

FACTORS INHIBITING OPTIMAL PROTEIN UTILIZATION AMONG CHILDREN: A NARRATIVE REVIEW

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Abstract

Background: Adequate protein intake is essential for child growth, yet optimal growth depends not only on protein quantity but also on the efficiency of protein utilization. Multiple biological and environmental factors may impair the conversion of dietary protein into functional body proteins, contributing to growth faltering despite sufficient protein intake.

Methods: This narrative review synthesized recent evidence published between 2020 and 2026 from PubMed, Scopus, ScienceDirect, and Google Scholar. Studies involving pediatric populations from birth to 18 years of age were considered, with priority given to peer-reviewed original studies, systematic reviews, meta-analyses, clinical guidelines, and consensus statements addressing factors affecting protein digestion, absorption, metabolism, and tissue protein synthesis. **Results:** Protein utilization is influenced by dietary protein quality, digestive function, intestinal absorption, environmental enteric dysfunction, gut microbiota, infection, inflammation, micronutrient status, energy adequacy, and socioeconomic and environmental conditions. These factors interact to reduce amino acid bioavailability, suppress anabolic pathways, increase protein catabolism, and impair tissue protein synthesis, thereby limiting linear growth. **Conclusions:** Optimizing child growth requires integrated nutrition strategies that combine high-quality protein intake with interventions supporting intestinal health, adequate energy and micronutrient intake, infection prevention, and improved environmental conditions to maximize protein utilization.

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Keywords: Protein utilization; Child growth; Protein quality; Environmental enteric dysfunction; Protein metabolism

Introduction

Child undernutrition remains one of the most persistent public health challenges worldwide, despite substantial progress in nutrition interventions over the past two decades. According to the 2024 Joint Child Malnutrition Estimates released by UNICEF, the World Health Organization (WHO), and the World Bank, an estimated of 150.2 million children under five years of age (23.2%) were stunted, while 42.8 million (6.6%) experienced wasting in 2024.¹ Growth faltering during early childhood has profound consequences, including impaired cognitive development, weakened immune function, reduced educational attainment, lower economic productivity in adulthood, and an increased risk of chronic diseases later in life.²⁻⁴

Protein is an essential macronutrient required for tissue accretion, skeletal muscle development, immune competence, enzyme production, and the synthesis of structural and functional proteins that support normal growth.⁵ During infancy and childhood, protein requirements increase substantially because of rapid linear growth and high rates of protein turnover. Adequate dietary protein intake has consistently been associated with improved height gain, lean body mass, and developmental outcomes.^{6,7} Current nutritional strategies therefore emphasize increasing both the quantity and quality of dietary protein, particularly through animal-source foods and high-quality complementary feeding.^{8,9} Animal-source proteins are particularly important during early childhood because they provide highly digestible indispensable amino acids that efficiently stimulate tissue protein synthesis and linear growth.¹⁰ Adequate protein intake alone does not always translate into optimal growth, indicating that factors beyond dietary intake influence the biological utilization of protein.

Protein utilization encompasses a series of physiological processes extending beyond protein consumption, including digestion, amino acid absorption, transport, cellular uptake, metabolic regulation, and protein synthesis. Disruption at any stage of this pathway may reduce the efficiency with which dietary protein is converted into functional body proteins.¹¹ Gastrointestinal infections, environmental enteric dysfunction, chronic inflammation, gut microbiota dysbiosis, inadequate energy intake, micronutrient deficiencies, and poor dietary protein quality have each been associated with impaired protein utilization in children. These conditions may increase protein catabolism, reduce amino acid bioavailability, suppress

anabolic signaling pathways, or impair intestinal absorptive capacity, thereby limiting growth even when protein intake appears sufficient.^{12,13}

The efficiency of protein utilization is also influenced by broader environmental and socioeconomic determinants. Children living in resource-limited settings are frequently exposed to recurrent infections, poor sanitation, food insecurity, and limited dietary diversity. Such conditions interact with biological mechanisms that regulate protein metabolism and contribute to persistent growth deficits.^{14,15} Nutritional interventions focusing solely on increasing protein intake often produce heterogeneous outcomes because they do not adequately address factors that compromise protein digestion, absorption, or metabolic utilization. This complexity underscores the importance of adopting a multidimensional perspective when evaluating protein-related interventions for child growth.^{16,17}

Although numerous reviews have examined dietary protein intake, protein quality, or the association between protein consumption and child growth, relatively few have synthesized the diverse biological, nutritional, and environmental factors that inhibit optimal protein utilization in children. Existing evidence is dispersed across studies investigating infection, intestinal health, micronutrient status, dietary composition, inflammatory responses, and socioeconomic conditions, making it difficult to establish an integrated understanding of how these factors collectively influence protein metabolism and growth. A comprehensive synthesis of these mechanisms is needed to support more effective nutrition policies and intervention strategies.

In this review, children are defined as individuals from birth to 18 years of age, encompassing infancy, childhood, and adolescence. This narrative review aims to synthesize current evidence regarding the biological, dietary, environmental, and socioeconomic factors that inhibit optimal protein utilization among children. The review also discusses the underlying mechanisms through which these factors interfere with protein digestion, absorption, metabolism, and protein synthesis, and highlights their implications for child growth and future nutrition interventions.

