

Selected Micronutrients and Gut Health: Relationships with Gut Microbiota, Intestinal Barrier Function, and Immunity

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Abstract

Deficiency of micronutrients has been linked to metabolic disorders like rickets, scurvy, and anemia for decades. But recent studies indicate that even deficiency of vitamins and minerals affects the function of the digestive tract and disrupts the immune system. Some important micronutrients like zinc, iron, and vitamins A, D, and B12 play a significant role in ensuring the balance between the host, gut bacteria, and the immune system. Deficiencies of these micronutrients can disrupt gut microbial composition, reduce SCFA-producing bacteria, and impair intestinal barrier function. Evidence from observational, experimental, and mechanistic studies suggests that micronutrient status is associated with differences in gut microbial composition, microbial metabolite production, intestinal barrier-associated processes, and immune regulation. However, the available evidence does not establish a single causal pathway from micronutrient deficiency to dysbiosis, barrier dysfunction, endotoxemia, and systemic immune dysregulation in humans. (Barone et al., 2022; Gombart et al., 2020; Guetterman et al., 2022)

This narrative review synthesizes evidence on the relationships between selected micronutrient deficiencies, gut microbial composition, intestinal barrier function, and immune regulation, with emphasis on the strength and limitations of evidence relevant to clinical nutrition.

To provide an overview of how micronutrient deficiency affects the microbial community of the gut, intestinal epithelium integrity, and immune regulation, the following figure shows the key mechanisms by which nutrition influences gut-immune homeostasis.

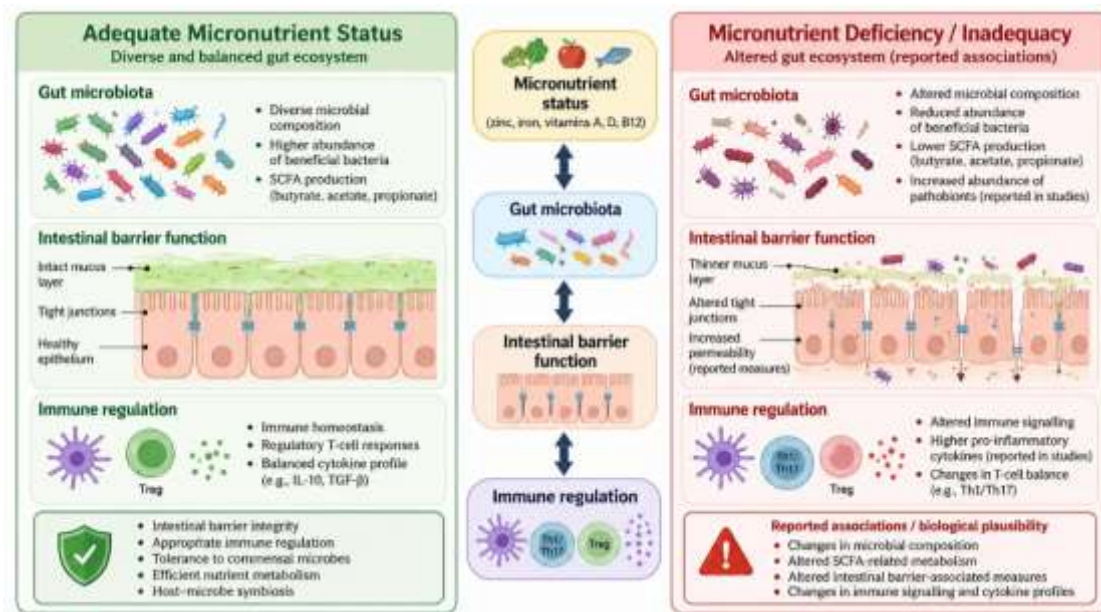


Figure 1. Proposed Relationships Between Micronutrient Status, Gut Microbiota, Intestinal Barrier Function, and Immune Regulation.

Note. Author-generated figure created using AI-assisted visualization tools based on concepts synthesized from Kau et al. (2011), Sekirov et al. (2010), Gombart et al. (2020), Barone et al. (2022), and Nishida et al. (2018).

SCFA = short-chain fatty acid; LPS = lipopolysaccharide; Treg = regulatory T cell; Th1 = T-helper 1 cell; Th17 = T-helper 17 cell.

Keywords: Dysbiosis; Gut microbiota; Immune dysregulation; Intestinal permeability; Micronutrient deficiency.

1. Introduction

Deficiencies of micronutrients were traditionally associated with metabolic disorders including rickets, scurvy, and anemia. However, growing evidence suggests that insufficient intake of essential vitamins and minerals also compromises integrity of the intestinal barrier, affects gut microbe population structure and immune system regulation (Gombart et al., 2020; Huskisson et al., 2007). Micronutrients besides their importance for cellular metabolism play an important part in maintenance of mucosal homeostasis and efficient immunity.

