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THE GLUTEN – FREE DIET BEYOND CELIAC DISEASE: TRENDS, RISKS AND NUTRITIONAL DEFICIENCIES

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ABSTRACT

Introduction: Gluten-free diet is effective treatment for celiac disease patients. However, the gluten-free diet has become increasingly popular in recent years, not only as a medical intervention for celiac disease but also as a lifestyle preference for individuals who perceive it as a healthier option. Additionally, there has been a growing number of studies investigating the use of gluten-free diets in the management of various medical conditions. Nevertheless, there are growing concerns regarding possible nutritional deficiencies associated with the exclusion of gluten-containing grains, as well as skepticism regarding the purported health benefits of a gluten-free diet in individuals without diagnosed gluten-related disorders.
Aim of the study: We aimed to systematically review the current knowledge about nutritional deficiencies and risks associated with gluten-free diet.
Methodology: An extensive search was conducted using electronic database PubMed to identify relevant studies published between 2010 and 2025. The search was based on keywords such as: 'gluten-free diet', 'celiac disease,' 'nutritional deficiencies,' and 'diet therapy,'.
Results and Discussion: Analysis of existing research suggests that individuals adhering to a gluten-free diet may be prone to inadequate intake of dietary fiber and several key micronutrients, including vitamins D, E, and B-group, along with critical minerals such as iron, zinc, calcium, and magnesium. Additionally, those consuming an imbalanced gluten-free diet often have a higher intake of total fat, particularly saturated fatty acids and cholesterol.
Conclusion: Current research indicates that adherence to a gluten-free diet is associated with specific micronutrient deficiencies. Individuals complying with this dietary regimen should be informed of the potential nutritional risks and adopt strategies to maintain an adequate and balanced nutrient intake. Clinical dietary oversight is recommended to identify and address common deficiencies linked to gluten exclusion.

KEYWORDS

Gluten-Free Diet, Nutritional Deficiencies, Gluten-Free, Fibre, Vitamins, Celiac, Disease

CITATION

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Introduction:

Celiac disease CD is chronic, systematic, autoimmune enteropathic disorder (*Ludvigsson* et al., 2013) that affects around 1% up to 2% of the general population (Catassi et al., 2022). The disease is triggered by gluten in genetically susceptible individuals causing complex immune reaction that results in inflammation and tissue damage of small intestinal mucosa as well as atrophy of the intestinal villi. The disease presents itself later with intestinal symptoms such as bloating, diarrhea, nausea, loss of appetite, stomach pain and weight loss, however since the disease is characterized as systemic, it affects also other organ systems such as skin, joint and muscles. Celiac disease can result in hospitalization due to complication such as significant hypoalbuminemia, cachexia, sarcopenia and electrolyte abnormalities (Caio et al, 2019). Non-classic celiac disease often manifests with vague gastrointestinal complaints, such as bloating, abdominal discomfort or constipation, along with a range of symptoms that are not directly linked to the digestive system. It may present with iron-deficiency anemia, osteoporosis, dermatitis herpetiformis or neurological manifestations such as headaches and peripheral neuropathy (Hujoel et al., 2018). Subclinical celiac disease describes a condition in which individuals exhibit no noticeable symptoms, yet still demonstrate the typical intestinal mucosal damage resulting from gluten exposure (Catassi et al., 2022).

Non-celiac gluten sensitivity (NCGS) is a condition in which individuals develop symptoms resembling those of celiac disease—such as gastrointestinal discomfort, fatigue, and headaches—despite the absence of a small intestinal mucosal damage. While the precise pathophysiologic mechanisms remain uncertain, NCGS is considered a separate entity from both celiac disease and wheat allergy. Symptom management generally

involves adherence to a gluten-free diet, which has been shown to improve clinical outcomes in affected individuals (Cardenas-Torres et, al. 2021).

