Department of Epidemiology and Global Health, Umeå University, 901 87, Umeå, Sweden. fredrik.norstrom@umu.se.
- ² Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden.
- ³ Department of Epidemiology and Global Health, Umeå University, 901 87, Umeå, Sweden.
Abstract

**Background:** Living with undiagnosed symptomatic coeliac disease is connected with deteriorated health, and persons with coeliac disease often wait a long time for their diagnosis. A mass screening would lower the delay, but its cost-effectiveness is still unclear. Our aim was to determine the cost-effectiveness of a coeliac disease mass screening at 12 years of age, taking a life course perspective on future benefits and drawbacks.

**Methods:** The cost-effectiveness was derived as cost per quality-adjusted life-year (QALY) using a Markov model. As a basis for our assumptions, we mainly used information from the Exploring the Iceberg of Celiacs in Sweden (ETICS) study, a school-based screening conducted in 2005/2006 and 2009/2010, where 13,279 12-year-old children participated and 240 were diagnosed with coeliac disease, and a study involving members of the Swedish Coeliac Association with 1031 adult participants.

**Results:** The cost for coeliac disease screening was 40,105 Euro per gained QALY. Sensitivity analyses support screening based on high compliance to a gluten-free diet, rapid progression from symptom-free coeliac disease to coeliac disease with symptoms, long delay from celiac disease with symptoms to diagnosis, and a low QALY score for undiagnosed coeliac disease cases.

**Conclusions:** A coeliac disease mass screening is cost-effective based on the commonly used threshold of 50,000 Euro per gained QALY. However, this is based on many assumptions, especially regarding the natural history of coeliac
disease and the effects on long-term health for individuals with coeliac disease still eating gluten.

**Keywords:** Adolescent; Coeliac disease; Compliance; Cost-effectiveness; Long delay; QALY; Screening.

**Conflict of interest statement**

The authors declare that they have no competing interests.

- 52 references
- 1 figure

**Full text links**

71. **Utility of gastric and duodenal biopsy sampling in adult eosinophilic esophagitis patients to rule out other gastrointestinal disorders**


**Authors**


**Affiliations**

- ¹ Department of Gastroenterology & Hepatology, Amsterdam University Medical Center, Amsterdam, The Netherlands.
- ² Department of Gastroenterology and Hepatology, University Medical Center Utrecht and St. Antonius Hospital Nieuwegein, Utrecht, The Netherlands.
Abstract

**Rationale:** According to consensus guidelines, if eosinophilic esophagitis (EoE) is suspected, not only esophageal but also gastric and duodenal biopsy specimens should be sampled in order to exclude other generalized or eosinophilic gastrointestinal (GI) disorders, such as eosinophilic gastroenteritis or celiac disease. However, the diagnostic yield for this remains unclear.

**Aim:** To assess the diagnostic yield of biopsy sampling from the stomach and duodenum in adult EoE patients to rule out generalized or eosinophilic GI disorders.

**Methods:** A retrospective chart-review was conducted in untreated adult EoE patients that underwent upper endoscopy with biopsies sampled from the esophagus, stomach and duodenum. Standardized (electronic) case-report forms were used to extract clinical, endoscopic and histologic data.

**Results:** In total, 93 adults (71% males, age 36.4 (interquartile range 28.4 - 49.1) years) with untreated EoE (≥15 eosinophils/high-power-field) were included. Symptoms of dysphagia and food impaction were reported in 93% and 58%, respectively of the patients. Typical endoscopic EoE-features were present in 77 (85%) patients. The yield of routinely sampled gastric and duodenal biopsy specimens in our cohort was 3.6% (95% confidence interval: 2.6-4.8%) (n/N = 1/93) for a relevant other generalized or eosinophilic GI diagnosis and 30% for other histological diagnosis such as non-specific or *H. Pylori* gastritis. In total, 62 (67%) patients presented with other GI symptoms and/or endoscopic abnormalities of the stomach and/or duodenum - which both may be suggestive for other relevant GI conditions. The diagnostic yield for a relevant generalized or eosinophilic GI disorder in this subgroup was, 4.8% (95%CI 3.4 - 6.7%) (n/N = 1/62).

**Conclusion:** Gastric and duodenal biopsy specimens seem to have limited diagnostic value for the exclusion of generalized or eosinophilic GI disorders in adults with EoE.

**KEY POINTS**

- Evidence is lacking on the diagnostic value of...
additional biopsies sampled from the stomach and duodenum to rule out other relevant generalized or eosinophilic gastrointestinal (GI) disorders. The yield of gastric and duodenal biopsies routinely sampled in our cohort was 3.6% for a relevant other generalized or eosinophilic GI diagnosis and 30% for other histological diagnosis such as non-specific or H. Pylori gastritis. The diagnostic yield for a relevant generalized or eosinophilic GI disorder in the subgroup of patients (67%) presenting with other GI symptoms and/or endoscopic abnormalities of the stomach and/or duodenum - which both may be suggestive for other relevant GI conditions was, 4.8%. Gastric and duodenal biopsy specimens seem to have limited diagnostic value for the exclusion of generalized or eosinophilic GI disorders in adults with EoE.

**Keywords:** Eosinophilic esophagitis; biopsy; diagnostic value; esophageal eosinophilia and allergy.

**Full text links**

72. [Non-responsive celiac disease in children on a gluten free diet](https://wjo.wjgnet.com/wjo/wjo27p1311.htm)


**Authors**

Gopal Veeraraghavan ¹, Amelie Therrien ², Maya Degroote ², Allison McKeown ², Paul D Mitchell ³, Jocelyn A Silvester ², Daniel A Leffler ⁴, Alan M Leichtner ², Ciaran P Kelly ⁴, Dascha C Weir ⁵

**Affiliations**

- ¹ Division of Gastro-enterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA 02115, United States.
- ² Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA 02115, United States.
- ³ Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, MA 02115, United States.
Abstract

**Background:** Non-responsive celiac disease (NRCD) is defined as the persistence of symptoms in individuals with celiac disease (CeD) despite being on a gluten-free diet (GFD). There is scant literature about NRCD in the pediatric population.

**Aim:** To determine the incidence, clinical characteristics and underlying causes of NRCD in children.

**Methods:** Retrospective cohort study performed at Boston Children's Hospital (BCH). Children < 18 years diagnosed with CeD by positive serology and duodenal biopsies compatible with Marsh III histology between 2008 and 2012 were identified in the BCH's Celiac Disease Program database. Medical records were longitudinally reviewed from the time of diagnosis through September 2015. NRCD was defined as persistent symptoms at 6 mo after the initiation of a GFD and causes of NRCD as well as symptom evolution were detailed. The children without symptoms at 6 mo (responders) were compared with the NRCD group. Additionally, presenting signs and symptoms at the time of diagnosis of CeD among the responders and NRCD patients were collected and compared to identify any potential predictors for NRCD at 6 mo of GFD therapy.

**Results:** Six hundred and sixteen children were included. Ninety-one (15%) met criteria for NRCD. Most were female (77%). Abdominal pain (odds ratio (OR) 1.8 95% confidence interval (CI) 1.1-2.9), constipation (OR 3.1 95%CI 1.9-4.9) and absence of abdominal distension (OR for abdominal distension 0.4 95%CI 0.1-0.98) at diagnosis were associated with NRCD. NRCD was attributed
to a wide variety of diagnoses with gluten exposure (30%) and constipation (20%) being the most common causes. Other causes for NRCD included lactose intolerance (9%), gastroesophageal reflux (8%), functional abdominal pain (7%), irritable bowel syndrome (3%), depression/anxiety (3%), eosinophilic esophagitis (2%), food allergy (1%), eating disorder (1%), gastric ulcer with *Helicobacter pylori* (1%), lymphocytic colitis (1%), aerophagia (1%) and undetermined (13%). 64% of children with NRCD improved on follow-up.

**Conclusion:** NRCD after ≥ 6 mo GFD is frequent among children, especially females, and is associated with initial presenting symptoms of constipation and/or abdominal pain. Gluten exposure is the most frequent cause.

**Keywords:** Abdominal pain; Celiac disease; Children; Constipation; Gluten-free diet; Non-responsive celiac disease.

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**Conflict of interest statement**

Conflict-of-interest statement: Leffler DA is employed by Takeda Pharmaceuticals International Co. Kelly CP has acted as a scientific advisor to companies attempting to develop new diagnostic and management approaches for Celiac disease including Cour Pharma, Glutenostics, Innovate, Immunogenx and Takeda. He also acts as Principal Investigator on a research grant on Celiac disease supported by Aptalis. Silvester JA has served on an advisory board for Takeda Pharmaceuticals and has received research funding from Biomedal S.L., Cour Pharma and Glutenostics.

- 24 references
- 2 figures

**Full text links**

73. [Associations of breastfeeding with childhood autoimmunity, allergies, and overweight: The Environmental...](#)
Determinants of Diabetes in the Young (TEDDY) study


Authors

Sandra Hummel 1, Andreas Weiß 1, Ezio Bonifacio 2, Daniel Agardh 3, Beena Akolkar 4, Carin A Aronsson 3, William A Hagopian 5, Sibylle Koletzko 6 7, Jeffrey P Krischer 8, Åke Lernmark 3, Kristian Lynch 8, Jill M Norris 9, Marian J Rewers 10, Jin-Xiong She 11, Jorma Toppari 12 13, Ulla Uusitalo 8, Kendra Vehik 8, Suvi M Virtanen 14 15 16 17, Andreas Beyerlein 1, Anette-G Ziegler 1, TEDDY Study Group

Affiliations

1 Institute of Diabetes Research, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich-Neuherberg, Germany; and Forschergruppe Diabetes, Technical University Munich, at Klinikum rechts der Isar, Munich, and Forschergruppe Diabetes eV, Neuherberg, Germany.

2 DFG Center for Regenerative Therapies Dresden, Faculty of Medicine, TU Dresden, Dresden, Germany.

3 Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden.

4 National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, USA.

5 Pacific Northwest Diabetes Research Institute, Seattle, WA, USA.

6 Department of Pediatrics, Dr. von Hauner Children's Hospital, University Hospital, LMU Munich, Munich, Germany.

7 Department of Pediatrics, Gastroenterology and Nutrition, School of Medicine, Collegium Medicum University of Warmia and Mazury, Olsztyn, Poland.

8 Health Informatics Institute, Morsani College of Medicine, University of South Florida, Tampa, FL, USA.

9 Department of Epidemiology, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.
Abstract

Background: Breastfeeding has beneficial effects on numerous health outcomes.

Objectives: We investigated whether breastfeeding duration is associated with the development of early childhood autoimmunity, allergies, or obesity in a multinational prospective birth cohort.

Methods: Infants with genetic susceptibility for type 1 diabetes (n = 8676) were followed for the development of autoantibodies to islet autoantigens or transglutaminase, allergies, and for anthropometric measurements to a median age of 8.3 y (IQR: 2.8-10.2 y). Information on breastfeeding was collected at 3 mo of age and prospectively thereafter. A propensity score for longer breastfeeding was calculated from the variables that were likely to influence any or exclusive breastfeeding. The risks of developing autoimmunity or allergy were assessed using Cox proportional hazards models, and the risk of obesity at 5.5 y of age was assessed using logistic regression with adjustment by the propensity score.
**Results:** Breastfeeding duration was not associated with a lower risk of either islet or transglutaminase autoimmunity (any breastfeeding >6 mo, adjusted HR: 1.07; 95% CI: 0.96, 1.19; exclusive breastfeeding >3 mo, adjusted HR: 1.03; 95% CI: 0.92, 1.15). Exclusive breastfeeding >3 mo was associated with a decreased risk of seasonal allergic rhinitis (adjusted HR: 0.70; 95% CI: 0.53, 0.92; P < 0.01). Any breastfeeding >6 mo and exclusive breastfeeding >3 mo were associated with decreased risk of obesity (adjusted OR: 0.62; 95% CI: 0.47, 0.81; P < 0.001; and adjusted OR: 0.68; 95% CI: 0.47, 0.95; P < 0.05, respectively).

**Conclusions:** Longer breastfeeding was not associated with a lower risk of childhood (islet or transglutaminase) autoimmunity in genetically at-risk children but was associated with decreased risk of seasonal allergic rhinitis and obesity at 5.5 y of age.

**Keywords:** allergic disease; breastfeeding; celiac disease; islet autoimmunity; obesity.

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**Full text links**

74. [Automated interpretation of biopsy images for the detection of celiac disease using a machine learning approach](https://doi.org/10.1016/j.cmpb.2021.106010)


**Authors**

Joel En Wei Koh, Simona De Michele, Vidya K Sudarshan, V Jahmunah, Edward J Ciaccio, Chui Ping Ooi, Raj Gururajan, Rashmi Gururajan, Shu Lih Oh, Suzanne K Lewis, Peter H Green, Govind Bhagat, U Rajendra Acharya
Affiliations

2. Department of Pathology and Cell Biology, Columbia University Irving Medical Center, USA.
3. School of Science and Technology, Singapore University of Social Sciences, Singapore.
4. Department of Medicine, Celiac Disease Center, Columbia University Irving Medical Center, USA.
5. School of Business, University of Southern Queensland Springfield, Australia.
6. Royal Brisbane and Women's Hospital, Queensland, Australia.
7. Department of Medicine, Celiac Disease Center, Columbia University Irving Medical Center, USA; Department of Pathology and Cell Biology, Columbia University Irving Medical Center, USA.
8. Department of Electronics and Computer Engineering, Ngee Ann Polytechnic, Singapore; School of Science and Technology, Singapore University of Social Sciences, Singapore; School of Business, University of Southern Queensland Springfield, Australia; Department of Bioinformatics and Medical Engineering, Asia University, Taiwan; International Research Organization for Advanced Science and Technology (IROAST) Kumamoto University, Kumamoto, Japan.

Electronic address: aru@np.edu.sg.

PMID: 33831693
DOI: 10.1016/j.cmpb.2021.106010

Abstract

**Background and objectives:** Celiac disease is an autoimmune disease occurring in about 1 in 100 people worldwide. Early diagnosis and efficient treatment are crucial in mitigating the complications that are associated with untreated celiac disease, such as intestinal lymphoma and malignancy, and the subsequent high morbidity. The current diagnostic methods using small intestinal biopsy histopathology, endoscopy, and video capsule endoscopy (VCE) involve manual interpretation of photomicrographs or images, which can be time-consuming and difficult, with inter-observer variability. In this paper, a machine learning technique was developed for the automation of
biopsy image analysis to detect and classify villous atrophy based on modified Marsh scores. This is one of the first studies to employ conventional machine learning to automate the use of biopsy images for celiac disease detection and classification.

**Methods:** The Steerable Pyramid Transform (SPT) method was used to obtain sub bands from which various types of entropy and nonlinear features were computed. All extracted features were automatically classified into two-class and multi-class, using six classifiers.

**Results:** An accuracy of 88.89%, was achieved for the classification of two-class villous abnormalities based on analysis of Hematoxylin and Eosin (H&E) stained biopsy images. Similarly, an accuracy of 82.92% was achieved for the two-class classification of red-green-blue (RGB) biopsy images. Also, an accuracy of 72% was achieved in the classification of multi-class biopsy images.

**Conclusion:** The results obtained are promising, and demonstrate the possibility of automating biopsy image interpretation using machine learning. This can assist pathologists in accelerating the diagnostic process without bias, resulting in greater accuracy, and ultimately, earlier access to treatment.

**Keywords:** Biopsy images; Celiac disease; Classifiers; Image analysis; Machine learning; Nonlinear features; Steerable pyramid transform.

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**Conflict of interest statement**

Declaration of Competing Interest None.

**Full text links**

[ELSEVIER FULL-TEXT ARTICLE](#)

75. [Perceived impact of information signals on opinions about gluten-free diets](#)
Understanding how people assimilate different types of information for food choices is integral to improving knowledge about diet and human health. This study evaluates the impact that 10 information signals have on the perceived healthiness of gluten. Signals include non-social signals such as personal eating experiences, scientific studies, and advice from doctors, but also includes social signals such as recommendations from attractive people, social media, the layout of a grocery store, and celebrities. An online survey of over 1,000 Americans is administered using indirect questioning where subjects are presented with a hypothetical other person and asked how the various signals would impact that person's opinion of gluten-free diets. Results show that advice from an attractive person is thought to have a slightly larger impact than reading about a new study regarding gluten, and seeing a grocery store develop a new gluten-free section has a larger impact than learning a celebrity consumes a gluten-free diet.

Conflict of interest statement

The authors have declared that no competing interests exist.
76. [New tools in the diagnosis of food hypersensitivity reactions: beyond IgE and prick testing]

[Article in French]

Authors

Sophie Vandenberghe-Durr ¹, Jean-Christoph Caubet ², David Spoerl ¹

Affiliations

- ¹ Service d'immunologie et allergologie, Département de médecine, HUG, 1211 Genève 14.
- ² Unité d'allergologie pédiatrique, HUG, 1211 Genève 14.

PMID: 33830697

Abstract

in English, French

Food hypersensitivity represents a group of adverse immunological reactions linked to food ingestions such as anaphylaxis or eosinophilic esophagitis. Identification of the responsible food is currently based on a detailed history and complementary exams, mostly prick testing and assessment of serum specific IgE, either by ImmunoCAP or multiplex assay. Other skin and laboratory tools such as functional in vitro or patch testing are currently not validated although some show promising results in the field of food allergy. This article presents the different diagnostic procedures that are commonly and less commonly used in the workup of food allergies and their potential for future use in the workup of food-induced hypersensitivity reactions. Non-
immunological reactions, rare entities (Heiner syndrome) and celiac disease will not be addressed in this review.

Les allergies alimentaires représentent un groupe hétérogène de réactions immunologiques secondaires à l’ingestion d’aliments. L’identification des aliments incriminés se base initialement sur l’anamnèse et des examens complémentaires, principalement les prick tests et les recherches d’immunoglobulines E spécifiques par immunoCAP ou tests multiplex. Avant d’envisager des tests de provocation, d’autres tests sont disponibles, notamment les tests fonctionnels in vitro ou les patch tests, qui ne sont pas validés pour cette indication, mais dont certains montrent un potentiel d’utilité à venir. Cet article fait une synthèse des différents outils à disposition actuels et à venir dans le diagnostic des allergies alimentaires. Les intolérances alimentaires non immunomédies, la maladie cœliaque et les raretés telles que le syndrome de Heiner ne seront pas abordées ici.

Conflict of interest statement

Les auteurs n’ont déclaré aucun conflit d’intérêts en relation avec cet article.

77. Cost, Nutritional Content and Number of Gluten-Free Staple Foods Available in Winnipeg, Manitoba, Canada


Authors

Olutola Jegede 1, Avery Enns 1, Marianna Kantounia 1, Taryn Preun 1, Kathy Vagianos 1 2
Miyoungh Suh 1 3, Heather Blewett 4 5 6

Affiliations

1 Department of Food and Human Nutritional Sciences, University of Manitoba, Winnipeg, MB, Canada.
2 Department of Nutrition and Food Services, Health Sciences Centre, Winnipeg, MB, Canada.
Abstract

Data has indicated that gluten-free (GF) foods are more expensive and have lower nutritional value than their gluten-containing (GC) counterparts. The aim of the present study was to compare the cost and nutrient content between GF and GC staple foods and determine whether the number and price of GF staple foods differed based on type of store or location within Winnipeg, Canada. Twelve grocery stores (2 chain stores/quadrant; 1 local store/quadrant) in the four quadrants (northwest, northeast, southwest, southeast) of Winnipeg were visited to identify GF staple products (bread, flour, cereal, pasta) along with a GC comparator. A total of 819 GF products along with GC comparators were identified. The median cost of GF products ($1.50/100 g) was 131 % greater than that of GC ($0.65/100 g) (p < 0.0001). The greatest difference in cost was between GF and GC flour, with the least difference occurring between GF and GC cereal. GF products were 58, 36 and 100 % lower in iron, protein and saturated fat (p < 0.0001) than their GC comparators, respectively. The number of GF staple products was 370 % higher (p < 0.007) at chain stores than at local stores, whereas store location did not significantly affect the number of GF products available. The greatest difference in number of different GF foods based on store type was for cereals, with the least being for flours. These results confirm that GF staple foods are more expensive and have lower nutritional value (mainly due to lower iron and protein content) compared to GC foods.

Keywords: Celiac disease; Cost; Gluten-containing; Gluten-free; Number; Nutrient content.
Endovascular Revascularization with Stent Implantation in Patients with Acute Mesenteric Ischemia due to Acute Arterial Thrombosis: Clinical Outcome and Predictive Factors


Authors

Federico Pedersoli 1, Kai Schönau 2, Maximilian Schulze-Hagen 2, Sebastian Keil 2, Peter Isfort 2, Alexander Gombert 3, Patrick Hamid Alizai 4, Christiane K Kuhl 2, Philipp Bruners 2, Markus Zimmermann 2

Affiliations

1 Department of Diagnostic and Interventional Radiology, University Hospital RWTH Aachen, Pauwelsstraße 30, 52074, Aachen, Germany. fpedersoli@ukaachen.de.
2 Department of Diagnostic and Interventional Radiology, University Hospital RWTH Aachen, Pauwelsstraße 30, 52074, Aachen, Germany.
3 Department of Vascular Surgery, University Hospital RWTH Aachen, Pauwelsstraße 30, 52074, Aachen, Germany.
4 Department of General, Visceral and Transplant Surgery, University Hospital RWTH Aachen, Pauwelsstraße 30, 52074, Aachen, Germany.

PMID: 33825061
DOI: 10.1007/s00270-021-02824-2
Abstract

**Purpose:** To determine 30-day-mortality rates and identify predictors for survival in patients undergoing endovascular revascularization for acute mesenteric ischemia (AMI) due to occlusion of the celiac (CA) or superior mesenteric artery (SMA) from arterial thrombosis in the setting of atherosclerosis at the vessel origin.

**Materials and methods:** A retrospective analysis on patients who underwent acute endovascular revascularization to treat AMI caused by thrombotic occlusion of the CA and/or SMA between January 2011 and December 2019 was conducted. 30-day-mortality rates were calculated. Univariate binomial logistic regression analyses (p < 0.05) were performed to assess whether the following factors were associated with 30-day mortality: sex, age, history of smoking, history of abdominal angina, signs of bowel necrosis on pre-interventional CT, one- vs. two-vessel disease, patency of the inferior mesenteric artery, outpatient or inpatient occurrence of ischemia, onset of AMI during ITU stay, elevated pre-interventional serum lactate levels, total leukocyte count, platelet/lymphocyte ratio and neutrophil/lymphocyte ratio.

**Results:** 40 patients were included in this analysis. 30-day-mortality rate was 25/40 (62.5%). Median overall survival of patients who survived the first 30 days was 36 ± 18 months. None of the analyzed factors was statistically significantly associated with 30-day mortality.

**Conclusion:** Although mortality of patients with AMI due to acute arterial thrombosis remains high, almost 40% of patient who underwent emergent endovascular revascularization survived longer than one month. Since no predictors for the outcome in these patients were identified, all patients with AMI should be offered an immediate revascularization effort.

**Keywords:** Celiac artery; Endovascular procedures; Mesenteric ischemia; Stents; Superior mesenteric artery.

- [26 references](#)

**Full text links**

[SpringerLink](https://link.springer.com/article/10.1007/s00270-020-09613-7)
Collagenous gastritis: Epidemiology and clinical associations


Authors

Robert M Genta ¹, Kevin O Turner ², Christopher J Morgan ², Amnon Sonnenberg ³

Affiliations

¹ Inform Diagnostics, Irving, TX, United States; Baylor College of Medicine, Houston, TX, United States. Electronic address: rmgenta@gastropath.com.
² Inform Diagnostics, Irving, TX, United States.
³ Division of Gastroenterology, Portland VA Medical Center and Oregon Health and Science University, United States.

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DOI: 10.1016/j.dld.2021.03.010

Abstract

Background: the rare occurrence of collagenous gastritis (CG) makes its epidemiology difficult to investigate. We designed a study to determine the demographic and clinical characteristics as well as the associations of CG with other upper gastrointestinal diseases in a large national clinicopathological database.

Methods: from the IDEA database we extracted all patients with histopathologically documented CG and, in a case-control study, we compared 168 subjects with and 1,286,165 subjects without CG using odds ratios (OR) with their 95% confidence intervals (CI).

Results: the prevalence of CG was 13 per 100,000 EGDs. CG was significantly more common among female than male patients (OR: 1.69, 95% CI: 1.20-2.39) and was characterized by a bi-modal age distribution (first peak in patients aged 10-19, second peak primarily in females aged >60 years). CG patients
presented with diarrhea (18%), anemia (12%), weight loss (11%), and vomiting (10%). CG was significantly associated with other lymphocytic disorders of the upper gastrointestinal tract, including celiac sprue (2.12, 1.55-2.88), duodenal intraepithelial lymphocytosis (3.71, 2.30-5.98), and lymphocytic gastritis (23.2, 10.9-49.5). CG persisted in 69% of patients who underwent multiple consecutive endoscopies.

**Conclusions:** the epidemiologic features of collagenous gastritis reflect on different etiologies contributing to its occurrence in children and adults.

**Keywords:** Autoimmune gastritis; Celiac disease; Collagenous gastritis; Duodenal intraepithelial lymphocytosis; Environmental risk factors; Epidemiology; Helicobacter pylori; Microscopic colitis.

