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REVIEW ARTICLES

Exploring Unique Insights into Cell Damage Pathways in Celiac Disease

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Abstract

Introduction: Celiac disease, or celiac sprue, is a T cell-mediated autoimmune disorder of the small intestine triggered by ingesting dietary gluten products in genetically susceptible individuals. The pathologic mechanism involves an immune response targeting gluten peptides, leading to inflammation, villous atrophy, and malabsorption in the small intestine. This research is a significant step in understanding the mechanisms of how CD4+ T cell (white blood cells that are an essential part of the human immune system) responses against gluten can lead to autoreactive B-cell responses and tissue destruction mediated by intraepithelial cytotoxic T cells in the small intestine.

Furthermore, the articles underscore the pivotal role of CD4+ T cells in the lamina propria, where they interact with gluten, undergo activation, proliferate, and subsequently secrete proinflammatory cytokines, ultimately leading to tissue damage characterized by crypt hyperplasia and villous atrophy.

Furthermore, the text explores the overexpression of IL-15 on enterocytes in active celiac disease, contributing to the condition's underlying pathogenesis.

It addresses challenges in understanding specific phenotypes of celiac disease, such as slow-responsive, potential, and seronegative forms.

Conclusion: The articles provide valuable insights into the cellular mechanisms underlying celiac disease, the immune responses involved, and the impact of gluten on intestinal cells. They also address the practical implications of this knowledge, such as the significance of dietary management in controlling the disease and preventing complications, thereby empowering the reader with actionable information.

Keywords: Celiac disease, T cell-mediated autoimmune disorder, CD4+ T cells, B-cell responses, Lamina propria, Proinflammatory cytokines, IL-15, Enterocytes.

Introduction

Celiac disease (CD) is a life-long autoimmune condition of the gastrointestinal tract. It is characterized by inflammatory damage to the small intestine after ingesting wheat gluten, barley, and rye products. [1]

Upon exposure to gluten peptides, intestinal epithelium undergoes immediate cytoskeletal rearrangement, and functional barrier integrity is lost. [2]

Understanding the mechanisms of cell damage in celiac disease is crucial for managing its gastrointestinal symptoms and addressing extraintestinal manifestations. This article delves into the interplay between gluten exposure, immune response, and cellular dysfunction, illuminating

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the pathways through which celiac disease inflicts damage beyond the gut barrier. It also explores different aspects of CD regarding their classification, structure, epidemiology, complications, and treatment.

Epidemiology: The prevalence of celiac disease (CD) is estimated to be between 0.5%-1% globally, with higher risk observed in populations with diabetes, autoimmune disorders, or relatives of CD individuals due to shared HLA typing. This global impact underscores the importance of our research in understanding and managing this condition.

The CD was initially believed to affect white Europeans predominantly but is now recognized as widely distributed worldwide. [4, 5]

Epidemiological studies conducted in areas previously thought free of CD, such as Africa, the Middle East, Asia, and South America, reveal that the disease was underdiagnosed. [6]

CD is considered one of the most common genetic diseases, influenced by environmental factors (gluten) and genetic factors (HLA and non-HLA genes).[7]

CD distribution globally correlates with historical patterns of wheat consumption and migratory flows, originating from the Middle East and spreading through Europe and beyond.[6]

The prevalence of CD in Western populations is close to 1%, with potential variations in different regions.[8]

Women have a higher prevalence of CD compared to men, with a male-to-female ratio of approximately 1:2.8, possibly due to delayed diagnosis in men.[6]

Cases of CD have been reported among immigrant children from various regions, indicating that genetic predisposition may manifest clinically with sufficient gluten intake.[8]

The prevalence of CD varies across different regions, with higher rates observed in Northern European countries like Scandinavia, Ireland, and the United Kingdom, ranging from 1.0%-1.5%.[7]

Possible triggers for CD include genetic predisposition (HLA, MYO9B), gluten consumption, pro-autoimmune genetic background, viral infections, tissue damage, early termination of breastfeeding, and gender differences.[9]

Pathogenesis of Celiac Disease:

Dietary cereal grains such as wheat, rye, and barley include proteins that activate CD. While "gluten" is commonly used to refer to the disease-causing proteins found in different grains, technically, gluten only consists of the disease-causing proteins found in wheat. [3]