Gluten is a protein found naturally in wheat, barley, and rye, (Biesiekierski et al., 2017) and is common in foods such as bread, pasta, cookies, and cakes. Gluten-containing grains offer a range of important nutritional advantages. They supply complex carbohydrates, dietary fiber, and key micronutrients such as iron, B vitamins including thiamine, riboflavin, niacin, and folate, along with minerals like magnesium and zinc. Moreover, whole grains that contain gluten support overall health by delivering beneficial antioxidants and phytochemicals (Melini et al.,2019).

Gluten-free diet is thoroughly studied as effective treatment available for celiac disease (Itzlinger et al., 2018). There is an abundance of data that confirms that a strict gluten-free diet is a key treatment strategy for celiac patients (Simon et al., 2023). Well maintained gluten free-diet leads to resolution of intestinal and extraintestinal symptoms, negativity of autoantibodies and the regrowth of the intestinal villi. However, this clinically validated therapeutic strategy is not without its challenges. A significant limitation of the gluten-free diet is the potential of micronutrient deficiencies (Caio et al., 2019). In patients with celiac disease, lifelong adherence to a strict gluten-free diet is essential, with no viable dietary alternative. While micronutrient deficiencies may initially appear to be a minor drawback, they can result in significant clinical complications over time.

Moreover, with a growing trend of gluten-free diet and an increase in its implications in treating various diseases, it comes a question of how well its use is medically assessed and confirmed by a wide range of medical research such as clinical trials, meta-analysis. Those concerns are of utmost importance when taking into account risks and disadvantages of a diet such as micronutrient deficiencies. Over the years, the growing interest of gluten-free diet resulted in expanding its clinical applications.

Piticchio et al. conducted first meta-analysis to examine the effect of gluten-free diet on autoimmune thyroiditis progression by monitoring TgAb, TPOAb, TSH, FT3 and FT4 levels in patients with Hashimoto thyroiditis and no symptoms or histology of celiac disease. A total of 87 patients were included in the analysis. The results of the meta-analysis indicate a tendency toward decreased levels of thyroid autoantibodies (TgAb and TPOAb) and significant improvements in thyroid function markers, particularly a reduction in TSH and an increase in FT4 levels, indicating potential clinical benefit. However, the reduction in autoantibodies levels were not statistically significant ($p > 0.05$), while changes in TSH and FT4 were significant ($p = 0.02$). FT3 levels remained stable, showing no notable variation. The authors stated that the results of the meta-analysis suggest a positive effect of gluten-free diet on thyroid function and its inflammation, however there is insufficient high-quality data to implement this dietary strategy in management of Hashimoto's thyroiditis.

Another area of interest is the assessment of the gluten-free diet's impact on the cardiovascular risk factors. Rohani et al, conducted systematic review and meta-analysis. A total of 19 studies met the inclusion criteria and were analyzed. Pooled results revealed that a gluten-free diet does not have a statistically significant impact on glucose metabolism parameters. Specifically, there were no meaningful changes observed in fasting glucose, insulin levels, or HbA1c following gluten-free diet intervention. These findings suggest that gluten-free diet may not influence glycemic control in a clinically relevant way. Moreover, the data demonstrated that adherence to a gluten-free diet was associated with a statistically significant increase in HDL levels, suggesting a favorable effect on this lipid parameter. However, the intervention did not yield significant changes in low-density lipoprotein cholesterol (LDL-C) or triglyceride (TG) concentrations. Furthermore, reduction in both systolic blood pressure (SBP) (WMD: –2.96 mmHg; 95% CI: –4.11 to –1.81; $p < 0.001$) and C-reactive protein (CRP) levels (WMD: –0.40 mg/L; 95% CI: –0.67 to –0.14; $p = 0.002$) were observed. Subgroup analyses revealed that gluten-free diet was associated with increased total cholesterol and HDL levels in individuals with celiac disease and when the dietary intervention exceeded 48 weeks. In contrast, shorter interventions and non-celiac populations exhibited less pronounced changes. These findings suggest that long-term adherence to a gluten-free diet may exert beneficial effects on select cardiovascular risk parameters, particularly in celiac patients, however, further high-quality, long-duration studies are needed to confirm these effects in broader populations.