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**Conflict of interest statement**

Declaration of Competing Interest RM Genta, KO Turner, and CJ Morgan are employed by Inform Diagnostics, Irving, TX. A Sonnenberg has no conflict of interest to declare. No funding was obtained for this study. Author Contributions: Study conception and design: A Sonnenberg, RM Genta; data analysis: A Sonnenberg, RM Genta, KO Turner; review of biopsy specimens and photographs: CJ Morgan; writing of manuscript: RM Genta, A Sonnenberg.

**Full text links**

[Identification of gluten-like proteins in selected pod bearing leguminous tree seeds](https://doi.org/10.1371/journal.pone.0249427)


**Authors**
Mostafa Taghvaei 1, Brennan Smith 1 2, Gamze Yazar 1, Scott Bean 3, Michael Tilley 3, Brian Ioerger 3

Affiliations

• 1 Animal, Veterinary and Food Sciences, University of Idaho, Moscow, Idaho, United States of America.
• 2 United States Department of Agriculture, Agricultural Research Service, Southern Regional Research Center, New Orleans, Louisiana, United States of America.
• 3 United States Department of Agriculture, Agricultural Research Service, Center for Grain and Animal Health Research, Manhattan, Kansas, United States of America.

• PMID: 33819280
• PMCID: PMC8021184
• DOI: 10.1371/journal.pone.0249427

Free PMC article

Abstract

The protein composition, molecular weight distribution, and rheological properties of honey locust, mesquite, Kentucky coffee tree, and carob seed germs were compared against wheat gluten. Polymeric and Osborne fractionation protocols were used to assess biochemical properties. Dynamic oscillatory shear tests were performed to evaluate protein functionality. All samples had similar ratios of protein fractions as well as high molecular weight disulfide linked proteins except for the Kentucky coffee tree germ proteins, which were found to have lower molecular weight proteins with little disulfide polymerization. Samples were rich in acidic and polar amino acids (glutamic acid and arginine,). Rheological analyses showed that vital wheat gluten had the most stable network, while Kentucky coffee seed proteins had the weakest. High molecular weight disulfide linked glutenous proteins are a common, but not universal feature of pod bearing leguminous trees.

Conflict of interest statement

The authors have declared that no competing interests exist.
Retrograde Catheterization of the Superior Mesenteric Artery and Celiac Axis as a Bailout Technique in a Complex FEVAR


Authors

Fernando Picazo Pineda ¹, Tishanthan Pathmarajah ¹, Kishore Sieunarine ¹ ²

Affiliations

1 Department of Vascular and Endovascular Surgery, Royal Perth Hospital, Perth, Western Australia, Australia.
2 Curtin University Medical School, Curtin University, Perth, Western Australia, Australia.

PMID: 33813979
DOI: 10.1177/15385744211000916

Abstract

Introduction: A retrograde approach of the celiac trunk (CT) and superior mesenteric artery (SMA) to catheterize the visceral vessels during a fenestrated endovascular aortic reparation (FEVAR) is a feasible option when standard access techniques have failed.

Report: In this report we describe a patient with a previous endoluminal repair of an infrarenal aortic aneurysm, complicated by a persistent type 1a endoleak despite treatment with endoanchor fixation. A decision was made to proceed with a proximal 4 vessel FEVAR to treat the type 1a endoleak. Due to angulation of the mesenteric vessels, and a rotation of the fenestrated stent
graft during deployment, the CT and SMA were unable to be catheterized. A decision was made to perform a median laparotomy for retrograde access of the aforementioned vessels, allowing successful catheterization and stenting. The patient was discharged 30 days following the procedure, without any major post-operative complications. Follow up at 6 weeks with a contrasted enhanced computerized tomography scan showed a stable repair with no residual type 1a endoleak.

**Discussion:** Catheterization of the target vessels during a FEVAR can be difficult, especially in patients with challenging anatomy. Prolonged surgical time in an attempt to catheterize the vessels can result in increased morbidity for the patient, and ultimately may result in the procedure being abandoned or conversion to an open repair of the aneurysm. Retrograde access of the target vessels as a bailout measure during fenestrated stent graft repair due to failure of an antegrade approach has rarely been reported in the literature. Only a few cases are described in the available literature, however, none of them describe retrograde approach of both the CT and SMA as described in this case. A median laparotomy for retrograde access is a feasible alternative in these situations, and should be considered if the patient is suitable.

**Keywords:** aortic aneurysm; fenestrated endovascular aneurysm repair; retrograde target vessel access.

**Full text links**

82. [Dietary gluten avoidance in Canada: a cross-sectional study using survey data](https://journals.sagepub.com/doi/10.9778/cmajo.20200082)


**Authors**

Adriana Mudryj, Anne Waugh, Joyce Slater, Donald R Duerksen, Charles N Bernstein, Natalie D Riediger
Affiliations

1 Department of Food and Human Nutritional Sciences (Mudryj, Waugh, Slater, Riediger), Faculty of Agricultural and Food Sciences, University of Manitoba; Department of Internal Medicine (Duerksen, Bernstein), Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba; Department of Community Health Sciences (Slater, Riediger), Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Man.

2 Department of Food and Human Nutritional Sciences (Mudryj, Waugh, Slater, Riediger), Faculty of Agricultural and Food Sciences, University of Manitoba; Department of Internal Medicine (Duerksen, Bernstein), Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba; Department of Community Health Sciences (Slater, Riediger), Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Man. Natalie.riediger@umanitoba.ca.

- PMID: 33795221
- PMCID: PMC8034255
- DOI: 10.9778/cmajo.20200082

Free PMC article

Abstract

Background: A gluten-free diet (GFD) is required for the management of some conditions, whereas some Canadians may follow a GFD for discretionary reasons. We sought to estimate the prevalence of Canadians who adhere to a GFD, identify factors associated with adherence to a GFD, and describe and compare the location of food preparation and consumption for those who follow a GFD, those who report no dietary avoidances and those reporting other dietary avoidances.

Methods: We used cross-sectional data from the 2015 Canadian Community Health Survey - Nutrition (n = 20,487). Demographic variables included sex, age group, ethnicity, highest level of household education and income adequacy. The relations between respondent characteristics and report of a GFD were estimated using logistic regression. Respondents were further
categorized as avoiding dietary gluten, other dietary avoidances and no dietary avoidances.

**Results:** An estimated 1.9% of Canadians follow a GFD. Women had 2 times higher odds (odds ratio [OR] 2.08, 95% confidence interval [CI] 1.32 to 3.27) of reporting a GFD than men. After adjustment for income adequacy, household education, sex, age group and ethnicity, residents of Ontario and Quebec had about half the odds (OR 0.52, 95% CI 0.31 to 0.87, and OR 0.55, 95% CI 0.32 to 0.94, respectively) of reporting a GFD compared with residents of Atlantic Canada. Canadians who followed a GFD consumed significantly fewer calories from foods prepared at restaurants than both Canadians who reported no dietary avoidances and those who reported dietary avoidances other than gluten. Canadians following a GFD reported that 2.0% (95% CI 1.1% to 2.9%) of their daily kilocalories were from foods prepared at restaurants, compared with 6.7% (95% CI 5.4% to 7.9%) for Canadians reporting 1 or more dietary avoidances other than gluten, and 6.4% (95% CI 6.0% to 6.9%) for those reporting no avoidances.

**Interpretation:** The estimated 1.9% prevalence of dietary gluten avoidance likely includes individuals with celiac disease, wheat allergies and nonceliac gluten sensitivity, as well as individuals excluding gluten in the management of irritable bowel syndrome or for reasons related to dietary trends. Canadians eating GFDs consume fewer daily calories from restaurant-prepared foods than other Canadians, which may have social implications.

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**Conflict of interest statement**

Competing interests: None declared.

- 41 references

**Full text links**

[Free full text on cmajopen.ca] [PMC Full text]
Persisting Villous Atrophy and Adherence in Celiac Disease: What Does the Patient Want? What Should a Clinician Advise?


Authors

Anupam Rej 1, Luca Elli 2, David Surendran Sanders 1 3

Affiliations

1 Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield, England.
2 Gastroenterology and Endoscopy Unit, Department of Pathophysiology and Transplantation, Center for Prevention and Diagnosis of Celiac Disease, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy.
3 Academic Unit of Gastroenterology, Department of Infection, Immunity, and Cardiovascular Disease, University of Sheffield, Sheffield, United Kingdom.

PMID: 33767095
DOI: 10.14309/ajg.0000000000001244

Abstract

Adherence to a gluten-free diet in celiac disease remains challenging. Clinicians may view mucosal healing as crucial. From the patient's perspective, avoidance of an invasive upper endoscopy may be desirable. A fundamental misconception is that noninvasive tools including symptoms, serology, dietary adherence questionnaires, and novel gluten immunogenic peptides may detect ongoing villous atrophy rather than assess adherence. Duodenal biopsies are the only reliable method for assessment of mucosal healing—however, we as clinicians should provide patients with the uncertainties of
this approach allowing them to make an informed decision on an individual basis.

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- 30 references

Full text links

84. **Gluten-free green banana flour muffins: chemical, physical, antioxidant, digestibility and sensory analysis**


Authors

Marjana Radünz ¹, Taiane Mota Camargo ¹, Camila Francine Paes Nunes ¹, Elisa Dos Santos Pereira ¹, Jardel Araújo Ribeiro ¹, Helen Cristina Dos Santos Hackbart ¹, Amanda Fabres Oliveira Radünz ², André Luiz Radünz ³, Márcia Arocha Gularte ⁴, Fabrizio Da Fonseca Barbosa ⁴

Affiliations

- ¹ Posgraduate Program in Food Science and Technology, Federal University of Pelotas City, Pelotas City, Rio Grande do Sul State 96050-500 Brazil.
- ² Posgraduate Program in Health Sciences, Community University of the Chapecó Region, Chapecó City, Santa Catarina State 89809-900 Brazil.
- ³ Departamen of Agronomia, Federal University of Fronteira Sul, Chapecó City, Santa Catarina State 89815-899 Brazil.
- ⁴ Center for Chemical, Pharmaceutical and Food Sciences, Federal University of Pelotas, Pelotas City, Rio Grande do Sul State 96050-500 Brazil.

- PMID: [33746257](https://doi.org/10.1007/s13197-020-04638-5)
Abstract

Considering the low availability of gluten-free products that are offered an affordable price and good sensory characteristics, the main objective of the study was developed a gluten-free muffin based on green banana flour and evaluate their physical-chemical and sensorial aspects. The quality of the muffin was analyzed through such moisture content, ashes, proteins, lipids, fiber, carbohydrates, total caloric content, yield mass, weight loss in the supply, antioxidant activity, protein digestibility, and hedonic scale. The results showed that the gluten-free muffin had a moisture content of 26.7%, ash of 2.39%, lipids of 15.4%, proteins of 10.3%, fibers of 1.2%, carbohydrates of 44.0%, the total caloric value of 261.2 kcal, high protein digestibility and moderate antioxidant activity. The acceptability index was 84.5%. It has been concluded that gluten-free muffin with green banana flour is a viable alternative for the reason that they have higher protein content than other alternative flours.

Keywords: Celiac disease; Eating habits; Functional foods; Nutritional value.

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85. **Indications, Contraindications, and Considerations for Video Capsule Endoscopy**


Authors

Jacquelyn G Bolwell ¹, Daniel Wild ²

Affiliations

¹ Duke University Medical Center, 1151 Duke South, Yellow Zone, Box 3534, Durham, NC 27710, USA.
Video capsule endoscopy is indicated in a broad range of clinical settings, most commonly in evaluating suspected small bowel bleeding. It is also useful in diagnosing Crohn's disease and monitoring patients with known Crohn's. Video capsule endoscopy has a role in evaluating patients with refractory celiac disease symptoms and in surveying patients with polyposis syndromes. The only absolute contraindication to video capsule endoscopy is luminal gastrointestinal tract obstruction. Despite manufacturer statement, video capsule endoscopy can be used safely in patients with implantable cardiac devices including pacemakers, defibrillators, and ventricular assist devices.

Keywords: Contraindications; Indications; Video capsule endoscopy.
Disorders of the nervous system can produce a variety of gastrointestinal (GI) dysfunctions. Among these, lesions in various brain structures can cause appetite loss (hypothalamus), decreased peristalsis (presumably the basal ganglia, pontine defecation center/Barrington's nucleus), decreased abdominal strain (presumably parabrachial nucleus/Kolliker-Fuse nucleus) and hiccups and vomiting (area postrema/dorsal vagal complex). In addition, decreased peristalsis with/without loss of bowel sensation can be caused by lesions of the spinal long tracts and the intermediolateral nucleus or of the peripheral nerves and myenteric plexus. Recently, neural diseases of inflammatory etiology, particularly those affecting the PNS, are being recognized to contribute to GI dysfunction. Here, we review neuroinflammatory diseases that potentially cause GI dysfunction. Among such CNS diseases are multiple sclerosis, neuromyelitis optica spectrum disorder, myelin oligodendrocyte glycoprotein associated disorder, and autoimmune encephalitis. Peripheral nervous system diseases impacting the gut include Guillain-Barre syndrome, chronic inflammatory demyelinating polineuropathy, acute sensory-autonomic neuropathy/acute motor-sensory-autonomic neuropathy, acute autonomic ganglionopathy, myasthenia gravis and acute autonomic neuropathy with paraneoplastic syndrome. Finally, collagen diseases, such as Sjogren syndrome and systemic sclerosis, and celiac disease affect both CNS and PNS. These neuro-associated GI dysfunctions may predate or present concurrently with brain, spinal cord or peripheral nerve.
dysfunction. Such patients may visit gastroenterologists or physicians first, before the neurological diagnosis is made. Therefore, awareness of these phenomena among general practitioners and collaboration between gastroenterologists and neurologists are highly recommended in order for their early diagnosis and optimal management, as well as for systematic documentation of their presentations and treatment.

**Keywords:** Acute autonomic ganglionopathy; Autoimmune disease; Multiple sclerosis; Neuroinflammatory diseases; Neuromyelitis optica spectrum disorder (NMOSD); Paraneoplastic syndrome.

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**Full text links**

87. **The Use of Fecal Calprotectin Testing in Paediatric Disorders: A Position Paper of the European Society for Paediatric Gastroenterology and Nutrition Gastroenterology Committee**


**Authors**

Carmen Ribes Koninckx 1, Ester Donat 1, Marc A Benninga 2, Ilse J Broekaert 3, Frederic Gottrand 4, Kaija-Leena Kolho 5, Paolo Lionetti 6, Erasmo Miele 7, Rok Orel 8, Alexandra Papadopoulos 9, Corina Pienar 10, Michela G Schäppi 11, Michael Wilschanski 12, Nikhil Thapar 13

**Affiliations**

1 Department of Paediatric Gastroenterology, Hepatology and Nutrition, La Fe University Hospital Valencia, Spain.
2 Department of Paediatric Gastroenterology and Nutrition, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands.

3 Department of Paediatrics, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany.

4 Department of Paediatric Gastroenterology, Hepatology and Nutrition, CHU Lille, University Lille, France.

5 Children’s Hospital, University of Helsinki, Helsinki, Finland and Tampere University, Tampere, Finland.

6 Department NEUROFARBA, University of Florence - Meyer Children's Hospital, Florence.

7 Department of Translational Medical Science, Section of Pediatrics, University of Naples "Federico II", Naples, Italy.

8 Department of Gastroenterology, Hepatology and Nutrition, University Children's Hospital, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.

9 Division of Gastroenterology and Hepatology, First Department of Paediatrics, University of Athens, Children's hospital «Agia Sofia», Athens, Greece.

10 Department of Paediatrics, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania.

11 Paediatric Centre, Clinique des Grangettes and Centre Médical Universitaire, Geneva, Switzerland.

12 Paediatric Gastroenterology Hadassah Hebrew University Medical Centre, Jerusalem, Israel.

13 Neurogastroenterology and Motility, UCL Great Ormond Street Institute of Child Health and Department of Gastroenterology, Great Ormond Street Hospital, London, UK.

14 Gastroenterology, Hepatology and Liver Transplant, Queensland Children's Hospital, Brisbane, Australia.

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DOI: 10.1097/MPG.0000000000003046
Abstract

**Objectives:** The aim of the study was to review the evidence regarding the clinical use and value of fecal calprotectin (FC) measurements in different gastrointestinal disorders in children.

**Methods:** A literature search was conducted in the PubMed, MEDLINE, EMBASE, and Cochrane databases until October 31, 2019. Subtopics were identified and each assigned to individual authors.

**Results:** A total of 28 recommendations were voted on using the nominal voting technique. Recommendations are given related to sampling, measurement methods, and results interpretation. The 14 authors anonymously voted on each recommendation using a 9-point scale (1 strongly disagree to 9 fully agree). Consensus was considered achieved if at least 75% of the authors voted 6, 7, 8, or 9.

**Conclusions:** Consensus was reached for all recommendations. Limitations for the use of FC in clinical practice include variability in extraction methodology, performance of test kits as well as the need to establish local reference ranges because of the influence of individual factors, such as age, diet, microbiota, and drugs. The main utility of FC measurement at present is in the diagnosis and monitoring of inflammatory bowel disease (IBD) as well as to differentiate it from functional gastrointestinal disorders (FAPDs). FC, however, has neither utility in the diagnosis of infantile colic nor to differentiate between functional and organic constipation. A rise in FC concentration, may alert to the risk of developing necrotizing enterocolitis and help identifying gastrointestinal involvement in children with Henoch-Schönlein purpura. FC measurement is of little value in Cow's Milk Protein Allergy, coeliac disease (CD), and cystic fibrosis. FC does neither help to distinguish bacterial from viral acute gastroenteritis (AGE), nor to diagnose Helicobacter Pylori infection, small intestinal bacterial overgrowth (SIBO), acute appendicitis (AA), or intestinal polyps.

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**Conflict of interest statement**
The authors report no conflicts of interest.

- 214 references

Full text links

88. **Celiac disease antibody levels reflect duodenal mucosal damage but not clinical symptoms**


Authors

Aki J Käräjämäki 1 2, Juha Taavela 3 4, Christian Nielsen 1, Mårten Lönnqvist 1, Marcus Svartbäck 5, Katri Kaukinen 4 6, Risto Tertti 1 7

Affiliations

- 1 Department of Internal Medicine, Vaasa Central Hospital, Vaasa, Finland.
- 2 Research Unit of Internal Medicine, Medical Research Center Oulu, Oulu University Hospital, and University of Oulu, Oulu, Finland.
- 3 Central Finland Central Hospital, Jyväskylä, Finland.
- 4 Celiac Disease Research Center, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland.
- 5 Department of Pathology, Vaasa Central Hospital, Vaasa, Finland.
- 6 Department of Internal Medicine, Tampere University Hospital, Tampere, Finland.
- 7 Department of Internal Medicine, University of Turku, Turku, Finland.

PMID: 33705679
DOI: 10.1080/00365521.2021.1899278
Abstract

**Objectives:** This study aimed to investigate, in a real-world population, whether the histological and clinical phenotype differ at baseline and during follow-up in patients with high and low CD (celiac disease) antibody titers.

**Materials and methods:** The study cohort consisted of 96 consecutive patients diagnosed to have CD during the years 2010-2018. The clinical parameters, symptoms and laboratory results were registered and histomorphometry was analyzed from the available duodenal biopsies taken during the primary and follow-up esophageal-gastric-duodenoscopies. Patients having immunoglobulin A transglutaminase antibody (tTG-ab) levels above 70 U/mL were classified as high titer patients.

**Results:** Measured by the villous-crypt ratio, the duodenal mucosa was more severely damaged in the high tTG-ab group than in the low tTG-group at baseline \((n = 70, 0.61 \pm 0.63 \text{ vs. } 1.02 \pm 0.87, p = .003)\) and during the follow-up when the patients were on gluten-free diet \((n = 27, 1.80 \pm 0.72 \text{ vs. } 2.35 \pm 0.64, p = .041)\). Interestingly, the high tTG-ab group members had fewer gastrointestinal symptoms at baseline than those in the low tTG-ab group \((43\% \text{ vs. } 68\%, p = .013)\) but lower vitamin D levels \((68 \pm 34 \text{ nmol/L vs. } 88 \pm 29 \text{ nmol/L, } p = .034)\) and more often microcytosis \((28\% \text{ vs. } 10\%, p = .040)\). During the follow-up, these differences were no longer detected.

**Conclusions:** At baseline, CD patients with high tTG-ab have more severe duodenum injury and signs of malabsorption but fewer symptoms. After gluten-free diet has been initiated, the mucosal healing in the high tTG-ab group is prolonged, but symptoms and signs of malabsorption recover equally in both groups.

**Keywords:** Celiac disease; anemia; gastrointestinal symptoms; histomorphometry; malabsorption; tissue transglutaminase antibody.
Improving the quality of gluten-free bread by a novel acidic thermostable α-amylase from metagenomics data


Authors

Seyedeh Fatemeh Sadeghian Motahar 1, Shohreh Ariaenejad 2, Maryam Salami 3, Zahra Emam-Djomeh 1, Atefeh Sheykh Abdollahzadeh Mamaghani 4

Affiliations

1 Department of Food Science and Engineering, University College of Agriculture & Natural Resources, University of Tehran, Karaj, Iran. 
2 Department of Systems and Synthetic Biology, Agricultural Biotechnology Research Institute of Iran (ABRII), Agricultural Research Education and Extension Organization (AREEO), Karaj, Iran. Electronic address: sh.ariaee@abrii.ac.ir.
3 Department of Food Science and Engineering, University College of Agriculture & Natural Resources, University of Tehran, Karaj, Iran. Electronic address: msalami@ut.ac.ir.
4 Department of Systems and Synthetic Biology, Agricultural Biotechnology Research Institute of Iran (ABRII), Agricultural Research Education and Extension Organization (AREEO), Karaj, Iran.

PMID: 33691209
DOI: 10.1016/j.foodchem.2021.129307

Abstract

Development of gluten-free products is important due to their role in gluten related disorders and health improvement. α-Amylase enzymes have shown to have a positive effect on wheat bread quality. This study aimed to screen in-silico a novel acidic-thermostable α-amylase (PersiAmy2) from the sheep rumen metagenome to increase the quality of gluten-free bread. The PersiAmy2 was cloned, expressed, purified and characterized. The enzyme
was highly stable at a wide range of pH, temperature and storage conditions. The PersiAmy2 had excellent activity in the presence of ions, inhibitors, and surfactants. Utilization of the acidic thermostable PersiAmy2 in gluten-free bread resulted in a softer crumb, higher specific volume, porosity, moisture content and caused a darker crust color. The rheological measurement showed a solid-elastic behavior in batters. Also the addition of this enzyme reduced the firmness. From the results of this study it can be concluded that the PersiAmy2 can be used to improve the quality of gluten-free bread.

**Keywords:** Bread quality; Gluten-free; In-silico screen; Metagenome; Novel-amylase.

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**Full text links**

90. [New developments in non-Hodgkin lymphoid malignancies](http://example.com)


**Authors**

Karthik A Ganapathi ¹, Laura E Brown ¹, Sonam Prakash ¹, Parul Bhargava ²

**Affiliations**

- ¹ Department of Laboratory Medicine, University of California San Francisco, CA, USA.
- ² Department of Laboratory Medicine, University of California San Francisco, CA, USA. Electronic address: Parul.Bhargava@ucsf.edu.

- PMID: [33685720](http://example.com)
- DOI: [10.1016/j.pathol.2021.01.002](http://example.com)
Abstract

The revised fourth edition of the World Health Organization (WHO) Classification of Tumours of Haematopoietic and Lymphoid Tissues (2017) reflects significant advances in understanding the biology, genetic basis and behaviour of haematopoietic neoplasms. This review focuses on some of the major changes in B-cell and T-cell non-Hodgkin lymphomas in the 2017 WHO and includes more recent updates. The 2017 WHO saw a shift towards conservatism in the classification of precursor lesions of small B-cell lymphomas such as monoclonal B-cell lymphocytosis, in situ follicular and in situ mantle cell neoplasms. With more widespread use of next generation sequencing (NGS), special entities within follicular lymphoma and mantle cell lymphoma were recognised with recurrent genetic aberrations and unique clinicopathological features. The diagnostic workup of lymphoplasmyacytic lymphoma and hairy cell leukaemia has been refined with the discovery of MYD88 L265P and BRAF V600E mutations, respectively, in these entities. Recommendations in the immunohistochemical evaluation of diffuse large B-cell lymphoma include determining cell of origin and expression of MYC and BCL2, so called 'double-expressor' phenotype. EBV-positive large B-cell lymphoma of the elderly has been renamed to recognise its occurrence amongst a wider age group. EBV-positive mucocutaneous ulcer is a newly recognised entity with indolent clinical behaviour that occurs in the setting of immunosuppression. Two lymphomas with recurrent genetic aberrations are newly included provisional entities: Burkitt-like lymphoma with 11q aberration and large B-cell lymphoma with IRF4 rearrangement. Aggressive B-cell lymphomas with MYC, BCL2 and/or BCL6 rearrangements, so called 'double-hit/triple-hit' lymphomas are now a distinct entity. Much progress has been made in understanding intestinal T-cell lymphomas. Enteropathy-associated T-cell lymphoma, type II, is now known to not be associated with coeliac disease and is hence renamed monomorphic epitheliotropic T-cell lymphoma. An indolent clonal T-cell lymphoproliferative disorder of the GI tract is a newly included provisional entity. Angioimmunoblastic T-cell lymphoma and nodal T-cell lymphomas with T-follicular helper phenotype are included in a single broad category, emphasising their shared genetic and phenotypic features. Anaplastic large cell lymphoma, ALK- is upgraded to a definitive entity with subsets carrying recurrent rearrangements in DUSP22 or TP63. Breast implant-associated anaplastic large cell lymphoma is a new provisional entity with indolent behaviour. Finally, cutaneous T-cell proliferations include a new provisional entity, primary cutaneous acral CD8-positive T-cell lymphoma, and
reclassification of primary small/medium CD4-positive T-cell lymphoma as lymphoproliferative disorder.

