ŚWIERCZ, Aleksandra, ŻUREK, Urszula, TOŁWIŃSKI, Ignacy, KĘDZIERSKA, Zofia, ANTKOWIAK, Klaudia, DADAS, Klaudia, MAŁACHOWSKA, Dominika, CIECIERSKI-KOŹLAREK, Hubert and SHVED, Kateryna. Does a gluten-free diet result in nutritional deficiencies? – a review of literature. Journal of Education, Health and Sport. 2023;34(1):140-153. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2023.34.01.012
https://apcz.umk.pl/JEHS/article/view/44881
https://zenodo.org/record/8206230

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 17.07.2023 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 17.07.2023 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159.
Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 02.07.2023. Revised:30.07.2023. Accepted: 31.07.2023. Published: 08.08.2023.

Does a gluten-free diet result in nutritional deficiencies? – a review of literature

Aleksandra Świercz

Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland

ORCiD: 0009-0007-1535-1590

e-mail: aleksandra.swiercz1996@gmail.com

Urszula Żurek

Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland

ORCiD: 0009-0008-3482-5381

e-mail: ula.zurek@gmail.com

Ignacy Tołwiński

Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland

ORCiD: 0000-0003-1362-6734

e-mail: ignacyt233@gmail.com

Zofia Kędzierska

Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland

ORCiD: 0000-0002-4181-4719

e-mail: zo.kedzierska@gmail.com

Klaudia Antkowiak

Szpital Średzki Serca Jezusowego z.o.o ul. Żwirki i Wigury 10, 63-000 Środa Wielkopolska, Poland

ORCiD: 0009-0008-3421-2200

e-mail: klaudia.antkowiak2021@gmail.com

Klaudia Dadas

Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland
ORCiD: 0009-0007-3352-9807
e-mail: klaudia.w.2703@gmail.com
Dominika Małachowska
Warszawski Szpital Południowy, ul. rtm. Witolda Pileckiego 99, 02-781 Warszawa, Poland
ORCiD: 0009-0008-6305-7959
e-mail: dominika1.malachowska@gmail.com
Hubert Ciecierski-Koźlarek
Wojewódzki Szpital Specjalistyczny w Olsztynie, ul. Żołnierska 18, 10-561 Olsztyn, Poland
ORCiD: 0009-0009-4062-6888
e-mail: hubertciecierski@icloud.com
Kateryna Shved
Wielospecjalistyczny Szpital Miejski im. Józefa Strusia, ul. Szwajcarska 3, 61-285 Poznań, Poland
ORCiD: 0009-0002-3773-7025
e-mail: katey.shved@gmail.com

Abstract

Introduction and purpose:

Gluten-free diet have gained immense popularity in recent years, both as a treatment for coeliac disease and as a lifestyle choice for those who believe it is healthier. However, concerns have been raised about potential nutrient inadequacies resulting from the elimination of gluten-containing grains. The purpose of this review is to assess the state of knowledge regarding the impact of a gluten-free diet on nutritional status.

Materials and methods:

A comprehensive search was conducted using electronic database PubMed to identify relevant studies published between 1999 and 2022. Keywords such as "gluten-free diet" and "nutritional deficiencies" were used in combination with Boolean operators to refine the search.

A brief description of the state of knowledge:

Analysis of studies revealed that individuals adhering to a gluten-free diet may be at risk of nutritional deficiencies including micronutrients such as vitamin D, vitamin E, vitamin B complex along with minerals, in particular iron, zinc, calcium, magnesium as well as fibre. Furthermore, higher levels of fat and sugar were observed in the composition of gluten-free products.

Conclusions:

Based on the current body of literature, it is evident that a gluten-free diet results in certain nutritional deficiencies. Individuals following gluten-free diet should be aware of potential risks and take appropriate measures to ensure a well-balanced and nutrient-rich diet. Nutritional guidance should be provided to individuals to address specific nutrient deficiencies associated with a gluten-free diet.