In recent years gluten-free diet became much more than dietary treatment for celiac disease. Due to its perceived health benefits in individuals without celiac disease, the gluten-free diet has gained popularity as a modern dietary trend, often endorsed by certain healthcare professionals and amplified through social media and commercial marketing campaigns (Borghini et al., 2024). The main objective of this article is to discuss and investigate the risk of nutritional deficiencies with gluten-free diet. This is especially important for patients suffering from celiac disease, as a strict gluten-free diet is the primary treatment they must adhere to rigorously,

therefore knowledge about its limitations is vital. On the other hand, with growing popularity of gluten-free diet and an increase in its clinical applications, that lack thorough, evidence-based research, understanding the possible side effects and its impact on long-term health is crucial in making an informed decision.

Methodology

A systematic review of full-text scientific publications available in the PubMed database was conducted. The search was based on keywords such as: 'gluten-free diet', 'celiac disease,' 'nutritional deficiencies,' and 'diet therapy,' combining them with AND and OR logical operators, as applicable. The search was primarily focused on the last 15 years (2010- 2025). Only studies conducted on human participants were considered. The relevance and source of publications were manually assessed based on titles and abstracts. The collected information was analysed and synthesized.

Results and Discussion

Patients suffering from celiac disease that are untreated or newly diagnosed, present with nutritional deficiencies. Introducing gluten-free diet, the main treatment for celiac patients results in regeneration of intestinal mucosa and lead to better nutritional absorption. A study showed that during a first year of introducing gluten-free diet, patients with celiac disease became less anemic, however hemoglobin and folate levels remained below appropriate values. This leads to the conclusion that supplements such as iron should be introduced in first year of gluten-free diet, before intestinal mucosa recovery (Cardo et al., 2021). Moreover, comparable findings have been observed in the assessment of vitamin D deficiency and bone structure parameters. Vitamin D value elevated after first year of introducing gluten-free diet, however vitamin D levels remained suboptimal and were still lower compared to those of healthy individuals. As previously stated, the correction of nutritional deficiencies is linked to the healing of the intestinal lining following the elimination of gluten from the diet. Nevertheless, some patients do not exhibit full mucosal recovery even after one year on a gluten-free diet (Zanchetta et al., 2017).

Macronutrients

Research indicates that gluten-free products often contain higher levels of carbohydrates and fats compared to their gluten-containing equivalents. Segura et al. examined the nutritional profile of various gluten-free breads and reported that these items are predominantly starch-based, exhibit a high glycemic index (ranging from approximately 83 to 96 compared to 71 in standard white wheat bread) and are characterized by reduced protein and elevated fat content. The analyses confirmed that celiac patients adhere to unbalanced diet with high fat proportions and consume nutrition with high saturated fatty acids and cholesterol composition (Jamieson et al., 2020) (Ballestero et al., 2021). This may result from insufficient consumption of plant-derived foods combined with a high intake of processed gluten-free products. Individuals with celiac disease adhering to a gluten-free diet often rely heavily on gluten-free products, which typically contain higher amounts of total fat and saturated fatty acids compared to their gluten-containing counterparts (Wild et al., 2010). Furthermore, data compiled by Wild et al. indicated that nearly half (47%) of the total energy intake in a gluten-free diet originated from processed food items.

The inclusion of lipid-rich ingredients in the production of gluten-free baked goods is a necessary technological component that is difficult to eliminate (Sue et al., 2018). In terms of lipid composition commercially available gluten-free biscuits tend to have a higher proportion of saturated fatty acids than their gluten-containing equivalents. These nutritional limitations may pose health risks as limited dietary options often lead to increased consumption of processed gluten-free items such as packaged snacks and biscuits (Penagini et al., 2013). Several studies have documented that children with celiac disease tend to consume significantly more total fat compared to their healthy colleagues (Kautto et al., 2013).

