

Heavy Metal Exposure in Gluten-Free Diets: Current Evidence and Future Perspectives

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ABSTRACT

The gluten-free diet (GFD) is increasingly adopted, not only by individuals with celiac disease but also by the general population, often due to the perception that gluten is linked to various health problems. Studies indicate that GFD can alter macro- and micronutrient intake as well as fiber consumption. In addition to these nutritional concerns, attention has recently focused on potential heavy metal exposure associated with GFD. This risk is primarily attributed to increased consumption of rice-based products, pesticide residues in raw materials, and possible metal release during processing. Moreover, differences in the absorption and retention of heavy metals among individuals with celiac disease may influence long-term exposure patterns. This review aims to critically evaluate recent findings on the potential heavy metal burden of GFD and to discuss their relevance for both celiac and non-celiac populations.

Keywords: Gluten-free diet, gluten-free foods, heavy metal contamination, dietary risk assessment, celiac disease

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INTRODUCTION

Gluten, composed of gliadin and glutenin proteins, is mainly found in wheat and rye (1). It has attracted considerable attention due to its association with wheat-related disorders (2). Three major conditions linked to gluten consumption are celiac disease, non-celiac gluten sensitivity, and wheat allergy (3). Among these, Celiac disease has been the primary focus of clinical and public health interest, leading to the widespread adoption of the gluten-free diet (GFD) (4, 5).

The foundation for GFD was laid in 1950 through the pioneering research of Dr. Willem Karel Dicke (6) who identified the harmful effects of gluten on individuals with celiac disease. Subsequent studies demonstrated that gluten exposure causes villus atrophy in the small intestine and that strict adherence to GFD restores mucosal integrity and is essential for long-term health (7). Today, celiac disease is diagnosed using serological tests, genetic markers, and small bowel biopsy (8). Although alternative therapies are under investigation, current guidelines from The European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), European Society for the Study of Coeliac Disease (ECD), and World Gastroenterology Organization (WGO) continue to emphasize strict lifelong adherence to GFD as the standard care (3, 9).

The prevalence of celiac disease has increased in recent years, largely due to improved screening and awareness, while the concept of broader “gluten-related disorders” remains debated (10). At the same time, the use of GFD has expanded beyond individuals with celiac disease or other gluten-related disorders. Data from the National Health and Nutrition Examination Surveys (NHANES) indicate that while the prevalence of celiac disease remained stable between 2009 and 2014, adherence to GFD increased significantly in the general population (11). This trend is expected to grow further in the coming years (12). However, the widespread adoption of GFD among individuals without a confirmed medical indication has raised concerns regarding nutritional imbalances and misconceptions about their health benefits (13).

The growing popularity of GFD among individuals without medical indication is largely driven by the perception that gluten contributes to various health problems and that gluten-free products are inherently healthier (14-16). However, current evidence does not support the routine implementation of GFD in conditions other than celiac disease, wheat allergy, and non-celiac gluten sensitivity (17-19). Therefore, clinical status and dietary patterns should be carefully evaluated before recommending GFD outside established indications.

Gluten-free products are now widely available in grocery stores, providing dietary alternatives that replace wheat-containing products and facilitate energy and nutrient intake (5, 20). According to U.S. Food and Drug Administration (FDA) regulations, a product may be labeled as “gluten-free” if it contains less than 20 ppm gluten, including possible contamination during production (4). Despite this regulatory clarity, a common misconception persists that gluten-free foods automatically offer superior health benefits. Many are produced using refined flours and starches, frequently with lower fiber content and less fortification compared to conventional products (14, 21). Studies suggest that GFD may alter macro- and micronutrient intake, potentially leading to lower levels of calcium, iron, magnesium, zinc, vitamin B12, folate, vitamin D, and fiber, alongside increased intake of fat and simple carbohydrates (1, 21, 22).

Beyond nutritional considerations, another emerging concern is the potential association between GFD and heavy metal exposure. Several studies have reported elevated concentrations of heavy metals in the blood and urine of individuals adhering to GFD (16, 23). This risk is primarily attributed to the frequent use of rice and rice-based ingredients in gluten-free products. Rice, cultivated in flooded conditions, readily accumulates inorganic arsenic and other heavy metals from soil and water (23).

Rice consumption is already high in Türkiye; according to the Turkey Nutrition Health Survey (2017), 45% of individuals consume rice at least two to three times per week (24). For individuals following GFD, especially those relying heavily on packaged rice-based products, cumulative exposure may be higher. Additionally, environmental contamination, pesticide residues, and potential metal release during processing may further contribute to total dietary exposure (25).