Keywords: gluten-free diet; nutritional deficiencies; gluten-free; fibre; vitamins; coeliac disease

Introduction

Under the common name gluten, there are individual components of the protein contained in cereals like wheat, rye and barley.[1] Coeliac disease is an autoimmune disorder caused by gluten intolerance and affects between 0,5 to 2% of the general population. In genetically predisposed people, intake of gluten proteins triggers a cascading immune response causing tissue damage and atrophy of the intestinal villi- protrusions of the intestinal mucosa responsible for the absorption of nutrients from food in the small intestine. It leads to malabsorption, malnutrition and nutrient deficiencies in the body. Coeliac disease can be classified into classical, non-classical, and subclinical forms based on the clinical features observed during diagnosis. Classical form of coeliac disease is characterized by gastrointestinal symptoms such as abdominal pain, bloating and diarrhoea. Other symptoms include weight loss, poor appetite, and muscle wasting. Non-classic coeliac disease presents with non-specific gastrointestinal symptoms such as bloating or constipation as well as symptoms that are not primarily related to gastrointestinal tract.[2] It may manifest as unexplained iron-deficiency anaemia, osteoporosis, neurological symptoms such as headaches and peripheral neuropathy, dermatitis herpetiformis or arthritis. [3] Subclinical Coeliac

Disease refers to cases where individuals have no apparent symptoms, despite having the characteristic intestinal damage caused by gluten ingestion. It is often detected through routine screening or investigation of related conditions. [2] The only effective treatment for coeliac disease is a strict and lifelong adherence to a gluten-free diet. A majority of coeliac patients experience symptom and serologic as well as histological remission when gluten is entirely eliminated from their diet. [4]According to reports, eliminating gluten can help prevent numerous disease complications, and in the case of children, following a gluten-free diet can facilitate a return to normal growth and development. [5] Non-coeliac gluten sensitivity is a form of gluten intolerance in which individuals experience symptoms similar to those of coeliac disease, such as digestive issues, fatigue and headaches, but without the characteristic damage to the small intestine seen in coeliac disease. Although the exact mechanisms are not fully understood, non-coeliac gluten sensitivity is distinct from coeliac disease and wheat allergy. A gluten-free diet is typically recommended for individuals with this condition to manage symptoms.[6] Besides the aforementioned indications, a gluten-free diet is also recommended for gluten allergy, dermatitis herpetiformis, and gluten ataxia.[7] There has been a significant increase in awareness and diagnosis of gluten-related disorders over past decades.[8] As a result, more patients are adopting gluten-free diet as a necessary medical requirement. There is also a growing perception that gluten-free diets are generally healthier, even for individuals without coeliac disease. [9]The media plays a role in shaping public opinion and trends. Increased media coverage of gluten-related disorders and endorsements by celebrities and influencers who claim to feel better on a gluten-free diet not only have helped raise awareness or popularize this dietary choice but also created a general belief that gluten is harmful or that removing gluten will automatically lead to improved health. [10]The food industry has responded to the growing demand for gluten-free options by expanding the availability of gluten-free products. Grocery stores, restaurants and cafes now offer a wider range of gluten-free alternatives, making it easier for individuals to adhere to a gluten-free diet. Many people associate a gluten-free dietary approach with weight loss, increased energy, and better digestion. While scientific evidence supporting these claims is limited for the general population, some individuals may experience improvements in these areas when they eliminate gluten due individual sensitivities. [11] The growing popularity of gluten-free diets has raised concerns about potential nutritional deficiencies in those following them. Gluten-free products often have a different nutritional composition compared to their gluten-containing counterparts. This review aims to evaluate the existing scientific literature

to determine if a gluten-free diet leads to nutrient deficiencies and to identify strategies to mitigate such deficiencies.