**Keywords:** 2017 World Health Organization Classification; EBV-positive mucocutaneous ulcer; NOS; anaplastic large cell lymphoma ALK−; breast implant-associated anaplastic large cell lymphoma; diagnostic criteria; high grade B-cell lymphoma; in situ follicular neoplasia; indolent mantle cell lymphoma; large B-cell lymphoma with IRF4 rearrangement; monoclonal B-cell lymphocytosis; monomorphic epitheliotropic intestinal T-cell lymphoma.

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91. NanoUPLC-MS reveals differential abundance of gluten proteins in wheat flours of different technological qualities


**Authors**

V C M Victorio, T O Alves, G H M F Souza, L C Gutkoski, L C Cameron, M S L Ferreira

**Affiliations**

1 Laboratory of Bioactives, Food and Nutrition Graduate Program, PPGAN, Federal University of the State of Rio de Janeiro, UNIRIO, Av. Pasteur, 296, 22290-240, RJ, Brazil. Electronic address: veronica.victorio@edu.unirio.br.

2 Laboratory of Bioactives, Food and Nutrition Graduate Program, PPGAN, Federal University of the State of Rio de Janeiro, UNIRIO, Av.
Gluten proteins contribute to the rheological properties of dough. Mass spectrometric techniques help to understand the contribution of these proteins to the quality of the end product. This work aimed to apply modern proteomic techniques to characterize and provide a better understanding of gluten proteins in wheat flours of different technological qualities. Nine Brazilian wheat flours (Triticum aestivum) classified by rheological gluten force were used to extract the proteins. Extracts were pooled together by technological qualities in low (LW), medium (MD), and superior (SP). Peptides were analyzed by nanoUPLC and mass spectrometry multiplex method (MS^6). Collectively, 3545 peptides and 1297 proteins were identified, and 116 proteins were found differentially abundant. Low molecular weight glutenin subunits (LMW-GS) were found up-regulated only in SP samples. Proteins related to wheat grain hardness, such as puroindoline-A, were found in significant concentration in LW samples. After domain prediction, LW presented a different pattern with a lower abundance of functional domains, and SP presented chaperones, known to be involved in adequate folding of the storage proteins. NanoUPLC-MS^6 was efficient in analyzing and distinguishing the proteomic pattern of wheat flours from different qualities,
pointing out the differentially abundant gluten proteins and providing a better understanding of wheat flour quality. SIGNIFICANCE: Common wheat is one of the most important staple food sources in the world. The improvement and comprehension of wheat quality has been a major objective of plant breeders and cereal chemists. Our findings highlighted the application of a modern proteomic approach to obtain a better understanding of the impact of gluten proteins on the technological quality of different wheat flours. The obtained data revealed different abundances of wheat quality-related proteins in superior quality flours when compared with samples of low rheological properties. In addition, multivariate statistical analysis clearly distinguished the flours of different qualities. This work contributes to the consolidation of research in the field of wheat technological quality.

Keywords: Foodomics; Protein abundance profile; SDS-PAGE; Storage proteins; Wheat quality.

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92. **Epitope mapping of anti-amelogenin IgG in untreated celiac children**


Authors

Sanja Petronijevic ¹, Solveig Stig ¹, Trond S Halstensen ¹ ²

Affiliations

- ¹ Institute of Oral Biology, Faculty of Dentistry, University of Oslo, Oslo, Norway.
- ² Medical Department, Lovisenberg Diaconal Hospital, Oslo, Norway.

PMID: 33656197
Abstract

Children with untreated celiac disease (CeD) may develop enamel defects, and children with severe CeD have significantly increased levels of IgG to amelogenin, which may interfere with normal amelogenesis depending on which epitope(s) they bind. Children with untreated CeD (n = 42), for whom CeD had been confirmed either by biopsy (n = 17, cohort 1) or by the presence of particularly high serum levels of anti-transglutaminase 2 (TG2) IgA (n = 25, cohort 2), were selected from 146 children with CeD, and 10 controls were selected from 34 children who did not have CeD. Samples from these 52 children were used for detailed IgG anti-amelogenin, X isoform (AMELX) epitope mapping using 31 overlapping, 10-22mer peptides in ELISA. Although sera from both groups showed reactivity to peptides containing sequences from the N and C terminus of AMELX, sera from children with CeD reacted more strongly to peptides from the central region (amino acids 75-150) containing both a binding site for transforming growth factor-β (TGF-β), as well as the enzymatic cleavage sites for matrix metalloproteinase-20 and for kallikrein-4. Antigen-specific extraction revealed that only IgG to the central region cross-reacted to gliadin. Thus, cross-reactive anti-gliadin/amelogenin IgG may affect normal amelogenesis by interfering with enzymatic degradation, proper folding, and/or TGF-β signaling in children with untreated CeD.

Keywords: autoimmunity; dental enamel; gluten; immunology.

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Psyllium (from Plantago ovata; ispaghula) is used as a dietary supplement and is supplied in the form of husk, granules, capsules, or powder. Consumers using psyllium-containing laxatives, healthcare workers handling these, and pharmaceutical workers in laxative-manufacturing plants are known to be at risk of sensitization and subsequent rhinitis, asthma, contact urticaria, and even anaphylaxis. To our knowledge, the case we present here is the first of baker's immunoglobulin E (IgE)-mediated occupational allergy due to psyllium exposure. Our patient, a 24-year-old female baker with no previous allergies, was referred to our clinic with suspected occupational rhinitis. After 1 year of baking with cereal flour or gluten-free flour-mix, she began to suffer from rhino-conjunctival symptoms during workdays. Skin prick tests with agents from the patient's workplace revealed allergies not only to wheat and rye flours but also to psyllium, with a remarkable 10 mm wheal. Subsequently, nasal provocation tests confirmed occupational allergic rhinitis to psyllium. We also found work-related sensitization to buckwheat, which she used in gluten-free baking. Due to the increased prevalence of celiac disease and the popularity of gluten-free and vegan food, psyllium has recently become a common ingredient in baking, used as a substitute for gluten or eggs. Bakers
handle allergens such as these in high concentrations and this may lie behind the emergence of respiratory and dermal symptoms. It is essential to consider new or recently introduced materials as possible allergens if it is suspected that a baker has work-related respiratory or allergic symptoms.

**Keywords:** allergy; baker; ispaghula; nasal provocation test; occupational rhinitis.

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- 17 references

**Full text links**

94. **Effects of thermal properties and behavior of wheat starch and gluten on their interaction: A review**


**Authors**

Zhen Wang ¹, Sen Ma ², Binghua Sun ³, Fengcheng Wang ¹, Jihong Huang ⁴, Xiaoxi Wang ¹, Qingdan Bao ¹

**Affiliations**

- ¹ College of Food Science and Engineering, Henan University of Technology, Zhengzhou, Henan 450001, China.
- ² College of Food Science and Engineering, Henan University of Technology, Zhengzhou, Henan 450001, China. Electronic address: masen@haut.edu.cn.
- ³ College of Food Science and Engineering, Henan University of Technology, Zhengzhou, Henan 450001, China. Electronic address: sbhfood@126.com.
Abstract

Starch and gluten, the most important macromolecules in wheat flour, vary in thermal properties. The thermal behavior of starch, gluten and their complexes during the manufacture and quality control of flour products need to be accurately understood. However, the high complexity of starch-gluten systems impedes the accurate description of their interactions. When heated within varying temperature ranges and when water molecules are involved, the behaviors of amylose and amylopectin change, and the properties of the starch are modified. Moreover, important indicators of starch granules such as gelatinization temperature, peak viscosity, and so on, which are encapsulated by the gluten matrix, are altered. Meanwhile, the high-temperature environment induces the opening of the intrachain disulfide bonds of gliadin, leading to an increase in the probability of interchain disulfide bond formation in the gluten network system. These behaviors are notable and may provide insights into this complex interaction. In this review, the relationship between the thermal behavior of wheat starch and gluten and the quality of flour products is analyzed. Several methods used to investigate the thermal characteristics of wheat and its flour products are summarized, and some thermal interaction models of starch and gluten are proposed.

Keywords: Gluten; Thermal behavior; Wheat starch.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing interests.

Full text links

[Full-text article link]
**Well-being and dietary adherence in patients with coeliac disease depending on follow-up**


**Authors**

Jesper Lexner 1 2, Henrik Hjortswang 3 4, Rickard Ekesbo 5, Klas Sjöberg 1 2

**Affiliations**

- 1 Department of Clinical Sciences, Lund University, Lund, Sweden.
- 2 Department of Gastroenterology, Skåne University Hospital, Malmö, Sweden.
- 3 Department of Gastroenterology and Hepatology, Linköping University, Linköping, Sweden.
- 4 Department of Health, Medicine, and Caring Sciences, Linköping University, Linköping, Sweden.
- 5 Department of Clinical Sciences, Lund University, Vårdsområde Malmö, Sweden.

- PMID: 33621157
- DOI: 10.1080/00365521.2021.1889024

**Abstract**

**Objective:** It is not clear how follow-up of coeliac disease should be optimally organised. In Malmö, Sweden, patients are followed up by general practitioners (GP), but in Linköping by gastroenterologists (GE). The aim of this study was to investigate if there were any differences in well-being and dietary adherence depending on type of follow-up.

**Methods:** All adult patients with newly diagnosed biopsy-verified coeliac disease in the cities between 2010 and 2014 were offered to participate. Data was retrieved comprising demography, laboratory analyses, questionnaires (Gastrointestinal Symptoms Rating Scale, Short Health Scale, Multidimensional...
Fatigue Inventory, Psychological General Well-being Index and Short Form 36) and follow-up.

**Results:** In the GP cohort 39/73 patients and in the GE cohort 58/121 agreed to participate (mean age 43 and 44 years, 69 and 60% women, respectively). A follow-up to a dietician was carried out in 31% and 93% of patients, respectively ($p < .001$). In the GP group 28% had eaten gluten-containing food during the last 4 weeks compared to 9% in the GE group ($p = .01$). Despite this, no differences could be seen in vitamin or mineral levels. The questionnaires did not indicate any major discrepancies in subjective health.

**Conclusion:** Irrespective of the design of the follow-up physical and mental well-being were comparable. Dietary adherence was not quite as good in the GP group but follow-up in a primary care setting can still be a suitable and equivalent alternative. However, it is crucial that the dietary counselling is structured in a way that ensures dietary adherence.

**Keywords:** Coeliac disease; diet; follow-up; quality of life; well-being.

**Full text links**

96. [The role of female endoscopists: are women gastroenterologists better at obtaining biopsies for celiac disease than men?](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8193286/)


**Authors**

Claire L Jansson-Knodell ¹, William R Kessler ¹

**Affiliation**
Abstract

Objectives: Celiac disease (CD) is commonly found in women. Given the sex differences in diagnosed patients, we hypothesized sex differences in physicians obtaining biopsies for CD may exist.

Materials and methods: We retrospectively reviewed duodenal biopsies for suspected CD excluding pre-existing CD patients. Appropriate biopsy practice was defined as ≥5 specimens per ACG guidelines.

Results: We included 125 patients (females, 92). There were 85 properly (68%) biopsied. Presence of a female endoscopist was associated with better adherence to biopsy guidelines (OR, 2.99, 95% CI, 1.19-7.54; p = .02) which remained significant after multivariable adjustment (adjusted OR, 2.7; p = .047).

Conclusions: Physician sex-based differences in biopsy patterns may exist.

Keywords: Sprue; diagnosis; duodenal biopsy; gender; practice patterns; sex.

Full text links

97. Quantification of the Hemodynamic Changes of Cirrhosis with Free-Breathing Self-Navigated MRI


Authors
Affiliations

- 1 Department of Radiology, Stanford University, Palo Alto, California, USA.
- 2 Department of Radiology, University of California San Diego, La Jolla, California, USA.
- 3 Division of Gastroenterology, Department of Medicine, University of California San Diego, La Jolla, California, USA.
- 4 Division of Epidemiology, Department of Family Medicine and Preventive Medicine, University of California San Diego, La Jolla, California, USA.
- 5 NAFLD Research Center, Department of Medicine, University of California San Diego, La Jolla, California, USA.

PMID: 33594733
DOI: 10.1002/jmri.27488

Abstract

**Background:** Non-invasive assessment of the hemodynamic changes of cirrhosis might help guide management of patients with liver disease but are currently limited.

**Purpose:** To determine whether free-breathing 4D flow MRI can be used to quantify the hemodynamic effects of cirrhosis and introduce hydraulic circuit indexes of severity.

**Study type:** Retrospective.

**Population:** Forty-seven patients including 26 with cirrhosis.

**Field strength/sequence:** 3 T/free-breathing 4D flow MRI with soft gating and golden-angle view ordering.

**Assessment:** Measurements of the supra-celiac abdominal aorta, supra-renal abdominal aorta (SRA), celiac trunk (CeT), superior mesenteric artery (SMA),
splenic artery (SpA), common hepatic artery (CHA), portal vein (PV), and supra-renal inferior vena cava (IVC) were made by two radiologists. Measures of hepatic vascular resistance (hepatic arterial relative resistance [HARR]; portal resistive index [PRI]) were proposed and calculated.

**Statistical analysis**: Bland-Altman, Pearson's correlation, Tukey's multiple comparison, and Cohen's kappa. P < 0.05 was considered significant.

**Results**: Forty-four of 47 studies yielded adequate image quality for flow quantification (94%). Arterial structures showed high inter-reader concordance (range; ρ = 0.948-0.987) and the IVC (ρ = 0.972), with moderate concordance in the PV (ρ = 0.866). Conservation of mass analysis showed concordance between large vessels (SRA vs. IVC; ρ = 0.806), small vessels (celiac vs. CHA + SpA; ρ = 0.939), and across capillary beds (CeT + SMA vs. PV; ρ = 0.862). Splanchnic flow was increased in patients with portosystemic shunting (PSS) relative to control patients and patients with cirrhosis without PSS (P < 0.05, difference range 0.11-0.68 liter/m). HARR was elevated and PRI was decreased in patients with PSS (3.55 and 1.49, respectively) compared to both the control (2.11/3.18) and non-PSS (2.11/2.35) cohorts.

**Data conclusion**: 4D flow MRI with self-navigation was technically feasible, showing promise in quantifying the hemodynamic effects of cirrhosis. Proposed quantitative metrics of hepatic vascular resistance correlated with PSS.

**Level of evidence**: 3 TECHNICAL EFFICACY STAGE: 2.

**Keywords**: 4D flow; TIPS; cirrhosis; liver; portal vein; splanchnic.

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- [39 references](#)

**Full text links**
Reliability of anti-tissue transglutaminase antibodies in children with malnutrition


Authors

Necati Balamtekin 1, Harun Erdal 2, Emira Gençkardeşler 3, Melike Arslan 1

Affiliations

1 Department of Pediatrics, Division of Pediatric Gastroenterology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey.
2 Department of Internal Medicine, Division of Gastroenterology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey.
3 Department of Pediatrics, University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Turkey.

PMID: 33590788
DOI: 10.1080/00365521.2021.1882554

Abstract

Objectives: Serological markers are used in the diagnosis of celiac disease. Among these, the most widely used are tissue transglutaminase antibodies (anti-TG2 antibodies). It has been suggested that the mechanisms that are set in motion by malnutrition cause the tight connections between enterocytes to expand, which allows gluten-derived peptides to pass through the epithelium. This causes the production of anti-TG2 antibodies without the presence of celiac disease.

Methods: The patients who were examined for malnutrition and had their anti-TG2 antibody levels measured at the same time, were accepted into the study. The patients who were investigated for suspected celiac disease,
showed no signs of malnutrition, and had their anti-TG2 antibody levels measured were accepted into a control group.

**Results:** The study population consisted of 126 children with mild malnutrition (54.8% female, 7.44 ± 5.38 years); 89 children with moderate malnutrition (54.8% female, 7.62 ± 5.43 years), and a control group of 200 children (53.2% female, 7.72 ± 5.05 years). According to the results, anti-TG2 IgG levels were significantly higher among patients in the mild and moderate malnutrition groups compared to patients in the control group ($p = .02$ and $p = .01$, respectively). However, there was no significant difference between the mild and moderate malnutrition groups ($p > .05$).

**Conclusions:** Malnutrition does not affect anti-TG2 IgA levels in children. However, anti-TG2 IgG levels increase in children suffering from malnutrition. When examining celiac disease, especially in people with a background IgA deficiency, doctors should consider whether malnutrition may be the cause of the increase in serum anti-TG2 IgG levels without celiac disease.

**Keywords:** Malnutrition; anti-tissue transglutaminase antibodies; children.

**Full text links**


**Authors**

D E Yung ¹, A R Robertson ¹, M Davie ², R Sidhu ³, M McAlindon ³, I Rahman ⁴, P Patel ⁴, L Sinha ⁵, S Mason ⁵, J Brzeszczyńska ², S Douglas ¹, J N Plevris ⁶, A Koulaouzidis ⁷

**Affiliations**
Abstract

**Introduction:** Capsule endoscopy (CE) is well established the investigation of small-bowel (SB) pathology. We compared the use of double-headed (DH) capsules, to conventional single-headed (SH), in a real-world patient cohort in the first multicentre British study.

**Methods:** Over 9 months, patients referred for routine SBCE at 4 tertiary referral centres in the UK underwent DH CE instead of conventional SH using MiroCam® MC2000 as per local protocols. One head (L/R) was chosen at random and reported by an expert reviewer. The DH recordings, anonymised and randomised, reported by another expert or re-read after a 4-week interval. For each CE, numbers and types of findings and overall conclusion/diagnosis were compared between SH and DH examinations.

**Results:** 211 CEs were performed. 7 failed to reach the SB; 204 analysed. Indications were: SB bleeding (n = 94); ?SB inflammation or reassessment of known inflammatory bowel disease (IBD) (n = 84); ?SB neoplasia including suspicious radiological imaging (n = 15); and, others e.g. ?celiac disease (n = 11). For SB bleeding: 27/94 (28.7%) examinations reported differences between SH and DH readings. In 17 (18.1%) the findings were clinically significant. SH CE missed angiectasias (5 pts), SB inflammation (7 pts),
oesophagitis (2 pts) and SB masses (2 pts). In 1 patient, the extent of angiectasias seen was greater on the DH reading. For IBD: findings differed in 30/84 (35.7%) of CEs; 11 (13.1%) were clinically significant. In 5, signs of active inflammation were missed by the SH reading. In 6, assessment of extent/severity differed. For SB neoplasia findings differed in 2/15 (13.3%) of examinations. Both were clinically significant. For others: 1/11 (9.1%) examinations differed; however, not deemed clinically significant. Overall, use of DH CE impacted the diagnosis in 30/204 (14.7%).

**Conclusions:** The use of DH CE provides more information with the potential to change clinical diagnosis and therefore management. Therefore, the routine adoption of DH CE in SB assessment should be considered.

**Keywords:** Bleeding; Capsule endoscopy; Double headed; Inflammatory bowel disease; Neoplasia; Small bowel.

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**Conflict of interest statement**

Declaration of Competing Interest The above authors have no COI but would like to disclose material support for this study by IntroMedic and SynMed.

**Full text links**

100. [Association Between Proton Pump Inhibitor Use and Risk of Asthma in Children](https://doi.org/10.1001/jamapediatrics.2020.5710)


**Authors**

Yun-Han Wang, Viktor Wintzell, Jonas F Ludvigsson, Henrik Svanström, Björn Pasternak
Affiliations

- 1 Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.
- 2 Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
- 3 Department of Pediatrics, Örebro University Hospital, Örebro, Sweden.
- 4 Division of Epidemiology and Public Health, University of Nottingham School of Medicine, Nottingham, United Kingdom.
- 5 Celiac Disease Center, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York.
- 6 Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark.

- PMID: 33555324
- PMCID: PMC7871209 (available on 2022-02-08)
- DOI: 10.1001/jamapediatrics.2020.5710

Abstract

Importance: The use of proton pump inhibitors (PPIs) in children has increased substantially in recent years, concurrently with emerging concerns that these drugs may increase the risk of asthma. Whether PPI use in the broad pediatric population is associated with increased risk of asthma is not known.

Objective: To investigate the association between PPI use and risk of asthma in children.

Design, setting, and participants: This nationwide cohort study collected registry data in Sweden from January 1, 2007, to December 31, 2016. Children and adolescents 17 years or younger were matched by age and propensity score into 80,870 pairs of those who initiated PPI use and those who did not. Data were analyzed from February 1 to September 1, 2020.

Exposures: Initiation of PPI use.
Main outcomes and measures: The primary analysis examined the risk of incident asthma with a median follow-up to 3.0 (interquartile range, 2.1-3.0) years. Cox proportional hazards regression was used to estimate hazard ratios (HRs).

Results: Among the 80,870 pairs (63.0% girls; mean [SD] age, 12.9 [4.8] years), those who initiated PPI use had a higher incidence rate of asthma (21.8 events per 1000 person-years) compared with noninitiators (14.0 events per 1000 person-years), with an HR of 1.57 (95% CI, 1.49-1.64). The risk of asthma was significantly increased across all age groups and was highest for infants and toddlers with an HR of 1.83 (95% CI, 1.65-2.03) in the group younger than 6 months and 1.91 (95% CI, 1.65-2.22) in the group 6 months to younger than 2 years (P < .001 for interaction). The HRs for individual PPIs were 1.64 (95% CI, 1.50-1.79) for esomeprazole, 1.49 (95% CI, 1.25-1.78) for lansoprazole, 1.43 (95% CI, 1.35-1.51) for omeprazole, and 2.33 (95% CI, 1.30-4.18) for pantoprazole. In analyses of the timing of asthma onset after PPI initiation, the HRs were 1.62 (95% CI, 1.42-1.85) for 0 to 90 days, 1.73 (95% CI, 1.52-1.98) for 91 to 180 days, and 1.53 (95% CI, 1.45-1.62) for 181 days to end of follow-up. The association was consistent through all sensitivity analyses, including high-dimensional propensity score matching (HR, 1.48; 95% CI, 1.41-1.55).

Conclusions and relevance: In this cohort study, initiation of PPI use compared with nonuse was associated with an increased risk of asthma in children. Proton pump inhibitors should be prescribed to children only when clearly indicated, weighing the potential benefit against potential harm.

Conflict of interest statement

Conflict of Interest Disclosures: Dr Ludvigsson coordinates, on behalf of the Swedish IBD quality register (SWIBREG), a study that has received funding from Janssen Global Services, LLC. Dr Svanström reported receiving consulting fees from Celgene Corporation and being employed by IQVIA outside of the submitted work. No other disclosures were reported.

Full text links
Novel parameters characterizing size distribution of A and B starch granules in the gluten network: Effects on dough stability in bread wheat


Authors

Liwei Yu 1, Lei Guo 1, Yingchun Liu 1, Yanrong Ma 1, Jianchu Zhu 1, Yang Yang 1, Donghong Min 1, Yanzhou Xie 1, Mingxun Chen 1, Jingyang Tong 2, Ata-Ur Rehman 3, Zhonghua Wang 4, Xinyou Cao 5, Xin Gao 6

Affiliations

1 State Key Laboratory of Crop Stress Biology in Arid Areas and College of Agronomy, Northwest A&F University, Yangling, Shaanxi 712100, China.
2 Institute of Crop Sciences/National Wheat Improvement Center, Chinese Academy of Agricultural Sciences, Beijing 100081, China.
3 Graham Centre for Agricultural Innovation, Charles Sturt University, Wagga Wagga, NSW 2650, Australia.
4 State Key Laboratory of Crop Stress Biology in Arid Areas and College of Agronomy, Northwest A&F University, Yangling, Shaanxi 712100, China. Electronic address: zhwangnew@126.com.
5 Crop Research Institute, Shandong Academy of Agricultural Sciences/National Engineering Laboratory for Wheat and Maize/Key Laboratory of Wheat Biology and Genetic Improvement in North Yellow and Huai River Valley, Ministry of Agriculture, Jinan 250100, China. Electronic address: caoxinyou@126.com.
6 State Key Laboratory of Crop Stress Biology in Arid Areas and College of Agronomy, Northwest A&F University, Yangling, Shaanxi 712100, China. Electronic address: bestgaoxin@nwsuaf.edu.cn.