Babio et al. conducted a study with 98 subjects with celiac disease and 98 participants as controlled group to compare the dietary pattern between two groups. Patients with celiac disease consumed significantly more added sugar ($p < 0.001$) and total fat ($p < 0.017$). Moreover, the study highlighted lower folic acid, calcium, iron and magnesium consumption in group with celiac disease patients.

Dietary Fibre

The gluten-free diet is often associated with reduced dietary fiber intake, largely due to the exclusion of fiber-rich whole grains and the reliance on gluten-free products made from refined flours and starches. These ingredients undergo processing that removes the fiber-dense outer grain layers, resulting in products with significantly lower fiber content. Studies, including those conducted in the United States among adults with celiac disease, have confirmed that individuals adhering to a gluten-free diet commonly fail to meet recommended fiber intake levels (Vici et al., 2016; Penagini et al., 2013). The significantly reduced fiber intake associated with gluten-free dietary that stems from decreased consumption of whole grains, may impair the prevention of lifestyle-related diseases such as obesity, type 2 diabetes and cardiovascular disorders (Taetzsch et al., 2018). Moreover, a low fibre diet may contribute to health conditions, including constipation or diverticulitis and higher likelihood of colorectal cancer (Penagini et al., 2013).

Micronutrients

Individuals with untreated celiac disease often present with multiple micronutrient deficiencies, such as iron, folate, fat-soluble vitamins (A, D, E, K), B-complex vitamins (B6, B12), zinc, and copper, due to malabsorption. Importantly, in some patients, these deficiencies persist despite adherence to a gluten-free diet, necessitating long-term supplementation to prevent ongoing nutritional imbalances. In certain treated cases, unresolved micronutrient deficits may contribute to extra-intestinal complications, including neurological conditions (e.g., neuropathy, ataxia, epilepsy, myelopathy, cognitive decline) and psychiatric symptoms such as anxiety, depression and paraesthesia. Additionally, these deficits can adversely affect bone health, increasing susceptibility to osteopenia and osteoporosis (Deora et al., 2017).

Moreover, research has demonstrated that many commercially available gluten-free products contain significantly lower levels of folate, iron, and B vitamins—particularly thiamine, riboflavin, and niacin, when compared to their gluten-containing equivalents. Two studies analyzing gluten-free products available in the United States revealed that these items are often inadequately fortified or enriched with key micronutrients. Comparative analysis confirmed that gluten-free alternatives consistently exhibited reduced concentrations of these essential nutrients relative to standard wheat-based products (Penagini et al. 2013).

Vitamin D

Vitamin D is responsible for bone health and plays a significant role in modulating immune system function. Patients with celiac disease present with low levels of bone mineral density due to multiple contributors such as inflammation, malabsorption and insufficient intake of calcium, vitamin D and K (Margulies et al., 2015). A gluten-free diet has been associated with notable improvements in bone mineral density within the first year of adherence. However, eliminating gluten alone may not be sufficient to fully restore bone density to normal levels. In many cases, following a gluten-free diet can lead to disruptions in calcium and vitamin D levels, contributing to ongoing skeletal health concerns. Research indicates that vitamin D supplementation alongside a gluten-free diet may help prevent continued bone demineralization, alleviate symptoms associated with osteomalacia, and restore normal calcium concentrations in the body (Zignone et al., 2018).

Vitamins B

Deficiencies in B-group vitamins, particularly B12 and folate, have been documented in individuals with celiac disease, even after long-term adherence to a gluten-free diet, as shown by Hallert et al., who also reported elevated homocysteine (tHcy) levels compared to the general population. Elevated tHcy is a known risk factor for cardiovascular disease, to which celiac patients are already more susceptible. These deficiencies are largely attributed to insufficient dietary intake rather than malabsorption. Supplementation with B vitamins has been shown to normalize tHcy levels, and thus regular dietary monitoring is essential, with particular emphasis on increasing folate intake through foods such as pseudo-cereals like quinoa and amaranth, as well as legumes and vegetables (Cardo et al., 2021).