Methods

This study was conducted as a narrative review to provide a comprehensive synthesis of current evidence on factors inhibiting optimal protein utilization among children. Unlike systematic reviews, a narrative review allows the integration of evidence from diverse study designs to explain complex biological, nutritional, and environmental mechanisms that influence protein utilization. The review focused on identifying and critically discussing key determinants affecting protein digestion, amino acid absorption, metabolism, and tissue protein synthesis.

A literature search was performed using four electronic databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The search primarily focused on articles published between January 2020 and June 2026 to capture recent evidence. Earlier landmark publications were retained selectively when they provided foundational concepts or mechanisms directly relevant to protein utilization. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to protein utilization and child nutrition. The primary search terms included *protein utilization, protein metabolism, protein digestion, protein absorption, protein quality, amino acid metabolism, children, child growth, stunting, wasting, gut microbiota, environmental enteric dysfunction, infection, inflammation, micronutrient deficiency, and malnutrition*. Boolean operators (AND, OR) were used to combine keywords according to the indexing system of each database.

Relevant publications were screened based on their titles and abstracts, followed by full-text assessment of potentially eligible articles. Studies involving pediatric populations from birth to 18 years of age, including infants, children, and adolescents, were considered when they addressed factors influencing protein digestion, absorption, utilization, metabolism, or growth. Priority was given to original research articles, systematic reviews, meta-analyses, clinical guidelines, and consensus statements published in peer-reviewed journals. Articles focusing exclusively on protein intake without discussing mechanisms related to protein utilization were considered only when they provided important contextual information. Editorials, conference abstracts, opinion papers, unpublished reports, and articles lacking sufficient methodological information were excluded as primary sources of evidence.

As this study was designed as a narrative review rather than a systematic review, formal PRISMA-style reporting of study identification, screening, and inclusion counts was not performed. The retrieved literature was synthesized using a thematic narrative approach. Evidence was organized into major themes according to biological plausibility and relevance to protein utilization. These themes included physiological aspects of protein utilization, dietary protein quality, gastrointestinal health, environmental enteric dysfunction, infectious diseases, inflammatory responses, gut microbiota, micronutrient interactions, energy adequacy, and environmental and socioeconomic determinants. Findings from different study designs were critically compared to identify consistent evidence, explain potential mechanisms, and highlight areas where current knowledge remains limited. Rather than quantitatively pooling results, this review emphasizes conceptual integration to provide a comprehensive understanding of factors that influence the efficiency of protein utilization in children.

Although a formal risk-of-bias assessment was not conducted because of the narrative review design, greater emphasis was placed on evidence derived from high-quality publications, including systematic reviews, meta-analyses, randomized controlled trials, prospective cohort studies, and international guidelines. Recent publications and studies with robust methodologies were prioritized to ensure that the discussion reflected current scientific evidence and advances in pediatric nutrition research.

Results and Discussion

1. Protein Utilization in Children: From Intake to Tissue Protein Synthesis

Optimal growth during childhood depends not only on adequate protein intake but also on the efficiency of protein utilization, a biological process that includes protein digestion, amino acid absorption, transport, cellular metabolism, and tissue protein synthesis. Dietary protein provides essential amino acids required for the development of muscle, bone, enzymes, hormones, and immune proteins.¹⁸ The physiological benefits of protein therefore depend on the body's capacity to convert ingested protein into functional body proteins rather than on protein intake alone. Impaired protein utilization may contribute to growth faltering even when dietary protein intake appears sufficient.^{10,19}

Protein digestion begins in the stomach through acid denaturation and pepsin activity and continues in the small intestine via pancreatic proteases, producing free amino acids and small peptides that are absorbed by specialized intestinal transporters. Once absorbed, amino acids enter the portal circulation and are distributed to peripheral tissues, where they support protein turnover and growth.^{20,21} The efficiency of this process is influenced by protein digestibility, amino acid composition, gastrointestinal integrity, and metabolic demands. Food processing, dietary composition, and intestinal health can modify amino acid bioavailability, thereby affecting the amount of protein available for tissue synthesis.²⁰

At the cellular level, indispensable amino acids, particularly leucine, activate the mechanistic target of rapamycin complex 1 (mTORC1), which regulates protein translation and tissue accretion. This anabolic response requires an adequate supply of all essential amino acids and sufficient energy intake.²² During energy deficiency or inflammatory conditions, amino acids are preferentially oxidized for energy production or redirected toward acute-phase protein synthesis and immune responses, reducing their availability for growth.^{23,24} Protein utilization is therefore determined by the interaction between nutrient availability, endocrine regulation, immune activation, and intestinal function rather than by dietary protein quantity alone.²⁵

Assessment of protein quality has also evolved from measuring total protein intake to evaluating digestible indispensable amino acid availability. The Digestible Indispensable Amino Acid Score (DIAAS) is increasingly recognized as a more accurate indicator of protein quality than the Protein Digestibility-Corrected Amino Acid Score (PDCAAS), as it better reflects ileal amino acid digestibility and metabolic availability.²⁶ Animal-source proteins generally provide higher digestibility and a more balanced indispensable amino acid profile than most plant-derived proteins, although appropriate food processing and complementary protein combinations can substantially improve the nutritional quality of plant-based diets.¹⁰ Understanding protein utilization as an integrated metabolic pathway provides a stronger framework for explaining growth impairment and forms the basis for identifying the biological and environmental factors discussed in the following sections.²⁷ Based on the evidence synthesized in this review, protein utilization in children can be conceptualized as a multistage

process involving dietary protein intake, gastrointestinal digestion, intestinal absorption, amino acid transport and metabolism, and tissue protein synthesis, ultimately contributing to child growth. These processes are influenced by interconnected factors, including dietary protein quality, infection, inflammation, micronutrient and energy status, gut microbiota, environmental enteric dysfunction, and socioeconomic and environmental conditions, as illustrated in Figure 1.

