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MALNUTRITION-INDUCED GROWTH FAILURE IN CHILDREN: A GLOBAL NARRATIVE REVIEW OF BIOCHEMICAL MECHANISMS AND CLINICAL IMPLICATIONS

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ABSTRACT

Malnutrition remains a major global public health challenge and a leading cause of growth failure among children, particularly in low- and middle-income countries. Although its clinical manifestations such as stunting and wasting are well recognized, the underlying biochemical mechanisms remain fragmented across endocrine, metabolic, immunological, and nutritional domains. This lack of integrated understanding limits advances in targeted diagnosis and treatment. This review therefore aimed to synthesize current evidence on the biochemical mechanisms underlying malnutrition-induced growth failure in children. A narrative review design guided by the PRISMA 2020 framework was adopted to ensure a systematic and transparent approach to literature identification, screening, eligibility assessment, and inclusion. A comprehensive search was conducted across PubMed, Scopus, Web of Science, and Google Scholar, supplemented by manual searches of reference lists. The review found that malnutrition-induced growth failure results from multiple interacting biochemical pathways. Central to this process is disruption of the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis, characterized by growth hormone resistance and reduced IGF-1 synthesis. Protein and energy malnutrition were associated with increased proteolysis, negative nitrogen balance, muscle wasting, and impaired tissue development. Micronutrient deficiencies, including iron, zinc, iodine, and vitamin D, were shown to impair enzymatic activity, endocrine regulation, and skeletal growth. Malnutrition-induced growth failure is a complex systemic biochemical disorder involving endocrine, metabolic, immune, and oxidative stress pathways. Effective management requires integrated strategies that go beyond caloric supplementation to include micronutrient correction, infection control, and inflammation reduction.

Keywords: Malnutrition, Growth Failure, Growth Hormone, Micronutrient Deficiency, Oxidative Stress

Introduction

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Malnutrition remains a major global public health challenge and a leading cause of growth failure, morbidity, and mortality among children, particularly in low- and middle-income countries. Despite advances in nutritional interventions, millions of children continue to experience stunting, wasting, and delayed developmental outcomes associated with inadequate nutrient intake. Growth failure resulting from malnutrition has traditionally been assessed using anthropometric indicators; however, these clinical manifestations are the downstream consequences of complex biochemical and physiological disturbances that affect normal growth and development. Understanding the mechanisms through which malnutrition impairs growth is therefore essential for improving prevention, diagnosis, and treatment strategies (Sturgeon et al., 2023; Vresk et al., 2025)."

Normal childhood growth depends on a coordinated interaction between nutrient availability, hormonal regulation, cellular metabolism, and tissue synthesis. Central to this process is the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis, which regulates skeletal growth, protein accretion, and cellular proliferation. Adequate dietary protein and energy are required to sustain hepatic production of IGF-1 and support anabolic activity. When nutrient intake becomes insufficient, endocrine regulation is disrupted, resulting in reduced IGF-1 production, impaired growth signaling, and diminished tissue development. These alterations contribute significantly to stunting and delayed physiological maturation observed in undernourished children (Cammisa et al., 2025; Carvalho et al. (2025).

Beyond endocrine dysfunction, malnutrition induces profound metabolic adaptations that prioritize survival over growth. During prolonged nutrient deprivation, the body increases proteolysis, gluconeogenesis, and lipolysis to maintain energy supply to vital organs. While these responses are initially protective, sustained catabolism leads to negative nitrogen balance, muscle wasting, impaired tissue repair, and reduced synthesis of structural and functional proteins necessary for normal growth. Consequently, chronic undernutrition compromises both body composition and organ development, increasing vulnerability to disease and developmental impairment (Ali & Mouzaki, 2024).

Micronutrient deficiencies further aggravate growth failure by disrupting enzymatic reactions and regulatory pathways essential for cellular function. Nutrients such as zinc, iron, iodine, and vitamin D play critical roles in DNA synthesis, oxygen transport, thyroid hormone production, bone mineralization, and immune regulation. Deficiencies in these micronutrients impair cellular proliferation, metabolic efficiency, and skeletal development, thereby limiting growth potential. In addition, inadequate antioxidant micronutrients weaken cellular defense systems, increasing susceptibility to oxidative stress and biochemical damage (Vresk et al., 2025; Shahzad et al., 2025).