PMID: 33541650
Our study on six wheat genotypes has revealed strong interaction between gluten and starch to affect dough stability. To establish gluten-starch interaction and its roles in dough stability, we randomly selected 16 wheat genotypes and investigated the physicochemical properties of gluten and starch. The manner in which the starch granules occupied available space in gluten network was quantitatively analyzed using gluten lacunarity and proportion of different sized A-type and B-type starch granules. Positive correlations were found between the morphological attributes (B/A/Lacunarity, B/Lacunarity) and dough stability. The correlation coefficient between B/A/Lacunarity and dough stability was highest, followed by the percentage of unextractable polymeric protein (UPP%), B/Lacunarity and dough stability. Dough mixing properties were strongly affected by gluten-starch interactions, as indicated by novel parameters. Whereas the effect of gluten on its own did not provide any evidence to suggest its concrete role in dough mixing properties because of the various genetic backgrounds.

**Keywords:** Interaction between gluten and starch; Physicochemical properties of gluten and starch; Regression analysis; Wheat dough.

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**Full text links**

**102. Colonic paracellular permeability and circulating zonulin-related proteins**


**Authors**

Felipe Meira de-Faria, Olga Bednarska, Magnus Ström, Johan D Söderholm, Susanna A Walter, Åsa V Keita
Abstract

**Objective:** Irritable bowel syndrome (IBS) is a gut-brain disorder associated with increased gut permeability. Zonulin has been suggested to regulate the gut barrier and claimed to be pre-haptoglobin 2 (pre-HP2) and circulating zonulin is often used as a proxy for gastrointestinal permeability. This study investigated the correlation between colonic paracellular permeability and levels of circulating zonulin and pre-HP2.

**Materials and methods:** Colonic biopsies from 32 patients with IBS and 15 healthy controls (HC) were used to measure permeability in Ussing chambers and levels of zonulin (Cusabio ELISA). Zonulin was also measured in blood samples from 40 HC, 78 patients with IBS and 20 patients with celiac disease (CeD), before and after a gluten-free diet. In addition, we verified HP genotype and circulating pre-HP2 using a monoclonal pre-HP2 antibody (Bio-Rad) by ELISA.

**Results:** Increased colonic paracellular permeability correlated positively with zonulin levels in IBS biopsies, but negatively with plasma zonulin. We found no agreement between circulating zonulin and pre-HP2. Genotyping revealed non-specificity of the zonulin kit, as all pre-HP2 non-producers presented detectable levels. Patients with CeD displayed higher pre-HP2 and zonulin levels compared to HC. A gluten-free diet in patients with CeD led to lower serum zonulin and pre-HP2 concentrations.

**Conclusions:** Our study suggests that neither circulating zonulin nor pre-HP2 mirror colonic permeability. Our data corroborate previous reports showing
the inability of the Cusabio zonulin kit to target zonulin and highlights that the results of studies using this kit must be re-examined with caution.

**Keywords:** Colonic paracellular permeability; ELISA; irritable bowel syndrome; pre-haptoglobin 2; zonulin.

**Full text links**

103. **Survival impact of distal pancreatectomy with en bloc celiac axis resection combined with neoadjuvant chemotherapy for borderline resectable or locally advanced pancreatic body carcinoma**


**Authors**

Yoshiaki Murakami 1, Naoya Nakagawa 2, Naru Kondo 2, Yasushi Hashimoto 3, Kenjiro Okada 2, Shingo Seo 2, Hiroyuki Otsuka 2

**Affiliations**

- 1 Department of Advanced Medicine, Hiroshima University, Hiroshima, Japan; Department of Surgery, Hiroshima Memorial Hospital, Hiroshima, Japan. Electronic address: mura777@hiroshima-u.ac.jp.
- 2 Department of Surgery, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.
- 3 Department of Surgery, Hiroshima Memorial Hospital, Hiroshima, Japan.

- PMID: 33526385
- DOI: 10.1016/j.pan.2021.01.008
Abstract

**Background:** The survival benefit associated with distal pancreatectomy with en bloc celiac axis resection (DP-CAR) for patients with borderline resectable or locally advanced pancreatic body carcinoma is controversial. The aim of this study was to evaluate the impact of DP-CAR following neoadjuvant chemotherapy on survival in patients with borderline resectable or locally advanced pancreatic body carcinoma.

**Methods:** Medical records of patients with pancreatic ductal adenocarcinoma who underwent distal pancreatectomy (DP, n = 102) and DP-CAR following neoadjuvant chemotherapy (n = 32) between 2008 and 2019 were analyzed retrospectively. Short- and long-term outcomes were compared between the two groups.

**Results:** All patients who underwent DP-CAR had tumor contact with the celiac axis. Of these, 30 patients underwent preoperative embolization of the common hepatic artery. The pretreatment tumor size of patients who underwent DP-CAR was larger (P < 0.001), and rates of blood transfusion (P = 0.003) and postoperative complications (P = 0.016) were higher in patients who underwent DP-CAR compared with patients who underwent DP. The 5-year survival rate of patients who underwent DP and DP-CAR were 50.6% and 41.1%, respectively (median survival time, 65.9 vs 37.0 months). For all 134 patients, pretreatment serum CA19-9 levels (P < 0.001), adjuvant chemotherapy (P < 0.001), and lymph node status (P = 0.035) were independent prognostic factors of overall survival by multivariate analysis.

**Conclusions:** DP-CAR following neoadjuvant chemotherapy for patients with borderline resectable or locally advanced pancreatic body carcinoma may bring the same survival impact as DP, despite increased morbidity.

**Keywords:** Distal pancreatectomy; Distal pancreatectomy with en bloc celiac axis resection; Neoadjuvant chemotherapy; Pancreatic body or tail carcinoma.

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**Conflict of interest statement**
Declaration of competing interest The authors declare that they have no conflicts of interest.

Full text links

Impact of a Gluten-Free Diet on Quality of Life and Health Perception in Patients With Type 1 Diabetes and Asymptomatic Celiac Disease


Authors

Daniel I Weiman ¹, Farid H Mahmud ¹, Antoine B M Clarke ¹, Esther Assor ¹, Charlotte McDonald ², Fred Saibil ³, Heather A Lochnan ⁴, Zubin Punthakee ⁵, Margaret A Marcon ⁶, CD-DIET Study Group

Collaborators

- CD-DIET Study Group:

Affiliations

- ¹ Division of Endocrinology, Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.
Abstract

**Context:** Celiac disease (CD) is a common comorbidity seen in patients with type 1 diabetes (T1D) and is frequently asymptomatic. As chronic conditions requiring significant lifestyle changes, there are limited reports assessing changes in health-related quality of life (HRQoL) during transition to a gluten-free diet (GFD) in patients with T1D who are asymptomatic for CD.

**Objective:** This work aims to prospectively assess HRQoL and health perception in children and adults with T1D and asymptomatic CD after random assignment to GFD vs usual diet.

**Methods:** Patients with T1D aged 8 to 45 years without CD symptoms were serologically screened for CD, with positive results confirmed with intestinal biopsy. Participants were randomly assigned in an open-label fashion to a GFD or gluten-containing diet (GCD) for 12 months. Generic and diabetes-specific HRQoL and self-perceived wellness (SPW) were assessed longitudinally.

**Results:** A total of 2387 T1D patients were serologically screened. CD was biopsy-confirmed in 82 patients and 51 participants were randomly assigned to a GFD (N = 27) or GCD (N = 24). Excellent adherence to the assigned diets was observed. Overall, no changes in generic (P = .73) or diabetes-specific HRQoL (P = .30), or SPW (P = .41) were observed between groups over 12
months. Hemoglobin A1c (HbA1c) and gastrointestinal symptoms were consistent predictors of HRQoL and SPW.

**Conclusion:** HRQoL and SPW were not significantly affected by the adoption of a GFD over 12 months, but worsened with symptom onset and increased HbA1c. Our findings indicate that transition to a GFD can be made successfully in this population without adversely affecting quality of life.

**Keywords:** celiac disease; gluten-free diet; health perception; quality of life; type 1 diabetes.

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**Full text links**


**Authors**

Vilma Xhakollari, Maurizio Canavari, Magda Osman

**Affiliations**

1 Department of Agricultural and Food Sciences, Alma Mater Studiorum-University of Bologna, Viale Giuseppe Fanin 50, 40127, Bologna, Italy. Electronic address: vilma.xhakollari@unibo.it.

2 Department of Agricultural and Food Sciences, Alma Mater Studiorum-University of Bologna, Viale Giuseppe Fanin 50, 40127, Bologna, Italy. Electronic address: maurizio.canavari@unibo.it.
Abstract

**Purpose:** To understand factors affecting adherence to GFD by celiac and non-celiac people through the application of behavioural theories, Integrative Model (IM) and Multi Theory Model (MTM).

**Methods:** Analyses were conducted for a sample of 308 subjects, majority females, celiac and non-celiac. Adherence to GFD was measured considering two scales, self-declared adherence and scored adherence, in order to discern possible inconsistencies between what subjects believe and what they really do. Subsequently, adherence to GFD was modelled by considering constructs of MTM and IM. Moreover, the constructs were designed based on literature review. Ordered logit (OL) model was used to test the IM and MTM theoretical models.

**Results:** The findings show that adherence to GFD is affected mainly by attitudes towards GFD, self-efficacy, injunctive norms, knowledge about GFD and health conditions. Between the two models, IM and MTM, results show that all constructs of IM explain the behaviour. Contrary, for MTM, results indicate only some constructs of the MTM explain adherence to GFD.

**Conclusions:** Results of this study should be considered for improving the adherence to GFD for celiac people. Furthermore, it is important to consider the non-celiac people's perceptions for GFD and GF products. In other words an accurate information about the diet and products it is relevant for supporting people to make healthier food choices. Finally, as the results show, IM explain adherence to GFD better than MTM.

**Keywords:** Adherence; Celiac; Gluten free diet; Integrative model; Multi theory model; Non-celiac.
Non-invasive peripheral focused ultrasound neuromodulation of the celiac plexus ameliorates symptoms in a rat model of inflammatory bowel disease


Authors

Kainat Akhtar 1, Zall Hirschstein 1, Allison Stefanelli 1, Emilia Iannilli 1, Aditya Srinivasan 1, Linda Barenboim 1, Mustafa Balkaya 1, Alexandra Cunha 1, Aliyah Audil 1, Eliyahu M Kochman 1, Fuyee Chua 1, Maya Ravi 1, Saisree Mikkilineni 1, Hanel Watkins 1, William O'Connor Jr 2, Ying Fan 3, Victoria Cotero 3, Jeffrey Ashe 3, Christopher Puleo 3, Tzu-Jen Kao 3, Damian S Shin 1 4

Affiliations

1 Department of Neuroscience & Experimental Therapeutics, Albany Medical College, Albany, NY, USA.
2 Department of Immunology and Microbial Disease, Albany Medical College, Albany, NY, USA.
3 General Electric Global Research Center, Niskayuna, NY, USA.
4 Department of Neurology, Albany Medical Center, Albany, NY, USA.

PMID: 33512049
DOI: 10.1113/EP088848

Abstract

New findings: What is the central question of this study? Does peripheral non-invasive focused ultrasound targeted to the celiac plexus improve inflammatory bowel disease? What is the main finding and its importance? Peripheral non-invasive focused ultrasound targeted to the celiac plexus in a
rat model of ulcerative colitis improved stool consistency and reduced stool bloodiness, which coincided with a longer and healthier colon than in animals without focused ultrasound treatment. The findings suggest that this novel neuromodulatory technology could serve as a plausible therapeutic approach for improving symptoms of inflammatory bowel disease.

Abstract: Individuals suffering from inflammatory bowel disease (IBD) experience significantly diminished quality of life. Here, we aim to stimulate the celiac plexus with non-invasive peripheral focused ultrasound (FUS) to modulate the enteric cholinergic anti-inflammatory pathway. This approach may have clinical utility as an efficacious IBD treatment given the non-invasive and targeted nature of this therapy. We employed the dextran sodium sulfate (DSS) model of colitis, administering lower (5%) and higher (7%) doses to rats in drinking water. FUS on the celiac plexus administered twice a day for 12 consecutive days to rats with severe IBD improved stool consistency scores from 2.2 ± 1 to 1.0 ± 0.0 with peak efficacy on day 5 and maximum reduction in gross bleeding scores from 1.8 ± 0.8 to 0.8 ± 0.8 on day 6. Similar improvements were seen in animals in the low dose DSS group, who received FUS only once daily for 12 days. Moreover, animals in the high dose DSS group receiving FUS twice daily maintained colon length (17.7 ± 2.5 cm), while rats drinking DSS without FUS exhibited marked damage and shortening of the colon (13.8 ± 0.6 cm) as expected. Inflammatory cytokines such as interleukin (IL)-1β, IL-6, IL-17, tumour necrosis factor-α and interferon-γ were reduced with DSS but coincided with control levels after FUS, which is plausibly due to a loss of colon crypts in the former and healthier crypts in the latter. Lastly, overall, these results suggest non-invasive FUS of peripheral ganglion can deliver precision therapy to improve IBD symptomology.

Keywords: Crohn's disease; IBD; bioelectric medicine; celiac plexus; dextran sulfate sodium; medical device; peripheral ganglion; superior mesenteric plexus; ulcerative colitis.

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- [63 references](#)

Full text links
The quality of gluten-free bread made of brown rice flour prepared by low temperature impact mill


Authors

Shunjing Luo 1, Xudong Yan 1, Yuteng Fu 1, Min Pang 2, Ruiyun Chen 1, Yunfei Liu 3, Jun Chen 4, Chengmei Liu 5

Affiliations

1 State Key Laboratory of Food Science and Technology, Nanchang University, No. 235 Nanjing East Road, Nanchang 330047, China.
2 Guilin Guiliu Modern Food Co, Ltd, Changjiang East Road, Guilin 541805, China.
3 Institute of Applied Chemistry, Jiangxi Academy of Sciences, 7777 Changdong Avenue, Nanchang 330096, China.
4 State Key Laboratory of Food Science and Technology, Nanchang University, No. 235 Nanjing East Road, Nanchang 330047, China. Electronic address: chen-jun1986@hotmail.com.
5 State Key Laboratory of Food Science and Technology, Nanchang University, No. 235 Nanjing East Road, Nanchang 330047, China. Electronic address: liuchengmei@aliyun.com.

PMID: 33508598
DOI: 10.1016/j.foodchem.2021.129032

Abstract

Our previous work reported that the brown rice flour prepared by low temperature impact mill possessed excellent physicochemical properties. The performance of brown rice flour in making gluten-free bread was further investigated. It was found that the starch crystal structure was destroyed and...
the damaged starch content increased as the particle size of brown rice flour decreased. The interaction between the starch and water in the model dough and the matrix structures among the endosperm masses were enhanced as the particle size decreased, making the gluten-free dough more viscoelastic. However, dough made with finer flour was too sticky, which limited the expansion of dough. Gluten-free bread prepared with medium-sized brown rice flour had favorable quality characterized by large specific volume, low hardness, numerous and homogeneous gas cells.

**Keywords:** Brown rice; Dough; Gluten-free bread; Low temperature impact mill; Particle size.

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**Full text links**

108. *Associations of TP53 codon 72 polymorphism with complications and comorbidities in patients with type 1 diabetes*


**Authors**

Bartosz Słomiński ¹, Maria Skrzypkowska ², Monika Ryba-Stanisławowska ², Małgorzata Myśliwiec ³, Piotr Trzonkowski ²

**Affiliations**

- ¹ Department of Medical Immunology, Faculty of Medicine, Medical University of Gdańsk, ul. Dębinki 1, 80-211, Gdańsk, Poland. bartosz@gumed.edu.pl.
- ² Department of Medical Immunology, Faculty of Medicine, Medical University of Gdańsk, ul. Dębinki 1, 80-211, Gdańsk, Poland.
Abstract

Wild-type TP53 plays an important role in the regulation of immune response and systemic inflammation. In type 1 diabetes (T1D), TP53 pathways are upregulated and an increased susceptibility to apoptosis is observed. We hypothesize that TP53 codon 72 polymorphism could be associated with complications and comorbidities in patients with T1D. We have investigated the associations of the TP53 codon 72 polymorphism with the T1D complications and comorbidities (retinopathy, nephropathy, hypertension, dyslipidemia, autoimmune thyroiditis, and celiac disease) in 350 patients. The key results of our approach are as follows: (1) In diabetic subjects, the Pro/Pro genotype is associated with an increased risk of microvascular complications, dyslipidemia, and celiac disease; (2) the Arg/Arg variant is associated with a decreased risk of autoimmune thyroiditis and celiac disease; (3) the Pro allele is associated with an increased risk of dyslipidemia, autoimmune thyroiditis, and celiac disease. Although further studies are required, our results for the first time indicate that the TP53 codon 72 polymorphism could be considered a genetic marker to predict the increased susceptibility to some T1D complications and comorbidities. KEY MESSAGES: We analyzed the TP53 codon 72 polymorphism in patients with T1D. Pro/Pro genotype is associated with an increased risk of microvascular complications, dyslipidemia, and celiac disease. The Arg/Arg variant is associated with a decreased risk of autoimmune thyroiditis and celiac disease. The Pro allele is associated with an increased risk of dyslipidemia, autoimmune thyroiditis, and celiac disease.

Keywords: Diabetes complications; TP53 codon 72 polymorphism; Type 1 diabetes.

• 42 references
Persistent Villous Atrophy in De Novo Adult Patients With Celiac Disease and Strict Control of Gluten-Free Diet Adherence: A Multicenter Prospective Study (CADER Study)


Authors

Fernando Fernández-Bañares ¹ ², Belén Beltrán ² ³, Antonio Salas ⁴, Isabel Comino ⁵, Raquel Ballester-Clau ⁶, Carme Ferrer ⁴, Javier Molina-Infante ² ⁷, Mercé Rosinach ¹, Inés Modolell ⁸, Francisco Rodríguez-Moranta ⁹, Beatriz Arau ¹ ², Verónica Segura ⁵, Luis Fernández-Salazar ¹⁰, Santos Santolaria ¹¹, Maria Esteve ¹ ², Carolina Sousa ⁵, CADER study group

Affiliations

¹ Department of Gastroenterology, Hospital Universitari Mutua Terrassa, Terrassa (Barcelona), Spain.
² Centro de Investigación Biomédica en Red de enfermedades hepáticas y digestivas (CIBERehd), Instituto de Salud Carlos III, Madrid, Spain.
³ Department of Gastroenterology, Hospital Universitario La Fe, Valencia, Spain.
⁴ Department of Pathology, Hospital Universitari Mutua Terrassa, Terrassa (Barcelona), Spain.
⁵ Department of Microbiology and Parasitology, Faculty of Pharmacy, University of Seville, Seville, Spain.
⁶ Department of Gastroenterology, Hospital Arnau de Vilanova, Lleida, Spain.
⁷ Department of Gastroenterology, Hospital Universitario de Cáceres, Cáceres, Spain.
⁸ Department of Gastroenterology, Consorci Sanitari, Terrassa, Spain.
⁹ Department of Gastroenterology, Hospital de Bellvitge, L'Hospitalet de Llobregat (Barcelona), Spain.
Abstract

Introduction: A substantial proportion of adult patients with celiac disease on a gluten-free diet exhibit persistent villous atrophy, and inadvertent gluten exposure may be one of the causes. The aim of the present study was to evaluate villous atrophy persistence after 2 years on a gluten-free diet in de novo adult patients with celiac disease with strict control of gluten exposure.

Methods: Symptomatic de novo adult patients with celiac disease were prospectively included. Clinical visits and dietary surveillance were scheduled every 6 months during a 2-year follow-up period. At each visit, fecal samples were collected and stored at -20 °C until analysis for gluten immunogenic peptides (f-GIPs). A follow-up duodenal biopsy was performed at 2 years. We evaluated the variables associated with persistent villous atrophy.

Results: Seventy-six patients completed the study (36.5 ± 1.6 years, 73% women); persistent villous atrophy was observed in 40 (53%), whereas 72.5% were asymptomatic and 75% had negative serology. Detectable f-GIP >0.08 μg/g in at least 1 fecal sample was seen in 69% of patients. There were no significant differences in the median f-GIP at each visit and median area under the curve over the serial measurements between patients with persistent villous atrophy and those who recovered. On multivariate analysis, only older age was associated with persistent villous atrophy (32% for 16-30 years; 67% for >30 years; P = 0.016).

Discussion: The rate of persistent villous atrophy after 2 years was high in adult patients with celiac disease on an intentionally strict gluten-free diet. Low-level ongoing inadvertent gluten exposure could be a contributing factor to persistent villous atrophy.

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110. Coeliac disease is associated with depression in children and young adults with type 1 diabetes: results from a multicentre diabetes registry


Authors

Sascha René Tittel 1 2, Désirée Dunstheimer 3, Dörte Hilgard 4, Burkhold Knauth 5, Elke Fröhlich-Reiterer 6, Angela Galler 7, Michael Wurm 8, Reinhard Walter Holl 9 10, DPV Initiative

Affiliations

1 Institute for Epidemiology and Medical Biometry, ZIBMT, Ulm University, Albert-Einstein-Allee 41, 89081, Ulm, Germany. sascha.tittel@uni-ulm.de.
2 German Center for Diabetes Research (DZD), Munich-Neuherberg, Germany. sascha.tittel@uni-ulm.de.
3 Paediatrics and Adolescent Medicine, Medical Faculty University of Augsburg, Augsburg, Germany.
4 Department of Pediatrics, Witten, Germany.
5 Department of Pediatrics and Adolescent Medicine, CJD Berchtesgaden, Berchtesgaden, Germany.
6 Division of General Pediatrics, Department of Paediatrics and Adolescent Medicine, Medical University Graz, Graz, Austria.
7 Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany.
Aims: To analyse the association between coeliac disease (CD) and depression in children, adolescents, and young adults with type 1 diabetes (T1D).

Methods: We included 79,067 T1D patients aged 6-20 years, with at least six months of diabetes duration, and treatment data between 1995 and 2019 were documented in the diabetes patient follow-up registry. We categorized patients into four groups: T1D only (n = 73,699), T1 + CD (n = 3379), T1D + depression (n = 1877), or T1D + CD + depression (n = 112).

Results: CD and depression were significantly associated (adjusted OR: 1.25 [1.03-1.53]). Females were more frequent in both the depression and the CD group compared with the T1D only group. Insulin pumps were used more frequently in T1D + CD and T1D + depression compared with T1D only (both p < .001). HbA1c was higher in T1D + depression (9.0% [8.9-9.0]), T1D + CD + depression (8.9% [8.6-9.2]), both compared with T1D only (8.2% [8.2-8.2], all p < .001). We found comorbid autism, attention deficit hyperactivity disorder, anxiety, schizophrenia, and eating disorders more frequently in the T1D + CD + depression group compared with T1D only (all p < .001).

Conclusions: CD and depression are associated in young T1D patients. The double load of T1D and CD may lead to an increased risk for depression. Depression was associated with additional psychological and neurological comorbidities. Aside from imperative CD screening after T1D diagnosis and regular intervals, depression screening might be helpful in routine care, especially in patients with diagnosed CD.

Keywords: Coeliac disease; DPV; Depression; Endocrinology; Paediatric.
111. **The multiple faces of autoimmune/immune-mediated myocarditis in children: a biopsy-proven case series treated with immunosuppressive therapy**


**Authors**

Renzo Marcolongo, Stefania Rizzo, Alessia Cerutti, Elena Reffo, Biagio Castaldi, Anna Baritussio, Cristina Basso, Giovanni Di Salvo, Alida L P Caforio

**Affiliations**

- 1 Hematology and Clinical Immunology, Department of Medicine, University of Padova, Padova, Italy.
- 2 Cardiovascular Pathology Unit, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Padova, Italy.
- 3 Pediatric Cardiology, Department of Woman and Child Health, University of Padova, Padova, Italy.
- 4 Division of Cardiology, Department of Cardiac Thoracic Vascular Sciences and Public Health, University of Padova, Padova, Italy.

- PMID: 33452872
- PMCID: PMC8006650
- DOI: 10.1002/ehf2.13163

Free PMC article
Abstract

The role of immunosuppressive therapy (IT) in paediatric autoimmune/immune-mediated myocarditis remains poorly defined. To explore its role, we present a series of three consecutive paediatric patients with biopsy-proven, virus negative, autoimmune/immune-mediated myocarditis, with distinct clinical and pathological features, who have been successfully treated with IT, a 14-year-old boy with Loeffler's fibroblastic parietal endomyocarditis, a 6-year-old child with celiac disease with chronic active lymphocytic myocarditis, and a 13-year-old boy with long-standing heart failure and active lymphocytic myocarditis. Patients started IT and entered follow-up between July 2017 and September 2019; the first patient completed IT. IT was associated with a substantial and sustained recovery of cardiac function in our patients, regardless of their heterogeneous clinical and pathological features. Combination IT was well tolerated and enabled tapering and weaning off steroids.

Keywords: Children; Endomyocardial biopsy; Immunosuppressive therapy; Myocarditis.