It is also important to consider whether altered intestinal absorption in individuals with celiac disease may influence heavy metal uptake. Intestinal atrophy at diagnosis and mucosal recovery following long-term GFD adherence may affect absorption dynamics, potentially modifying systemic metal levels.

Given the increasing prevalence of GFD and the growing body of literature addressing heavy metal concentrations in gluten-free products and biological samples, a comprehensive evaluation of current evidence is warranted. This review aims to summarize and critically assess available data on heavy metal content in gluten-free foods and heavy metal exposure among individuals adhering to GFD, with attention to both celiac and non-celiac populations.

Heavy Metal Levels in Gluten-Free Food Products

Exposure to heavy metals is of particular concern in individuals adhering to GFD, as increased consumption of rice and fish may result in elevated levels of these metals in the body. Rice, cultivated in flooded fields, readily absorbs inorganic arsenic from soil and water. Consequently, rice and rice-based gluten-free products may pose health concerns due to their potential heavy metal content (19, 26).

Despite the significant increase in the consumption of gluten-free foods, their composition and nutritional profiles have not been comprehensively evaluated. A critical aspect of food quality and safety is the potential presence of contaminants, both organic and inorganic. Attention is given to non-degradable substances that can bioaccumulate within the food chain. Such contaminants may be found in gluten-free foods due to the intensive use of pesticides or their release from raw materials used during the production process (25).

A U.S.-based study examined the nutrient content of gluten-containing and gluten-free products. The products were categorized into three groups: (i) flour types, (ii) rice types, and (iii) ready-to-eat foods. The analysis revealed that “rice” was among the initial three ingredients listed in most gluten-free products. It was determined that the total arsenic concentration in rice flour (rice: 112 ng/kg; wheat: 11 ng/kg; others: 12 ng/kg; $p < 0.05$) and ready-to-eat foods containing rice (rice-containing: 141 ng/kg; non-rice-containing: 13 ng/kg; $p < 0.0001$) was significantly higher compared with products derived from other grains. Similarly, mercury concentrations in rice were considerably higher than in other grains ($p < 0.0001$) (23). In contrast, Collumb et al. (27) that certain metals were more prevalent in selected gluten-containing products than in gluten-free alternatives. However, the detected amounts were below the action levels set by the WHO (2004) and were not expected to produce adverse effects in the context of a healthy diet. Nevertheless, the possibility of chronic toxicity due to long-term, low-level exposure to metal-containing gluten-free or gluten-containing foods cannot be excluded (27). A study conducted in Saudi Arabia assessed the heavy metal content of foods labeled as gluten-free and sold in local markets. The findings revealed that the levels of chromium (e.g., coconut biscuit: 0.268 ± 0.035 mg/kg), iron (e.g., rice cereal: 2009 ± 8 mg/kg), lead (e.g., chocolate balls: 0.66 ± 0.02 mg/kg), nickel (e.g., rice cereal (42.3 ± 3.8 mg/kg), and manganese levels (e.g., spaghetti: 100.3 ± 0.7 mg/kg) were found to exceed the permissible limits established by the reference authorities (WHO, Turkish Food Codex, NAS/NRC Food and Nutrition Board, Brazilian Ministry of Health, European Commission). To ascertain the similarities between the selected sample and other products, a hierarchical cluster analysis (HCA) was conducted. The

results of the HCA indicated that the rice cereal and flour mixture were in the same group and that their metal contents were similar. This finding suggests that consumers' preferences may be influenced by the similarity of heavy metal contents within the same group (28). A similar study was conducted in Kayseri/Türkiye, which revealed that the mean levels of zinc (8.30 ± 0.36 mg/kg; Turkish Food Codex reference value: 5 mg/kg) and cadmium (0.14 ± 0.03 mg/kg; WHO reference value: 0.057–0.071 mg/day) in some selected samples; nickel (1.65 ± 0.19 mg/kg; Turkish Food Codex reference value: 0.2 mg/kg) in all samples were higher than acceptable levels. The calculations of the metal contamination index revealed that cocoa cookies (4.83), flour (3.85), and spaghetti (3.52) exhibited the highest concentrations of metals among the gluten-free products. The analyzed heavy metal contents represented 7.55–35.3% of acceptable daily intake levels, suggesting that the gluten-free products tested had low nutritional quality indices (29). Another Turkish study analyzing 41 gluten-free food samples reported the highest trace element levels in specific products: popcorn and crunch for copper (51.45 ± 5.37 mg/kg), chocolate sauce for iron (137.43 ± 6.72 mg/kg), pre-cooked chickpea flour for manganese (20.80 ± 3.42 mg/kg), carob flour for strontium (12.85 ± 2.28 mg/kg), and yeast for zinc (91.98 ± 6.32 mg/kg). The analysis also revealed that pre-cooked pea flour (15.21) and chocolate sauce (15.02) exhibited the highest metal pollution index. It was also demonstrated that consuming 100 grams per day of pasta (104.49%), popcorn and crunch (497.01%), or noodles (313.08%) may exceed the recommended daily intake of copper. Similarly, the study found that foods such as tarhana soup (117.52%), baby biscuits (108.76%), chocolate sauce (166.29%), and cornflakes (140.62%) were shown to potentially surpass the recommended daily intake of iron (30).