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The effects of malnutrition on growth are also influenced by chronic inflammation and recurrent infection. Conditions such as environmental enteric dysfunction and persistent immune activation impair nutrient absorption, increase metabolic demands, and suppress anabolic pathways through inflammatory cytokine activity. These processes interact with endocrine and metabolic disturbances to create a persistent catabolic state that hinders tissue growth and recovery. As a result, growth impairment in malnourished children reflects the cumulative impact of hormonal dysregulation, metabolic imbalance, micronutrient insufficiency, inflammation, and oxidative stress rather than the effects of inadequate food intake alone (Carvalho et al. (2025; Suryowati, 2024).

Although numerous studies have documented the prevalence and clinical consequences of childhood malnutrition, evidence on the underlying biochemical mechanisms remains dispersed across different areas of nutritional, endocrine, and metabolic research. This fragmentation limits a comprehensive understanding of how multiple biochemical pathways interact to influence growth outcomes. Synthesizing current evidence on these mechanisms is important for identifying potential biomarkers, informing targeted nutritional therapies, and improving strategies for the prevention and management of malnutrition-related growth failure.

Therefore, this review examined the biochemical mechanisms underlying malnutrition-induced growth failure in children by focusing on four key areas: disruption of the GH–IGF-1 axis, alterations in protein and energy metabolism, the role of micronutrients in enzymatic and endocrine regulation of growth, and the impact of inflammation and oxidative stress on growth-related biochemical pathways. By integrating evidence across these domains, the review provides a comprehensive understanding of the molecular and metabolic processes linking malnutrition to impaired growth and highlights potential pathways for improving clinical assessment and nutritional rehabilitation.

Conceptual framework

The conceptual framework illustrates the biological mechanisms linking malnutrition to growth failure in children. It shows how nutritional deficiencies initiate endocrine, metabolic, and immunological disturbances that converge to impair cellular growth and skeletal development.

At the center of the model is malnutrition (protein, energy, and micronutrient deficiency), which triggers three primary pathways: disruption of the GH–IGF-1 axis, protein-energy metabolic imbalance, and micronutrient-related dysfunction. These pathways are further amplified by inflammation and oxidative stress, culminating in impaired cellular proliferation, reduced tissue accretion, and skeletal growth failure, clinically manifesting as stunting, wasting, and delayed development.

Theoretical framework

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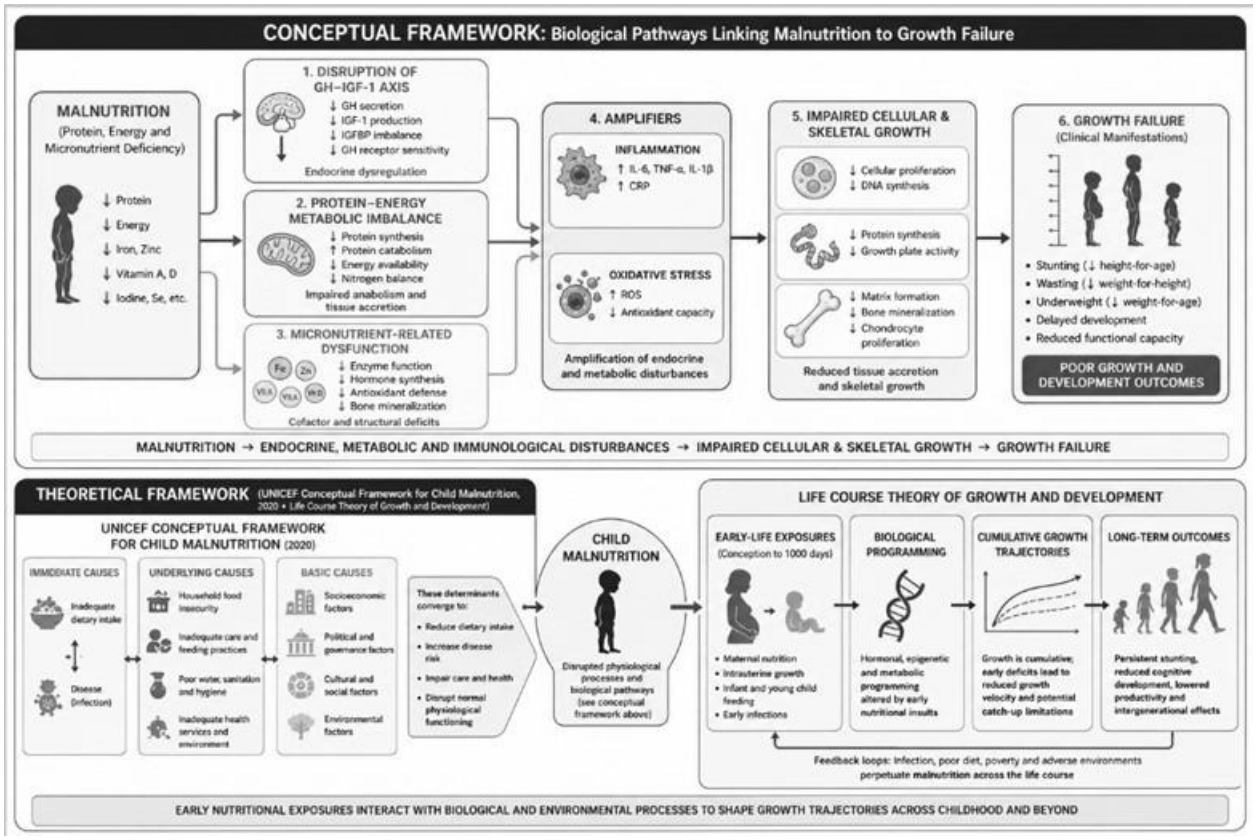
This narrative review is anchored on the UNICEF Conceptual Framework for Child Malnutrition (2020) and the Life Course Theory of Growth and Development. Together, these frameworks explain how early-life nutritional exposures interact with biological and environmental processes to shape growth trajectories across childhood.