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Conflict of interest statement

All authors have completed the ICMJE disclosure form and declare no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

• 15 references
• 3 figures

Full text links

Absence of the celiac trunk and anomalous very low origin of the common hepatic
artery arising independently from the abdominal aorta just above aortic bifurcation in patient undergoing radical pancreaticoduodenectomy


Authors

Sławomir Mrowiec 1, Robert Król 2, Beata Jabłońska 3

Affiliations

1 Department of Digestive Tract Surgery, Medical University of Silesia, Medyków 14 St. 40-752, Katowice, Poland.
2 Department of General, Vascular and Transplant Surgery, Medical University of Silesia, Katowice, Poland.
3 Department of Digestive Tract Surgery, Medical University of Silesia, Medyków 14 St. 40-752, Katowice, Poland. bjablonska@poczta.onet.pl

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• PMCID: PMC8021532
• DOI: 10.1007/s00276-020-02666-6

Free PMC article

Abstract

Purpose: Knowledge of anomalies of the celiac trunk is very important during various surgical procedures (such as pancreatic and gastric resections including Appleby operation, liver resections and liver transplantations) and as well as radiologic procedures (such as chemoembolization of pancreatic and hepatic tumors).

Methods: A 77-years-old woman was admitted to our department for surgical treatment of ampullary adenocarcinoma G2 confirmed in endoscopic retrograde cholangiopancreatography (ERCP) with papillotomy and ampullary
biopsy. In the contrast-enhanced computed tomography, the ampullary tumor was not visible, but the main pancreatic duct within pancreatic head and isthmus was dilated (indirect radiological tumor signs). An absence of the celiac trunk (CT) was established via computed tomography. Therefore, computed tomography-based angiography (angio-CT) of the abdominal aorta (AA) was performed before operation.

Results: Angio-CT confirmed an extremely rare vascular anomaly: an absence of CT. The left gastric (LGA), splenic (SA), and common hepatic (CHA) arteries connected above origin of the superior mesenteric artery (SMA) from the AA. Pylorus-preserving pancreaticoduodenectomy (PD) was performed. This anomaly was also confirmed intraoperatively. The postoperative course was uneventful and the patient was discharged on postoperative day 10. There were no signs of recurrence of the tumor during the 6 months follow-up.

Conclusion: The proper preoperative identification of anomalies within major abdominal vessels and its relationship to the tumor is very important to avoid intraoperative vascular injury and major postoperative complications.

Keywords: Anatomic variation; Anomaly; Celiac trunk; Common hepatic artery; Pancreaticoduodenectomy.

Conflict of interest statement

The authors declare no conflicts of interest.

- 3 references
- 2 figures

Full text links

113. Dermatitis Herpetiformis: An Update on Diagnosis and Management

Dermatitis herpetiformis (DH), presenting with an intense itch and blistering symmetrical rash, typically on the elbows, knees, and buttocks, is a cutaneous manifestation of celiac disease. Though overt gastrointestinal symptoms are rare, three-fourths of patients with DH have villous atrophy in the small bowel, and the rest have celiac-type inflammatory changes. DH affects mostly adults and slightly more males than females. The mean age at onset is about 50 years. DH diagnosis is confirmed by showing granular immunoglobulin A deposits in the papillary dermis. The DH autoantigen, transglutaminase 3, is deposited at the same site in tightly bound immune complexes. At present, the DH-to-celiac disease prevalence is 1:8. The incidence of DH is decreasing, whereas that of celiac disease is increasing, probably because of improved diagnostics. In DH, the treatment of choice for all patients is a gluten-free diet (GFD) in which uncontaminated oats are allowed. At onset, most patients need additional dapsone to rapidly control the rash and itching. Dapsone can be stopped after a mean of 2 years, and a strict lifelong GFD alone is required. Dietary adherence offers an excellent long-term prognosis for patients with DH, with a normal quality of life and all-cause mortality.
Phosvitin-wheat gluten complex catalyzed by transglutaminase in the presence of Na$_2$SO$_3$: Formation, cross-link behavior and emulsifying properties


Authors

Lu Yang, Jie Jia, Xuefu Zhou, Meichen Liu, Qunjun Zhang, Liangjie Tian, Wen Tan, Yanjun Yang, Xuebo Liu, Xiang Duan

Affiliations

1 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: yanglu1116@nwafu.edu.cn.
2 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: jiajili@nwafu.edu.cn.
3 Department of Food Science and Technology, Shanghai Jiao Tong University, Shanghai 200240, PR China. Electronic address: shiftzhou@sjyu.edu.com.
4 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: liumeichen@nwafu.edu.cn.
5 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: qinjunzhang1110@163.com.
6 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: tianlj8@163.com.
7 College of Food Science and Engineering, Northwest A&F University, Yangling 712100, PR China. Electronic address: wentan@nwafu.edu.cn.
8 School of Food Science and Technology, Jiangnan University, Wuxi 214122, PR China. Electronic address: yangyj@jiangnan.edu.cn.
Phosvitin (PSV) is considered as a good emulsifier, although it has a low proportion of hydrophobic regions and steric hindrance. Wheat gluten (WG) possesses excellent hydrophobicity and macromolecular network structure. In this work, WG was subjected to a series of Na₂SO₃ solution, followed by cross-linking with PSV under transglutaminase (TGase) catalyzation. The results showed that Na₂SO₃ could break disulfide bonds of WG and increase its solubility from 7.33% to 42.82% with 1200 mg/L of Na₂SO₃. Correspondingly, the cross-linking degree was significantly enhanced. Compared to PSV, the cross-linked PSV-WG exhibited a higher surface hydrophobicity and thermal stability, with a lower zeta potential and apparent viscosity. The emulsifying activity of PSV-WG reached 17.42, 20.63 and 20.28 m²/g with Na₂SO₃ concentration of 300, 600 and 900 mg/L, which were all higher than that of PSV (15.19 m²/g). This work provided a novel strategy to elevate emulsifying properties of PSV by cross-link reaction.

**Keywords:** Cross-link; Emulsifying property; Phosvitin; Transglutaminase; Wheat gluten.

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**ELSEVIER FULL-TEXT ARTICLE**

115. The impact of autoimmune systemic inflammation and associated medications on male reproductive health in patients
with chronic rheumatological, dermatological, and gastroenterological diseases: A systematic review


Authors

Renata Finelli ¹, Kristian Leisegang ², Federica Finocchi ³, Salvatore De Masi ⁴, Ashok Agarwal ¹, Giovanni Damiani ⁵ ⁶

Affiliations

¹ American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH, USA.
² School of Natural Medicine, University of the Western Cape, Cape Town, South Africa.
³ Division of Endocrinology, Department of Clinical and Molecular Sciences, Umberto I Hospital, Polytechnic University of Marche, Ancona, Italy.
⁴ Clinical Trial Office, University Hospital Meyer, Florence, Italy.
⁵ Clinical Dermatology, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy.
⁶ Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy.

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DOI: 10.1111/aji.13389

Abstract

Autoimmune disorders currently affect 5%-8% of the global population, characterized by an aberrant chronic inflammatory response to self-antigens. The aim of this study was to systematically review the current available evidence investigating the impact of systemic autoimmune diseases and associated immunosuppressive treatment on fertility parameters of adult men. Clinical trials, observational studies, and case reports written in English and reporting semen analysis, evaluation of seminal oxidative stress, and/or
sperm DNA fragmentation in patients affected by psoriasis and psoriatic arthritis, celiac disease, inflammatory bowel diseases, systemic lupus erythematosus, ankylosing spondylitis, hidradenitis suppurativa, uveitis, dermatomyositis, and rheumatoid arthritis were collected by searching on PubMed, EMBASE, OVID, Scopus, and Cochrane Library databases, with no limit of time. The study quality and the extent of bias in design, methods, and outcome assessment were evaluated by applying the Joanna Briggs Institute Critical Appraisal tools. Evidence suggested that various autoimmune diseases or relevant medications can adversely affect male fertility parameters and that patients may benefit of counseling and sperm cryopreservation. Clinical trials further investigating any adverse effect of autoimmunity and related thereby on male infertility are warranted, to develop appropriate guidelines for males diagnosed and treated for autoimmune disorders.

**Keywords:** autoimmunity; chronic inflammation; male infertility; semen analysis.

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- Cited by 1 article
- 100 references

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116. **Usefulness of Transesophageal Echocardiography in the Evaluation of Celiac Trunk and Superior Mesenteric Artery Involvement in Acute Aortic Dissection**


**Authors**
Mesenteric ischemia is a serious complication of acute aortic dissection (AAD), and its early diagnosis is vital for prognosis and appropriate treatment indication. Arteries affected by this complication are the celiac trunk and superior mesenteric artery, and their evaluation is usually based on computed tomographic angiography. Transesophageal echocardiography is also a useful technique for diagnosing AAD and is essential in monitoring surgical or endovascular treatment when computed tomographic angiography is not available. However, the usefulness of transesophageal echocardiography for evaluating celiac trunk and superior mesenteric artery involvement and mesenteric ischemia mechanisms in AAD is not well established. Real-time information on mesenteric malperfusion is needed at the bedside, in primary
care facilities, and in the operating room to achieve prompt diagnosis and better therapeutic management. The aims of this review are to assess the role of TEE to diagnose celiac trunk and superior mesenteric artery involvement in AAD, determine the mechanisms that can cause flow obstruction in patients with mesenteric ischemia, and analyze possible implications in the treatment of this complication.

**Keywords:** Acute aortic dissection; Celiac trunk; Mesenteric ischemia; Superior mesenteric artery; Transesophageal echocardiography.

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**Full text links**

**Exploring the alpha-gliadin locus: the 33-mer peptide with six overlapping coeliac disease epitopes in Triticum aestivum is derived from a subgroup of Aegilops tauschii**


**Authors**

Jan G Schaar, Elma M J Salentijn, Svetlana V Goryunova, Charity Chidzanga, Danny G Esselink, Nick Gosman, Alison R Bentley, Luud J W J Gilissen, Marinus J M Smulders

**Affiliations**

1 Plant Breeding, Wageningen University and Research, Droevendaalsesteeg 1, NL-6708 PB Wageningen, the Netherlands.

2 The John Bingham Laboratory, NIAB, 93 Lawrence Weaver Road, Cambridge, CB3 0LE, UK.
Abstract

Most alpha-gliadin genes of the Gli-D2 locus on the D genome of hexaploid bread wheat (Triticum aestivum) encode for proteins with epitopes that can trigger coeliac disease (CD), and several contain a 33-mer peptide with six partly overlapping copies of three epitopes, which is regarded as a remarkably potent T-cell stimulator. To increase genetic diversity in the D genome, synthetic hexaploid wheat lines are being made by hybridising accessions of Triticum turgidum (AB genome) and Aegilops tauschii (the progenitor of the D genome). The diversity of alpha-gliadins in A. tauschii has not been studied extensively. We analysed the alpha-gliadin transcriptome of 51 A. tauschii accessions representative of the diversity in A. tauschii. We extracted RNA from developing seeds and performed 454 amplicon sequencing of the first part of the alpha-gliadin genes. The expression profile of allelic variants of the alpha-gliadins was different between accessions, and also between accessions of the Western and Eastern clades of A. tauschii. Generally, both clades expressed many allelic variants not found in bread wheat. In contrast to earlier studies, we detected the 33-mer peptide in some A. tauschii accessions, indicating that it was introduced along with the D genome into bread wheat. In these accessions, transcripts with the 33-mer peptide were present at lower frequencies than in bread wheat varieties. In most A. tauschii accessions, however, the alpha-gliadins do not contain the epitope, and this may be exploited, through synthetic hexaploid wheats, to breed bread wheat varieties with fewer or no coeliac disease epitopes.

Keywords: Aegilops tauschii; Triticum aestivum; D genome; SHW; T-cell epitope; alpha-gliadin; coeliac disease; gluten; re-synthesised bread wheat; synthetic hexaploid wheat.

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Characterization of T-cell receptor transgenic mice recognizing immunodominant HLA-DQ2.5-restricted gluten epitopes


Authors

Christian B Lindstad 1 2, Shuo-Wang Qiao 1 2, Marie K Johannesen 1 2, Lars Fugger 3, Ludvig M Sollid 1 2 4, M Fleur du Pré 1 4

Affiliations

1 K.G. Jebsen Coeliac Disease Research Centre, University of Oslo, Oslo, Norway.
2 Department of Immunology, University of Oslo, Oslo, Norway.
3 Oxford Centre for Neuroinflammation, Nuffield Department of Clinical Neurosciences, Division of Clinical Neurology and Medical Research Council Human Immunology Unit, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, Oxford, UK.
4 Department of Immunology, Oslo University Hospital, Oslo, Norway.

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DOI: 10.1002/eji.202048859

Abstract

We created a TCR transgenic mouse with CD4+ T cells recognizing the immunodominant DQ2.5-glia-ω2 gluten epitope. We show that these cells respond to deamidated gluten feed in vivo and compare them to previously
published α2- and γ1-specific mice. These mice may help enlighten key aspects of celiac disease pathogenesis.

**Keywords:** HLA-DQ2.5; TCR; celiac; gluten; mouse.

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- 6 references

**Full text links**

**119. Effect of degree of milling and defatting on proximate composition, functional and texture characteristics of gluten-free muffin of bran of long-grain indica rice cultivars**


**Authors**

Amandeep Kaur ¹, Amardeep Singh Virdi ¹, Narpinder Singh ¹, Amandeep Singh ¹, Raj Sukhwinder Singh Kaler ²

**Affiliations**

- ¹ Department of Food Science and Technology, Guru Nanak Dev University, Amritsar, India.
- ² Department of Food Science and Technology, Guru Nanak Dev University, Amritsar, India. Electronic address: rsskaler@yahoo.com.

- PMID: 33348134
- DOI: 10.1016/j.foodchem.2020.128861
Abstract

Effect of different degrees of milling (DoM: 2%, 4%, 6% and 8%) and defatting on the proximate composition, protein characteristics, functional properties of bran of long grain rice cultivars and texture characteristics of bran (RB) supplemented muffins were evaluated. Protein, ash content, redness and yellowness increased while fat content decreased for RB by extended DoM and defatting. A higher proportion of β sheets, random coils, α-helix and β-turns for all fractions of RB of both cultivars after defatting were also observed. Defatting and extended DoM both improved the essential amino acid content in RB. A higher level of prolamines (15-18 kDa) in RB and DF-RB of PUSA1121 than PR111 was observed. Muffins made from 2% DoM bran from PUSA1121 showed improved texture characteristics and achieved the highest score for sensory attributes. Therefore, DoM and defatting improved the proximate, protein profiling, and functionality of the different fraction of RB.

Keywords: Amino acid composition; FTIR analysis; Muffins; Protein profiling; Proximate composition; Rice bran.

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Deamidated Gliadin Antibodies: Do They Add to Tissue Transglutaminase-IgA Assay in Screening for Celiac Disease?


Authors

Ashraf Abdulrahim 1, Mosa Fagih 2 3, Riccardo Troncone 4, Muhammed Salman Bashir 5, Ali Asery 1, Muhanad Alruwaithi 1, Abdullah N Al-Jurayyan 5, Ibrahim Al-Alallah 5, Abdulrahman Al-Hussaini 1 6 7
Abstract

**Objectives:** Use of deamidated gliadin peptide (DGP) test kits as adjunctive to tissue-transglutaminase-IgA (TTG-IgA) for the diagnosis of celiac disease (CD) has been a controversial issue. The objectives of our study were to evaluate the diagnostic performance of DGP antibodies compared with TTG-IgA and to evaluate the correlation between DGP-antibody titers and degree of enteropathy.

**Methods:** We included children who underwent endoscopy and biopsies because of positivity of any of the serology tests in the "celiac profile" (TTG-IgA, DGP-IgA, and DGP-IgG) from 2012 to 2019. We divided children into clinically suspected cases of CD (group 1) and asymptomatic cases screened as they were from a high-risk group (group 2).

**Results:** Group 1 constituted 52 children and group 2 included 81 children (76 type-1 diabetes [T1D]). The sensitivity and positive-predictive value (PPV) of
DGP-IgG in group 1 (90%, 98%) and group 2 (91%, 85.5%) were comparable with TTG-IgA (98%, 92% in group 1; 100%, 80% in group 2). By adding DGP-IgG to TTG-IgA, the performance of TTG-IgA has improved marginally in group 1 (sensitivity 100%, PPV 92.3%). All cases with DGP-IgG titer 2 times ULN in group 1, and >4 times ULN in group 2 had villous atrophy. All T1D patients with TTG IgA >10 times ULN had villous atrophy.

Conclusions: DGP-IgG assay did not add to the performance of TTG-IgA. DGP-IgG titer correlated with enteropathy. The diagnosis of CD can be made in asymptomatic T1D child with TTG-IgA titer >10 times ULN and positive endomyseal antibodies.

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Conflict of interest statement

The authors report no conflicts of interest.

- 35 references

Full text links

121. The Knowledge About Celiac Disease Among Healthcare Professionals and Patients in Central Europe


Authors

Petra Riznik ¹, Luigina De Leo ², Jasmina Dolinsek ³, Judit Gyimesi ⁴, Martina Klemenak ¹, Berthold Koletzko ⁵ ⁶, Sibylle Koletzko ⁶ ⁷, Tunde Koltai ⁸, Ilma Rita Korponay-Szabó ⁴ ⁹, Tomaz Krcncnik ¹, Marina Milinovic ¹⁰, Tarcisio Not ², Goran Palcevski ¹¹, Daniele Sblattero ¹², Katharina Julia Werkstetter ⁶, Jernej Dolinsek ¹ ¹³
Affiliations

1. Department of Pediatrics, Gastroenterology, Hepatology and Nutrition Unit, University Medical Centre Maribor, Maribor, Slovenia.
2. IRCCS Burlo Garofolo Trieste, Institute for Maternal and Child Health, Trieste, Italy.
4. Heim Pál National Pediatric Institute, Coeliac Disease Centre, Budapest, Hungary.
5. Stiftung Kindergesundheit (Child Health Foundation) at Dr. von Hauner Children's Hospital.
6. Dr. von Hauner Children's Hospital, Clinical Medical Centre, LMU, Munich, Germany.
7. Department of Pediatrics, Gastroenterology and Nutrition, School of Medicine Collegium Medicum University of Warmia and Mazury, Olsztyn, Poland.
9. Department of Pediatrics, Faculty of Medicine, University of Debrecen, Debrecen, Hungary.
11. Department for Gastroenterology, Pediatrics Clinic, University Hospital Rijeka, Rijeka, Croatia.
12. Department of Life Sciences, University of Trieste, Trieste, Italy.
13. Department of Pediatrics, Medical Faculty, University of Maribor, Maribor, Slovenia.

PMID: 33346575
DOI: 10.1097/MPG.0000000000003019

Abstract

Objectives: Celiac disease (CD) remains undiagnosed for a long time in many adult and pediatric patients. We assessed the knowledge about CD among healthcare professionals (HCPs) and CD patients in Central Europe (CE).

Methods: HCPs and CD patients from 5 CE countries were asked to complete the web-based questionnaire about CD. The questions were divided into subsections on epidemiology, clinical presentation, diagnostics, treatment, and follow-up. Achieved scores of different specialists managing patients with
CD were compared and regional differences in patients' knowledge were analyzed.

**Results:** Questionnaire was completed by 1381 HCPs and 2262 CD patients or their caregivers from Croatia, Hungary, Germany, Italy, and Slovenia. Mean score achieved by HCPs was 50.9%, and by CD patients 56.4%. Pediatric gastroenterologists scored the highest (69.4%; P < 0.001). There were significant differences in knowledge of patients from different CE regions with German participants scoring the highest (58.3%). Members of CD societies scored higher compared with nonmembers (mean score 58% vs 53.2%; P < 0.001) and patients diagnosed less than 5 years ago scored higher compared with those diagnosed more than 10 years ago (mean score 57.3% vs 54.6%; P < 0.001).

**Conclusions:** The knowledge about CD among HCPs and CD patients is not satisfactory. Further awareness-raising and learning activities are needed to improve HCPs' knowledge and to minimize the number of unrecognized patients and unnecessary diagnostic delays. Patients should be better informed about their disease to reach higher compliance with the gluten-free diet.

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**Conflict of interest statement**

The authors report no conflicts of interest.

- 46 references

**Full text links**

122. Metabolic-associated fatty liver disease (MAFLD) in coeliac disease

Abstract

**Background and aims:** Coeliac disease (CD) is considered a high-risk condition for developing non-alcoholic fatty liver disease (NAFLD) and other related metabolic disorders, particularly after commencing gluten-free diet (GFD). Recently, a new concept of metabolic-associated fatty liver disease (MAFLD) has been proposed to overcome the limitations of NAFLD definition. This study aimed at exploring the prevalence of NAFLD and MAFLD in CD patients at the time of CD diagnosis and after 2 years of GFD. Furthermore, we evaluated the role of PNPLA3 rs738409 in the development of NAFLD and MAFLD in the same population.

**Methods:** We retrospectively enrolled all newly diagnosed CD patients who underwent clinical, laboratory and ultrasonography investigations both at diagnosis and after 2 years of follow-up. Moreover, a PNPLA3 rs738409 genotyping assay was performed.

**Results:** Of 221 newly diagnosed CD patients, 65 (29.4%) presented NAFLD at CD diagnosis, while 32 (14.5%) met the criteria for MAFLD (κ = 0.57). There were no significant differences between NAFLD and MAFLD, except for the
higher rate of insulin resistance (IR) of MAFLD patients (75% vs 33.8%, P < .001). At 2 years of follow-up, 46.6% of patients developed NAFLD while 32.6% had MAFLD (k = 0.71). MAFLD subjects had higher transaminases (P = .03), LDL-cholesterol (P = .04), BMI and waist circumference and higher IR than NAFLD patients. MAFLD patients showed higher non-invasive liver fibrosis scores than NAFLD subjects (APRI = 1.43 ± 0.56 vs 0.91 ± 0.62, P < .001; NFS=-1.72 ± 1.31 vs -2.18 ± 1.41, P = .03; FIB-4 = 1.27 ± 0.77 vs 1.04 ± 0.74, P = .04). About PNPLA3 polymorphisms, at 2 years follow-up, NAFLD subjects presented a higher rate of heterozygosis (40.8%) and homozygosis (18.4%) polymorphisms than non-NAFLD (26.3% and 7.6%, respectively, P = .03 and 0.02), while no correlation between PNPLA3 polymorphisms and MAFLD was seen.

**Conclusions:** The new MAFLD definition better reflects the metabolic alterations following GFD in CD population. This new classification could be able to identify patients at higher risk of worse metabolic outcome, who need a close multidisciplinary approach for their multisystemic disease.

**Keywords:** MAFLD; coeliac disease; metabolic syndrome; steatosis.

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- [47 references](#)

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123. [Interactions between gluten and water-unextractable arabinoxylan during the thermal treatment](#)


**Authors**
Abstract

This study aimed to investigate the interactions between gluten and water-unextractable arabinoxylan (WUAX), which changed the conformation and aggregation of gluten during the thermal treatment. In this work, the interactions between water-unextractable arabinoxylan and wheat gluten during thermal treatment were extensively evaluated by different techniques. The results showed that the extra WUAX could impair the viscoelasticity as well as weaken the thermal properties of gluten. The fluorescence spectra revealed the extra WUAX changed the conformation of gluten molecules. Besides, chemical interaction measurement indicated that the extra WUAX prevented the formation of partial disulfide bonds and had a major effect on the hydrophobic interaction of gluten. In summary, these results indicated that WUAX disrupted the covalent crosslinking by affecting disulfide bonds between gluten proteins, and dominated the folding/unfolding process of gluten via the competition with gluten for water, resulting in the poor quality of whole wheat-based foods.
Keywords: Aggregation behavior; Chemical interactions; Gluten; Thermal process; Water-unextractable arabinoxylan.

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Full text links

124. Clinical Presentation in Children With Coeliac Disease in Central Europe


Authors

Petra Riznik 1, Luigina De Leo 2, Jasmina Dolinsek 3, Judit Gyimesi 4, Martina Klemenak 1, Berthold Koletzko 5, 6, Sibylle Koletzko 6, 7, Ilma Rita Korponay-Szabó 4, 8, Tomaz Krenčnik 1, Tarcisio Not 2, Goran Palcevski 9, Daniele Sblattero 10, Katharina Julia Werkstetter 6, Jernej Dolinsek 1

Affiliations

1 Department of Paediatrics, Gastroenterology, Hepatology and Nutrition Unit, University Medical Centre Maribor, Maribor, Slovenia.
2 IRCCS Burlo Garofolo Trieste, Institute for Maternal and Child Health, Trieste, Italy.
3 Municipality of Maribor, Project Office, Maribor, Slovenia.
4 Heim Pál National Paediatric Institute, Coeliac Disease Centre, Budapest, Hungary.
5 Stiftung Kindergesundheit (Child Health Foundation), Dr. von Hauner Children’s Hospital.
6 Dr. von Hauner Children's Hospital, Clinical Medical Centre, LMU, Munich, Germany.
7 Department of Paediatrics, Gastroenterology and Nutrition, School of Medicine Collegium Medicum, University of Warmia and Mazury, Olsztyn, Poland.
Abstract

Objectives: During the past decades, there has been a shift in the clinical presentation of coeliac disease (CD) to nonclassical, oligosymptomatic, and asymptomatic forms. We assessed clinical presentation of CD in children and adolescents in Central Europe.

Methods: Paediatric gastroenterologists in 5 countries retrospectively reported data of their patients diagnosed with CD. Clinical presentation was analyzed and the differences among very young (<3 years) and older children and adolescents were studied.