Microbiota of the gut contributes to nutrient metabolism, bioactive compound synthesis, and immune maturation (Sekirov et al., 2010; Kau et al., 2011; Nishida et al., 2018). Human and experimental studies have reported associations between micronutrient status and changes in gut microbial composition, microbial metabolic activity, and intestinal barrier-related processes. However, the direction and causality of these relationships remain incompletely established and may vary according to the micronutrient, population, underlying disease, and study design (Barone et al., 2022; Gombart et al., 2020; Barra et al., 2021). These alterations have been associated with changes in microbial balance, intestinal permeability-related measures, and immune regulation, although evidence for a direct causal sequence remains limited in humans (Barone et al., 2022; Gombart et al., 2020).

However, the clinical interpretation of these relationships is still challenging, as the evidence available is heterogeneous regarding study design, populations, and outcomes. Nevertheless, the relationships between micronutrient status, gut microbiota, intestinal barrier function and immune regulation have been described in previous reviews.

In particular, the evidence from human observational studies, intervention studies, animal models and mechanistic studies does not provide similar support for causal inference. Furthermore, the association between gut health and micronutrient status is potentially bidirectional, as gastrointestinal disease, inflammation, altered absorption, dietary restriction and changes in dietary intake can all contribute to micronutrient deficiency.

This narrative review discusses the reported relationships of gut microbial composition, intestinal barrier function, and immune regulation, as well as zinc, iron, and vitamins A, D and B12. Synthesis of evidence is also provided. Special emphasis is placed on differentiating evidence by study design and identifying areas where the findings from experimental or observational research are not yet ready for translation into clinical recommendations. The review considers the implications of these relationships for clinical nutrition practice and nutritional assessment, including the interpretation of micronutrient biomarkers in inflammatory and gastrointestinal diseases.

1.1. Rationale for the Selection of Micronutrients

Zinc, iron, and vitamins A, D, and B12 were selected as the focus of this narrative review because they represent distinct biological pathways through which micronutrient status may interact with the gut microbiota, intestinal barrier function, and immune regulation. Zinc is involved in epithelial maintenance and immune function, while iron has a complex relationship with microbial growth, host nutritional immunity, and intestinal homeostasis (Gombart et al., 2020; Yilmaz & Li, 2018; Seyoum et al., 2021). Vitamins A and D participate in mucosal immune regulation and epithelial function, whereas vitamin B12 is involved in host metabolism and has also been investigated in relation to the gastrointestinal microbiome (Akimbekov et al., 2020; Lv et al., 2016; Sun, 2018; Guetterman et al., 2022).

Examining these micronutrients together provides an opportunity to compare different biological mechanisms and assess the extent to which experimental findings are supported by human evidence. Previous literature has described interactions between micronutrients and the gut microbiome, including relationships involving mineral availability, microbial metabolism, epithelial function, and immune regulation (Barone et al., 2022; Gombart et al., 2020; Guetterman et al., 2022).

Other micronutrients, including vitamin K and additional B vitamins, also participate in microbial metabolism and host physiological processes (Barone et al., 2022; Yoshii et al., 2019). However, a comprehensive evaluation of all micronutrients is beyond the scope of this focused narrative review. The discussion is therefore restricted to zinc, iron, and vitamins A, D, and B12, with particular attention to differences between mechanistic findings, observational associations, and evidence relevant to clinical nutrition.

2. Fundamental Mechanisms: Micronutrients at the Host–Microbe Interface

2.1. Microbial Requirements for Essential Vitamins and Trace Minerals

The gut microbiota requires enough vitamins and minerals to facilitate metabolic activities and ecosystem stability. While some bacterial species produce certain vitamins, including vitamin K and specific B vitamins, many others depend on nutrients acquired from the host organism and other microorganisms (Guetterman et al., 2022). Vitamin B12 is involved in microbial metabolism and DNA synthesis, and

interactions between vitamin B12 and the gastrointestinal microbiome have been reported. However, available evidence is heterogeneous, and current evidence does not establish that vitamin B12 deficiency directly causes clinically relevant alterations in the human gut microbiome (Guetterman et al., 2022; Yoshii et al., 2019).