The UNICEF framework posits that child malnutrition arises from a complex interplay of immediate causes (inadequate dietary intake and disease), underlying causes (food insecurity, inadequate care practices, and poor health services), and basic causes (socioeconomic, political, and environmental factors). These determinants converge to disrupt normal physiological functioning.

Complementing this, the Life Course Theory emphasizes that growth is a cumulative biological process influenced by early nutritional insults, which can produce lasting effects through hormonal programming and altered metabolic regulation.



Methodology

Study Design

This study adopted a narrative review design guided by the PRISMA 2020 framework to ensure a transparent and systematic process for identifying, screening, assessing eligibility, and including relevant literature. While the synthesis was narrative in nature, the review

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followed structured reporting standards consistent with systematic review methodology to enhance rigor, transparency, and reproducibility.

Information Sources and Search Strategy

A comprehensive literature search was conducted across four electronic databases: PubMed (n = 102 records), Scopus (n = 118 records), Web of Science (n = 86 records), and Google Scholar (n = 50 records), yielding a total of 356 records. In addition, manual searches of reference lists of relevant studies were carried out to identify additional eligible articles that may not have been captured in the database search.

Eligibility Criteria

Studies were included if they were peer-reviewed journal articles published in English, had full-text availability, and focused on biochemical, metabolic, endocrine, or nutritional mechanisms related to growth or malnutrition in humans or relevant experimental models. Eligible designs included original research such as cross-sectional, cohort, case-control, and experimental studies. Studies were excluded if they were duplicates, irrelevant to the study objectives after title and abstract screening, non-original publications (such as editorials, commentaries, or opinion pieces), review articles without primary data (where applicable), or studies with inaccessible full texts.

Study Selection and Screening Process

The study selection followed a PRISMA-guided stepwise process. A total of 356 records were initially identified. After removal of duplicates, automation-removed records, and other exclusions (n = 118), 238 records remained for title and abstract screening. At this stage, 202 records were excluded due to irrelevance to the study objectives, leaving 36 full-text articles for eligibility assessment.

Full-Text Eligibility Assessment

During full-text review, six reports could not be retrieved, and 24 studies were excluded due to non-relevant populations, outcomes, study designs, or publication types. This resulted in a final set of six studies that met all inclusion criteria and were included in the narrative synthesis.

Data Synthesis and Analysis

The included studies were analyzed using narrative synthesis. Findings were organized thematically according to key biochemical and biological mechanisms relevant to the research objectives. The analysis focused on identifying patterns, similarities, and differences across studies to generate an integrated interpretation of the evidence.