Minerals and other vitamins

Clinical research examining the nutritional status of individuals following a gluten-free diet has demonstrated that their intake of minerals like calcium, iron, magnesium, and zinc is often below recommended levels. These studies suggest that a gluten-free diet may contribute to long-term deficiencies in essential micronutrients (Vici et al., 2016).

Furthermore, the literature frequently identifies iron, calcium, and magnesium as the most prevalent mineral deficiencies. Additionally, inadequate levels of iodine, potassium, and zinc are also commonly reported. Some studies demonstrate reduced intake of minerals such as selenium, sodium and manganese (Cardo et al., 2021).

Anemia is a frequent extraintestinal manifestation of celiac disease, affecting 5–40% of patients in Western countries and over 80% in developing regions. Iron deficiency anemia is the most prevalent type, though anemia in celiac disease can have multiple causes, including chronic disease, mixed nutrient deficiencies and even aplastic anemia. Research has shown a strong association between the severity of anemia and the degree of intestinal villous atrophy. Iron levels may take longer than six months to normalize even after mucosal healing, indicating that iron deficiency remains a persistent issue. Additionally, since gluten-free flours are not routinely fortified with iron like wheat flours, celiac disease patients face a higher risk of deficiency and should be encouraged to consume iron-rich foods such as red meat, vegetables, and fruits (Nardo et al., 2019).

When adhering to a gluten-free diet, it is crucial to choose gluten-free alternatives that are fortified with essential vitamins or to obtain these nutrients from other dietary sources. Furthermore, consuming a wide range of fruits, vegetables, lean protein options and dairy or suitable plant-based substitutes can support adequate intake of vital micronutrients (Penagini et al., 2013).

Approaches to Mitigate the Risk of Nutritional Deficiencies

Awareness about potential nutritional deficiencies that comes with gluten-free diet are a key element for maintaining well balanced diet and healthy lifestyle. Patients that plan to adhere to long lasting gluten-free diet should be advised to consult a dietitian. Presenting educational materials to address patients' most urgent needs such as recipes, reading labels as well as longer-term coping strategies for travel and eating out are vital. Furthermore, patients are advised to stay informed about updated clinical guidelines related to their condition and dietary management, as issued by reputable medical organizations. Patients should refrain from depending on unverified sources such as social media platforms or non-expert influencers for health-related information. A well-planned gluten-free diet that includes a variety of fruits, vegetables and fiber-rich foods does not necessarily lead to nutritional deficiencies. Prioritizing food that are naturally gluten-free rather than searching for processed gluten-free products is recommended. Encouraging increased consumption of plant-based foods such as fruits, vegetables, legumes, nuts, naturally gluten-free whole grains and pseudocereals has proven beneficial. Pseudocereals like quinoa and amaranth are affordable options and offer important micronutrients like folate, riboflavin, vitamin C, and vitamin E. Reducing poor quality fats and simple sugars and increasing complex carbohydrates in patients' diet is recommended (Cardo et al., 2021) (Itzlinger et al., 2018) (Wild et al., 2010).

Conclusion

These findings suggest that adhering to a gluten free diet can result in nutritional deficiencies. Patients are at risk of suffering from vitamins, multiple micronutrient and dietary fiber deficiencies. Moreover, they are exposed to higher levels of carbohydrates and fats in their everyday diet. Since celiac disease patients must adhere to a gluten-free diet rigorously as it is effective and thoroughly studied treatment, they should keep a well-balanced diet composed of high-quality products. Moreover, knowledge about diet's disadvantages and risks such as nutritional deficiencies give opportunity to supplement vitamins and micronutrients and monitor nutritional levels.

Recent clinical applications of the gluten-free diet indicate a growing trend of its use beyond the treatment of celiac disease. However, further research is needed to determine the mechanisms of action of this dietary plan on other diseases and its effect on patient's health. Moreover, more research with larger datasets and patient populations is necessary to develop clear indications and guidelines regarding the diseases in which a gluten-free diet is effective and preferred over other dietary interventions. Current evidence is limited by heterogeneous study designs and small sample sizes.

Disclosures

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