Gliadins and glutenins, the two main protein types found in gluten, include peptides that trigger illness. Hordeins and secalins, two closely related proteins found in barley and rye, respectively, are the proteins that trigger CD. [1]

Proline and glutamine levels are high in gliadins, glutenins, hordeins, and secalins. Because gastric, pancreatic,

< 5%	5%-20%	20%
HLA-DQ2		
Albania	Belarus Algeria	Algeria
Canada BC (Athabaskans)	Cameroon	Australia
Cook Islands	Congo	Belgium
Indonesia	Costa Rica	Central African Republic
Japan	China	Croatia
Jordan	Cuba	England
Papua New Guinea	Ecuador Africans	Equatorial Guinea Bioko Island
Philippines	France	Ethiopia
Samoa	India	Germany
	Malaysia	Greece
	Mexico	Iran
	Poland	Ireland South
	Russia	Israel
	Singapore	Italy
	South Korea	Mongolia
	Spain	New Zealand

*Table 1. Frequency of human leukocyte antigen-DQ2, encoded by human leukocyte Antigen-DQB1*02, and human leukocyte antigen-DQ8, encoded by human leukocyte antigen-DQA1*0301-DQB1*0302*

and brush border enzymes in the human intestine lack prolyl endopeptidase activity, the high proline concentration of these proteins makes them resistant to complete proteolytic digestion. As a result, the small intestine may accumulate comparatively large peptide fragments high in proline and glutamine. However, CD cannot be caused by the significantly poor digestion of these proteins. [1]

Host genetic factors have a significant role in the etiology of CD. It is well established that specific MHC class II alleles corresponding to the HLA-DQ gene are linked to CD. [2]

Nearly all individuals with biopsy-confirmed CD express HLA-DQ alleles that encode particular HLA-DQ2 or specific HLA-DQ8 heterodimers, and these alleles are relatively common in the white population. [2, 3]

Four distinct components interact in the affected individual: T cells, tissue transglutaminase (TG2), HLA-DQ2/8, and gluten. Gluten is broken down into relatively large pieces in the stomach by the action of the pepsin enzyme. Because gluten is high in proline, relatively big fragments remain even if small intestine enzymes may further reduce these pieces. Specific molecules can bind to HLA-DQ2 or HLA-DQ8 molecules with low affinity, and CD patients have occasionally been discovered to have T cells that are reactive to these DQ-peptide complexes. However, tissue damage could result from these T-cell responses, most likely in combination with the development of innate responses. Innate responses, non-specific immune responses that occur immediately or within hours of an antigen's appearance in the body, also play a role in the pathogenesis of celiac disease. [1, 2]

As a result, the TG2 enzyme would be released, which can alter gluten peptides in the extracellular environment high in calcium. The process, known as deamidation, changes glutamine, a neutral amino acid, into glutamic acid, a negatively charged amino acid. Deamidated gluten peptides bind to HLA-DQ2 or HLA-DQ8 with a substantially higher affinity due to introducing a negative charge. These HLA molecules prefer to bind peptides with one or more negatively charged residues. [1, 2]

Furthermore, many gluten peptides can be altered this way, expanding and enhancing the lamina propria's gluten-specific T-cell response. Proinflammatory cytokines, including IFNγ, are secreted during this reaction, which fuels the local inflammation. More significantly, these findings explain the known fact that those who are HLA-DQ2 and/or -DQ8 positive virtually exclusively acquire CD. [2]

Innate immunity response:

Innate immunity plays a crucial role in the initiation of CD. Cytokines like interleukin (IL)-15 and interferon α can prime the innate immune response by polarizing dendritic cells and intraepithelial lymphocyte function. [1, 2, 4]

Gliadin peptides induce enterocyte proliferation via EGFR and IL-15, causing structural changes, vesicular trafficking alterations, and innate immune activation. Alpha-amylase/trypsin inhibitors in wheat engage TLR4-MD2-CD14, leading to proinflammatory cytokine release in CD patients. [3] Gliadin-mediated zonulin release disrupts epithelial barrier function, allowing toxic peptides into the lamina propria, while also inducing IL-8 production, contributing to CD enteropathy. Gliadin directly attracts neutrophils via interaction with the fMLP receptor 1. [3]

Adaptive immunity response:

In CD, the adaptive immune response is initiated by gluten peptides interacting with HLA-DQ2/8-restricted T cells, facilitated by post-translational deamidation by transglutaminase 2. This response involves CD4+ T cells, activated by gluten presentation via various antigen-presenting cells, producing proinflammatory cytokines and growth factors. [1, 2, 3]

Overexpression of IL-15 promotes NK receptor expression by IELs, contributing to tissue damage. Crypt hyperplasia in CD may result from a balance between mucosal damage and stem cell compensation, involving expansion of progenitor cells and downregulation of Hedgehog signaling. [3]

Tissue TGase, released in the intestinal mucosa during tissue injury, plays a role in tissue repair and cross-links proteins by forming isopeptide bonds between glutamine and lysine residues. [1]

Histological view of Celiac Disease:

When viewed through a dissecting microscope, the luminal surface of a small intestinal mucosal biopsy from a healthy subject has abundant villi. In contrast, the luminal surface of a small intestinal mucosal biopsy from a patient with severe CD manifests a complete loss of villi, with a flat mucosal surface accentuated by ridges and numerous crypt openings. [1] When tissue sections of the mucosa of the small intestine are stained with H&E to visualize mucosal structure and the individual cells, the mucosa of healthy individuals is characterized by tall villi lined by a single layer of columnar epithelial cells with nuclei located near the basal surface; a smattering of intraepithelial lymphocytes (IELs) (approximately 1 per 6–10 epithelial cells); lymphocytes and plasma cells in the lamina propria in numbers consistent with the "physiologic inflammation" that is normal in the small intestine; and a ratio of villous height to crypt depth of approximately 4:1 to 5:1. In contrast, the small-intestinal mucosa of patients with severe CD shows total villous atrophy. The complete loss of villi is accompanied by the presence of markedly abnormal squamoid surface epithelial cells, an increase in the number of IELs, a marked increase in the number of lymphocytes and plasma cells in the lamina propria, and striking crypt hypertrophy with increased crypt mitoses. Pathologic changes in less severe CD are not as marked. They can be characterized by increased numbers of IELs, less extensive villous atrophy, and crypt hypertrophy, subtotal villous atrophy. [1]

Symptoms:

The pathologic alterations indicate great variety, but the clinical manifestations differ significantly. Very few patients exhibit the "classic" symptoms of severe malnourishment, steatorrhea, and weight loss. [1] By contrast, a large number of people with CD are either relatively asymptomatic (i.e., identified only because they have affected family members) or exhibit primarily extraintestinal symptoms and findings (e.g., unexplained iron deficiency anemia, premature-onset osteoporosis, irritability, and depression). Many traits of a chronic inflammatory disease are present in CD. In line with this, biopsies from either milder or more severe diseases do not show a significant neutrophil infiltration of the mucosa, indicative of an initial inflammatory response. [1]

Classification of Celiac Disease (CD)

Potential CD:

Definition: Patients with positive CD-related antibodies (IgA EmA and anti-tTG) and HLA-DQ2/HLA-DQ8 lack villous atrophy.

Intestinal Mucosa: May be normal (Marsh 0) or slightly inflamed (increased number of IELs, Marsh 1).

Symptoms: Can be GI and/or extraintestinal or entirely asymptomatic.

Controversy: Treatment with a gluten-free diet (GFD) [12] is debated. Symptomatic patients benefit from a GFD, while asymptomatic patients may continue a gluten-containing diet with close monitoring.

Follow-up: Regular clinical, serological, and histological evaluations are recommended, with some patients experiencing spontaneous normalization of serological markers.

Seronegative CD:

Definition: Patients with villous atrophy on duodenal histology but negative for CD-specific antibodies.

Diagnosis: Genetic testing for CD is crucial, with negative results ruling out the disease and prompting further investigations for other causes of villous atrophy.

Confirmation: Improvement in symptoms and histology is observed after 1 year of a GFD.

Differential Diagnosis: Includes parasitic infections, autoimmune enteropathy, drug-induced enteropathy, intestinal lymphoma, Crohn's disease, tropical sprue, HIV enteropathy, and Whipple disease.

Clinical Features: Classic phenotype with diarrhea and malabsorption, more prevalent in females, and associated with a higher risk of morbidity and mortality compared to antibody-positive CD patients.

Association with Autoimmune Diseases: Seronegative CD patients are more associated with autoimmune diseases and a higher risk of developing refractory disease.