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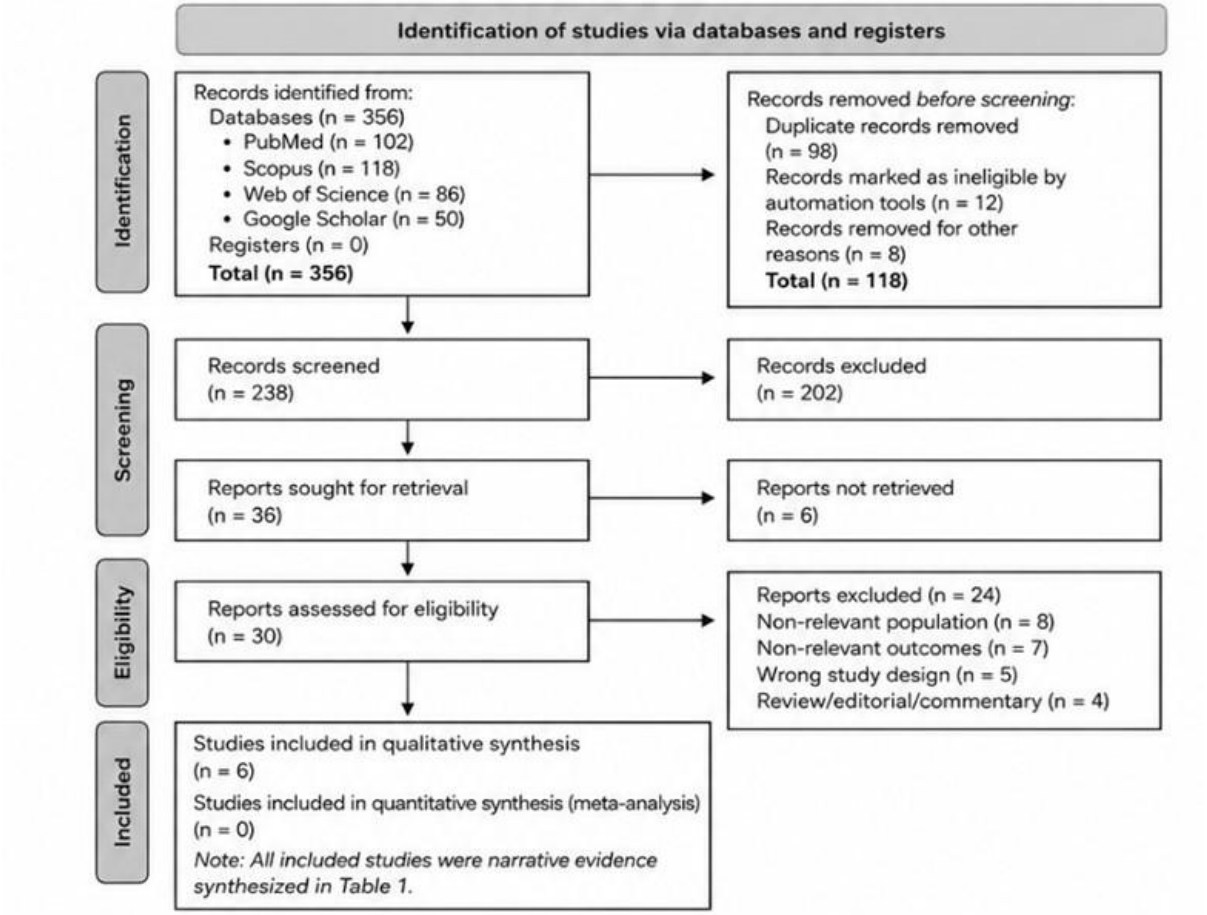
PRISMA Flow Summary of Study Selection

The study selection process followed the PRISMA 2020 framework, ensuring transparent documentation of each stage: identification (n = 356), screening (n = 238), eligibility assessment (n = 30), and final inclusion (n = 6). This structured approach ensured methodological rigor while maintaining the interpretive flexibility characteristic of a narrative review.