Methods

To identify suitable literature, the authors employed a comprehensive search strategy. They extensively searched electronic database PubMed, utilizing relevant keywords and combinations such as “gluten-free diet” and “nutritional deficiencies”. Studies investigating the effect of gluten-free diet on nutrient intake, both in individuals with coeliac disease and those without any diagnosed gluten-related disorders, were included. The selected studies were critically analysed to assess the impact of gluten-free diets on macronutrient and micronutrient intake, as well as any associated deficiencies. Searches for studies constituting the basis of the article took place in the period from March to June 2023 and included only articles in English. As a result of the search, 89 articles were collected, of which 64 were rejected because they presented a different topic, unrelated to the main issue of the review. The remaining articles were found to meet the search criteria and our research objective.

Nutritional composition of gluten-containing grains

As is well known, products that typically contain gluten in their composition are wheat-based products: bread, pasta, cereal, flour, couscous, crackers, and baked goods like cookies, cakes, and pastries, barley-based products: barley malt, malt vinegar, malted beverages, and certain cereals, rye-based products: rye bread, rye flour, and some types of rye beer, other grains: some oats may contain gluten due to cross-contamination during processing. Processed foods such as sauces, dressings, soups, gravies, processed meats and packaged snacks can also contain hidden sources of gluten. Gluten is a mixture of proteins found in wheat, barley and rye. These proteins are called prolamins due to the large share of prolamin and glutamine residues in their structure. Wheat prolamins consist of gliadins and glutenins, while rye prolamins are called hordeins and barley prolamins are called secalins.[12] These proteins ensure the stability and extensibility of the gluten, which gives the dough an elastic consistency and makes it easier to rise during baking.[1] Grains containing gluten provide several nutritional benefits. They are a good source of carbohydrates, dietary fibre, and essential nutrients like iron, B vitamins such as thiamine, riboflavin, niacin, folate, and minerals like magnesium and zinc. Additionally, whole grains containing gluten can contribute to a healthy diet by providing antioxidants and phytochemicals.[13]

Nutritional deficiencies in patients with coeliac disease

When individuals with coeliac disease consume gluten, their immune system reacts by attacking the mucosa of the small intestine, causing inflammation and damage to the villi. The damaged villi are less effective in absorbing nutrients, such as iron, calcium, folate, vitamin D, vitamin B12, zinc and magnesium. The destruction of the villi decreases the surface area available for nutrient absorption. As a result, the overall absorption capacity of the small intestine is compromised. Secondary lactose intolerance is common in patients with coeliac disease due to decreased production of lactase by damaged villi. Limiting the consumption of milk and dairy products to avoid lactose as well as malabsorption can contribute to calcium, phosphorus and vitamin D deficiency.[14] Due to impaired iron absorption in the proximal small intestine, coeliac disease is known to be associated with iron deficiency anaemia. Coeliac disease can also affect the absorption of fats, leading to deficiencies in fat-soluble vitamins like vitamin A, vitamin E, vitamin D, and vitamin K. Vitamin A deficiency can manifest as night blindness or conjunctival dryness. Vitamin D deficiency may cause ostelomalacia, which manifests itself as muscle pain and weakness. Low levels of vitamin E may be associated with neuropathy and gait disorders, while vitamin K deficiency causes a decrease in synthesis coagulation factors II, VII, IX and X and the occurrence of haemorrhages. Insufficient absorption of folic acid and vitamin B12 can lead to red blood cell macrocytosis. Zinc deficiency states in the body are manifested by immunodeficiency, poor wound healing and alopecia. [15]The chronic inflammation in the small intestine can disrupt the normal functioning of the digestive system, affecting the production of digestive enzymes and the release of bile acids, which are necessary for proper digestion and absorption of nutrients. Moreover, people with coeliac disease often experience gastrointestinal symptoms such as diarrhoea, abdominal pain, and bloating, which can also further contribute to malabsorption and nutritional deficiencies. The severity of the previously mentioned nutritional deficiencies is influenced by various factors, including the duration of living with the undiagnosed yet active disease, the level of damage to the intestinal tract, and the extent of malabsorption. [14]It is crucial for individuals with coeliac disease to avoid gluten exposure and allow the intestines to heal. The adoption of a strict gluten-free diet in the majority of patients is undeniably associated with improvements in histological lesions, blood biochemistry, clinical manifestations, and the overall risk of complications related to coeliac disease.[16] Nevertheless, certain research has indicated that complete adherence to a gluten-

free diet fails to eradicate all pre-existing nutritional deficiencies[15][17] and in some cases, nutritional deficiencies developed only after many years of following a gluten-free diet.[18]