In addition, micronutrients affect the mechanisms of host organism to maintain balance in the microbial population. For instance, vitamin D helps maintain the integrity of the epithelium and its antimicrobial functions via vitamin D receptors, while vitamin A assists in sustaining mucosal membrane and developing goblet cells (Akimbekov et al., 2020; Sun, 2018; Lv et al., 2016). At the same time, iron and zinc are vital to the functioning of both microorganisms and host organism. Lack of trace elements leads to the disruption of microbial homeostasis and impairment of the immune response and development of dysbiosis; however, too much iron is associated with an increase in the number of pathogenic microorganisms (Chai et al., 2024; Cheng et al., 2024; Yilmaz & Li, 2018; Seyoum et al., 2021).

There is mutual dependency between the microbiota and nutrition: the presence of micronutrients impacts microbial community, while microbiota affects the way nutrients are metabolized and absorbed by host cells. Thus, micronutrient deficiency and dysbiosis may occur simultaneously, and their relationship may be bidirectional: altered microbial and intestinal function may influence nutrient metabolism and absorption, while micronutrient status may in turn influence microbial and host processes (Barone et al., 2022; Guetterman et al., 2022).

2.2. Nutritional Immunity: Host Regulation of Micronutrients During Infection

The term 'nutritional immunity' refers to an innate immunity response where the host deprives the pathogens of essential nutrients to limit their survival. Iron regulation is one of the ways the body uses to achieve this purpose. Hepcidin-induced iron sequestration during infection leads to decreased iron intake from the intestines and reduced iron availability for microbes (Yilmaz & Li, 2018; Seyoum et al., 2021). Despite being an effective way to limit pathogen infection, the lack of iron may cause anemia and change gut microbiota composition (Yilmaz & Li, 2018; Seyoum et al., 2021).

Also, zinc is tightly regulated when infections occur because it is a crucial factor that influences microbial reproduction and immune functions in the host. The lack of zinc leads to increased risk of inflammation and infections due to impaired function of epithelium, oxidative stress and immune response (Chai et al., 2024; Gombart et al., 2020).

Moreover, fat-soluble vitamins participate in mucosal immunity. Specifically, vitamin D plays the role of regulating antimicrobial peptide production and barrier function of epithelium while vitamin A affects mucosal tolerance, lymphocytes differentiation, and secretion of IgA (Akimbekov et al., 2020; Sun, 2018; Lv et al., 2016). Thus, the lack of those micronutrients affects mucosal immunity and increases the risk of development of the disorders.

2.3. Impact of Micronutrient Depletion on Gut Epithelial Barrier Integrity

The intestinal epithelium functions as a selective barrier that separates luminal contents from the host immune system. Vitamins and trace elements are necessary for epithelial integrity, mucus production and immune regulation and therefore the maintenance of this barrier requires adequate micronutrient availability. Deficiency of key micronutrients may impair barrier function and increase intestinal permeability, thereby contributing to chronic inflammatory disorders.

Vitamins D and A have important roles in mucosal homeostasis. Vitamin D receptor signalling supports tight junctions and antimicrobial peptide production, and vitamin A supports epithelial differentiation and mucus secretion through its effects on goblet cells (Akimbekov et al., 2020; Sun, 2018; Lv et al., 2016).

Deficiencies in either vitamin can compromise the integrity of the barrier and increase susceptibility to microbial translocation.

Trace elements like zinc and iron are also required for epithelial maintenance and immune function. Zinc deficiency affects epithelial repair and the integrity of tight junctions, while changes in iron homeostasis can alter microbial balance and intestinal physiology (Chai et al., 2024; Cheng et al., 2024; Seyoum et al., 2021; Yilmaz & Li, 2018). These changes combined facilitate the translocation of microbial products, such as lipopolysaccharides (LPS), into the circulation resulting in systemic inflammation and chronic disease (Hakansson & Molin, 2011; Valdes et al., 2018).

3. Specific Micronutrient Deficiencies: Impact on Dysbiosis and Immune Signalling

3.1. Zinc Deficiency: T-Cell Differentiation and Altered Gut Microbial Composition

Zinc has an impact on maintenance of the intestinal barrier, repair of the epithelium and regulation of immune responses. Since zinc uptake takes place predominantly in the gastrointestinal tract, zinc deficiency has been associated with changes in gut microbial composition and intestinal homeostasis in experimental and observational studies (Chai et al., 2024; Cheng et al., 2024). The changes in the ratio of Firmicutes/Bacteroidetes, loss of commensal organisms and enrichment of pro-inflammatory microbial population have been linked to zinc deficiency (Chai et al., 2024; Cheng et al., 2024).

Experimental and observational evidence suggests that inadequate zinc status may be associated with alterations in microbial metabolites, intestinal barrier-related processes, and host immune responses; however, the extent to which these findings represent direct causal effects in humans remains uncertain (Chai et al., 2024; Cheng et al., 2024; Gombart et al., 2020).