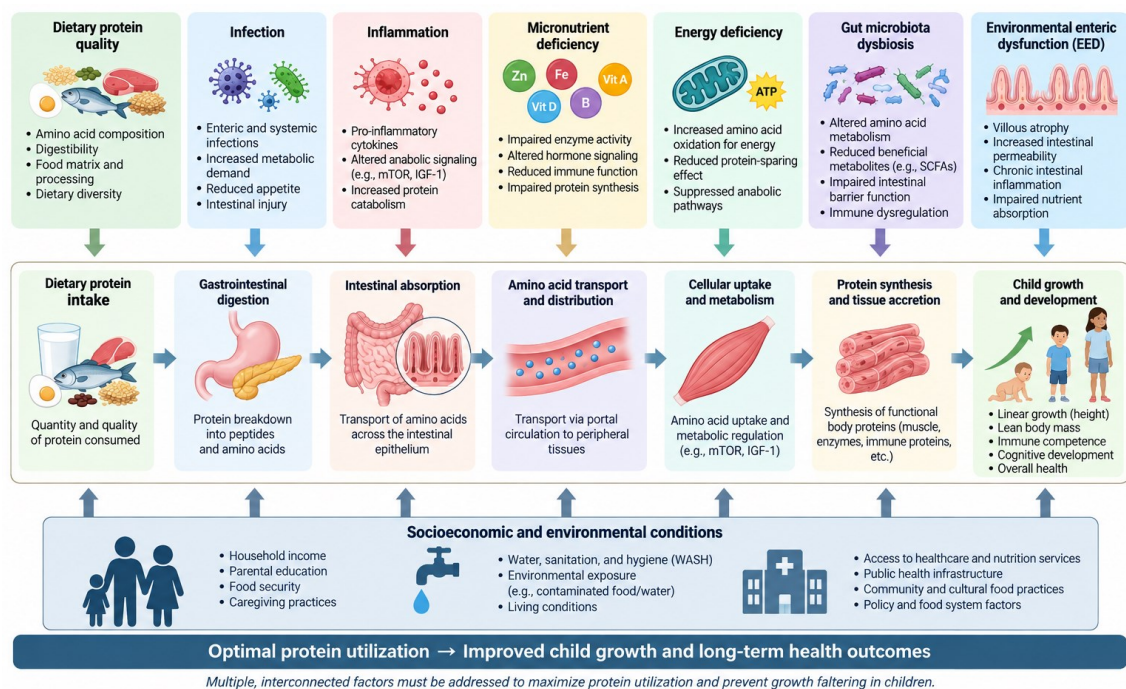


Figure 1. Integrated Biological and Environmental Factors Affecting Protein Utilization in Children

2. Dietary Protein Quality as a Determinant of Protein Utilization

Dietary protein quality is a fundamental determinant of protein utilization because it influences the amount of digestible indispensable amino acids available for tissue protein synthesis. Protein quality is determined by amino acid composition, digestibility, and bioavailability rather than total protein content alone. A protein source that provides all indispensable amino acids in adequate proportions and is efficiently digested is more likely to support positive nitrogen balance, muscle protein synthesis, and linear growth. The

importance of evaluating dietary proteins based on digestible amino acid availability, with DIAAS regarded as the most physiologically relevant method for assessing protein quality. Unlike the PDCAAS, DIAAS estimates ileal digestibility of individual indispensable amino acids and provides a more accurate reflection of the amino acids available for metabolic utilization.^{26,28,29}

Animal-source proteins, including milk, eggs, fish, and meat, generally exhibit higher digestibility and a more balanced indispensable amino acid profile than most plant-derived proteins, although some plant protein sources have relatively favorable indispensable amino acid profiles and digestibility compared with other plant-based sources.^{30–32} In contrast, many cereal- and legume-based proteins may contain limiting amino acids, such as lysine in cereals and methionine in legumes, and may also contain antinutritional compounds that can reduce protein digestibility and amino acid absorption.³¹ Although food processing techniques such as fermentation, germination, and thermal treatment may improve protein digestibility and reduce some antinutritional factors, the nutritional quality of plant-based proteins may remain variable depending on the source and processing method.³²

Improving protein utilization requires attention to both protein quantity and protein quality. Increasing dietary diversity, incorporating animal-source foods where feasible, and combining complementary plant protein sources can enhance indispensable amino acid balance and digestibility. These approaches increase amino acid bioavailability and support more efficient tissue protein synthesis, highlighting dietary protein quality as a critical component of strategies to optimize child growth and nutritional status.³³