An Italian study reported elevated metal pollution indices in breadsticks (0.44), lasagna (0.42), and local bread (0.41). The findings underscored the potential health risks associated with cadmium, lead, and copper contamination (31). A study by Orecchio et al. (32). examined the heavy metal content of gluten-free products in Italy. The analysis revealed that specific food items, including noodles, finger biscuits, grissini, and croutons, could potentially exceed the established daily reference limits for lithium. In Nordic countries, nickel ($p=0.001$) and lead ($p=0.004$) concentrations were found to be elevated in gluten-free products compared with gluten-containing counterparts. While lead concentrations remained below the EU standard of 20 $\mu\text{g}/100$ g, no comparable standard exists for nickel (33). A recent Polish study evaluating naturally gluten-free cereals and pseudocereals reported that cadmium and lead concentrations in selected products exceeded EU limits. However, calculated Target Hazard Quotient (THQ)

and Cancer Risk (CR) values remained below risk thresholds, suggesting no immediate health concern under reported consumption levels (34). Similarly, another Polish study, found that gluten-free bread contained lower cadmium levels than wheat-rye bread and did not pose significant cancer or non-cancer risk based on calculated CR values. Nevertheless, constant consumption of cadmium-contaminated bread may present a potential cancer risk in young children (35).

Overall, studies conducted across multiple countries indicate that gluten-free products—particularly those based on rice—often contain higher concentrations of certain heavy metals compared with gluten-containing counterparts. While most reported levels remain below regulatory limits, specific products or consumption patterns may approach or exceed reference values. Even when concentrations do not indicate immediate toxicity, the potential effects of chronic low-level exposure warrant careful consideration. Therefore, comprehensive dietary assessments are essential to better understand cumulative exposure and its possible health implications.

Heavy Metal Exposure in Individuals Following a Gluten-Free Diet and in Celiac Disease

Data from the NHANES examined blood and urine heavy metal levels in individuals adhering to GFD. The analysis revealed significantly higher concentrations of blood mercury ($p=0.008$), lead ($p=0.007$), cadmium ($p=0.03$), and urine arsenic ($p=0.002$) among individuals following GFD. In a subsequent analysis excluding individuals with celiac disease, elevated blood and urine levels of heavy metals remained significant ($p>0.05$) among those on GFD, except for cadmium ($p=0.06$). Furthermore, when the analysis was restricted to individuals who had consumed fish in the last 30 days, those on GFD exhibited higher mercury levels than non-adherents, suggesting that other foods, in addition to seafood, may contribute to this association. These findings indicate that individuals adhering to GFD without a celiac disease diagnosis may still be at risk for elevated heavy metal exposure, independent of fish consumption (36).

In contrast, Kamycheva et al. (40), also using NHANES 2009–2012 data, reported a significant association between celiac seropositivity and lower blood lead and mercury levels in children aged 6–17 years, while no such association was observed in adults. The authors suggested that reduced intestinal absorption due to villous atrophy at diagnosis might contribute to lower systemic metal levels in children with untreated celiac disease (37). Elli et al. (38) further investigated mercury concentrations in a cohort of 30 patients with celiac disease (20 treated and 10 with intestinal atrophy) and 20 healthy controls, considering potential confounding factors such as fish consumption and dental amalgam fillings. Treated celiac patients showed

higher blood ($10.2 \pm 6.7 \mu\text{g/L}$) and urinary mercury levels ($2.2 \pm 3.0 \mu\text{g/L}$) compared with patients with persistent atrophy ($2.4 \pm 2.3 \mu\text{g/L}$; $1.0 \pm 1.4 \mu\text{g/L}$, respectively) and healthy controls ($3.7 \pm 2.7 \mu\text{g/L}$; $1.3 \pm 1.2 \mu\text{g/L}$, respectively) ($p < 0.05$). These findings suggest that mucosal recovery following long-term adherence to GFD may influence mercury absorption. However, urinary mercury levels did not increase proportionally, indicating that additional mechanisms, including possible genetic predisposition, may be involved.