Results: Data from 653 children and adolescents (median age 7 years 2 months; 63.9% girls) from Croatia, Germany, Hungary, Italy, and Slovenia were available for the analysis. One fifth (N = 134) of all children were asymptomatic. In symptomatic children, the most common leading symptom was abdominal pain (33.3%), followed by growth retardation (13.7%) and diarrhoea (13.3%). The majority of symptomatic children (47.6%; N = 247) were polysymptomatic. Abdominal pain was the most common symptom in polysymptomatic (66.4%) as well as in monosymptomatic children (29.7%). Comparing clinical presentation of CD in very young children (younger than 3 years) with older children (3 years or older), we found that symptoms and signs of malabsorption were significantly more common in younger (P < 0.001), whereas abdominal pain and asymptomatic presentation were more common in older children and adolescents (both P < 0.001).

Conclusion: In children with CD, abdominal pain has become the most common symptom. However, in younger children, symptoms of malabsorption are still seen frequently. This raises a question about the
underlying mechanism of observed change in clinical presentation in favour of nonclassical presentation and asymptomatic disease at certain age.

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Conflic of interest statement

The authors report no conflicts of interest.

- 50 references

Full text links

125. The effect of Celiac disease on cardiac functions and aortic elasticity parameters in children


Authors

Fatos Alkan ¹, Guzide Dogan ², Erhun Kasırga ³, Senol Coskun ¹

Affiliations

- ¹ Celal Bayar University, School of Medicine, Division of Pediatric Cardiology, Department of Pediatrics, Manisa, Turkey.
- ² Bezmialem Vakif University, School of Medicine, Division of Pediatric Gastroenterology, Department of Pediatrics, Istanbul, Turkey.
- ³ Maltepe University, School of Medicine, Division of Pediatric Gastroenterology, Department of Pediatrics, Istanbul, Turkey.

PMID: 33300485
Abstract

**Aim:** We aimed to investigate the effect of Celiac disease on myocardial functions and aortic elasticity parameters.

**Materials and methods:** Thirty children with Celiac disease and 30 healthy children were enrolled in the study. Both the groups were similar in terms of age and gender. Cardiac functions of all children in the patients and control group were evaluated using conventional transthoracic echocardiography and tissue Doppler imaging. Aortic strain, distensibility, and stiffness index were calculated by M-mode echocardiography.

**Results:** The demographic findings, height, weight, and body mass index of cases were similar among two groups. No statistical difference was found between E wave velocity for conventional transthoracic echocardiography and tissue Doppler imaging measurements of the mitral valve; early diastolic flow peak velocity, A wave velocity; late diastolic flow peak velocity; and E/A ratio. Isovolumetric relaxation time and isovolumetric contraction time ratios were statistically different between the groups (p = 0.000, p = 0.000, p = 0.000). The myocardial performance index calculated according to the pulse Doppler measurement results was found to be statistically different between the groups (p = 0.000). There was no statistical difference between the groups in terms of aortic strain, distensibility, and stiffness index.

**Conclusion:** In this study, both conventional transthoracic echocardiography and tissue Doppler imaging revealed the affection of the myocardial functions during systole and diastole in children with Celiac disease. Therefore, early follow-up and routine cardiac evaluation of celiac patients may be appropriate due to the increased risk of cardiac affection.

**Keywords:** Celiac disease; myocardial performance index; tissue Doppler echocardiography.

**Full text links**
Chemical modifications and their effects on gluten protein: An extensive review


Authors

E Abedi 1, K Pourmohammadi 2

Affiliations

1 Department of Food Science and Technology, College of Agriculture, Fasa University, Fasa, Iran. Electronic address: e.abedi@fasau.ac.ir.
2 Department of Food Science and Technology, College of Agriculture, Fasa University, Fasa, Iran. Electronic address: Kpourmohammadi@fasau.ac.ir.

PMID: 33268180
DOI: 10.1016/j.foodchem.2020.128398

Abstract

Gluten protein as one of the plant resources is susceptible to genetic, physical, chemical, enzymatic and engineering modifications. Chemical modifications have myriad advantages over other treatments, including short reaction times, low cost, no requirement for specialized equipment, and highly clear modification effects. Therefore, chemical modification of gluten can be mainly conducted via acylation, glycosylation, phosphorylation, and deamidation. The present review investigated the impact of different chemical compounds on conformations of gluten and its subunits. Moreover, their effects on the physico-chemical, morphological, and rheological properties of gluten and their subunits were studied. This allows for the use of gluten for a variety of purposes in the food and non-food industry.

Keywords: Chemical modifications; Conformation; Gluten; Physico-chemical properties.
A 47-year-old female presented with a lengthy history of dyspeptic symptoms, weight loss, and occasional diarrhea. A computed tomography (CT) scan showed several mesenteric nodular lesions, with peripheral calcifications, inversion of the fold pattern of the small intestine loops and an atrophic spleen.
Celiac disease can be predicted by high levels of tissue transglutaminase antibodies in children and adolescents with type 1 diabetes


Authors

Mara Cerqueiro Bybrant 1, Elin Udén 2, Filippa Frederiksen 3, Anna L Gustafsson 4, Carl-Göran Arvidsson 5, Anna-Lena Fureman 6, Gun Forsander 7 8, Helena Elding Larsson 9, Sten A Ivarsson 10, Marie Lindgren 10 11, Johnny Ludvigsson 12 13, Claude Marcus 14, Auste Pundziute Lycka 8, Martina Persson 15, Ulf Samuelsson 12 13, Stefan Särnblad 16, Karin Åkesson 17 18, Eva Örtqvist 1, Annelie Carlsson 10

Affiliations

1. Pediatric Endocrinology Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden.
2. Lund University, Lund, Sweden.
4. Children Clinic, Halland's Hospital, Halmstad, Sweden.
5. Department of Pediatrics, Västmanland's Hospital, Västerås, Sweden.
6. Children's clinic, Östersund Hospital, Sweden.
7. Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.
8. Department of Pediatrics, Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden.
9. Department of Clinical Sciences, Lund University/Clinical Research Centre, Skåne University Hospital, Malmö, Sweden.
10. Department of Clinical Sciences, Lund University, Skåne University Hospital, Pediatrics, Lund, Sweden.
12. Crown Princess Victoria's Children's and Youth Hospital, University Hospital, Linköping, Sweden.
Abstract

Objectives: Children with type 1 diabetes (T1D) are not included in guidelines regarding diagnosis criteria for celiac disease (CD) without a diagnostic biopsy, due to lack of data. We explored whether tissue transglutaminase antibodies (anti-tTG) that were ≥ 10 times the upper limit of normal (10× ULN) predicted CD in T1D.

Methods: Data from the Swedish prospective Better Diabetes Diagnosis study was used, and 2035 children and adolescents with T1D diagnosed between 2005-2010 were included. Of these, 32 had been diagnosed with CD before T1D. The children without CD were repeatedly screened for CD using anti-tTG antibodies of immunoglobulin type A. In addition, their human leukocyte antigen (HLA) were genotyped. All children with positive anti-tTG were advised to undergo biopsy. Biopsies were performed on 119 children and graded using the Marsh-Oberhüber classification.

Results: All of the 60 children with anti-tTG ≥10x ULN had CD verified by biopsies. The degree of mucosal damage correlated with anti-tTG levels. Among 2003 screened children, 6.9% had positive anti-tTG and 5.6% were confirmed CD. The overall CD prevalence, when including the 32 children with CD before T1D, was 7.0% (145/2035). All but one of the children diagnosed with CD had HLA-DQ2 and/or DQ8.
Conclusions: As all screened children and adolescents with T1D with tissue transglutaminase antibodies above 10 times the positive value 10x ULN had CD, we propose that the guidelines for diagnosing CD in screened children, when biopsies can be omitted, should also apply to children and adolescents with T1D as a noninvasive method.

Keywords: biopsy; celiac disease; screening; tissue transglutaminase antibodies; type 1 diabetes.

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- 37 references
- 3 figures

Full text links

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A Distinct EEG Marker of Celiac Disease-Related Cortical Myoclonus


Authors

Emily Swinkin 1, Karlo J Lizárraga 1 2, Musleh Algarni 1 3, Luis Garcia Dominguez 4, Julianne K Baarbe 5 6, James Saravanamuttu 5, Robert Chen 1 5, Elizabeth Slow 1, Anthony E Lang 1 5, Richard A Wennberg 4

Affiliations

1 Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital and Division of Neurology, UHN, Division of Neurology, University of Toronto, Toronto, Ontario, Canada.

2 Motor Physiology and Neuromodulation Program, Division of Movement Disorders and Center for Health and Technology (CHeT), Department of Neurology, University of Rochester, Rochester, New York, USA.
Abstract

**Background:** Celiac disease is associated with motor cortex hyperexcitability and neurological manifestations including cortical myoclonus. Electroencephalography abnormalities have been described, but no distinct pattern has been reported.

**Methods:** We describe the neurophysiological characteristics of 3 patients with celiac-associated cortical myoclonus using electroencephalography, magnetoencephalography, and transcranial magnetic stimulation.

**Results:** Electroencephalography in all cases demonstrated lateralized low-amplitude, electropositive beta-frequency polyspike activity over the central head region, corresponding to motor cortex contralateral to the myoclonic limb. Jerk-locked back-averaging demonstrated a preceding cortical potential; magnetoencephalography source localization revealed a cortical generator in the posterior wall of the precentral gyrus for the back-averaged potential and oscillatory abnormality. In 1 patient, cerebellar inhibition of the motor cortex was physiologically normal.

**Conclusions:** Central head oscillatory, low-amplitude, electropositive electroencephalography polyspike activity may be a distinct marker of celiac-related cortical myoclonus and is consistent with celiac-related motor cortex hyperexcitability, which may not necessarily result from cerebellar disinhibition. © 2020 International Parkinson and Movement Disorder Society.
In this paper, the inhibitory effects of sorbitol on the collapse of gluten network and textural deterioration of fresh noodles during storage were investigated, based on the changes in macroscopic and microscopic characteristics of gluten protein. Appropriate addition (≤2%) of sorbitol
increased dough viscoelasticity and extension energy. Sorbitol significantly inhibited the increase of cooking loss and adhesiveness of fresh noodles, and the decrease of hardness, springiness, LA-SRC value, and GMP weight during storage. SEM images showed that sorbitol retarded the deterioration of gluten network, with maintained continuous and ordered structure after 48 h. Sorbitol enhanced the hydrogen bond interactions in gluten system and promoted dynamic depolymerization and repolymerization of gluten protein molecules during processing and cooking, this may induce the texture stability. Sorbitol as a low-molecular polyol can inhibit the deterioration in gluten network and fresh noodle texture during storage, although showing no influence on the growth of microorganisms.

**Keywords:** Fresh noodle; Gluten collapse; Repolymerization; Sorbitol; Texture.

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**Full text links**

131. [Endovascular Treatment of Giant Celiac Artery Aneurysm in Behcet's Disease](https://doi.org/10.1177/1538574420975906)


**Authors**

Arika Dwivedi ¹, Erik Wayne ², Daisy Sangroula ², Abindra Sigdel ²

**Affiliations**

- ¹ Bioengineering, College of Engineering, 1848Northeastern University, Boston, MA, USA.
- ² 5170University of Louisville, Louisville, KY, USA.

- PMID: 33243094
- DOI: 10.1177/1538574420975906
Abstract

We report a case of a 17-year-old male with Behcet's disease (BD) with giant celiac artery aneurysm and impending rupture. Over the past 8 weeks, patient began having intermittent back and abdominal pain that worsened and became persistent over the past few days. This was accompanied by anorexia and non-bilious vomiting. Computed tomography angiogram (CTA) demonstrated a wide neck large celiac artery aneurysm (60 mm diameter). Endovascular repair of the aneurysm was performed using stent graft of the aorta and transcatheter coil embolization of the aneurysm sac. Technical success was confirmed by interruption of flow in the aneurysm, and preservation of distal native circulation at the conclusion of the procedure. One-week post-embolization, a CTA demonstrated complete thrombosis of the aneurysm. On follow-up CTA at 3, 6, and 12 months after embolization, the aneurysm has completely thrombosed and decreased in size to 24 mm. Patient remains asymptomatic till date.

Keywords: Behcet’s disease; celiac artery aneurysm; endovascular; transcatheter coil embolization.

Full text links

132. **Balanced by iron. Hereditary hemochromatosis and celiac disease**


Authors

Javier Jiménez Sánchez ¹, Miguel Ruiz Moreno ², Juan José Martínez Crespo ²

Affiliations

- ¹ Gastroenterología, Hospital General Universitario Reina Sofía, España.
- ² Aparato Digestivo, Hospital General Universitario Reina Sofía, España.
We present the case of a healthy 14-year-old adolescent who was referred to our hospital for an incidental alteration of the iron profile (Fe 225 ug/dl, transferrin 186 mg/dl, IST 63.93 %, ferritin 253 ng/ml). The blood count, proteinogram and renal, lipid and liver function tests were in the normal range. Abdominal ultrasound was requested with no findings of interest. The genetic analysis for hereditary hemochromatosis (HH) confirmed that the patient was homozygous for the C282Y mutation.

Full text links

133. A serial SPECT-CT study in a celiac disease patient with cerebellar ataxia and psychiatric symptoms


Authors

Juliana J Schmidt ¹, Guilherme J Schmidt ², Julio C Tolentino ², Eunice N Simoes ², Angela Obongo ³, Yolanda Tolentino ², Francisco A Coelho ⁴, Maria C P P Landesmann ⁴, Lea M B Fonseca ⁴, Glenda C B Lacerda ², Sergio L Schmidt ²

Affiliations

¹ Department of Neurology, Federal University of the State of Rio de Janeiro, Mariz and Barros street, 775, Tijuca, Rio de Janeiro, RJ, 20270-001, Brazil. julianaschmidtjaneiro@gmail.com.
Abstract

Celiac disease (CD) is an immune-mediated systemic disorder triggered by gluten and related prolamins in genetically predisposed individuals. Here, we described a case of a 31-year-old Caucasian woman who exhibited cerebellar and psychiatric dysfunctions. The patient underwent single-photon emission computed tomography (SPECT-CT) before and after a gluten-free diet (GFD). There was an improvement in cerebellar perfusion accompanied by a remission of cerebellar manifestations. The maintenance of the psychiatric manifestations was related to the persistence of the hypoperfusion in the frontal lobes. The patient's psychiatric symptoms did not change after 4 months under a GFD in the hospital. To our knowledge, this is the first case that shows the relationship between improvement in cerebellar perfusion and remission of cerebellar clinical manifestations in a CD patient under a GFD.

Keywords: Celiac disease; Cerebellar perfusion; Cerebellum; SPECT-CT.

Full text links

Is Celiac Disease Testing Necessary in Functional Abdominal Disorders? A Study in Predominantly Latino Children
Abstract

**Background:** Functional abdominal pain disorders (FAPDs) are among the most common causes of consultation in general pediatrics and pediatric gastroenterology. The Rome IV criteria recommend testing for celiac disease (CD) in children with irritable bowel syndrome-diarrhea (IBS-D) and leaves testing in cases of other FAPDs to the practitioner's discretion. These recommendations were based on a single study that showed a 4-fold increase of CD among patients with IBS in Italy. It is unclear if these findings can be extrapolated to other populations. Understanding whether those results are reproducible in areas with different racial/ethnic backgrounds can optimize patient care.

**Aim:** The aim of the study was to assess the prevalence of CD in a sample of children consulting for FAPDs to a tertiary care center in Miami.

**Methods:** The charts of all pediatric patients consulting for FAPDs from January 2016 to November 2019 at the University of Miami were reviewed. Demographics, diagnosis, and CD testing for each child were analyzed.

**Results:** One hundred eighty-one children with FAPDs and celiac testing were seen. Mean age of 12.89 years, girls 61.34%. 84 (46.40%) had a diagnosis of IBS and 97 (53.59%) had a diagnosis of other FAPD. One of 181 children with
FAPDs (0/84 with IBS and 1/97 with other FAPDs) had positive CD serological testing and EGD confirmation.

**Conclusions:** Our study suggests that the prevalence of CD among children with FAPDs is similar to the community prevalence. This data questions the benefit of testing all children FAPDS (including IBS) for CD. Studies with larger sample size and various racial/ethnic makeup should be done to confirm our findings.

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**Conflict of interest statement**

The authors report no conflicts of interest.

- 15 references

**Full text links**

135. Proteolysis efficiency and structural traits of corn gluten meal: Impact of different frequency modes of a low-power density ultrasound


**Authors**

Yang Wang ¹, Zhaoli Zhang ¹, Ronghai He ², Benjamin Kumah Mintah ², Mokhtar Dabbour ³, Wenjuan Qu ², Dandan Liu ², Haile Ma ⁴

**Affiliations**
Abstract

The influence of varying frequency modes of a low-power density ultrasound (LPDU) on the enzymolysis efficacy and structural property of corn gluten meal (CGM) was investigated. Sonication pretreatment (of CGM) with sequential and simultaneous duple-frequency modes enhanced notably the relative enzymolysis efficiency, compared to other LPDU frequency modes. With a sequential duple-frequency of 20/40 kHz showing the most significant effect, the maximum value of enzymolysis efficiency and protein dissolution rate were 15.99% and 61.69%, respectively. Changes in the surface hydrophobicity, secondary structure and microstructure revealed alterations of conformation of CGM by ultrasound-induced effect. Furthermore, the molecular weight distribution CGM hydrolysates primarily distributed in 200-500 Da following ultrasonication. Sonication efficaciously enhanced the susceptibility of CGM to alcalase proteolysis. Thus, the use of various LPDU frequency modes in pretreating target proteins (CGM) may be considered as a practical approach to improve protein-enzyme reactions (proteolysis).

Keywords: Corn gluten meal; Enzymolysis; Frequency modes; Low-power density ultrasound; Microstructure; Surface hydrophobicity.
Abstract

Background: High-volume systemic-to-pulmonary ductus arteriosus shunts in premature infants are associated with adverse neonatal outcomes. The role of an atrial communication (AC) in modulating the effects of a presumed hemodynamically significant patent ductus arteriosus (PDA) is poorly studied.
The objective of this study was to characterize the relationship between early AC and echocardiographic indices of PDA shunt volume and clinical neonatal outcomes.

**Methods:** A retrospective review of preterm infants (born at <32 weeks' gestation) who underwent echocardiography in the first postnatal week was performed. The cohort was divided into four groups on the basis of presence of a presumed hemodynamically significant PDA (≥1.5 vs <1.5 mm) and AC size (≤1 vs >1 mm), and echocardiographic measures of PDA shunt volume were then compared. Clinical outcomes, including chronic lung disease and intraventricular hemorrhage, were also compared among all four groups.

**Results:** A total of 199 preterm infants (mean birth weight, 928 ± 632 g; mean gestational age, 26.6 ± 1.5 weeks) were identified; 159 infants had PDAs ≥ 1.5 mm, of whom 52 had ACs ≤ 1 mm and 107 had ACs > 1 mm. The remaining 40 infants had PDAs < 1.5 mm, of whom 23 had ACs ≤ 1 mm and 17 had ACs > 1 mm. Infants with PDAs ≥ 1.5 mm and ACs > 1 mm had higher pulmonary vein D-wave velocities (P < .05), higher left ventricular output (P < .005), higher PDA scores (P < .001), and increased rates of reversed diastolic flow in the descending aorta (P < .001), celiac artery (P < .001), and middle cerebral artery (P < .001) than infants with either PDAs < 1.5 mm or PDAs ≥ 1.5 mm and ACs ≤ 1 mm. There was no difference in the incidence of intraventricular hemorrhage, but infants with PDAs ≥ 1.5 mm and ACs > 1 mm had a higher risk for a composite outcome of chronic lung disease or death before hospital discharge (P < .05).

**Conclusions:** Echocardiographic evidence of ACs > 1 mm in patients with PDAs ≥ 1.5 mm during the first postnatal week may be a marker of a more pathologic hemodynamically significant PDA in premature infants. Future investigations should evaluate if early identification and treatment of patients with both high-volume PDAs and larger atrial-level communications may help mitigate adverse outcomes, such as chronic lung disease or death, in this high-risk patient population.

**Keywords:** Atrial septal defect; Chronic lung disease; Echocardiography; Hemodynamics; Patent ductus arteriosus; Prematurity; Shunt volume.

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Conflict of interest statement

Declaration of Interests: None

Full text links

137. Celiac axis stenosis and digestive disease: Diagnosis, consequences and management


Authors

J Dembinski ¹, B Robert ², M-A Sevestre ³, M Freyermuth ⁴, T Yzet ², S Dokmak ⁵, J-M Regimbeau ⁶

Affiliations

¹ Department of Digestive Surgery, University Hospital of Amiens Picardie et Université de Picardie Jules Verne, 1, rue du Professeur Christian Cabrol, 80054 Amiens, France; Clinical research unit SSPC (Simplifications des Soins des Patients Complexes) UR UPJV 7518, University of Picardie Jules Verne, Amiens, France.
² Radiology Department, University Hospital of Amiens Picardie and Picardie Jules Verne University, Amiens, France.
³ Vascular Medicine Department, University Hospital of Amiens Picardie and Picardie Jules Verne University, Amiens, France.
⁴ Vascular Surgery Department, University Hospital of Amiens Picardie and Picardie Jules Verne University, Amiens, France.
⁵ Department of Hepatobiliary Surgery and Liver Transplantation, Assistance Publique-Hôpitaux de Paris and Paris University, Clichy, France.
⁶ Department of Digestive Surgery, University Hospital of Amiens Picardie et Université de Picardie Jules Verne, 1, rue du Professeur Christian Cabrol, 80054 Amiens, France; Clinical research unit SSPC (Simplifications des Soins des Patients Complexes) UR UPJV 7518,
Abstract

Arterial blood flow to the organs of the upper abdomen is provided by the celiac axis (CA) and the superior mesenteric artery (SMA) that communicate between each other via the gastro-duodenal artery, the anterior and posterior pancreatico-duodenal arcades, the branches of the dorsal pancreatic artery and inconsistently, though a supplementary arcade that connects the CA and the SMA (arcade of Bühler). Celiac axis stenosis may or may not have a hemodynamic impact on the splanchnic circulation. Hemodynamically significant CA stenosis can be asymptomatic, or symptomatic with variables clinical consequences. Management depends on whether the mechanism of stenosis is extrinsic or intrinsic. When upper gastrointestinal interventional radiology or surgery is indicated, stenosis can pose technical difficulties or create severe ischemia requiring good understanding of this entity in the planning of operative steps and adapted management. Management of CA stenosis is therefore multidisciplinary and may involve interventional radiologists, gastrointestinal surgeons, vascular surgeons as well as medical physicians. Even though the prevalence of CA stenosis is relatively low (between 5 and 10%) and irrespective of its etiology, surgeons, radiologists and physicians must be aware of it because it can intervene in the management of upper gastrointestinal disease. It must be sought, and treatment must be adapted to each particular situation to avoid potentially severe complications.

Keywords: Atheromatous stenosis; Celiac axis; Median arcuate ligament.
Postural Orthostatic Tachycardia Syndrome and Disordered Eating: Clarifying the Overlap


Authors

Julia Benjamin ¹, Leslie Sim ¹, Michele Tsai Owens ², Andrea Schwichtenberg ³, Tracy Harrison ⁴, Cindy Harbeck-Weber ¹

Affiliations

¹ Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN. Dr. Benjamin is now with the Department of Health Psychology, American Family Children's Hospital - UW Health, Madison, WI.
² Department of Anesthesiology and Pain Medicine, Division of Pain Medicine, Seattle Children's Hospital, University of Washington Medicine, Seattle, WA.
³ Department of Nursing, Mayo Clinic, Rochester, MN.
⁴ Department of Anesthesiology, Division of Pain Medicine, Mayo Clinic, Rochester, MN.

PMID: 33181565
DOI: 10.1097/DBP.0000000000000886

Abstract

Objective: Postural orthostatic tachycardia syndrome (POTS) is estimated to occur in up to 1% of adolescents, with symptoms of dizziness, fatigue, and pain impacting daily functioning. However, many risk factors and symptoms for POTS overlap with those of youth with disordered eating, and adolescents with POTS may be at increased risk for developing eating disorders. Therefore, the present study sought to better understand this overlap. We hypothesized that patients with POTS would have higher than expected rates of weight change, restrictive eating patterns, and food sensitivities.
Methods: We conducted a retrospective chart review of 96 adolescents and young adults diagnosed with POTS who were participating in a 3-week intensive interdisciplinary pain rehabilitation program. We conducted descriptive and correlational statistical analyses on data from self-report measures, biomarkers of nutritional status, and abstracted information about eating and weight concerns from medical notes.

Results: Nearly 3 quarters of participants described engaging in restrictive eating, and more than half of them described experiencing weight loss. They also endorsed experiencing food allergies, celiac disease, and eating disorder at higher rates than would be expected in the general population. One-fifth of the sample had experienced invasive interventions to correct for nutritional imbalances, such as having a feeding tube.

Conclusion: Weight and eating are clear areas of risk for patients with orthostatic intolerance. It is essential that treatment team members thoroughly screen for eating disturbances and make recommendations that support regular and balanced eating habits.

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Conflict of interest statement

Disclosure: The authors declare no conflict of interest.