Latent CD:

Definition: Defined as standard small bowel architecture but positive serology and presence of HLA-DQ2 and/or HLA-DQ8.

Diagnosis: Made when blood tests are favorable for the condition, but a visual examination of your intestines reveals no damage to the villi that line the organ.

Confirmation: Confirmed by the presence of characteristic small intestinal mucosal changes [13].

Differential Diagnosis: Bacterial gastroenteritis, malabsorption, collagenous and lymphocytic colitis.

Clinical Features: Chronic bloating, diarrhea, constipation, gas, abdominal pain, nausea or vomiting, bulkiness.

Atypical CD:

Definition: Characterized by the absence of "typical" GI manifestations.

Diagnosis: Bones disease, anemia, reproductive problems, neurological problems.

Confirmation: via endoscopy with duodenal biopsies (Duodenal biopsies showed increased numbers of intraepithelial lymphocytes.

Differential Diagnoses: Anorexia nervosa, Giardiasis [14], Hipogammaglobulina, Intestinal lymphoma, Radiation enteritis, and Chron's Disease.

Clinical Features: depression, headaches, diarrhea, osteoporosis, fatigue, vomiting, liver disorders, weight loss, failure to thrive.

Complications of Celiac Disease

Malnutrition: Coeliac disease can lead to malnutrition and a critical lack of nutrients, causing fatigue, dizziness, and confusion. Severe cases can cause stunted growth in children and delayed development. Treatment involves increasing calorie intake and taking supplements.

Lactose Intolerance: Untreated coeliac disease can lead to lactose intolerance, causing symptoms like bloating, diarrhea, and abdominal discomfort. While lactose doesn't harm the body, it may cause gut-related symptoms. Treatment involves not eating dairy products containing lactose and taking calcium supplements. Once gut recovery occurs, lactose intolerance usually improves.

Cancer: Coeliac disease increases the risk of certain cancers, including small bowel cancer, small bowel lymphoma, and Hodgkin lymphoma [15], but most people will not develop these. Following a gluten-free diet reduces the risk of these types of cancer.

Pregnancy with CD: Poorly controlled coeliac disease in pregnancy can increase the risk of developing pregnancy-related complications, such as giving birth to a baby with a low birth weight.

Malabsorption, marked by the body's impaired ability to absorb essential nutrients fully, can lead to deficiencies in

vitamins and minerals, resulting in conditions such as iron deficiency anemia, vitamin B12 or folate deficiency anemia, and osteoporosis.

Hyposplenism: Around 30% of adult CD patients may have anatomical or functional hyposplenism, increasing to 80% in those with complications. Detection includes a small spleen on abdominal ultrasound, Howell–Jolly bodies, or pitted red cells on the peripheral blood smear, indicating splenic hypofunction. Splenic hypofunction is associated with a higher risk of encapsulated bacterial infections, requiring anti-pneumococcal and anti-meningococcal vaccinations.

Refractory CD (RCD)*:* Represents about 10% of OACD cases and 1–1.5% of total CD cases. Characterized by persistent villous atrophy and symptoms of malabsorption despite strict adherence to a GFD. -Subdivided into type 1 (normal CD3+CD8+ phenotype) and type 2 (clonal presentation of surface CD3−/ intracytoplasmic CD3+ IELs), with type 2 having a higher mortality rate due to the risk of intestinal lymphoma. Diagnosis involves ruling out other causes of persistent villous atrophy and performing phenotyping of the intestinal lymphocytic population.

Small Bowel Adenocarcinoma is more common in CD patients than in the general population. It is typically found in the jejunum and may present with sudden intestinal (sub) occlusion or anemia. Diagnosis requires a comprehensive imaging work-up, including CT/MR-enterography, PET, capsule endoscopy, and enteroscopy.

Follow-up for CD in adults: Managing celiac disease (CD) in adults requires a comprehensive approach that involves regular follow-up visits, diagnostic tests, symptom management, nutritional counseling, and addressing complications.

Follow-up visits should occur within 6 months of diagnosis and then every 12-24 months or more frequently (every 3-6 months) in case of complications. These visits aim to confirm compliance with a gluten-free diet (GFD), rule out autoimmune diseases, monitor metabolic changes, and detect complications early.