3. Digestive Function and Intestinal Protein Absorption

Efficient protein utilization depends on the integrity of the digestive system, as protein must be adequately hydrolyzed and absorbed before amino acids become available for tissue protein synthesis. Protein digestion begins in the stomach through gastric acid secretion and pepsin activity, followed by enzymatic hydrolysis in the small intestine by pancreatic proteases and brush-border peptidases.³⁴ The resulting amino acids and small peptides are absorbed through specialized intestinal transporters, providing the substrates required for growth, tissue repair, and metabolic regulation. Disruption of any stage in this process reduces amino

acid bioavailability and limits the efficiency of protein utilization, even when dietary protein intake is sufficient.³⁵

The absorptive capacity of the small intestine is closely linked to intestinal morphology and epithelial function. Healthy villi, intact tight junctions, adequate digestive enzyme activity, and functional amino acid transporters are essential for efficient nutrient uptake. Damage to the intestinal mucosa, whether caused by recurrent enteric infections, chronic inflammation, food protein-induced enteropathy, or other gastrointestinal disorders, impairs digestive enzyme activity, decreases absorptive surface area, and compromises amino acid transport across the intestinal epithelium. These alterations reduce the availability of indispensable amino acids for protein synthesis and contribute to impaired growth in children.^{36,37}

Digestive efficiency is also influenced by the physicochemical characteristics of the diet. Protein digestibility varies according to protein source, food matrix, and processing methods. Thermal processing, fermentation, and germination may improve protein digestibility by denaturing protein structures and reducing antinutritional compounds, whereas excessive heat treatment or the presence of phytates, tannins, and protease inhibitors can decrease enzymatic hydrolysis and amino acid absorption. These factors become particularly relevant in populations relying predominantly on cereal-based diets, where lower digestibility and reduced indispensable amino acid availability may compromise protein utilization despite adequate protein intake.^{28,30}

Intestinal dysfunction contributes to growth impairment through mechanisms extending beyond nutrient malabsorption.³⁸ Environmental enteropathy is characterized by villous blunting, increased intestinal permeability, chronic mucosal inflammation, and altered digestive function, all of which reduce nutrient absorption and metabolic efficiency.^{13,39,40} Protein requirements may increase under these conditions because inflammation accelerates protein turnover and amino acids are redirected toward immune responses and tissue repair rather than somatic growth.⁴¹ This interaction between impaired intestinal function and increased metabolic demand provides a biological explanation for the limited effectiveness of protein supplementation in some children living in environments with a high burden of enteric disease.^{42,43}

Maintaining gastrointestinal health is therefore a prerequisite for optimal protein utilization. Nutritional strategies that focus solely on increasing protein intake are unlikely to achieve maximal benefits when digestive function and intestinal absorptive capacity remain compromised. Interventions that preserve intestinal integrity, improve digestive efficiency, and reduce chronic enteric inflammation should be considered integral components of child nutrition programs aimed at optimizing protein utilization and supporting healthy growth.^{13,39,40,42,43}

4. Environmental Enteric Dysfunction and Gut Barrier Impairment

Environmental enteric dysfunction (EED) is increasingly recognized as a major biological barrier to optimal protein utilization among children living in low- and middle-income countries. EED is a chronic subclinical disorder of the small intestine characterized by villous blunting, crypt hyperplasia, impaired epithelial regeneration, increased intestinal permeability, and persistent mucosal inflammation.¹³ Unlike acute gastrointestinal disease, EED often develops without obvious clinical symptoms but substantially compromises digestive and absorptive function, making it an important contributor to growth faltering and poor nutritional outcomes.⁴⁰

The impaired intestinal barrier associated with EED reduces the efficiency of protein digestion and amino acid absorption. Structural damage to the intestinal mucosa decreases the absorptive surface area and disrupts nutrient transport, while chronic inflammation suppresses digestive function and increases intestinal permeability. These changes limit the availability of indispensable amino acids for tissue protein synthesis, even when dietary protein intake is adequate. At the same time, ongoing immune activation increases metabolic demand and redirects amino acids toward the synthesis of acute-phase proteins and immune mediators rather than somatic growth, reducing net protein accretion.^{40,44,45}

Repeated exposure to enteric pathogens resulting from inadequate water, sanitation, and hygiene (WASH) is considered a principal driver of EED.⁴⁶ Continuous microbial exposure disrupts epithelial integrity, promotes microbial translocation, and sustains low-grade systemic inflammation, creating a cycle of impaired nutrient utilization and growth failure.¹³ Recent evidence indicates that biomarkers reflecting intestinal permeability, epithelial injury,

intestinal inflammation, and systemic inflammation are consistently associated with poorer linear growth among children under five years of age, supporting the role of EED as a key mediator linking adverse environmental conditions with childhood stunting.⁴⁷

The nutritional consequences of EED extend beyond protein malabsorption. Chronic intestinal dysfunction also impairs the absorption of other macronutrients and micronutrients, exacerbating energy deficits and metabolic disturbances that further compromise protein utilization.^{45,48} Current evidence suggests that nutritional supplementation alone often produces limited improvements when underlying intestinal dysfunction persists, highlighting the need for integrated interventions that combine dietary improvement with strategies to reduce enteric infections, strengthen gut barrier integrity, and improve environmental hygiene. Addressing EED should therefore be considered an essential component of nutrition programs aimed at optimizing protein utilization and supporting healthy child growth.⁴⁹