• 30 references

Full text links

Optimization of gluten-free sponge cake fortified with whey protein concentrate using mixture design methodology

Abstract

This study aimed to optimize mixtures of whey protein concentrate (WPC) and two flours of rice and maize flours for the production of gluten-free sponge cakes. This was obtained by using mixture design methodology. WPC incorporation had positive effects on specific volume and baking loss of cakes, whilst, their incorporation increased their hardness. Considering all cakes properties, two formulas F1 (78.5% Maize, 15% Rice and 6.5% WPC) and F2 (82.4% Maize, 12% Rice and 5.6% WPC) were optimized using a mixture design. The microstructure F1 was more organized and very well structured with smaller aggregates. According to the organoleptic evaluation, F1 was also most appreciated by the tasting panel. The findings of the present study indicated that maize and rice flours, and WPC could be used as a substitute for wheat flour in producing sponge cakes of high quality.
Accuracy of a no-biopsy approach for the diagnosis of coeliac disease across different adult cohorts


Authors

Hugo A Penny 1, Suneil A Raju 1, Michelle S Lau 1, Lauren Js Marks 1, Elisabeth Mr Baggus 1, Julio C Bai 2, Gabrio Bassotti 3, Hetty J Bontkes 4, Antonio Carroccio 5, Mihai Danciu 6, Mohammad H Derakhshan 7, Arzu Ensari 8, Azita Ganji 9, Peter H R Green 10, Matt W Johnson 11, Saeid Ishaq 12, Benjamin Lebwohl 10, Adam Levene 11, Roxana Maxim 13, Hamid Mohaghegh Shalmani 14, Mohammad Rostami-Nejad 14, David Rowlands 15, Irene A Spiridon 6, Amitabh Srivastava 16, Umberto Volta 17, Vincenzo Villanacci 18, Graeme Wild 1, Simon S Cross 1, Kamran Rostami 19, David S Sanders 20

Affiliations

1 Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK.
2 Medicine, Gastroenterology Hospital 'Dr C Bonorino Udaondo', Buenos Aires, Argentina.
3 Gastroenterology & Hepatology Section, Department of Medicine, University of Perugia Medical School, Perugia, Italy.
4 Department Clinical Chemistry, Amsterdam Gastroenterology and Metabolism and Infection and Immunity Institutes, Amsterdam UMC, Amsterdam, The Netherlands.
• 5 Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy.
• 6 Pathology Department, Grigore T. Popa University of Medicine and Pharmacy Iasi, Iasi, Romania.
• 7 Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK.
• 8 Department of Pathology, Ankara University Medical School, Ankara, Turkey.
• 9 Department of Gastroenterology and Hepatology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
• 10 Celiac Disease Center, Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, USA.
• 11 Gastroenterology, Luton and Dunstable Hospital NHS Foundation Trust, Luton, UK.
• 12 Department of Gastroenterology, Dudley Group NHS Foundation Trust, Birmingham City University, Birmingham, UK.
• 13 Gastroenterology Department, Grigore T. Popa University of Medicine and Pharmacy Iasi, Iasi, Romania.
• 14 Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
• 15 Department of Gastroenterology, Queen Elizabeth II Hospital, Hertfordshire, UK.
• 16 Pathology, Brigham and Women's Hospital, Boston, Massachusetts, USA.
• 17 Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy.
• 18 Department of Pathology, Spedali Civili, Brescia, Italy.
• 19 Department of Gastroenterology, MidCentral District Health Board, Palmerston North, New Zealand.
• 20 Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK david.sanders1@nhs.net.

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• DOI: 10.1136/gutjnl-2020-320913

Free PMC article
Abstract

Objective: We aimed to determine the predictive capacity and diagnostic yield of a 10-fold increase in serum IgA antitissue transglutaminase (tTG) antibody levels for detecting small intestinal injury diagnostic of coeliac disease (CD) in adult patients.

Design: The study comprised three adult cohorts. Cohort 1: 740 patients assessed in the specialist CD clinic at a UK centre; cohort 2: 532 patients with low suspicion for CD referred for upper GI endoscopy at a UK centre; cohort 3: 145 patients with raised tTG titres from multiple international sites. Marsh 3 histology was used as a reference standard against which we determined the performance characteristics of an IgA tTG titre of ≥10×ULN for a diagnosis of CD.

Results: Cohort 1: the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for IgA tTG levels of ≥10×ULN at identifying individuals with Marsh 3 lesions were 54.0%, 90.0%, 98.7% and 12.5%, respectively. Cohort 2: the sensitivity, specificity, PPV and NPV for IgA tTG levels of ≥10×ULN at identifying individuals with Marsh 3 lesions were 50.0%, 100.0%, 100.0% and 98.3%, respectively. Cohort 3: the sensitivity, specificity, PPV and NPV for IgA tTG levels of ≥10×ULN at identifying individuals with Marsh 3 lesions were 30.0%, 83.0%, 95.2% and 9.5%, respectively.

Conclusion: Our results show that IgA tTG titres of ≥10×ULN have a strong predictive value at identifying adults with intestinal changes diagnostic of CD. This study supports the use of a no-biopsy approach for the diagnosis of adult CD.

Keywords: coeliac disease.

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Conflict of interest statement

Competing interests: DSS receives an educational grant from Dr Schär (a gluten-free food manufacturer). PHRG serves on the advisory board of
ImmusanT, Cellimmune and ImmunogenX, and is an unpaid member of Nima’s Scientific Advisory Board. The remaining authors disclose no conflicts.

- Cited by 4 articles
- 43 references
- 5 figures

Full text links

141. **Influence of ε-poly-l-lysine treated yeast on gluten polymerization and freeze-thaw tolerance of frozen dough**


**Authors**

Lu Lu ¹, Jun-Jie Xing ¹, Zhen Yang ¹, Xiao-Na Guo ¹, Ke-Xue Zhu ²

**Affiliations**

- ¹ State Key Laboratory of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, Jiangsu Province, PR China; School of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, Jiangsu Province, PR China.
- ² State Key Laboratory of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, Jiangsu Province, PR China; School of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, Jiangsu Province, PR China. Electronic address: kxzhu@jiangnan.edu.cn.

- PMID: 33127224
- DOI: 10.1016/j.foodchem.2020.128440
Abstract

The effects of ε-poly-L-lysine (ε-PL) treated yeast on gluten polymerization of frozen dough and quality of steamed bread after freeze-thaw cycles were investigated. Compared with steamed bread made from frozen dough containing ε-PL and untreated yeast (PUTY) or only untreated yeast, steamed bread made from frozen dough containing ε-PL treated yeast (PTY) had a larger specific volume, lower hardness and more porous. A dynamic rheological and scanning electron microscopic analysis demonstrated that using PTY instead of yeast could reduce dough elasticity and damage protein network after freeze-thaw cycles. Lower sodium dodecyl sulfate (SDS) soluble polymeric proteins and monomeric proteins, and higher SDS insoluble proteins were found in frozen dough containing PTY, which indicates a reduced depolymerization of gluten proteins after freeze-thaw cycles. After 4 freeze-thaw cycles, the lower glutathione and free sulphydryl in dough containing PTY indicate that the interchain disulfide bonds between proteins were preserved.

Keywords: Freeze–thaw cycles; Frozen dough; Gluten polymerization; ε-Poly-L-lysine treated yeast.

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Full text links

Clinical Characteristics and Management of 50 Patients with Anti-GAD Ataxia: Gluten-Free Diet Has a Major Impact


Authors

M Hadjivassiliou 1, P G Sarrigiannis 2, P D Shanmugarajah 2, D S Sanders 2, R A Grünewald 2, P Zis 2, N Hoggard 2 3
Abstract

The objective of this study is to report the clinical characteristics and treatment of patients with progressive cerebellar ataxia associated with anti-GAD antibodies. We performed a retrospective review of all patients with anti-GAD ataxia managed at the Sheffield Ataxia Centre over the last 25 years. We identified 50 patients (62% females) with anti-GAD ataxia. The prevalence was 2.5% amongst 2000 patients with progressive ataxia of various causes. Mean age at onset was 55 and mean duration 8 years. Gaze-evoked nystagmus was present in 26%, cerebellar dysarthria in 26%, limb ataxia in 44% and gait ataxia in 100%. Nine patients (18%) had severe, 12 (24%) moderate and 29 (58%) mild ataxia. Ninety percent of patients had a history of additional autoimmune diseases. Family history of autoimmune diseases was seen in 52%. Baseline MR spectroscopy of the vermis was abnormal at presentation in 72%. Thirty-five patients (70%) had serological evidence of gluten sensitivity. All 35 went on gluten-free diet (GFD). Eighteen (51%) improved, 13 (37%) stabilised, 3 have started the GFD too recently to draw conclusions and one deteriorated. Mycophenolate was used in 16 patients, 7 (44%) improved, 2 stabilised, 6 have started the medication too recently to draw conclusions and one did not tolerate the drug. There is considerable overlap between anti-GAD ataxia and gluten ataxia. For those patients with both, strict GFD alone can be an
effective treatment. Patients with anti-GAD ataxia and no gluten sensitivity respond well to immunosuppression.

**Keywords**: Anti-GAD Ataxia; Gluten Ataxia; Gluten Free Diet; Immune Ataxia; MR Spectroscopy.

**Conflict of interest statement**

The authors declare that they have no conflict of interest.

- Cited by 3 articles
- 30 references
- 2 figures

**Full text links**

143. *Modified Appleby Procedure, Distal Splenopancreatectomy with Celiac Axis Resection*


**Authors**

Haitham Triki¹, Damien Bergeat¹ ² ³, Marie Bougard¹, Fabien Robin¹ ³ ⁴, Laurent Sulpice⁵ ⁶ ⁷ ⁸

**Affiliations**

- ¹ CHU Rennes, Service de Chirurgie Hépatobiliaire et Digestive, Hôpital Pontchaillou, Centre Hospitalier Universitaire, Université de Rennes 1, Rennes, France.
- ² UMR NuMeCan (Nutrition, Métabolismes, Cancer), INRA, ALICE, St Gilles, France.
- ³ University of Rennes, Rennes, France.
- ⁴ UMR NuMeCan, INSERM U1241, Rennes, France.
Abstract

**Background:** Modified Appleby procedure could be indicated in stage III locally advanced body pancreatic ductal adenocarcinoma (PDAC) involving the celiac axis after neoadjuvant treatment.

**Patients and methods:** We report the case of a 38-year-old woman presenting a tumor arising from the body of the pancreas, involving the celiac trunk with the common hepatic artery and having contact with the anterior surface of the superior mesenteric artery. A fine-needle aspirate biopsy confirmed the diagnosis of PADC. Eight cycles of FOLFIRINOX followed by chemoradiotherapy (50.4 Gy) were conducted. After 6 months, the CA19-9 levels were normalized, and the tumor remained stable without local growth or distant metastasis. To reduce the risk of ischemia-related complications and develop the pancreaticoduodenal arcades, a preoperative embolization of the common hepatic artery was performed. Then, surgical resection was considered 4 weeks after embolization.

**Results:** The patient underwent a modified Appleby procedure including distal splenopancreatectomy with en bloc celiac axis resection combined with lateral portal vein resection. Venous reconstruction was carried out using peritoneal patch.1 Pathologic evaluation revealed a 2.5-cm PDAC with negative resection margins. Postoperative course was marked by acute ischemic cholecystitis requiring reoperation at postoperative day 3. The treatment was completed with four cycles of FOLFIRINOX, and she was free of disease 6 months after surgery.
Conclusions: Nowadays, modified Appleby procedure is more frequently performed due to improvements in responses to chemotherapy and radiotherapy which have led to better local control and more aggressive approaches in highly selected patients.

- 1 reference

Full text links

144. Insight into the advantages of premixing yeast-wheat gluten and combining ultrasound and transglutaminase pretreatments in producing umami enzymatic protein hydrolysates


Authors

Guowan Su 1, Xin Zheng 1, Jin Zou 1, Geoffrey Ivan Neil Waterhouse 2, Dongxiao Sun-Waterhouse 3

Affiliations

- 1 School of Food Science and Engineering, South China University of Technology, Guangzhou 510640, China; Guangdong Food Green Processing and Nutrition Regulation Technologies Research Center, Guangzhou 510650, China.
- 2 School of Chemical Sciences, University of Auckland, Auckland 1142, New Zealand.
- 3 School of Food Science and Engineering, South China University of Technology, Guangzhou 510640, China; Guangdong Food Green Processing and Nutrition Regulation Technologies Research Center, Guangzhou 510650, China; School of Chemical Sciences, University of...
Abstract

This study aimed to utilize effectively industrial byproducts, yeast suspension (Y) and wheat gluten (W), to produce umami protein hydrolysates as seasonings. Y and W were mixed to yield YW, followed by a pretreatment (ultrasound, transglutaminase (TG), or their combination) and then proteolysis with a yeast extract enzyme and trypsin. Premixing Y and W promoted their dispersibility, and suppressed gluten aggregation and hydrolysate's bitterness. All pretreatments increased protein recovery. Ultrasound alone or ultrasound with TG increased the embedding of yeasts in W, umami and salty tastes, hydrolysis degree and proportion of molecules < 3 kDa of the YW hydrolysate. For the first time, premixing Y and W, and pretreating YW (by ultrasound then TG-catalyzed protein crosslinking), were found to increase the β-sheet and random coil contents and decreased the β-turn content and surface hydrophobicity, leading to a low-cost umami and non-bitter protein hydrolysate with 56% of species < 1 kDa.

Keywords: Byproduct utilization; Enzymatic crosslinking; Proteolysis; Seasoning; Secondary structure.

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Full text links

145. Autoimmunity Features in Patients With Non-Celiac Wheat Sensitivity

Abstract

Introduction: Nonceliac wheat sensitivity (NCWS) is characterized by intestinal and extraintestinal manifestations consequent to wheat ingestion in subjects without celiac disease and wheat allergy. Few studies investigated the
relationship between NCWS and autoimmunity. The aim of this study is to evaluate the frequency of autoimmune diseases (ADs) and autoantibodies in patients with NCWS.

**Methods:** Ninety-one patients (13 men and 78 women; mean age of 40.9 years) with NCWS, recruited in a single center, were included. Seventy-six healthy blood donors (HBD) and 55 patients with a diagnosis of irritable bowel syndrome (IBS) unrelated to NCWS served as controls. Autoantibodies levels were measured. Human leukocyte antigen haplotypes were determined, and duodenal histology performed in all patients carrying the DQ2/DQ8 haplotypes. Participants completed a questionnaire, and their medical records were reviewed to identify those with ADs.

**Results:** Twenty-three patients with NCWS (25.3%) presented with ADs; autoimmune thyroiditis (16 patients, 17.6%) was the most frequent. The frequency of ADs was higher in patients with NCWS than in HBD (P = 0.002) and in patients with IBS (P = 0.05). In the NCWS group, antinuclear antibodies tested positive in 71.4% vs HBD 19.7%, and vs patients with IBS 21.8% (P < 0.0001 for both). The frequency of extractable nuclear antigen antibody (ENA) positivity was significantly higher in patients with NCWS (21.9%) than in HBD (0%) and patients with IBS (3.6%) (P = 0.0001 and P = 0.004, respectively). Among the patients with NCWS, 9.9% tested positive for antithyroglobulin, 16.5% for antithyroid peroxidase, and 14.3% for antiparietal cell antibodies; frequencies were not statistically different from controls. The presence of ADs was related to older age at NCWS diagnosis, female sex, duodenal lymphocytosis, and eosinophil infiltration.

**Discussion:** One in 4 patients with NCWS suffered from AD, and serum antinuclear antibodies were positive in a very high percentage of cases. These data led us to consider NCWS to be associated to ADs.

**Trial registration:** ClinicalTrials.gov NCT02248545.

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- 36 references

**Full text links**
Feasibility and effects on the gut microbiota of a 12-week high-intensity interval training plus lifestyle education intervention on inactive adults with celiac disease


Authors

Cassandra Warbeck ¹, A Justine Dowd ¹, Liam Kronlund ¹, Candice Parmar ¹, Julia T Daun ¹, Kathryn Wytsma-Fisher ¹, Guillaume Y Millet ², Alana Schick ³, Raylene A Reimer ¹ 4 5, Tak Fung ⁶, S Nicole Culos-Reed ¹ ⁷

Affiliations

¹ Faculty of Kinesiology, University of Calgary, Calgary, AB T2N 1N4, Canada.
² Univ Lyon, UJM-Saint-Etienne, Inter-university Laboratory of Human Movement Biology, EA 7424, F-42023, Saint-Etienne, France.
³ International Microbiome Centre, Snyder Institute for Chronic Diseases, University of Calgary, Calgary, AB T2N 1N4, Canada.
⁴ Department of Biochemistry and Molecular Biology, Cumming School of Medicine, University of Calgary, Calgary, AB T2N 1N4, Canada.
⁵ Alberta Children's Hospital Research Institute, Calgary, AB T3B 6A8, Canada.
⁶ Research Computing Services, Information Technologies, University of Calgary, Calgary, AB T2N 1N4, Canada.
⁷ Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB T2N 1N4, Canada.

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DOI: 10.1139/apnm-2020-0459
Abstract

This study assessed the feasibility and benefits of high-intensity interval training (HIIT) plus lifestyle education among inactive adults with celiac disease. Forty-one participants were randomized to receive the intervention (HIIT plus lifestyle education; HIIT+) for 12 weeks or waitlist control (WLC). Testing was completed at baseline, immediately post-intervention, and 3 months post-intervention. Generalized estimating equations were used to assess changes in the outcome variables over time between the groups. Mean percent of age-predicted maximum heart rate was 97.9% and average rating of perceived exertion was 6.33 (out of 10) during HIIT intervals. Following the intervention, the HIIT+ showed enrichment in relative abundance of Parabacteroides and Defluviitaleaceae_UCG_011 while WLC showed enrichment in relative abundance of Roseburia intestinalis, Klebsiella, and Adlercreutzia. A unique set of taxa were differentially abundant between the groups at 3 months post-intervention. HIIT+ participants experienced a reduction in resting heart rate (-6.6 bpm) immediately post-intervention compared with WLC. Further research is needed to establish an optimal HIIT protocol that may improve maximal oxygen uptake and metabolic syndrome biomarkers. Findings from this pilot study provide preliminary evidence that an HIIT intervention is feasible for inactive adults with celiac disease and leads to favourable changes in resting heart rate alongside potentially beneficial shifts in gut microbiota. Trial registration number: ClinicalTrials.gov number NCT03520244. Novelty: HIIT leads to potentially beneficial changes in the gut microbiota of adults with celiac disease. An HIIT exercise intervention is feasible and well tolerated for patients with celiac disease.

Keywords: celiac disease; entraînement par intervalles à haute intensité; gastro-intestinal; gastrointestinal; gut health; gut microbiota; high-intensity interval training; intervention d’éducation au mode de vie; lifestyle education intervention; maladie coeliaque; metabolic syndrome; microbiote intestinal; santé intestinale; syndrome métabolique.

Full text links
[Diagnosis of celiac disease in clinical practice: present and future]

[Article in Spanish]

Authors

Elena Crehuá-Gaudiza 1, Ana Barrés Fernández 2, Carmen Jovani Casano 3, María Latorre Tejerina 3, Ester María Largo Blanco 4, María Antonia Moreno Ruiz 5, Alicia Berghezan Suárez 6, Mónica García-Peris 7, Raquel Gil Piquer 7, Alicia Coret Sinisterra 8, Sandra Martínez-Barona 9, Cristina Salido-Capilla 10, María Ángeles Requena Fernández 11, José Vicente Arcos-Machancoses 12, Cecilia Martinez-Costa 2

Affiliations

• 1 Sección Gastroenterología y Nutrición Pediátrica, Hospital Clínico Universitario, Valencia, España. Electronic address: elenacrehua@gmail.com.
• 2 Sección Gastroenterología y Nutrición Pediátrica, Hospital Clínico Universitario, Valencia, España.
• 3 Sección Gastroenterología y Nutrición Pediátrica, Hospital General de Castellón, Castellón de la Plana, España.
• 4 Servicio de Pediatría, Consorcio Hospital General Universitario de Valencia, Valencia, España.
• 5 Servicio de Pediatría, Hospital de Manises, Manises (Valencia), España.
• 6 Servicio de Pediatría, Hospital de Denia, Denia (Alicante), España.
• 7 Servicio de Pediatría, Hospital Lluís Alcanyís de Xàtiva, Silla (Valencia), España.
• 8 Servicio de Pediatría, Hospital de Sagunto, Sagunto (Valencia), España.
• 9 Servicio de Pediatría, Hospital General de Requena, Requena (Valencia), España.
• 10 Servicio de Pediatría, Hospital Universitario La Plana, Villarreal (Castellón), España.
• 11 Servicio de Pediatría, Hospital de Hellín. Calle Juan Ramón Jiménez, Hellín (Albacete), España.
Abstract

**Introduction:** European guidelines for the diagnosis of celiac disease (CD) have been updated in 2020. The primary objective was to review the compliance with the diagnostic criteria for CD, according to ESPGHAN 2012. Secondarily, to describe the clinical characteristics of the patients and to assess the changes that would be implied by the application of the new 2020 criteria.

**Patients and methods:** Retrospective multicenter study in which 10 centers participated. Patients from 0 to 16 years old with a new diagnosis of CD in 2018-2019 were included. Clinical, serological variables and the performance of intestinal biopsy (IB) were collected.

**Results:** 163 patients were included (57% female) with a median age of 7.6 years (SD 4.4). The form of presentation was: 47.8% classical, 30.7% no classical and 21.5% asymptomatic, with differences depending on age. Total IgA and anti-transglutaminase IgA antibodies were performed in all centers as the first diagnostic step. IgA anti-endomysial antibodies (EMA) were performed in 80%, and HLA haplotype in 95%. Of the total, 78 cases (47.9%) met criteria for not performing intestinal biopsy (IB). IB was indicated in the remaining 85 patients, but was not performed in 29 cases (17.8%). The performance of IB was lower in the secondary hospitals than in the tertiary ones (p < 0.05). If we applied the ESPGHAN 2020 criteria, we would disregard the HLA study, and 21 more patients would not have required IB (going from 47.9% to 60.7% of the total).

**Conclusions:** Discrepancies are observed in the application of the ESPGHAN 2012 diagnostic criteria due to the different accessibility to EMA and endoscopic IB in secondary centers. With the ESPGHAN-2020 criteria, around 60% of patients will be able to be diagnosed without IB, provided that the determination of EMA is ensured.
Family socio-economic status and childhood coeliac disease seem to be unrelated-A cross-sectional screening study


Authors

Fredrik Norström 1, Fredinah Namatovu 2, Annelie Carlsson 3, Lotta Högberg 4, Anneli Ivarsson 1, Anna Myléus 1 5

Affiliations

1 Department of Epidemiology and Global Health, Umeå University, Umeå, Sweden.
2 Department of Historical, Philosophical and Religious Studies, Umeå University, Umeå, Sweden.
3 Department of Pediatrics, Clinical Sciences, Skåne University Hospital, Lund University, Lund, Sweden.
4 Department of Paediatrics, Norrköping Hospital, Linköping University, Norrköping, Sweden.
5 Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden.

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PMCID: PMC7983879
DOI: 10.1111/apa.15562
Aim: The aim of our study was to examine whether there is a difference in coeliac disease prevalence in regard to parents' education level and occupation, and whether this differs between screened and clinically diagnosed children at the age of 12 years.

Methods: The study, Exploring the Iceberg of Celiacs in Sweden (ETICS), was a school-based screening study of 12-year-old children that was undertaken during the school years 2005/2006 and 2009/2010. Data on parental education and occupation were reported from parents of the children. Specifically, by parents of 10 710 children without coeliac disease, 88 children diagnosed with coeliac disease through clinical care, and 231 who were diagnosed during the study.

Results: There were no statistically significant associations between occupation and coeliac disease for either the clinically detected (prevalence ratio 1.16; confidence interval 0.76-1.76) or screening-detected coeliac disease cases (prevalence ratio 0.86; confidence interval 0.66-1.12) in comparison with children with no coeliac disease. Also, there were no statistically significant associations for parental education and coeliac disease diagnosis.

Conclusion: There was no apparent relationship between coeliac disease and socio-economic position. Using parents' socio-economic status as a tool to help identify children more likely to have coeliac disease is not recommended.

Keywords: children; coeliac disease; education; occupation; screening.


Conflict of interest statement

The authors report no conflicts of interest.

- 28 references
Organic food consumption and gluten-free diet, is there a link? Results in French adults without coeliac disease


Authors

Laëtitia Perrin ¹, Benjamin Allès ¹, Chantal Julia ¹,², Serge Hercberg ¹,², Mathilde Touvier ¹, Denis Lairon ³, Julia Baudry ¹, Emmanuelle Kesse-Guyot ¹

Affiliations

¹ Université Sorbonne Paris Nord, CRESS - EREN (Nutritional Epidemiology Research Team) INSERM, INRA, CNAM, 74 rue Marcel Cachin, 93017Bobigny, France.
² Public Health Department, Avicenne Hospital, AP-HP, 93017Bobigny, France.
³ Aix Marseille Université, INSERM (U1062), INRA (U1260), C2VN, Faculté de Médecine de la Timone, 13005Marseille, France.