Diagnostic tests play a crucial role in monitoring CD. Blood tests, including complete blood count, anti-tTG IgA (or IgG if IgA deficient), thyroid stimulating hormone, thyroid antibodies, ferritin, folate, vitamin D3, transaminases, and metabolic profile are recommended. Screening for antinuclear antibodies and non-organ-specific autoantibodies should also be considered. Bone density scans should be conducted after 12-18 months on GFD, with repeat scans if abnormalities are detected. An abdominal ultrasound is also recommended at the start of GFD to exclude spleen abnormalities.

Symptom management is vital, especially addressing abdominal symptoms resembling irritable bowel syndrome (IBS) with dietary recommendations and symptomatic drug therapy if needed. Nutritional counseling should focus on preventing metabolic complications and vitamin deficiencies, with supplementation of vitamins if necessary, particularly in cases of asthenia or deficiency symptoms. Constipation associated with GFD should be managed using non-irritant laxatives.

Complications should be closely monitored, with more frequent follow-up visits (every 3-6 months) and additional tests, including protein electrophoresis, lactate dehydrogenase, beta-2 microglobulin, upper endoscopy with duodenal biopsies, abdominal ultrasound, and advanced imaging modalities, as needed.

A follow-up duodenal biopsy should be considered only in patients who exhibit persistent symptoms and demonstrable micronutrient deficiencies, despite current guidelines advising against it due to the slow rate of villi regrowth following a gluten-free diet, which can take up to 3 years.

Stool sample assessment for gluten immunogenic peptides (GIP) may help monitor adherence to GFD, although further validation is needed in this area.

Effective management of Crohn's disease in adults necessitates a multifaceted approach encompassing regular monitoring, symptom management, nutritional support, and proactive measures to prevent complications, ultimately yielding optimal health outcomes for patients.

*Follow-up for CD in children***:** It is recommended that children diagnosed with celiac disease (CD) undergo an initial follow-up visit approximately six months after diagnosis, followed by annual visits thereafter. These follow-up appointments serve as crucial checkpoints to evaluate various aspects of the child's health post-diagnosis. During these visits, healthcare providers assess symptomatic improvement, adherence to the gluten-free diet (GFD), quality of life, and the normalization of CD-related antibodies. Regular monitoring ensures that any issues or challenges the child faces in managing their condition can be addressed promptly, optimizing their overall well-being.

The laboratory testing and biochemical evaluation approach should be tailored case-by-case, considering individual patient factors and clinical presentation. Standard tests performed during follow-up visits may include a complete blood count to assess for anemia or other blood abnormalities, measurement of CD-related antibodies (such as tissue transglutaminase antibodies), and additional tests as clinically indicated based on the child's symptoms or comorbidities. Given the increased prevalence of thyroid disorders in individuals with CD, it is also recommended to screen for autoimmune thyroiditis routinely.

In most cases, duodenal biopsies are considered unnecessary once a gluten-free diet has been initiated and symptoms have improved. However, in instances where there is either no or only partial clinical response to gluten withdrawal or if ongoing mucosal damage is suspected despite adherence to the diet, a duodenal histopathology may be warranted. This allows for a direct assessment of the intestinal mucosa to determine the extent of any ongoing inflammation or damage, guiding further management decisions and ensuring optimal therapeutic outcomes for the child.

While complications of celiac disease are relatively rare in children, it is essential to remain vigilant, particularly in cases of refractory CD. Refractory celiac disease, though uncommon, is characterized by persistent symptoms and villous atrophy despite adherence to a strict gluten-free diet. While such cases are infrequent, they require specialized management and may necessitate additional interventions, such as immunosuppressive therapy or dietary modifications. Regular follow-up visits facilitate the early Detection and management of potential complications, thereby minimizing their impact on the child's health and well-being.

Conclusion

This article's final section aims to deliver a detailed and complete description of celiac disease (CD) by pinpointing its complex panorama and how the main genetic, environmental, and immunological factors concur. From looking at the epidemiological trends of CD subjects to the molecular happenings of the disease to each detail given, this is another aspect of the autoimmune condition that serves as a puzzle solution. Based on the disease course variation from mild to severe, this system demonstrates the changes in the clinical picture of Crohn's disease that can run through intestinal and out-of-intestinal manifestations, leading to a precise and reliable diagnosis, necessitating a comprehensive therapy approach. On top of that, the problem of possible health complications should be under one brush, with paramount attention paid to constant monitoring and individual care given to the CD (Celiac disease) people. Ultimately, this data can be transformed to work among clinicians and patients, with the outcome being more functional, emotional, and heartwarming diagnostics, leading to positive results for CD patients. Through concerted collaborations in research, healthcare, and patient advocacy, we can picture a CD-free future, with the least complications and happier inhabitants, living with the disease while positively managing and not compromising the quality of living.