5. Gut Microbiota and Amino Acid Metabolism

The gut microbiota has emerged as an important regulator of protein utilization through its influence on amino acid metabolism, intestinal homeostasis, and host metabolic function.⁵⁰ Beyond facilitating nutrient digestion, the intestinal microbiota participates in the synthesis, degradation, and biotransformation of amino acids, thereby modifying the availability of substrates required for tissue protein synthesis.⁵⁰ A balanced microbial ecosystem also supports epithelial integrity, regulates immune responses, and promotes the production of short-chain fatty acids (SCFAs), which contribute to intestinal health and nutrient absorption. Alterations in microbial composition, commonly referred to as gut dysbiosis, may therefore impair protein utilization even when dietary protein intake is adequate.⁵¹

Gut dysbiosis disrupts amino acid homeostasis through several mechanisms. Changes in microbial composition may increase microbial utilization of luminal amino acids, reduce the production of beneficial metabolites, and promote intestinal inflammation. These alterations impair epithelial barrier function, decrease absorptive efficiency, and reduce the availability of indispensable amino acids for anabolic processes.⁵² Chronic intestinal inflammation further increases protein turnover and redirects amino acids toward immune responses and tissue

repair instead of skeletal growth. This metabolic shift lowers net protein accretion and contributes to suboptimal growth among children exposed to persistent enteric insults.⁵³

Microbial metabolites act as signaling molecules regulating host nutrient metabolism. Short-chain fatty acids, particularly butyrate, enhance epithelial integrity, improve intestinal barrier function, and modulate inflammatory pathways that support efficient nutrient utilization.^{54,55} In contrast, disturbances in microbial amino acid metabolism may alter the availability of branched-chain amino acids, tryptophan, and other bioactive metabolites involved in cellular growth, endocrine regulation, and immune function. These interactions highlight that the gut microbiota influences protein utilization not only by affecting nutrient absorption but also by regulating metabolic pathways involved in protein synthesis and amino acid homeostasis.^{55,56}

Evidence from pediatric populations consistently demonstrates associations between gut microbial dysbiosis and impaired linear growth, although the specific microbial taxa differ across geographical settings and dietary patterns.³⁹ Rather than individual bacterial species, reduced microbial functionality, impaired metabolite production, and persistent intestinal inflammation appear to be the major mechanisms linking dysbiosis with poor nutrient utilization.⁵⁷ Strategies that preserve microbial diversity through improved dietary quality, breastfeeding, appropriate complementary feeding, infection prevention, and restoration of intestinal health may therefore enhance protein utilization and support healthy child growth.

6. Infection, Inflammation, and Protein Catabolism

Infection and inflammation are major determinants of impaired protein utilization because they alter nutrient metabolism and shift protein use from growth toward host defense.⁵⁸ During infection, activation of the innate and adaptive immune systems increases metabolic demands and induces a systemic inflammatory response characterized by the release of pro-inflammatory cytokines, including tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6).⁵⁹ These mediators stimulate the hepatic synthesis of acute-phase proteins, increase resting energy expenditure, and promote skeletal muscle proteolysis to provide amino acids required for immune cell proliferation, inflammatory mediator

production, and tissue repair.^{60,61} As a result, fewer amino acids remain available for tissue protein synthesis and linear growth.⁶²

Persistent inflammation also suppresses anabolic signaling pathways that regulate protein synthesis. Cytokine-induced insulin resistance and reduced activity of the insulin-like growth factor-1 (IGF-1) axis impair activation of the mTORC1, decreasing muscle protein synthesis while accelerating protein breakdown.⁶³ This imbalance produces a negative nitrogen balance that may persist even after dietary protein intake has been restored. In children experiencing recurrent or prolonged infections, repeated episodes of protein catabolism can substantially reduce lean body mass and compromise catch-up growth.

Common childhood infections, including diarrhea, pneumonia, malaria, intestinal parasitic infections, and recurrent enteric diseases, further reduce protein utilization by decreasing appetite, impairing gastrointestinal function, and increasing endogenous nutrient losses.⁶⁴ Diarrheal diseases may reduce amino acid absorption through mucosal injury, whereas chronic infections sustain inflammatory responses that prolong protein catabolism.⁶⁵ These metabolic adaptations are initially protective because they support immune function; however, prolonged activation diverts nutrients away from growth and contributes to growth faltering and undernutrition, particularly in children exposed to repeated infectious episodes.^{66,67}

The interaction between infection, inflammation, and protein metabolism creates a self-perpetuating cycle in which impaired nutritional status weakens immune function, increasing susceptibility to subsequent infections and sustaining metabolic stress. Breaking this cycle requires integrated interventions that combine adequate protein intake with effective infection prevention, timely clinical management, immunization, improved water, sanitation and hygiene (WASH), and strategies to reduce chronic inflammation. Addressing these factors is essential to maximize protein utilization and support optimal growth during childhood.

7. Micronutrient Deficiencies and Impaired Protein Utilization

Micronutrients play an essential role in protein utilization by regulating protein digestion, amino acid metabolism, cellular signaling, and tissue protein synthesis. Adequate dietary protein alone is insufficient to support optimal growth when key vitamins and minerals

required for anabolic processes are deficient.⁶⁸ Several micronutrients act as enzyme cofactors and metabolic regulators that facilitate protein synthesis, maintain nitrogen balance, and preserve normal muscle and skeletal development.⁶⁹ Deficiencies of these nutrients impair the metabolic efficiency of dietary protein, limiting its conversion into functional body proteins despite adequate protein intake.