Gluten-free diet

A gluten-free product contains <20 ppm of gluten, accounting for potential contamination during production. [19]A gluten-free diet involves avoiding foods that contain wheat, barley, rye, and their derivatives. This includes products like bread, pasta, cereals, baked goods, and many processed foods that may contain hidden sources of gluten. However, there are numerous naturally gluten-free foods that can be enjoyed, such as fruits, vegetables, meat, fish, dairy products, legumes, nuts, and gluten-free grains like rice, corn, quinoa, and millet. Over time, the advancement of scientific research, intense marketing efforts, and media attention regarding the advantages of a gluten-free diet have prompted food companies to increase their production of gluten-free options. This significant rise in gluten-free alternatives enables individuals with coeliac disease to adopt dietary habits and patterns similar to the general population. To assist consumers who follow a gluten-free diet, the Food and Drug Administration (FDA) implemented a rule for gluten-free labelling, specifying the legal obligations for labelling products as "gluten-free", "free of gluten", "without gluten" or "no gluten". Additionally, local organic food stores commonly offer gluten-free products like bread and pasta, albeit at a slightly higher price and with a distinct flavour compared to their gluten-containing counterparts.[20] For years, a gluten-free diet has been widely recognized as the only effective remedy for coeliac disease. Complying strictly with this diet has proven to bring about substantial improvement, if not complete restoration of the intestinal mucosa. [21]By promoting small bowel recovery, the gluten-free diet helps alleviate symptoms related to malabsorption, such as diarrhoea, steatorrhea, and weight loss. Additionally, various studies have highlighted notable improvements in bone mineral density in patients following the diet. Despite numerous research efforts to explore alternative treatments for coeliac disease, the gluten-free diet remains the sole effective option currently available. [22] Nevertheless, adopting a gluten-free diet brings about significant lifestyle changes that can present numerous difficulties. Those adhering to a gluten-free diet face the daily challenge of cross-contamination, as sharing cupboards, countertops and kitchen appliances with individuals who don't follow the same diet can create opportunities for unintentional gluten exposure that hampers the effectiveness of the diet. Moreover, processed foods that contain gluten-based ingredients raise concerns, as hidden sources of gluten can be found in certain soups, processed meat, French fries, seasonings and beer. Finally, gluten-free products tend to be

more costly compared to their gluten-containing counterparts, and there are apparent nutritional drawbacks associated with the gluten-free diet.[20]

Nutrient deficiencies in individuals on a gluten-free diet

Dietary fibre

Following a gluten-free diet is a potential for low fibre intake. Fibre insufficiency may arise both at the time of diagnosis of coeliac disease and while adhering to a gluten-free diet. Upon diagnosis, the deficiency can be attributed to reduced absorption caused by villi atrophy. While following a gluten-free diet, it may be linked to the subpar quality of gluten-free products, individual choices made by patients, and the exclusion of various fibre-rich foods. [5] Whole grains are an important source of dietary fibre, and their elimination from the diet can result in a lower fibre intake.[23] The composition of numerous gluten-free foods, predominantly consisting of starches and refined flours lacking in fibre, is highly probable as the underlying cause for this phenomenon. Through the process of refinement, the outer layer of grain, which harbours a significant portion of the fibre, is stripped away, leaving behind solely the inner starchy layer. Low fibre intake is associated with various health problems, including constipation, diverticulitis, and increased risk of colorectal cancer. Therefore, people on a gluten-free diet should aim to consume fibre-rich foods, such as fruits, vegetables, nuts, and seeds.[24]