In a recent study by Du et al. (39), elevated urinary arsenic levels ($3.3 \mu\text{g/L}$ vs. $13.6 \mu\text{g/L}$, $p < 0.001$) and total nail arsenic levels ($0,082 \mu\text{g/g}$ vs. $0,139 \mu\text{g/g}$, $p = 0,024$) were demonstrated in newly diagnosed children and adolescents living in the United States. The results of three-day food consumption records indicate that individuals' consumption of rice-containing sources of arsenic increased after six months of adherence to GFD (3.2 vs. 6.8 servings, $p < 0.001$). Although the correlation between urinary arsenic levels and rice consumption, an important marker of arsenic exposure was weak ($r = 0.22$), and urinary arsenic levels remained below toxicity thresholds, this study highlights the need for a more detailed examination of the relationship between celiac disease and arsenic exposure.

Taken together, although the number of studies in this area remains limited, the existing literature highlights the importance of investigating the interplay between GFD adherence, celiac disease, and heavy metal burden. Current evidence suggests that elevated heavy metal levels may be linked to GFD adherence, the physiological consequences of celiac disease, or a combination of both factors. Future research should adopt longitudinal designs, include larger and more diverse cohorts, and apply detailed dietary assessments to clarify these mechanisms. Additionally, exploring genetic predispositions, the duration of GFD adherence, and the extent of intestinal recovery may provide further insight into the complex relationship between heavy metal uptake, diet, and celiac disease.

Possible Effects of Heavy Metal Accumulation

Metals of toxicological concern include mercury, lead, cadmium, and arsenic. Their global prevalence has increased due to extensive industrial and agricultural activities, contributing to environmental contamination and subsequent entry into the food chain (19).

Heavy metal toxicity may manifest as either acute or chronic, depending on several factors such as the exposure dose, the developmental stage of the individual, and the duration of exposure. A critical determinant of associated health outcomes is the degree of bioaccumulation within biological tissues. Bioaccumulation occurs in all living organisms through continuous exposure

to heavy metals from dietary and environmental sources. In addition, their release during food production and packaging processes further contributes to exposure, thereby posing potential health risks (25).

Accumulation of heavy metals in vital organs has been demonstrated to induce oxidative stress, which can lead to the generation of reactive oxygen species, carcinogenesis, and neurological disorders (19). Moreover, their endocrine-disrupting properties may adversely affect hormonal regulation, enzyme activities, and the body's antioxidant defense capacity (40).

An important mechanism underlying heavy metal toxicity involves epigenetic modifications. These metals can influence epigenetic regulatory mechanisms, including DNA methylation, histone modifications, and non-coding RNA expressions. Alterations in gene expression mediated through these epigenetic pathways are considered significant contributors to cancer development (41, 42).

CONCLUSION AND RECOMMENDATIONS

Although accumulating evidence highlights the potential heavy metal burden associated with the GFD, its clinical significance remains uncertain. A central challenge in understanding this relationship lies in evaluating how strictly individuals adhere to GFD and which alternative foods are consumed in place of gluten-containing products. If GFD does contribute to heavy metal exposure, it is important to recognize that long-term, cumulative exposure may result in bioaccumulation within the body.

The current evidence is heterogeneous, as studies analyzing the heavy metal content of gluten-free products show considerable variation. This variability may be attributed to differences in environmental conditions where raw materials are cultivated, disparities in agricultural practices, and inconsistencies in food processing and packaging. While many studies report that heavy metal concentrations remain below regulatory thresholds, the long-term health effects of chronic, low-level exposure remain insufficiently understood. Given the well-documented metabolic, neurological, and carcinogenic effects of heavy metals, even low-level accumulation warrants concern.

Particular caution is required when interpreting studies involving individuals with celiac disease. It remains necessary to distinguish whether elevated heavy metal levels arise primarily from dietary patterns associated with GFD or from pathophysiological changes related to the disease itself, such as altered intestinal absorption. Although GFD remains the only effective

treatment for celiac disease, individuals without a confirmed diagnosis should be carefully evaluated before adopting long-term dietary restriction, considering potential heavy metal exposure, nutritional adequacy, and overall sustainability.

The increasing prevalence of childhood celiac disease further emphasizes the importance of this issue, as prolonged lifelong exposure to gluten-free products may contribute to cumulative metal intake. From a public health perspective, individuals adhering to GFD should be informed about the potential risks associated with excessive reliance on rice-based products. Encouraging dietary diversification—through the inclusion of alternative gluten-free grains such as sorghum, millet, buckwheat, amaranth, and quinoa—may help reduce dependency on rice and mitigate potential exposure.

Future research should prioritize longitudinal study designs, larger and more diverse cohorts, and standardized methodologies for assessing heavy metal concentrations in both food products and biological samples. Comprehensive dietary assessment tools and evaluation of genetic or physiological factors influencing metal absorption may further clarify the complex relationship between GFD adherence, celiac disease, and heavy metal burden.

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