Clinically, zinc deficiency may be relevant in patients with enteric infections, chronic gastrointestinal inflammation, or conditions associated with inadequate intake or impaired absorption. Zinc status can be corrected through dietary or supplemental intake when deficiency is confirmed or clinically indicated; however, excessive supplementation may have adverse effects and may alter the balance of other trace elements.

3.2. Iron Deficiency and Excess: Luminal Availability, Pathogen Outgrowth, and Inflammation

Iron is involved in metabolism of microbes, functions of the epithelium and regulation of immune responses, thus iron homeostasis is an important factor determining the state of gut. Both iron deficiency and excess iron availability have been associated with changes in microbial composition and intestinal physiology. Iron deficiency causes impairment of energy metabolism of the epithelium, impairment of immune system functioning and decreased numbers of bacteria producing short chain fatty acids.

However, too much iron in the lumen of the intestine cause proliferation of opportunistic bacteria, oxidative stress and inflammation of the mucosa (Yilmaz & Li, 2018; Seyoum et al., 2021). Sequestration of iron under the influence of hepcidin is important for suppression of pathogens during inflammation, however, this process leads to anemia and changes in composition of microbial community.

3.3. Vitamin A Deficiency: Secretory IgA Impairment and Loss of Mucosal Immune Tolerance

Vitamin A, through its active metabolite retinoic acid, plays a crucial role in maintaining intestinal barrier integrity and regulating mucosal immunity. Deficiency impairs epithelial cell differentiation, weakens immune regulation, and increases susceptibility to infection (Lv et al., 2016).

Vitamin A deficiency has been associated with alterations in gut microbial composition and mucosal immune function. In children with persistent diarrhoea, vitamin A deficiency has been associated with alterations in gut microbial composition; however, because gastrointestinal disease itself may affect

nutrient intake and status, these findings do not establish a unidirectional causal relationship (Lv et al., 2016).

Vitamin A status is also relevant to goblet-cell function, mucus production, and mucosal barrier maintenance. In children with persistent diarrhoea, low vitamin A status has been associated with differences in gut microbial composition and microbial diversity (Lv et al., 2016). However, these findings should be interpreted in the context of the underlying gastrointestinal condition, as diarrhoeal disease may itself influence dietary intake and micronutrient status.

3.4. Vitamin D Deficiency: Antimicrobial Peptide Suppression and Pro-Inflammatory Immune Activation

Through the activation of vitamin D receptors (VDRs) expressed in immunological and epithelial cells, vitamin D has a significant role in regulating intestinal immunity and microbial homeostasis (Akimbekov et al., 2020; Sun, 2018). VDR signalling stimulates the synthesis of antimicrobial peptides, including defensins and cathelicidins, which aid in preserving microbial equilibrium and preventing pathogenic colonization.

Vitamin D deficiency has been associated with differences in microbial diversity, the abundance of butyrate-producing bacteria, and intestinal barrier-related measures. Experimental studies suggest that vitamin D receptor signalling may influence epithelial integrity and immune regulation; however, the extent to which vitamin D deficiency directly causes microbial translocation or chronic inflammation in humans remains uncertain (Akimbekov et al., 2020; Sun, 2018). Vitamin D also participates in the regulation of adaptive immune responses, including regulatory T-cell and Th1/Th17-related pathways, although the clinical significance of these effects may vary according to the underlying condition.

Vitamin D deficiency with its effects on dysbiosis, impaired barrier function, and susceptibility to inflammatory diseases is associated with failure of VDR-mediated pathways, thereby underscoring the role of vitamin D in the maintenance of gut–immune homeostasis (Akimbekov et al., 2020; Sun, 2018). The major effects of micronutrient deficiencies on gut microbiota, intestinal barrier function, and immune responses are summarized in Table 1.

Table 1. Effects of micronutrients on Gut and Immune Health

Micronutrient	Gut microbiota / barrier / immune effects	Potential clinical relevance
Zinc	Associated with alterations in microbial composition, epithelial integrity and immune function	May be relevant in conditions involving deficiency, impaired intake or intestinal dysfunction
Iron	Iron availability can influence microbial growth and intestinal microbial ecology; both deficiency and excess may alter host–microbe interactions	Relevant to iron deficiency, supplementation and conditions involving altered iron homeostasis
Vitamin A	Associated with mucosal immune function, epithelial maintenance and microbial composition	Deficiency may be relevant in populations with inadequate intake or malabsorption
Vitamin D	Associated with microbial composition, epithelial barrier-related processes and immune regulation	Relevant to conditions involving vitamin D deficiency and altered immune function

Source: Compiled and adapted from Akimbekov et al. (2020); Chai et al. (2024); Cheng et al. (2024); Lv et al. (2016); Seyoum et al. (2021); Sun (2018); Yilmaz & Li (2018).