Vitamins

Coeliac patients, particularly when left untreated, experience vitamin deficiencies primarily caused by malabsorption in the small intestine. However, the latest research shows that the introduction of a gluten-free diet does not eliminate nutritional deficiencies. [5] Numerous studies have demonstrated that following a gluten-free diet results in deficiencies in vitamin D and vitamin E, alongside insufficient intake of B complex vitamins such as folate (B9), thiamine (B1), riboflavin (B2), and pyridoxine (B6).[5, 23] Certain gluten-free cereal products may be associated with reduced vitamin intake. Several studies indicate that these specific products contain lesser quantities of folate when compared to their gluten-containing alternatives. [18,24] Folate supplementation is recommended when following a gluten-free diet. Some naturally gluten-free products may serve as a beneficial folate source. Quinoa and amaranth have a notable quantity of folic acid. Additionally, these grains are rich in vitamins such as riboflavin, vitamin C, and vitamin E. Gluten-containing grains are fortified with various vitamins, especially B vitamins such as thiamine, riboflavin, niacin, and folic acid.

Reduced levels of B group vitamins have been linked to a decline in overall quality of life, while taking supplements of these vitamins has been shown to enhance general well-being.[25] When following a gluten-free diet, it's important to ensure alternative gluten-free products are also fortified or to seek other dietary sources of these vitamins. Additionally, incorporating a variety of fruits, vegetables, lean proteins and dairy or dairy alternatives (if tolerated) can help provide a range of essential vitamins.[24] Consuming a minimum of five servings of fruits and vegetables daily is crucial, especially for individuals with coeliac disease. This recommendation is essential because these foods contain antioxidants, which play a protective role in preventing issues related to oxidative damage. Patients with coeliac disease are at a significant risk of developing osteoporosis. Regrettably, simply removing gluten from the diet does not consistently restore normal bone mineral density, and adopting a gluten-free diet often leads to an imbalance in calcium and Vitamin D. Multiple studies have indicated that individuals with coeliac disease tend to consume lower levels of calcium and vitamin D than what is recommended. [14,24] Calcium levels can be brought back to normal by using a combination of gluten-free diet and the addition of vitamin D supplements.[5]

Minerals

Research has demonstrated that certain gluten-free products contain reduced levels of iron, magnesium, zinc, manganese, selenium, calcium or lack consistent fortification/enrichment when compared to their gluten-containing alternatives.[14,23] Iron deficiency anaemia can be a complication of a gluten-free diet. Therefore, it is crucial to advise patients to incorporate naturally gluten-free foods that are high in iron, such as meat and vegetables, into their diet. Additionally, they should diligently examine food labels of gluten-free products to assess their iron content. Whole grains, which are eliminated in a gluten-free diet, are a significant source of magnesium. Magnesium is involved in various bodily processes, including energy production, muscle function, and nerve transmission. Deficiency of magnesium can lead to symptoms like muscle cramps, weakness, and abnormal heart rhythms. Zinc is commonly found in gluten-containing foods like wheat germ and fortified cereals. Zinc is essential for immune function, wound healing, and cell growth. Inadequate zinc intake can result in weakened immune function and delayed wound healing.[5] Many gluten-containing foods are also good sources of calcium, such as fortified cereals, bread, and pasta. Insufficient calcium consumption may also be associated with limited dairy intake due to lactose intolerance. Consequently, in cases where patients have lactose intolerance and adhere to a gluten-free diet,

it might be worth considering calcium supplements as dairy consumption is likely to be significantly reduced or eliminated.[25]

Macronutrients

Individuals who adhere to a gluten-free diet face inadequate intake of macronutrients and energy. This may be attributed to the emphasis on avoiding gluten, which often overlooks the significance of ensuring nutritional adequacy in food choices. It is commonly recognized that gluten-free products generally contain higher amounts of carbohydrates and lipids, especially saturated fatty acids, compared to their gluten-containing counterparts. When it comes to proteins, animal food is typically the primary source in a gluten-free diet. Nonetheless, a number of studies have indicated that certain minor cereals and pseudo-cereals contain a higher protein content than commonly consumed cereals.[5] Continuing with the topic of macronutrient intake, it has been noticed that individuals adhering to a gluten-free diet often consume excessive amounts of fat. This is primarily due to the fact that gluten-free products are typically higher in fat content, as they use fat as a substitute for gluten. The extent of the consumption of specific gluten-free products is noteworthy, and certain studies indicate a correlation between following a gluten-free diet and elevated levels of saturated fatty acids.[25] The excessive consumption of dietary fats plays a significant role in the onset of conditions like coronary heart disease and obesity.[14]