Figure 1. PRISMA 2020 Flow Diagram of Study Selection



Results

Biochemical mechanisms underlying malnutrition-induced growth failure

Table 1 presents a synthesis of evidence from recent studies on the major biochemical mechanisms through which malnutrition contributes to growth failure in children. The reviewed literature highlights the multifaceted nature of malnutrition-induced growth impairment, encompassing endocrine dysregulation, alterations in protein and energy metabolism, micronutrient deficiencies, and inflammation-mediated oxidative stress. Across the studies, disruption of the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis emerged as a critical pathway linking inadequate nutrient intake to impaired linear growth. Similarly, chronic protein and energy deficits were associated with negative nitrogen balance, muscle wasting, and reduced tissue synthesis.

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The evidence further demonstrates the essential role of micronutrients in supporting enzymatic reactions, cellular proliferation, and hormonal regulation required for normal growth and development. In addition, persistent inflammation and oxidative stress were consistently identified as factors that exacerbate metabolic dysfunction by suppressing anabolic pathways, increasing nutrient demands, and promoting cellular damage. Collectively, the findings summarized in Table 1 provide an integrated understanding of the biochemical pathways underlying malnutrition-induced growth failure and their implications for diagnosis, treatment, and nutritional rehabilitation.

Table 1: Review Results on the Biochemical Mechanisms Underlying Malnutrition-Induced Growth Failure

Author	Disruption of the GH–IGF-1 Axis in Malnutrition	Alterations in Protein and Energy Metabolism during Nutrient Deficiency	Role of Micronutrients in Enzymatic and Endocrine Regulation of Growth	Impact of Inflammation and Oxidative Stress on Growth-Related Biochemical Pathways
Cammisa et al. (2025)	Reported that chronic undernutrition impairs hepatic IGF-1 synthesis through inadequate amino acid and energy supply, resulting in growth hormone resistance characterized by elevated GH and reduced IGF-1 levels, thereby contributing to stunting and impaired growth.	Not specifically addressed.	Not specifically addressed.	Not specifically addressed.
da Cruz Carvalho et al. (2025)	Demonstrated that nutrient deprivation disrupts GH–IGF-1 signaling and that chronic inflammation further suppresses hepatic IGF-1 production and receptor sensitivity, limiting linear growth and developmental outcomes.	Not specifically addressed.	Not specifically addressed.	Showed that inflammatory cytokines associated with gut inflammation and environmental enteric dysfunction interfere with GH–IGF-1 signaling, exacerbating growth impairment.
Ali and Mouzaki (2024)	Not specifically addressed.	Reported that protein–energy malnutrition promotes proteolysis, negative nitrogen balance, muscle wasting, impaired tissue repair, hypoalbuminemia, and edema, reflecting severe disruption of protein	Highlighted the importance of iron, zinc, vitamin D, and iodine in haemoglobin synthesis, DNA replication, bone mineralization, thyroid hormone production, and overall growth regulation.	Indirectly linked micronutrient deficiencies with impaired metabolic adaptation and poor growth outcomes.

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Author	Disruption of the GH–IGF-1 Axis in Malnutrition	Alterations in Protein and Energy Metabolism during Nutrient Deficiency	Role of Micronutrients in Enzymatic and Endocrine Regulation of Growth	Impact of Inflammation and Oxidative Stress on Growth-Related Biochemical Pathways
		and energy metabolism.		
Vresk et al. (2025)	Identified IGF-1 as a useful biomarker for assessing growth impairment associated with malnutrition.	Reported that multiple micronutrient deficiencies contribute to prolonged catabolism and delayed recovery despite nutritional rehabilitation.	Demonstrated that deficiencies in essential micronutrients worsen metabolic dysfunction and recovery outcomes in children with acute malnutrition.	Proposed the use of inflammatory markers such as CRP alongside micronutrient indicators to improve diagnosis and monitoring of malnutrition-related growth failure.
Suryowati (2024)	Reported that inflammatory cytokines suppress anabolic pathways including IGF-1 expression, thereby reducing growth potential.	Showed that infection-induced inflammation increases resting energy expenditure and redirects nutrients away from growth processes toward immune defense.	Not specifically addressed.	Demonstrated that chronic infection and inflammation create a persistent catabolic environment, impair nutrient utilization, and worsen growth failure.
Shahzad et al. (2025)	Not specifically addressed.	Reported that undernutrition alters glucose homeostasis and metabolic regulation.	Identified deficiencies of antioxidant micronutrients such as zinc, selenium, and vitamin A as contributors to impaired cellular defense mechanisms.	Demonstrated that oxidative stress resulting from excess reactive oxygen species damages proteins, lipids, and DNA, disrupts cellular signaling, and impairs bone growth and tissue repair.