Among the essential micronutrients, zinc has the strongest biological association with protein utilization and linear growth. Zinc participates in numerous enzymatic reactions involved in DNA replication, RNA transcription, cell proliferation, and protein synthesis.⁷⁰ It also regulates the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis and intracellular signaling pathways, including mechanistic target of rapamycin complex 1 (mTORC1), which controls muscle protein synthesis and tissue accretion. Zinc deficiency suppresses these anabolic pathways, reduces appetite, delays tissue repair, and increases susceptibility to infection, collectively lowering the efficiency of protein utilization and increasing the risk of growth faltering.^{71,72,73}

Other micronutrients also contribute to efficient protein metabolism through complementary mechanisms. Iron supports oxygen transport and cellular energy production required for protein synthesis. Emerging evidence also indicates that dietary proteins may influence iron metabolism through the modulation of microRNA expression involved in iron homeostasis, suggesting a molecular interaction between protein nutrition and iron utilization that may affect growth and erythropoiesis.⁷⁴ Vitamin A maintains epithelial integrity, immune competence, and normal cellular differentiation.⁷⁵ Vitamin D influences muscle development and protein turnover through vitamin D receptor-mediated signaling, whereas vitamin B6 functions as an essential coenzyme in amino acid transamination and other reactions involved in amino acid metabolism.^{76,77} Deficiencies in these micronutrients reduce metabolic efficiency, impair tissue repair, and increase the likelihood that absorbed amino acids will be diverted toward maintenance and immune responses rather than growth.

Micronutrient deficiencies frequently coexist with infection, intestinal dysfunction, and poor dietary diversity, creating multiple barriers to efficient protein utilization.^{78,58,79} Chronic inflammation and impaired intestinal absorption reduce both micronutrient bioavailability

and amino acid uptake, while inadequate micronutrient status further weakens intestinal integrity and immune function.⁸⁰ This interaction perpetuates a cycle of impaired nutrient utilization, increased metabolic demand, and reduced protein accretion. Addressing micronutrient deficiencies through diversified diets, food fortification, supplementation, and interventions that improve intestinal health should therefore accompany efforts to increase dietary protein intake. Such integrated strategies are more likely to optimize protein utilization and support healthy growth among children than approaches focused solely on increasing protein consumption.

8. Energy Deficiency and Protein Sparing

Adequate energy intake is essential for efficient protein utilization because dietary protein is preferentially used for tissue synthesis only when energy requirements are met. Under normal physiological conditions, carbohydrates and fats serve as the primary energy substrates, allowing amino acids to be preserved for protein synthesis, tissue growth, and cellular repair. This metabolic phenomenon, known as the protein-sparing effect, is particularly important during childhood, when rapid growth substantially increases the demand for protein accretion. When dietary energy is insufficient, amino acids are increasingly oxidized to support energy production through gluconeogenesis rather than being incorporated into structural and functional proteins, thereby reducing the efficiency of protein utilization.^{81,82}

Energy deficiency also alters hormonal and metabolic pathways involved in protein anabolism. Reduced energy availability suppresses insulin secretion and the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis while decreasing activation of the mTORC1, a key regulator of protein synthesis.⁸³ At the same time, protein breakdown is accelerated to provide amino acids for energy production and maintenance of essential physiological functions. Prolonged negative energy balance therefore results in negative nitrogen balance, loss of lean body mass, and impaired linear growth, even in children whose dietary protein intake meets recommended levels.⁸⁴

The interaction between inadequate energy intake and poor protein utilization is particularly relevant in children experiencing undernutrition or recurrent illness. Infection

increases resting energy expenditure while reducing appetite and food intake, creating an energy deficit that further limits the availability of amino acids for tissue protein synthesis. This metabolic adaptation diverts protein toward energy production, immune responses, and tissue repair instead of somatic growth, contributing to persistent growth faltering.⁸⁵ Similar mechanisms may also occur in children with chronic gastrointestinal disorders or environmental enteric dysfunction, where reduced nutrient absorption exacerbates both energy and protein deficits.^{13,43}

Optimizing protein utilization therefore requires adequate energy intake in addition to sufficient dietary protein. Nutritional interventions that improve total energy adequacy through balanced carbohydrate, fat, and protein intake are more likely to preserve the protein-sparing effect, maintain positive nitrogen balance, and maximize tissue protein synthesis. This integrated approach provides a stronger physiological basis for promoting healthy growth than strategies focused exclusively on increasing protein intake.

9. Socioeconomic and Environmental Determinants

Socioeconomic and environmental conditions strongly influence protein utilization by shaping dietary quality, exposure to infectious diseases, and access to health-promoting resources. Household income, parental education, food security, sanitation, healthcare access, and caregiving practices determine whether children receive sufficient quantities of high-quality protein and whether physiological conditions support efficient nutrient utilization. These determinants interact throughout the pathway of protein utilization, affecting digestion, absorption, metabolism, and tissue protein synthesis rather than dietary intake alone.^{86,87}