Following a gluten-free diet involves refraining from consuming cereals that contain gluten, which happen to be the most commonly eaten cereals and serve as the foundation of balanced diet. Therefore, without appropriate guidelines, following this diet can lead to an imbalance. Individuals adhering to a gluten free diet often have a reduced intake of carbohydrates because they fear gluten consumption and consequently avoid cereals, particularly those rich in complex carbohydrates. However, their total carbohydrate intake may still be adequate due to the excessive consumption of simple sugars and processed foods.[25] Furthermore, when discussing carbohydrates, an important factor to consider is the glycaemic index (GI). People following a gluten-free diet may face an elevated risk of obesity due to the high glycaemic index of gluten-free foods. When comparing the nutritional composition of gluten-free bread and its regular counterpart, it was discovered that gluten-free products exhibit a high glycaemic index.[24] Additionally, these products tend to have low protein content and increased fat content. Hence, it can be inferred that the observed imbalances are not solely attributable to the limited or non-existent consumption of cereals containing gluten, but also to the high intake of processed gluten-free products and the insufficient consumption of

vegetables and legumes. It is essential to carefully examine food labels and the content of macronutrients, especially fat, when adhering to a strict gluten-free diet.[5]

Strategies to prevent nutrient deficiencies

Obtaining guidance from a nutrition expert is strongly recommended when starting a gluten-free diet. It is important to regularly monitor patients and enhance their understanding of a gluten-free diet. It should be noted that a well-balanced and diverse gluten-free diet, containing plenty of fruits, vegetables and fibres, does not inevitably result in malnutrition. One effective recommendation would be to enhance the diet by encouraging greater consumption of plant-based foods, including fruits, vegetables, legumes, nuts, naturally gluten-free whole grain cereals, and pseudocereals, while simultaneously reducing the intake of gluten-free products. In terms of macronutrients, the focus should be on reducing the intake of low-quality fats and simple sugars while increasing the consumption of complex carbohydrates. Incorporating pseudo-cereals like quinoa and amaranth is highly recommended as they are cost-effective and serve as valuable sources of micronutrients such as folate, riboflavin, vitamin C, and vitamin E. [25]

Conclusion

When examining the nutritional value of the gluten-free diet, it is common to find significant deficiencies in both essential macronutrients and micronutrients. Specifically, there is a noticeable decrease in vitamins and minerals and increased risk of obesity due to the high glycaemic index and high saturated fat content of the gluten-free diet. Some individuals who follow a gluten-free diet as well as patients with coeliac disease may continue to experience deficiencies in important nutrients, particularly fibre, vitamin B complex, vitamin D, calcium, iron, zinc, and magnesium. To address these issues, it is important to incorporate nutrition education into the treatment plan, helping individuals understand the significance of food labels, making appropriate food choices, and ensuring an adequate combination of macro- and micronutrients. Additionally, the dietary approach should promote the consumption of naturally gluten-free products, such as pseudo-cereals and minor cereals which have represented a good source of carbohydrate, dietary fibre, minerals, vitamins and phenols.[14] For those without diagnosed gluten-related disorders, adopting a gluten-free diet should be carefully considered, taking into account potential nutritional consequences. Further research is needed to better understand the long-term effects of gluten-free diets on nutritional status and the role of dietary interventions to mitigate potential deficiencies.

Author's contribution

Conceptualization: A.Ś.; Data curation: A.Ś., U.Ż., I.T., Z.K., K.A.; Writing- rough preparation: A.Ś., K.D., D.M., H.C.K.; Writing – review and editing: A.Ś., K.S., U.Ż, Z.K., K.D., D.M.; Supervision: A.Ś.; Project administration: A.Ś., K.D. All authors have read and agreed with the published version of the manuscript.