COI Statement: This paper has yet to be submitted in parallel, presented fully or partially at a meeting, podium, or congress, published, or submitted for consideration beforehand.

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References:

1. Martin F. Kagnoff. J Clin Invest. 2007;117(1):41-49. https://doi.org/10.1172/JCI30253.
2. Parzanese, I., Qehajaj, D., Patrinicola, F., Aralica, M., Chiriva-Internati, M., Stifter, S., Elli, L., & Grizzi, F. (2017). Celiac disease: From pathophysiology to treatment. *World journal of gastrointestinal pathophysiology*, *8*(2), 27–38. https://doi.org/10.4291/wjgp.v8.i2.27
3. Caio, G., Volta, U., Sapone, A., Leffler, D. A., De Giorgio, R., Catassi, C., & Fasano, A. (2019). Celiac disease: a comprehensive current review. *BMC medicine*, *17*(1), 142. https://doi.org/10.1186/s12916-019-1380-z
4. Lerner A. (2010). New therapeutic strategies for celiac disease. *Autoimmunity reviews*, *9*(3), 144–147. https://doi.org/10.1016/j.autrev.2009.05.002
5. Gujral, N., Freeman, H. J., & Thomson, A. B. (2012). Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World journal of gastroenterology, 18(42), 6036–6059. https://doi.org/10.3748/wjg.v18.i42.6036
6. Fasano, A., & Catassi, C. (2001). Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology*, *120*(3), 636–651. https://doi.org/10.1053/gast.2001.22123
7. Catassi C, Yachha SK. The global village of celiac disease. In: Fasano A, Troncone R, Branski D, editors. Frontiers in celiac disease. Basel: Switzerland Karger; 2008. pp. 23–31.
8. Cataldo, F., & Montalto, G. (2007). Celiac disease in the developing countries: a new and challenging public health problem. *World journal of gastroenterology*, *13*(15), 2153–2159. https://doi.org/10.3748/wjg.v13.i15.2153
9. 7 Sollid, L. M., & Lie, B. A. (2005). Celiac disease genetics: current concepts and practical applications. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, *3*(9), 843–851. https://doi.org/10.1016/s1542-3565(05)00532-x
10. Dubé, Catherine, Rostom, Alaa Sy, et al. The prevalence of celiac disease in average-risk and at-risk Western European populations: A systematic review Elsevier Gastroenterology; Vol 128, Issue 4, S57-67, doi: https://doi.org/10.1053/j.gastro.2005.02.014
11. Mocan, O., & Dumitrașcu, D. L. (2016). The broad spectrum of celiac disease and gluten-sensitive enteropathy. *Clujul medical (1957)*, *89*(3), 335–342. https://doi.org/10.15386/cjmed-698
12. Mazzola, A. M., Zammarchi, I., Valerii, M. C., Spisni, E., Saracino, I. M., Lanzarotto, F., & Ricci, C. (2024). Gluten-Free Diet and Other Celiac Disease Therapies: Current Understanding and Emerging Strategies. *Nutrients*, *16*(7), 1006. https://doi.org/10.3390/nu16071006
13. Tye-Din J. (2018). Interpreting tests for coeliac disease: Tips, pitfalls and updates. *Australian journal of general practice*, *47*(1-2), 28–33. https://doi.org/10.31128/AFP-10-17-4357
14. Hrunka, M., Janda, L., Šťastná, M., Pinkasová, T., Pecl, J., Kunovský, L., Dítě, P., & Jabandžiev, P. (2023). Celiac Disease: Promising Biomarkers for Follow-Up. *Journal of gastrointestinal and liver diseases: JGLD*, *32*(4), 536–544. https://doi.org/10.15403/jgld-4926
15. Pelizzaro, F., Marsilio, I., Fassan, M., Piazza, F., Barberio, B., D'Odorico, A., Savarino, E. V., Farinati, F., & Zingone, F. (2021). The Risk of Malignancies in Celiac Disease-A Literature Review. *Cancers*, *13*(21), 5288. https://doi.org/10.3390/cancers13215288