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Abstract

The rising popular belief that gluten is unhealthy has led to growth in gluten avoidance in people without coeliac disease. Little information is available on their dietary profiles and their dietary behaviours. Our aim was to compare the consumption of organic foods between gluten avoiders and non-avoiders, and their places of food purchase. We described their sociodemographic and dietary profiles. The study population included participants of the NutriNet-
Santé cohort who completed both a food exclusion questionnaire and an organic semi-quantitative FFQ (n 23 468). Food intake and organic food consumption ratios were compared using multivariable adjusted ANCOVA models. Associations between gluten avoidance and organic food consumption as well as places of food purchase were investigated with multivariable logistic regression. Participants avoiding gluten were more likely to be women and had a healthier dietary profile. Organic food consumption was higher among gluten avoiders (48·50 % of total diet for total avoiders, 17·38 % for non-avoiders). After adjustments for confounders, organic food consumption and purchase in organic stores were positively associated with gluten avoidance: adjusted OR (aOR)Q5 v.Q1 organic food = 4·95; 95 % CI 3·70, 6·63 and aOROrganic stores v.supermarkets = 1·82; 95 % CI 1·42, 2·33 for total avoiders. Our study highlights that individuals avoiding gluten are high organic consumers and frequently purchase their foods in organic stores which propose an extended offer of gluten-free food. Further research is needed to determine the underlying common motivations and the temporality of the dietary behaviours of healthy people avoiding gluten.

**Keywords:** Consumers; Gluten avoidance; Organic food; Places of purchase.

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[HAL](https://hal.archives-ouvertes.fr/)

150. **Late Aortic Expansion After Thoracic Endovascular Aortic Repair for Chronic DeBakey IIIb Dissection**


**Authors**

Chikara Ueki 1, Hiroshi Tsuneyoshi 2

**Affiliations**
Abstract

**Background:** The efficacy of thoracic endovascular aortic repair (TEVAR) for chronic DeBakey IIIb aortic dissection is still under discussion. This study was performed to investigate the incidence of and risk factors for late aortic expansion after TEVAR for chronic DeBakey IIIb aortic dissection.

**Methods:** From March 2014 to April 2019, a total of 35 patients with chronic DeBakey IIIb aortic dissection underwent TEVAR in our institution. Risk factors for aortic expansion events were examined by stepwise Cox regression analysis. Aortic expansion events were defined as reintervention for expansion or aortic expansion of greater than 5 mm.

**Results:** No operative death occurred, and the 2-year survival rate was 96.8%. The 1- and 2-year rates of freedom from reintervention were 87.8% and 80.2%, respectively. During follow-up, 11 patients had late aortic expansion events (4 with expansion of the thoracic aorta and 7 with expansion of the abdominal aorta). The 1- and 2-year rates of freedom from aortic expansion were 87.8% and 68.7%, respectively. Significant risk factors for expansion events were aortic dilation at the celiac level (hazard ratio [HR], 1.11; P = .015), saccular aneurysm formation of the false lumen (HR, 5.08; P = .049), and high number of residual large reentries (>5 mm) (HR, 2.78; P = .027).

**Conclusions:** In patients undergoing TEVAR for chronic DeBakey IIIb aortic dissection, late aortic expansion in both the thoracic and abdominal aorta remains an important issue. Aggressive additional intervention should be considered for high-risk patients with residual large reentries and aortic dilation at the celiac level.

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Celiac disease and reproductive failures: An update on pathogenic mechanisms


Authors

Nicoletta Di Simone 1 2, Matteo Gratta 2, Roberta Castellani 2, Silvia D'Ippolito 1 2, Monia Specchia 2, Giovanni Scambia 2 3, Chiara Tersigni 1 2

Affiliations

1 U.O.C. di Ostetricia e Patologia Ostetrica, Dipartimento di Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy.
2 Istituto di Clinica Ostetrica e Ginecologica Università Cattolica del Sacro Cuore, Rome, Italy.
3 U.O.C. di Ginecologia Oncologica, Dipartimento di Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy.

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Abstract

Celiac disease (CD) is an autoimmune disorder that occurs in genetically predisposed people in which the ingestion of gluten leads to damage in the small intestine that clinically presents with malabsorption-related symptoms. CD can also be the underlying cause of several non-gastrointestinal symptoms. This review summarizes evidence on the relationship between CD and gynecological/obstetric disorders like reproductive failures. Although much has been reported on such a linkage, the pathogenic mechanisms remain unclear, especially those underlying extra-gastrointestinal clinical
manifestations. Studies conducted on celiac subjects presenting gynecological/obstetric disorders have pointed to intestinal malabsorption, coagulation alterations, immune-mediated tissue damage, and endometrial inflammation as the main responsible pathogenic mechanisms. Currently, however, the knowledge of such mechanisms is insufficient, and further studies are needed to gain a more thorough understanding of the matter.

**Keywords:** autoimmunity; celiac disease; personalized medicine; pregnancy; reproductive failures.

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- 51 references

**Full text links**

152. **Effect of celiac axis compression on target vessel-related outcomes during fenestrated-branched endovascular aortic repair**


**Authors**

Francesco Squizzato 1, Gustavo S Oderich 1, Emanuel R Tenorio 1, Bernardo C Mendes 1, Randall R DeMartino 2

**Affiliations**

- 1 Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, Minn.
- 2 Division of Vascular and Endovascular Surgery, Mayo Clinic, Rochester, Minn. Electronic address: demartino.randall@mayo.edu.
Abstract

**Objective:** To report the effect of median arcuate ligament (MAL) compression on outcomes and technical aspects of celiac artery (CA) stenting during fenestrated-branched endovascular aneurysm repair for thoracoabdominal aortic aneurysms (TAAA) or pararenal aortic aneurysms.

**Methods:** We retrospectively reviewed the clinical and anatomic data on 300 consecutive patients enrolled in a prospective nonrandomized physician-sponsored investigational device exemption study from 2013 to 2018. From this group, 230 patients with CA incorporation by fenestration or directional branch were included. MAL compression was defined by preoperative computed tomography angiogram as a J-hook narrowing of the proximal CA at the level of the ligament; the shift angle between the downward and upward segments within the CA was measured. End points were technical success, rates of intraoperative or early (30-days) CA branch revision, and freedom from target vessel instability, defined by any death or rupture owing to target vessel complication, occlusion, or reintervention for stenosis, endoleak, or disconnection.

**Results:** CA incorporation was performed using fenestrations in 118 patients (51%) and directional branches in 112 (49%). MAL compression was present in 97 patients (42%), resulting in a stenosis of more than 50% in 48 (49%). MAL compression was more often present in patients with extent I to III TAAAs compared with extent IV TAAA-pararenal aortic aneurysms (56% vs 31%; P < .001). Technical success rate was 99%. Patients with MAL compression more often received a directional branch (65% vs 37%; P < .001), self-expanding bridging stent grafts (32% vs 16%; P = .007), adjunctive bare metal stents (46% vs 24%; P = .001), and coverage of the gastric artery (44% vs 22%; P < .001). An intraoperative (n = 6, 2.6%) or early (n = 1, 0.4%) revision of the CA branch was required in seven patients (3%) owing to dissection/occlusion (n = 2 [0.9%]), kinking/stenosis (n = 3 [1.3%]), stent dislodgement (n = 1 [0.4%]), or type IC endoleak (n = 1 [0.4%]). A shift angle of less than 120° was the most significant factor associated with CA branch revision (odds ratio, 10.9; 95% confidence interval, 2.3-88.9; P = .013). Freedom from CA branch instability was 97 ± 2% at 4 years, and this outcome was not associated with MAL compression.
(hazard ratio, 0.83; 95% confidence interval, 0.14-5.02; P = .588) or any other predictor.

**Conclusions:** MAL compression was more common in extent I to III TAAAs, and related to additional challenges for CA stenting in fenestrated-branched endovascular aneurysm repair. This process may include bare metal stenting, gastric artery coverage, or early revision, especially in presence of an angulation of less than 120°. However, durable results can be achieved for CA incorporation despite these difficulties.

**Keywords:** Aortic aneurysm; Celiac artery; Fenestrated and branched endovascular aortic repair; Median arcuate ligament syndrome; Pararenal aortic aneurysm; Thoracoabdominal aortic aneurysm.

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**Full text links**

153. **Assessment of disease severity on capsule endoscopy in patients with small bowel villous atrophy**


**Authors**

Stefania Chetcuti Zammit ¹, Mark E McAlindon ¹, David S Sanders ¹, Reena Sidhu ¹

**Affiliation**

- ¹ Gastroenterology Department, Sheffield Teaching Hospitals, Sheffield, UK.

**PMID:** 32808308
Abstract

**Background and aim:** There is a lack of uniformity of reporting on features of celiac disease (CD) on small bowel capsule endoscopy (SBCE). This makes determining extent of disease and comparison of severity of disease challenging.

**Methods:** De-identified SBCEs of 300 patients (78 CD [26%], 18 serology negative villous atrophy [6%], and 204 controls with normal duodenal histology [68%]) were included. Videos were reviewed by two experts. All patients had duodenal histology taken within 2 weeks of SBCE. The degree of agreement in CD features and extent of disease was then determined. The resulting score for each factor was used to determine overall severity of disease.

**Results:** There was substantial agreement in the kappa coefficient for the detection of CD features between reviewers (0.67). Agreement for extent of affected small bowel (SB) mucosa was high (0.97). On multiple regression analysis, several features of CD correlated with extent of affected SB mucosa for both reviewers. The odds ratios derived from this analysis were then used to score features of CD, enabling scores of severity to be calculated for each patient. The median overall scores for patients increased significantly according to the independent classification of severity by the capsule reviewers: mild (20, 0-79), moderate (45, 25-123), and severe (89, 65-130) (P = 0.0001).

**Conclusion:** The good correlation of CD scores between expert reviewers confirms the validity of features of CD on SBCE. An objective score of CD features in the SB is useful in the follow up of patients with CD and serology negative villous atrophy.

**Keywords:** celiac disease; serology negative villous atrophy; severity score; small bowel capsule endoscopy.

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Extrahepatic autoimmune diseases in primary biliary cholangitis: Prevalence and significance for clinical presentation and disease outcome


Authors


Affiliations

1 Department of Gastroenterology, Gazi Yaşargil Education and Research Hospital, Diyarbakir, Turkey.
2 Department of Rheumatology, Ankara University Hospital, Ankara, Turkey.
3 Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.
4 Division of Gastroenterology, University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada.
5 University of Alberta Division of Gastroenterology and Liver Unit, Edmonton, Alberta, Canada.
6 Division of GI and Hepatology, Beth Israel Medical Center, Harvard Medical School, Boston, Massachusetts, USA.
7 Department of Gastroenterology, Medical Faculty, Uludag University, Bursa, Turkey.
8 Division of Gastroenterology, Clinic and Polyclinic for Oncology, Hepatology, Infectious Diseases and Pneumology, University Clinic Leipzig, Leipzig, Germany.
9 Division of Liver Diseases, The Mount Sinai Medical Center, New York, New York, USA.
10 Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
11 Center for the Study and Treatment of Autoimmune Diseases of the Liver and Biliary System, University of Bologna, Bologna, Italy.
12 Department of Gastroenterology, Hacettepe University, Ankara, Turkey.
13 Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden.
14 Department of Gastroenterology and Hepatology, Uppsala University Hospital, Uppsala, Sweden.
15 Department of Gastroenterology and Hepatology, Skåne University Hospital, Malmö, Sweden.
16 Department of Clinical Sciences, Gastroenterology Division, Skåne University Hospital, Lund, Sweden.
17 Department of Hepato-Gastroenterology, CHU Reims, Reims, France.
18 Division of Gastroenterology and Hepatology, Kantonsspital St. Gallen, St. Gallen, Switzerland.
19 Department of Gastroenterology, Ankara City Hospital, Ankara, Turkey.
20 Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.
21 Epatocentro Ticino, Lugano, Switzerland.
22 Hepatology Division, Centre for Digestive Diseases, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden.

PMID: 32790935
DOI: 10.1111/jgh.15214
Abstract

**Background and aim:** The prevalence and clinical significance of extrahepatic autoimmune diseases (EHAIDs) have not been evaluated in a large cohort of primary biliary cholangitis (PBC).

**Methods:** The medical records of 1554 patients with PBC from 20 international centers were retrospectively reviewed. Development of decompensated cirrhosis (ascites, variceal bleeding, and/or hepatic encephalopathy) and hepatocellular carcinoma were considered clinical endpoints.

**Results:** A total of 35 different EHAIDs were diagnosed in 440 (28.3%) patients with PBC. Patients with EHAIDs were more often female (92.5% vs 86.1%, P < 0.001) and seropositive for anti-mitochondrial antibodies (88% vs 84%, P = 0.05) and antinuclear antibodies and/or smooth muscle antibodies (53.8% vs 43.6%, P = 0.005). At presentation, patients with EHAIDs had significantly lower levels of alkaline phosphatase (1.76 vs 1.98 × upper limit of normal [ULN], P = 0.006), aspartate aminotransferase (1.29 vs 1.50 × ULN, P < 0.001), and total bilirubin (0.53 vs 0.58 × ULN, P = 0.002). Patients with EHAIDs and without EHAIDs had similar rates of GLOBE high-risk status (12.3% vs 16.1%, P = 0.07) and Paris II response (71.4% vs 69.4%, P = 0.59). Overall, event-free survival was not different in patients with and without EHAIDs (90.8% vs 90.7%, P = 0.53, log rank). Coexistence of each autoimmune thyroid diseases (10.6%), Sjögren disease (8.3%), systemic sclerosis (2.9%), rheumatoid arthritis (2.7%), systemic lupus erythematosus (1.7%), celiac disease (1.7%), psoriasis (1.5%), and inflammatory bowel diseases (1.3%) did not influence the outcome.

**Conclusions:** Our study confirms that EHAIDs are frequently diagnosed in patients with PBC. The presence of EHAIDs may influence the clinical phenotype of PBC at presentation but has no impact on PBC outcome.

**Keywords:** Ankylosing spondylitis; Anti-phospholipid syndrome; Autoimmune hemolytic anemia; Idiopathic thrombocytopenic purpura; IgA nephropathy; Multiple sclerosis; Polyarteritis nodosa; Polymyositis; Sarcoidosis; Temporal arteritis.
Utilization of quinoa flour (Chenopodium quinoa Willd.) in gluten-free pasta formulation: Effects on nutritional and sensory properties


Authors

Berat Demir ¹, Nermin Bilgiçli ²

Affiliations

¹ Bahri Dağdaş International Agricultural Research Institute, Konya, Turkey.
² Department of Food Engineering, Engineering and Architecture Faculty, 226846Necmettin Erbakan University, Konya, Turkey.

PMID: 32781850
DOI: 10.1177/1082013220940092

Abstract

In this study, raw and germinated quinoa seed flour was utilized in gluten-free pasta formulation. Rice:corn semolina (50:50) blend was used in gluten-free pasta as a control group. Quinoa flours were replaced with rice:corn semolina blend at different (0-30%) ratios in gluten-free pasta formulation. Guar gum
(3%) was also used to tolerate structural defects caused by gluten deficiency. Trials were conducted according to (2 × 4) × 2 factorial design. Color values, cooking properties, and chemical and sensory attributes of gluten-free pasta samples were determined. Quinoa flour type and quinoa flour addition ratio factors significantly (p < 0.05) affected the L*, a* color values and all of the cooking properties of the gluten-free pasta samples. Utilization of germinated quinoa flour in gluten-free pasta revealed lower water uptake, volume increase, firmness, and higher cooking loss values than that of raw quinoa flour. Quinoa flour especially improved the mean values of protein, total phenolic content, antioxidant activity from 8.1%, 0.7 mg GAE/g, and 13.4%, up to 12.7%, 1.5 mg GAE/g, and 28.8%, respectively. A significant (p < 0.05) increment was observed in Ca, Fe, K, Mg, P, and Z content of the gluten-free pasta and all addition ratios of quinoa flour. As a result, increasing amount of quinoa flour enriched the nutritional composition of gluten-free pasta but high utilization ratio resulted in slight sensory losses.

**Keywords:** Germination; gluten free; pasta; phenolic compounds; quinoa.

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156. **Gluten intake and metabolic health: conflicting findings from the UK Biobank**


**Authors**

Inken Behrendt 1, Mathias Fasshauer # 2 3 4, Gerrit Eichner # 5

**Affiliations**

- 1 Institute of Nutritional Science, Justus-Liebig-University of Giessen, Goethestr. 55, 35390, Giessen, Germany. inken.behrendt@ernaehrung.uni-giessen.de.
Purpose: The impact of gluten intake on metabolic health in subjects without celiac disease is unclear. The present study aimed to assess the association between gluten intake and body fat percentage (primary objective), as well as a broad set of metabolic health markers.

Methods: Gluten intake was estimated in 39,927 participants of the UK Biobank who completed a dietary questionnaire for assessment of previous 24-h dietary intakes. Multiple linear regression analyses were performed between gluten intake and markers of metabolic health with Holm adjustment for multiple comparisons.

Results: Median gluten intake was 9.7 g/day (male: 11.7 g/day; female: 8.2 g/day; p < 0.0001). In multiple linear regression analysis, association between gluten intake and percentage body fat was negative in males (β = -0.028, p = 0.0020) and positive in females (β = 0.025, p = 0.0028). Furthermore, gluten intake was a negative predictor of total cholesterol (male: β = -0.031, p = 0.0154; female: β = -0.050, p < 0.0001), high-density lipoprotein cholesterol (male: β = -0.052, p < 0.0001; female: β = -0.068, p < 0.0001), and glomerular filtration rate (sexes combined: β = -0.031, p < 0.0001) in both sexes. In females only, gluten intake was positively associated with waist circumference (β = 0.041, p < 0.0001), waist-to-height ratio (β = 0.040, p < 0.0001), as well as body mass index (β = 0.043, p < 0.0001), and negatively related to low-density
lipoprotein cholesterol ($\beta = -0.035$, $p = 0.0011$). A positive association between gluten intake and triglycerides was observed in males only ($\beta = 0.043$, $p = 0.0001$).

**Conclusion:** This study indicates that gluten intake is associated with markers of metabolic health. However, all associations are weak and not clinically meaningful. Limiting gluten intake is unlikely to provide metabolic health benefits for a population in total.

**Keywords:** Body composition; Dyslipidemia; Gluten; Hypertension; Metabolic health; Obesity.

**Conflict of interest statement**

The authors declare that they have no conflict of interest.

- Cited by 1 article
- 54 references
- 2 figures

**Full text links**

157. **Detection of gluten in duplicate portions to determine gluten intake of coeliac disease patients on a gluten-free diet**


**Authors**

**H J van der Fels-Klerx**$^1$$^2$, **N G E Smits**$^1$, **M G E G Bremer**$^1$, **J M Schultink**$^3$, **M M Nijkamp**$^1$, **J J M Castenmiller**$^4$, **J H M de Vries**$^3$

**Affiliations**
Abstract

This study determined the gluten content of foods and meals consumed by coeliac disease (CD) patients who adhere to a gluten-free diet, and to estimate the total daily intake of gluten of these patients. CD patients fulfilling defined inclusion criteria were preselected and approached for participation in the study. Duplicate portions (DP) of foods and mixed dishes were collected from the CD patients for evaluating complete daily food intake during two individual days. Also, for these days, written food records were completed by the participants. From each DP, a laboratory sample was prepared and analysed for its gluten concentration and total daily gluten intake was calculated. Each individual's total daily intakes of energy and macronutrients were calculated using the Dutch food composition database. In total, twenty-seven CD patients participated, seven males and twenty females, aged between 21 and 64 years. In thirty-two (6 %) of 499 food samples collected in total, more than 3 mg/kg gluten was present. In four of these thirty-two samples, the gluten concentration was above the European legal limit of 20 mg/kg and three of the four samples had a gluten-free label. The maximal gluten intake was 3·3 mg gluten/d. The gluten tolerance for sensitive CD patients (>0·75 mg/d) was exceeded on at least six out of fifty-four study days. To also protect these sensitive CD patients, legal thresholds should be re-evaluated and the detection limit of analytical methods for gluten analysis lowered.

Keywords: Coeliac disease; Dietary intake; ELISA; Gluten; Gluten-free diet.
Estimating the Impact of Verification Bias on Celiac Disease Testing


Authors

Isabel A Hujoel 1, Claire L Jansson-Knodell 2, Philippe P Hujoel 3, Margaux L A Hujoel 4, Rok Seon Choung 1, Joseph A Murray 1, Alberto Rubio-Tapia 5

Affiliations

1 Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.
2 Division of Gastroenterology and Hepatology, Indiana University, Indianapolis, IN.
3 Department of Epidemiology, School of Public Health, University of Washington, Seattle, WA.
4 Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA.
5 Department of Gastroenterology and Hepatology, Cleveland Clinic, Cleveland, OH.

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Abstract

Goal: The goal of this study was to estimate the impact of verification bias on the diagnostic accuracy of immunoglobulin A tissue transglutaminase (IgA tTG) in detecting celiac disease as reported by an authoritative meta-analysis, the 2016 Comparative Effectiveness Review (CER).
Background: Verification bias is introduced to diagnostic accuracy studies when screening test results impact the decision to verify disease status.

Materials and methods: We adjusted the sensitivity and specificity of IgA tTG reported by the 2016 CER with the proportion of IgA tTG positive and negative individuals who are referred for confirmatory small bowel biopsy. We performed a systematic review from January 1, 2007, to July 19, 2017, to determine these referral rates.

Results: The systematic review identified 793 articles of which 9 met inclusion criteria (n=36,477). Overall, 3.6% [95% confidence interval (CI): 1.1%-10.9%] of IgA tTG negative and 79.2.2% (95% CI: 65.0%-88.7%) of IgA tTG positive individuals were referred for biopsy. Adjusting for these referral rates the 2016 CER reported sensitivity of IgA tTG dropped from 92.6% (95% CI: 90.2%-94.5%) to 57.1% (95% CI: 35.4%-76.4%) and the specificity increased from 97.6% (95% CI: 96.3%-98.5%) to 99.6% (95% CI: 98.4%-99.9%).

Conclusions: The CER may have largely overestimated the sensitivity of IgA tTG due to a failure to account for verification bias. These findings suggest caution in the interpretation of a negative IgA tTG to rule out celiac disease in clinical practice. More broadly, they highlight the impact of verification bias on diagnostic accuracy estimates and suggest that studies at risk for this bias be excluded from systematic reviews.

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Conflict of interest statement
Conflict of Interest: None

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Prevalence and Progression of Recurrent Abdominal Pain, From Early Childhood to Adolescence


Authors

Jessica Sjölund 1, Agneta Uusijärvi 2, Navkiran T Tornkvist 3, Inger Kull 4, Anna Bergström 5, Johan Alm 4, Hans Törnblom 3, Ola Olén 6, Magnus Simrén 7

Affiliations

1 Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. Electronic address: jessica.sjolund@gu.se.
2 Department of Clinical Science and Education, Södersjukhuset, Stockholm, Sweden; Astrid Lindgren Children's Hospital, Karolinska University Hospital, Huddinge, Sweden.
3 Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.
4 Department of Clinical Science and Education, Södersjukhuset, Stockholm, Sweden; Department of Pediatric Gastroenterology and Nutrition, Sachs' Children's Hospital, Stockholm, Sweden.
5 Institute of Environmental Medicine, Stockholm, Sweden; Centre for Occupational and Environmental Medicine, Stockholm County Council, Stockholm, Sweden.
6 Department of Pediatric Gastroenterology and Nutrition, Sachs' Children's Hospital, Stockholm, Sweden; Division of Clinical Epidemiology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.
7 Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; Centre for Functional GI and Motility Disorders, University of North Carolina, Chapel Hill, North Carolina.
Abstract

**Background & aims:** Little is known about the natural history of childhood recurrent abdominal pain (RAP). We investigated the prevalence and progression of childhood RAP and its association with Rome III abdominal pain-related functional gastrointestinal disorders (AP-FGID) and irritable bowel syndrome (IBS) during adolescence.

**Methods:** We collected data from a prospective population-based birth cohort study of 4089 children, born from 1994 through 1996 in Sweden. We analyzed data from 2455 children with complete follow-up evaluation at ages 1, 2, 12, and 16 years and no parent-reported diagnoses of inflammatory bowel diseases or celiac disease at ages 12 or 16 years. A subpopulation of 2374 children who had answered questions based on the Rome III criteria at age 16 years was identified. We assessed RAP at 3 assessment points and defined it as parent-reported attacks of colic in early childhood (1-2 years) and as self-reported weekly abdominal pain at ages 12 years and 16 years. AP-FGID at age 16 years was defined according to the Rome III criteria.

**Results:** RAP was reported by 26.2% of children on at least 1 of 3 assessment points, of which 11.3% reported symptoms more than once. Children with RAP at 12 years had persistent symptoms at 16 years in 44.9% of cases and increased risks for RAP (relative risk, 2.2; 95% CI, 1.7-2.8), any AP-FGID (relative risk, 2.6; 95% CI, 1.9-3.6), and IBS (relative risk, 3.2; 95% CI, 2.0-5.1) at 16 years. Early childhood RAP was not associated significantly with any outcome.

**Conclusions:** RAP affects many children from early childhood through age 16 years, but most children do not have persistent symptoms throughout childhood. RAP at age 12 years is a risk factor for RAP, any Rome III AP-FGID, and IBS, at age 16 years.

**Keywords:** BAMSE; Dyspepsia; FAP; FD; Pediatric.

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