Disclosures

The authors received no financial support for this study. The authors declare no conflict of interest.

References

1. Biesiekierski JR. What is gluten? J Gastroenterol Hepatol. 2017 Mar;32 Suppl 1:78-81. doi: 10.1111/jgh.13703. PMID: 28244676.
2. Catassi C, Verdu EF, Bai JC, Lionetti E. Coeliac disease. Lancet. 2022 Jun 25;399(10344):2413-2426. doi: 10.1016/S0140-6736(22)00794-2. Epub 2022 Jun 9. PMID: 35691302.
3. Hujoel IA, Reilly NR, Rubio-Tapia A. Celiac Disease: Clinical Features and Diagnosis. Gastroenterol Clin North Am. 2019 Mar;48(1):19-37. doi: 10.1016/j.gtc.2018.09.001. Epub 2018 Dec 13. PMID: 30711209.
4. Varma S, Krishnareddy S. Novel Drug Therapeutics in Celiac Disease: A Pipeline Review. Drugs. 2022 Oct;82(15):1515-1526. doi: 10.1007/s40265-022-01784-2. Epub 2022 Oct 17. PMID: 36251239.
5. Vici G, Belli L, Biondi M, Polzonetti V. Gluten free diet and nutrient deficiencies: A review. Clin Nutr. 2016 Dec;35(6):1236-1241. doi: 10.1016/j.clnu.2016.05.002. Epub 2016 May 7. PMID: 27211234.
6. Cárdenas-Torres FI, Cabrera-Chávez F, Figueroa-Salcido OG, Ontiveros N. Non-Celiac Gluten Sensitivity: An Update. Medicina (Kaunas). 2021 May 24;57(6):526. doi: 10.3390/medicina57060526. PMID: 34073654; PMCID: PMC8224613.
7. Lerner A, O'Bryan T, Matthias T. Navigating the Gluten-Free Boom: The Dark Side of Gluten Free Diet. Front Pediatr. 2019 Oct 15;7:414. doi: 10.3389/fped.2019.00414. PMID: 31681712; PMCID: PMC6803387.
8. Taraghikhah N, Ashtari S, Asri N, Shahbazkhani B, Al-Dulaimi D, Rostami-Nejad M, Rezaei-Tavirani M, Razzaghi MR, Zali MR. An updated overview of spectrum of gluten-related disorders: clinical and diagnostic aspects. BMC Gastroenterol. 2020

Aug 6;20(1):258. doi: 10.1186/s12876-020-01390-0. PMID: 32762724; PMCID: PMC7409416.