Food insecurity and limited dietary diversity remain major barriers to optimal protein utilization in many low- and middle-income countries. Community-based nutrition education promoting local food utilization has also been shown to improve caregivers' nutritional knowledge, which may contribute to better dietary practices supporting child growth.⁸⁸ Households with constrained economic resources often rely on inexpensive staple foods that provide energy but contain lower-quality protein and fewer indispensable amino acids. Limited consumption of animal-source foods and inadequate dietary diversity reduce amino

acid adequacy and increase the likelihood of concurrent micronutrient deficiencies, diminishing the efficiency of protein synthesis during periods of rapid growth.^{10,18} Evidence consistently indicates that nutrition-sensitive interventions that improve household food production, food access, and dietary diversity enhance children's dietary quality and create more favorable conditions for protein utilization.⁸⁹

Environmental conditions also play a central role in determining how efficiently dietary protein is utilized. Inadequate water, sanitation, and hygiene (WASH) increase children's exposure to enteric pathogens, recurrent infections, and environmental enteric dysfunction, leading to chronic intestinal inflammation and impaired nutrient absorption. Repeated infectious episodes elevate metabolic demands and redirect amino acids toward immune responses instead of tissue growth. These findings demonstrate that poor environmental conditions reduce the biological efficiency of dietary protein even when protein intake is relatively adequate.^{13,90,91}

Maternal education and access to health and nutrition services further influence protein utilization through infant feeding practices, complementary feeding quality, infection prevention, and timely management of childhood illness. Caregivers with better nutritional knowledge are more likely to provide diverse diets, appropriate meal frequency, and hygienic feeding practices that preserve intestinal health and improve nutrient bioavailability.⁸⁸ These factors reinforce the importance of integrating nutrition-specific interventions with nutrition-sensitive strategies addressing poverty reduction, food systems, education, and environmental health. Such a multisectoral approach provides a stronger foundation for optimizing protein utilization and promoting healthy child growth than interventions focused solely on increasing dietary protein intake.

10. Critical Synthesis of Evidence

The evidence synthesized in this review indicates that the relationship between dietary protein intake and child growth is not necessarily linear and may be strongly modified by biological and environmental conditions. Although adequate protein intake is consistently recognized as necessary for growth, improvements in growth outcomes following increased protein provision are not uniform across populations. This heterogeneity may reflect

differences in baseline nutritional status, protein quality, energy adequacy, infection burden, intestinal function, dietary diversity, and environmental exposure. Protein supplementation may therefore have limited effects when intestinal dysfunction, recurrent infection, inflammation, or energy deficiency continues to restrict the utilization of absorbed amino acids.^{6,7,13}

Similar heterogeneity is evident in evidence concerning the gut microbiota. Although dysbiosis has been associated with impaired linear growth and altered amino acid metabolism, the specific microbial taxa associated with these outcomes differ across geographical settings and dietary patterns. This variation suggests that microbial functionality, metabolite production, and host–microbiota interactions may be more relevant to protein utilization than the presence or absence of individual bacterial taxa.^{39,50–57}

Evidence regarding environmental enteric dysfunction also suggests that nutritional supplementation alone may not consistently improve growth when underlying intestinal dysfunction persists. This indicates that the effectiveness of nutritional interventions may depend on whether the physiological barriers to nutrient absorption and utilization are simultaneously addressed. Therefore, apparently inconsistent intervention outcomes may reflect differences in the biological and environmental context of the children studied rather than contradictory effects of dietary protein itself.^{13,40,44–49}

These findings support the interpretation of protein utilization as an integrated process rather than an isolated nutritional outcome. Dietary protein quality, gastrointestinal integrity, energy availability, immune activation, micronutrient status, gut microbiota, and socioeconomic and environmental conditions interact across multiple stages of the pathway. This integrated perspective provides a more plausible explanation for differences in growth responses across studies and supports multidimensional strategies to optimize protein utilization in children.^{10,13,23,39,50,52,54,56,68,86}

Table 1. Summary of Factors Affecting Protein Utilization in Children

Factor	Underlying mechanism	Effect on protein utilization	Potential impact on child growth	References
Dietary protein quality	Limiting indispensable	Reduces the availability of	Reduced protein accretion and	10, 26, 28, 29, 31–33

Factor	Underlying mechanism	Effect on protein utilization	Potential impact on child growth	References
Digestive dysfunction	amino acids, lower digestibility, and reduced amino acid bioavailability Impaired gastric, pancreatic, or intestinal digestion and reduced digestive enzyme activity	indispensable amino acids for tissue protein synthesis Reduces protein hydrolysis and the availability of absorbable amino acids	impaired linear growth Poor nutrient utilization and impaired growth	20, 21, 35–37
Environmental enteric dysfunction (EED)	Villous blunting, increased intestinal permeability, epithelial injury, and chronic mucosal inflammation	Impairs amino acid absorption and increases metabolic demand through immune activation	Growth faltering and impaired linear growth	13, 40, 44–49
Gut microbiota dysbiosis	Altered microbial amino acid metabolism, metabolite production, intestinal barrier function, and immune regulation	Alters amino acid homeostasis, nutrient absorption, and metabolic regulation	Impaired nutrient utilization and linear growth	39, 50–52, 54–57
Infection	Increased metabolic demand, reduced appetite, gastrointestinal injury, and increased protein catabolism	Diverts amino acids toward immune responses and tissue repair rather than growth	Reduced lean tissue accretion and growth faltering	42, 43, 64–67
Inflammation	Cytokine-mediated alterations in protein turnover, insulin/IGF-1 signaling, and mTORC1 activity	Suppresses tissue protein synthesis and increases protein breakdown	Impaired lean tissue development and growth	23, 24, 59
Micronutrient deficiency	Impaired enzyme activity, cellular signaling, immune function, and anabolic pathways	Reduces metabolic efficiency and tissue protein synthesis	Impaired growth, tissue repair, and lean tissue development	68–78
Energy deficiency	Increased amino acid oxidation for energy and	Reduces the protein-sparing effect and	Negative nitrogen balance, loss of lean body	23, 81–85