4. Systemic Consequences: The Gut–Immune Axis

4.1. Loss of Short-Chain Fatty Acid Production and Metabolic Endotoxemia

Fermentation of dietary fiber by microbes results in the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, all of which play an important role in gut health (Ranjbar et al., 2021). Mucin production from SCFAs, the maintenance of epithelial cell tight junctions, energy supply to colonocytes, and the regulation of immune functions are all supported by SCFAs (Simpson & Campbell, 2015). Micronutrient deficiencies can affect the composition of gut microbes and decrease the number of SCFA-producing bacteria, reducing the availability of SCFA. Butyrate helps maintain intestinal permeability, supports epithelial barrier integrity, and promotes the translocation of bacterial products such as lipopolysaccharides (LPS) into the bloodstream (Brahe et al., 2016). Low-grade chronic inflammation and metabolic endotoxemia result from this process. Additionally, by enhancing the activity of regulatory T cells and reducing excessive inflammatory responses, SCFAs also contribute to immune homeostasis. Therefore, decreased SCFA production may promote immune dysregulation and increase the risk of developing inflammatory and autoimmune disorders (Kim, 2023).

4.2. Local Mucosal Inflammation and Systemic Immune Hyper-Responsiveness

The gastrointestinal tract has a crucial role in maintaining immune tolerance and protecting the host from potentially pathogenic microbes. The dynamic interactions among the intestinal epithelium, the resident microbiome, microbial-derived metabolites, and immune cells are key players in modulating this delicate homeostasis (Garabatos & Santamaria, 2022).

When disrupted due to microbial dysbiosis and micronutrient deficiency, these interactions can lead to prolonged immune activation, increased intestinal permeability, and impaired barrier function. Decreased microbial diversity and lowered production of potentially beneficial metabolites, such as short-chain fatty acids, increase pro-inflammatory immune responses, and as a result, increase CD4⁺ Th1 and Th17 cell activity while reducing regulatory T cell function (Candelli et al., 2021). Chronic intestinal inflammation and pathology associated with IBD and autoimmune diseases have been attributed to ongoing activation of inflammatory pathways.

In addition, the translocation of microbial products and inflammatory mediators from the intestine into the systemic circulation promotes systemic inflammation, increased oxidative stress, and immune dysregulation, which may contribute to the pathogenesis of extra-intestinal diseases, including cardiovascular disease, diabetes mellitus, neurodegenerative disorders, and allergic diseases (Valdes et al., 2018; Prescott et al., 2016; Violi et al., 2023).

4.3. Chronic Inflammatory and Autoimmune Consequences of Nutrient–Dysbiosis Interactions

Disruption of the gut microbiome–immune system axis has been linked to a growing number of chronic inflammatory and autoimmune diseases. Commensal bacteria and metabolites produced by commensal bacteria play a key role in helping develop immune tolerance and a healthy immune response (Garabatos & Santamaria, 2022; Levy et al., 2017; Hakansson & Molin, 2011). However, microbial dysbiosis, reduction of short-chain fatty acid production, or compromised intestinal barrier integrity may lead also to increased chronic immune system activation and loss of immune tolerance.

One possible explanation for this loss of immune tolerance is ‘molecular mimicry’, in which microbial antigens mimic host proteins, which leads to an inappropriate immune response to the body’s own tissues

(Suliman, 2024). The increased permeability of the intestine allows for greater exposure to endotoxins and microbial antigens, which can increase the duration of autoimmune activity and chronic inflammation. Each of these changes has been associated with rheumatoid arthritis, Type 1 diabetes, multiple sclerosis, systemic lupus erythematosus, and autoimmune thyroid disease (Kim, 2023). Additionally, chronic low-level inflammatory diseases related to dysbiosis have been linked to metabolic syndrome, obesity, cardiovascular disease, liver disease and allergy-related diseases (Valdes et al., 2018; Prescott et al., 2016). Collectively, these data demonstrate the importance of restoring gut microbial balance and barrier function when developing prevention strategies for chronic inflammatory diseases.

5. Clinical Perspectives and Therapeutic Interventions

5.1. Biomarkers of Concurrent Deficiencies and Dysbiosis

Conventional indicators like serum ferritin, zinc, retinol, and vitamin B12 are helpful in detecting micronutrient deficiencies, but they don't tell us much about how they affect the integrity of the gut barrier, the makeup of microbes, and immune function. As a result, integrating nutritional, inflammatory, permeability, and microbiome-related biomarkers is becoming more and more necessary for thorough evaluation.