9. Diez-Sampedro A, Olenick M, Maltseva T, Flowers M. A Gluten-Free Diet, Not an Appropriate Choice without a Medical Diagnosis. J Nutr Metab. 2019 Jul 1;2019:2438934. doi: 10.1155/2019/2438934. PMID: 31354988; PMCID: PMC6636598.
10. Germone M, Wright CD, Kimmons R, Coburn SS. Twitter Trends for Celiac Disease and the Gluten-Free Diet: Cross-sectional Descriptive Analysis. JMIR Infodemiology. 2022 Dec 5;2(2):e37924. doi: 10.2196/37924. PMID: 37113453; PMCID: PMC9987182.
11. Lerner BA, Green PHR, Lebwohl B. Going Against the Grains: Gluten-Free Diets in Patients Without Celiac Disease-Worthwhile or Not? Dig Dis Sci. 2019 Jul;64(7):1740-1747. doi: 10.1007/s10620-019-05663-x. PMID: 31102129.
12. Balakireva AV, Zamyatnin AA. Properties of Gluten Intolerance: Gluten Structure, Evolution, Pathogenicity and Detoxification Capabilities. Nutrients. 2016 Oct 18;8(10):644. doi: 10.3390/nu8100644. PMID: 27763541; PMCID: PMC5084031.
13. Melini V, Melini F. Gluten-Free Diet: Gaps and Needs for a Healthier Diet. Nutrients. 2019 Jan 15;11(1):170. doi: 10.3390/nu11010170. PMID: 30650530; PMCID: PMC6357014.
14. Saturni L, Ferretti G, Bacchetti T. The gluten-free diet: safety and nutritional quality. Nutrients. 2010 Jan;2(1):16-34. doi: 10.3390/nu20100016. Epub 2010 Jan 14. PMID: 22253989; PMCID: PMC3257612.
15. Naik RD, Seidner DL, Adams DW. Nutritional Consideration in Celiac Disease and Nonceliac Gluten Sensitivity. Gastroenterol Clin North Am. 2018 Mar;47(1):139-154. doi: 10.1016/j.gtc.2017.09.006. Epub 2017 Dec 7. PMID: 29413009.
16. Bascuñán KA, Vespa MC, Araya M. Celiac disease: understanding the gluten-free diet. Eur J Nutr. 2017 Mar;56(2):449-459. doi: 10.1007/s00394-016-1238-5. Epub 2016 Jun 22. PMID: 27334430.
17. Thompson T, Dennis M, Higgins LA, Lee AR, Sharrett MK. Gluten-free diet survey: are Americans with coeliac disease consuming recommended amounts of fibre, iron, calcium and grain foods? J Hum Nutr Diet. 2005 Jun;18(3):163-9. doi: 10.1111/j.1365-277X.2005.00607.x. PMID: 15882378.
18. Hallert C, Grant C, Grehn S, Grännö C, Hultén S, Midhagen G, Ström M, Svensson H, Valdimarsson T. Evidence of poor vitamin status in coeliac patients on a gluten-free

diet for 10 years. Aliment Pharmacol Ther. 2002 Jul;16(7):1333-9. doi: 10.1046/j.1365-2036.2002.01283.x. PMID: 12144584.

19. Jones AL. The Gluten-Free Diet: Fad or Necessity? Diabetes Spectr. 2017 May;30(2):118-123. doi: 10.2337/ds16-0022. PMID: 28588378; PMCID: PMC5439366.
20. Aljada B, Zohni A, El-Matary W. The Gluten-Free Diet for Celiac Disease and Beyond. Nutrients. 2021 Nov 9;13(11):3993. doi: 10.3390/nu13113993. PMID: 34836247; PMCID: PMC8625243.
21. Itzlinger A, Branchi F, Elli L, Schumann M. Gluten-Free Diet in Celiac Disease-Forever and for All? Nutrients. 2018 Nov 18;10(11):1796. doi: 10.3390/nu10111796. PMID: 30453686; PMCID: PMC6267495.
22. Wungjiranirun M, Kelly CP, Leffler DA. Current Status of Celiac Disease Drug Development. Am J Gastroenterol. 2016 Jun;111(6):779-86. doi: 10.1038/ajg.2016.105. Epub 2016 Mar 29. PMID: 27021196..
23. Wild D, Robins GG, Burley VJ, Howdle PD. Evidence of high sugar intake, and low fibre and mineral intake, in the gluten-free diet. Aliment Pharmacol Ther. 2010 Aug;32(4):573-81. doi: 10.1111/j.1365-2036.2010.04386.x. Epub 2010 Jun 4. PMID: 20528829.
24. Penagini F, Dilillo D, Meneghin F, Mameli C, Fabiano V, Zuccotti GV. Gluten-free diet in children: an approach to a nutritionally adequate and balanced diet. Nutrients. 2013 Nov 18;5(11):4553-65. doi: 10.3390/nu5114553. PMID: 24253052; PMCID: PMC3847748.
25. Cardo A, Churruca I, Lasa A, Navarro V, Vázquez-Polo M, Perez-Junkera G, Larretxi I. Nutritional Imbalances in Adult Celiac Patients Following a Gluten-Free Diet. Nutrients. 2021 Aug 21;13(8):2877. doi: 10.3390/nu13082877. PMID: 34445038; PMCID: PMC8398893.