Factor	Underlying mechanism	Effect on protein utilization	Potential impact on child growth	References
Socioeconomic and environmental conditions	suppression of anabolic signaling	availability of amino acids for tissue synthesis	mass, and impaired linear growth	13–15, 86–91
	Food insecurity, low dietary diversity, poor WASH, limited healthcare access, and inadequate caregiving resources	Indirectly compromises dietary quality, intestinal health, infection control, and nutrient utilization	Persistent growth deficits and increased risk of undernutrition	

11. Implications for Nutrition Programs and Future Perspectives

The evidence presented in this review indicates that optimizing child growth requires a broader perspective than increasing dietary protein intake alone. Protein utilization is influenced by multiple interconnected biological and environmental factors, including protein quality, digestive capacity, intestinal integrity, gut microbiota, inflammation, micronutrient status, energy adequacy, and socioeconomic conditions. These interactions explain why protein supplementation does not always produce consistent improvements in growth, particularly among children living in settings with a high burden of infection, poor sanitation, and limited dietary diversity. Nutrition programs should therefore adopt integrated strategies that address both nutrient intake and the physiological conditions necessary for efficient protein utilization.^{10,13}

From a programmatic perspective, interventions should prioritize access to high-quality protein sources with balanced indispensable amino acid profiles while ensuring adequate energy intake to preserve the protein-sparing effect. Dietary diversification, promotion of breastfeeding and appropriate complementary feeding, food fortification, and targeted micronutrient supplementation remain essential components of child nutrition programs. These nutrition-specific interventions should be implemented alongside nutrition-sensitive approaches, including improvements in water, sanitation and hygiene (WASH), infection prevention, food security, maternal nutrition education, and equitable access to primary

healthcare. Such integrated interventions are more likely to improve the efficiency of protein utilization than strategies focused solely on increasing protein consumption.^{88,91}

Future research should move beyond measuring dietary protein intake as the primary indicator of nutritional adequacy and incorporate biomarkers that better reflect protein utilization and metabolic responses. Advances in metabolomics, proteomics, stable isotope techniques, and gut microbiome profiling offer opportunities to characterize amino acid metabolism, protein turnover, and nutrient utilization more precisely. Longitudinal studies are also needed to clarify the interactions among dietary protein quality, intestinal health, inflammation, and growth across different stages of childhood. Such evidence will strengthen the development of nutrition policies and precision nutrition strategies tailored to children living in diverse environmental and socioeconomic contexts.

A comprehensive understanding of protein utilization provides a stronger scientific basis for preventing childhood growth faltering than reliance on protein intake alone. Integrating nutritional, clinical, environmental, and social interventions has the potential to maximize the biological value of dietary protein, improve growth outcomes, and accelerate progress toward global child nutrition targets.

12. Limitations of the Review

This review has several limitations. First, the narrative review design does not follow a fully systematic review protocol, and a formal risk-of-bias assessment was not performed. Although priority was given to recent and methodologically robust studies, the selection and interpretation of evidence may therefore be influenced by publication selection and reviewer judgment. Second, the literature search was conducted using PubMed, Scopus, ScienceDirect, and Google Scholar, and primarily focused on publications from January 2020 to June 2026. Relevant evidence indexed in other databases or published outside the primary search period may therefore have been missed, although selected earlier publications were retained when they provided foundational evidence. Third, substantial heterogeneity exists across the literature in terms of children's age, nutritional status, health conditions, dietary patterns, environmental exposures, and outcome measures, limiting direct comparison between studies. Finally, many studies evaluate individual determinants such as infection, intestinal

dysfunction, dietary quality, or micronutrient status rather than protein utilization as an integrated biological outcome. Therefore, the interactions presented in the conceptual framework should be interpreted as evidence-informed and biologically plausible relationships rather than definitive causal pathways.

Conclusion

Optimal protein utilization in children depends not only on adequate protein intake but also on the efficiency of protein digestion, amino acid absorption, metabolism, and tissue protein synthesis. This review highlights that dietary protein quality, digestive function, intestinal integrity, gut microbiota, infection, inflammation, micronutrient status, energy adequacy, and socioeconomic and environmental conditions collectively influence the biological utilization of dietary protein. Disruptions in these processes reduce amino acid availability for growth and increase the risk of growth faltering despite sufficient protein intake.

Improving child growth therefore requires an integrated approach that extends beyond increasing protein consumption. Nutrition programs should combine the provision of high-quality protein with interventions that promote intestinal health, adequate energy and micronutrient intake, infection prevention, dietary diversity, and improved environmental conditions. Addressing these interconnected determinants is essential to maximize protein utilization and support optimal growth and nutritional status among children.

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Declaration of Generative AI and AI-assisted Technologies

During the preparation of this manuscript, the authors used generative AI tools to assist with language editing, grammar refinement, and development of the conceptual framework in Figure 1. All AI-assisted content was critically reviewed and verified by the authors, who

take full responsibility for the accuracy, integrity, and originality of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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