Intestinal permeability and endotoxemia markers such as zonulin, intestinal fatty acid-binding protein (I-FABP), lipopolysaccharide (LPS), lipopolysaccharide-binding protein (LBP), and faecal calprotectin can shed light on intestinal inflammation and barrier dysfunction (Candelli et al., 2021; Violi et al., 2023). Concurrently, inflammatory mediators such TNF- α , IL-6, IL-17, and C-reactive protein (CRP) may indicate continuous immunological activity. Microbial diversity, the number of beneficial bacterial taxa, and the amounts of short-chain fatty acids (SCFAs), which are markers of microbial metabolic activity and gut health, may all be assessed thanks to developments in microbiome analysis (Kim, 2023; Yu et al., 2025).

No single biomarker is adequate for diagnosing dysbiosis since it is influenced by numerous nutritional, genetic, environmental, and clinical factors. Therefore, integrated diagnostic approaches combining nutritional, inflammatory, permeability, and microbiological markers may provide a more comprehensive assessment of the gut-immune-nutrition axis. Key biomarkers are summarized in Table 2.

Table 2. Integrated Biomarkers for Assessing the Gut-Immune-Nutrition Axis

Biomarker Class	Specific Markers	Clinical Utility & Target
Traditional Nutritional	Serum ferritin, zinc, retinol, vitamin B12.	Confirms baseline systemic nutrient deficiencies, though limited in showing localized gut damage.
Systemic Inflammation & Endotoxemia	Circulating lipopolysaccharide (LPS), TNF-alpha, IL-6, IL-17, C-reactive protein.	Indicates metabolic endotoxemia and chronic immune activation driven by microbial translocation.
Intestinal Permeability	Zonulin, lipopolysaccharide-binding protein (LBP), intestinal fatty acid-binding protein (I-FABP), faecal calprotectin.	Confirms tight junction degradation, structural barrier failure, and active mucosal inflammation.

Microbial & Metabolic	Short-chain fatty acids (butyrate, acetate, propionate), microbial sequencing.	Identifies stalled bacterial fermentation, loss of microbial diversity, and pro-inflammatory shifts in flora.
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Source: Compiled and adapted from Candelli et al. (2021); Kim (2023); Violi et al. (2023); Yu et al. (2025).

5.2. Challenges in Targeted Micronutrient Supplementation: Avoiding Pathogen Promotion

Micronutrient deficits must be corrected, although supplementing may be less successful in people with severe intestinal inflammation and gut dysbiosis. Reduced nutrient absorption and, in certain situations, a changed response to supplementation might result from compromised barrier function and altered microbial composition.

This difficulty is exemplified by iron supplementation. Excess luminal iron may encourage the growth of opportunistic bacteria and raise oxidative stress in the gut environment, despite being essential for treating iron shortage (Yilmaz & Li, 2018; Seyoum et al., 2021). In a similar vein, taking too much zinc supplements might upset the microbial balance and prevent other trace elements from being absorbed. The degree of intestinal inflammation and absorptive dysfunction may also affect how well vitamins A, D, and B12 supplements work. Therefore, restoring serum nutrient levels should not be the only goal of effective care of micronutrient deficiencies; underlying dysbiosis and compromised gut function should also be addressed. Alternative distribution methods may be taken into consideration in specific situations to enhance treatment results.

5.3. Precision Nutrition: Integrating Prebiotics, Probiotics, and Micronutrients

Precision nutrition, which takes into account the relationships between food, gut microbiota, and immune function rather than concentrating just on nutrient replacement, is becoming more and more important in the management of micronutrient deficiency-associated dysbiosis (Barone et al., 2022; Valdes et al., 2018). In order to enhance gut and immunological function, this strategy seeks to restore both nutritional status and microbial balance.

Prebiotics, such as resistant starch, pectin, inulin, and other indigestible fibers, encourage the growth of good bacteria and increase the synthesis of short-chain fatty acids (SCFAs), especially butyrate, which maintains the integrity of the epithelial barrier and regulates the immune system (Gibson et al., 2017; Collins & Reid, 2016). By enhancing microbial balance and lowering intestinal inflammation, probiotics—particularly *Lactobacillus* and *Bifidobacterium* species—may further aid in microbial restoration (Vyas & Ranganathan, 2012; Collins & Reid, 2016).

A positive feedback loop that promotes recovery from micronutrient insufficiency may be created by restoring a healthy microbiome, which may also enhance nutrient metabolism and absorption (Barone et al., 2022; Guetterman et al., 2022). Combined approaches incorporating dietary change, prebiotics, probiotics, and targeted nutrient supplementation seem to be more successful than single therapies, despite ongoing issues with strain selection, individual variability, and long-term efficacy.

5.4. Dietary Sources and Recommended Intake of Key Micronutrients

Deficiency of certain micronutrients constitutes one of the biggest causes of disruption of normal gut microbiota, impaired epithelial barrier function, and dysregulated immunity. Whereas clinical cases of deficiencies necessitate therapeutic treatment, ensuring sufficient dietary intake of certain nutrients represents a sustainable and physiologically optimal way to ensure healthy levels. The main micronutrients responsible for maintenance of normal microbial diversity and regulation of immune response include

zinc, iron, vitamins A, D, and B12. Sources and bioavailability of each nutrient may vary significantly depending on whether the person consumes a plant- or animal-based diet.

Heme iron is absorbed by the body much faster than non-heme iron found in plants; moreover, while the latter is readily available, vitamin B12 is almost exclusively found in foods of animal origin. In addition, unlike other nutrients discussed above, vitamin D cannot be taken from the diet, thus making sunlight the best source of this vitamin. It is crucial to consume adequate amounts of these micronutrients not only in order to prevent classic deficiency diseases but also to maintain gut-microbiota-immune axis balance. (Gombart et al., 2020; Barone et al., 2022; Guetterman et al., 2022). To help make the application of diet easier, Table 3 provides the recommended daily allowances, primary sources, and the physiological roles played by the micronutrients essential for gut and immune function.

Table 3. Recommended Dietary Allowances (RDA), dietary sources, and physiological functions of key micronutrients involved in gut and immune health.

Nutrient	RDA for Adults*	Major Vegetarian Sources	Major Non-Vegetarian Sources	Key Physiological Functions
Zinc	Men: 11 mg/day; Women: 8 mg/day	Pumpkin seeds, sesame seeds, chickpeas, lentils, cashew nuts, whole grains	Oysters, beef, lamb, poultry, eggs	Supports immune function, epithelial repair, antioxidant defence, and microbial homeostasis
Iron	Men: 8 mg/day; Women: 18 mg/day	Spinach, amaranth, lentils, soybeans, rajma, jaggery, sesame seeds	Liver, red meat, poultry, fish, shellfish	Essential for oxygen transport, cellular metabolism, immune competence, and microbial balance
Vitamin A	Men: 900 µg RAE/day; Women: 700 µg RAE/day	Carrots, sweet potato, pumpkin, spinach, kale, mango, papaya	Liver, egg yolk, dairy products, fish liver oil	Maintains epithelial integrity, mucus production, and mucosal immune tolerance
Vitamin D	15 µg/day (600 IU)	UV-exposed mushrooms, fortified milk, fortified cereals	Salmon, sardines, mackerel, egg yolk, fish liver oil	Regulates antimicrobial peptide production, calcium metabolism, and immune modulation
Vitamin B12	2.4 µg/day	Fortified cereals, fortified plant-based milk, nutritional yeast, dairy products	Liver, fish, shellfish, poultry, meat, eggs	Required for DNA synthesis, red blood cell formation, neurological health, and microbial metabolism

*RDA values based on Dietary Reference Intakes for healthy adults (Trumbo et al., 2001; Gombart et al., 2020; Dominguez et al., 2021).

6. Future Directions and Conclusion

6.1. Knowledge Gaps: Causality and Translational Limitations

Although recent studies suggest that micronutrient deficiency can lead to gut dysbiosis and immune disorders, the exact nature of these interrelated phenomena needs further investigation (Barone et al., 2022; Hou et al., 2025). The current evidence base includes human observational studies, intervention studies, animal experiments, mechanistic investigations, systematic and narrative reviews, and genetic or Mendelian-randomization analyses. These study designs provide different levels and types of evidence, and their findings should therefore be interpreted according to their methodological limitations and capacity to support causal inference. (Barone et al., 2022; Guetterman et al., 2022; Hou et al., 2025)

Moreover, numerous mechanistic studies use animal models, which prevents the generalization of results to humans. Thus, future studies need to be longitudinal and include the data related to nutrition, the microbiome, immunity, and metabolism. The application of multi-omics will allow getting a deeper insight into the interaction between nutrients, gut barrier, microbiome, and immune system to develop diagnostics and therapy of the diseases.

6.2. Conclusion

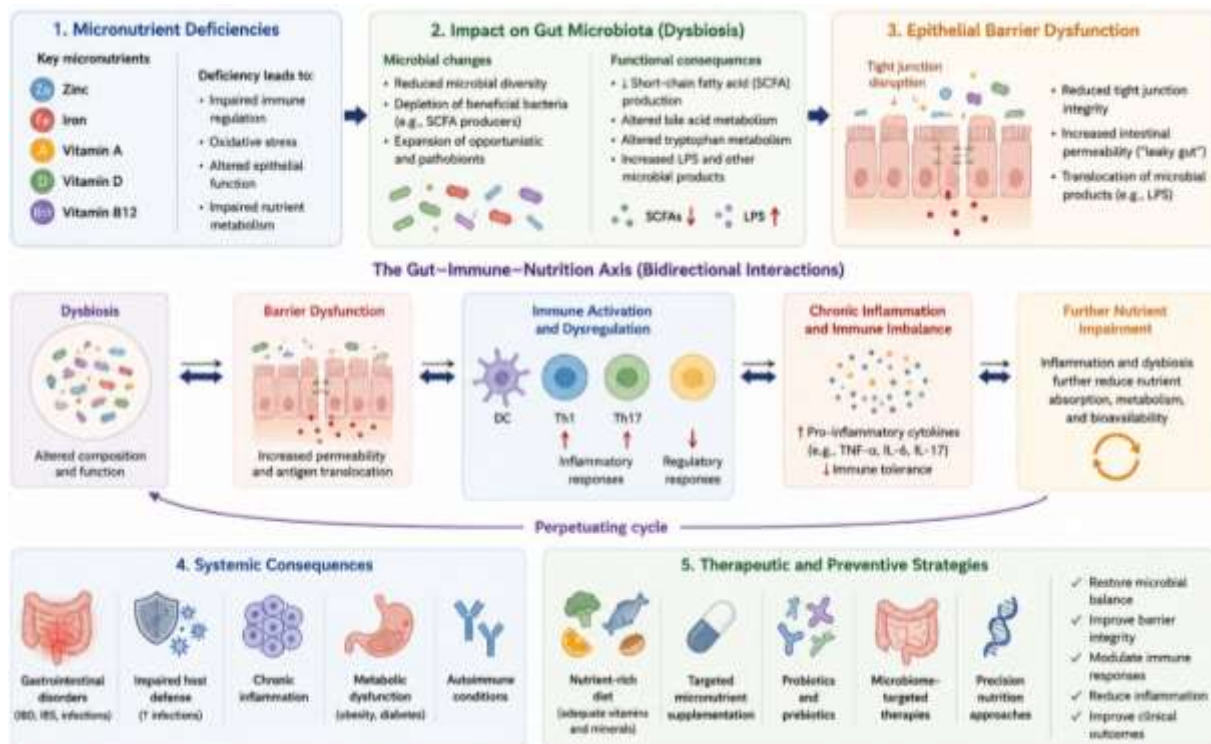
Micronutrients are crucial for maintenance of the balance of the gut microbiome, integrity of the intestine barrier, and immune homeostasis. Available evidence indicates that micronutrient status is associated with gut microbial composition, intestinal barrier-related processes, and immune regulation. However, the strength and direction of these relationships vary across micronutrients, populations, underlying diseases, and study designs. Evidence from observational and experimental studies supports biological plausibility, but does not consistently establish a direct causal pathway from micronutrient deficiency to dysbiosis, barrier dysfunction, or systemic inflammation in humans.

The relationship between micronutrient status, gut microbiota, intestinal barrier function, and immunity is reciprocal. Gastrointestinal disease, inflammation, altered absorption, reduced dietary intake, and increased nutritional requirements may contribute to micronutrient deficiency, while micronutrient inadequacy may also influence microbial, epithelial, and immune processes. Consequently, the presence of micronutrient deficiency alongside gut dysfunction should not by itself be interpreted as evidence of a unidirectional causal pathway.

Current studies show that the treatment of such disorders needs approaches other than simple supplementation of missing micronutrients. Nutritional, microbial, and immunological interventions can be more successful. With further development of knowledge about the interconnection between gut, immunity, and nutrition, personalized treatments including changes in diet, administration of prebiotics, probiotics, and supplements may become a perspective strategy of prevention and treatment of chronic inflammatory conditions (Barone et al., 2022; Gombart et al., 2020).

The relationships among micronutrient deficiencies, gut dysbiosis, intestinal barrier dysfunction, and immune impairment are summarized in Figure 2.

Figure 2. Proposed Interactions Between Micronutrient Status, Gut Microbiota, Intestinal Barrier Function, and Immune Health.



Note. Author-generated figure created using AI-assisted visualization tools based on findings synthesized from Akimbekov et al. (2020), Chai et al. (2024), Cheng et al. (2024), Lv et al. (2016), Yilmaz and Li (2018), Seyoum et al. (2021), and Gombart et al. (2020).

SCFA = short-chain fatty acid; LPS = lipopolysaccharide; DC = dendritic cell; Th1 = T-helper 1 cell; Th17 = T-helper 17 cell; IBD = inflammatory bowel disease; IBS = irritable bowel syndrome.

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