Table 1 summarizes evidence from selected studies on the biochemical mechanisms associated with malnutrition-induced growth failure in children. The reviewed studies identified disruptions in the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis, alterations in protein and energy metabolism, micronutrient deficiencies, and inflammation- and oxidative stress-related pathways as key biochemical mechanisms.

Studies by Cammisa et al. (2025) and da Cruz Carvalho et al. (2025) reported that chronic undernutrition impairs hepatic IGF-1 synthesis, resulting in growth hormone resistance characterized by elevated GH levels and reduced IGF-1 concentrations. Da Cruz Carvalho et al. (2025) further reported that chronic inflammation suppresses hepatic IGF-1 production and receptor sensitivity, thereby affecting growth signaling pathways. Vresk et al. (2025)

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identified IGF-1 as a potential biomarker for assessing growth impairment associated with malnutrition, while Suryowati (2024) reported that inflammatory cytokines suppress anabolic pathways, including IGF-1 expression.

Alterations in protein and energy metabolism were reported by Ali and Mouzaki (2024), who observed that protein–energy malnutrition promotes proteolysis, negative nitrogen balance, muscle wasting, impaired tissue repair, hypoalbuminemia, and edema. Suryowati (2024) reported that infection-induced inflammation increases resting energy expenditure and redirects nutrients toward immune responses. Shahzad et al. (2025) also documented alterations in glucose homeostasis and metabolic regulation associated with undernutrition. Vresk et al. (2025) reported that multiple micronutrient deficiencies contribute to prolonged catabolism and delayed recovery.

The role of micronutrients in growth regulation was highlighted in several studies. Ali and Mouzaki (2024) reported that deficiencies in iron, zinc, vitamin D, and iodine affect haemoglobin synthesis, DNA replication, bone mineralization, thyroid hormone production, and growth regulation. Vresk et al. (2025) found that deficiencies in essential micronutrients worsen metabolic dysfunction and recovery outcomes among children with acute malnutrition. Similarly, Shahzad et al. (2025) identified deficiencies in antioxidant micronutrients, including zinc, selenium, and vitamin A, as contributors to impaired cellular defense mechanisms.

Evidence on inflammation and oxidative stress was reported across multiple studies. Da Cruz Carvalho et al. (2025) found that inflammatory cytokines associated with gut inflammation and environmental enteric dysfunction interfere with GH–IGF-1 signaling. Suryowati (2024) reported that chronic infection and inflammation create a persistent catabolic environment that impairs nutrient utilization. Shahzad et al. (2025) documented that oxidative stress resulting from excessive reactive oxygen species damages proteins, lipids, and DNA and disrupts cellular signaling pathways. Vresk et al. (2025) proposed the use of inflammatory biomarkers, including C-reactive protein, alongside micronutrient indicators for monitoring malnutrition-related growth impairment.

Discussion

The evidence synthesized in this review demonstrates that malnutrition-induced growth failure is a complex biochemical process involving interconnected endocrine, metabolic, immunological, and cellular pathways rather than merely a consequence of inadequate food intake. The findings show that disruption of the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis represents one of the most critical mechanisms linking nutrient deprivation to impaired growth.

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Reduced hepatic synthesis of IGF-1 in the presence of elevated circulating growth hormone concentrations suggests the development of growth hormone resistance, a phenomenon that limits linear growth, protein synthesis, and tissue development despite physiological attempts to maintain growth homeostasis. This finding reinforces the understanding that childhood stunting and growth retardation are not solely anthropometric manifestations of undernutrition but reflect profound endocrine dysfunction. Similar observations have been reported in studies demonstrating that nutrient-sensitive regulation of IGF-1 is essential for skeletal development, cellular proliferation, and anabolic metabolism, and that chronic undernutrition disrupts these processes through impaired hormonal signaling and reduced cellular responsiveness (Cammisa et al., 2025; Carvalho et al., 2025); Vresk et al., 2025).

The additional observation that inflammatory cytokines further suppress hepatic IGF-1 synthesis highlights the multifactorial nature of growth impairment, suggesting that nutritional rehabilitation alone may be insufficient where chronic inflammation persists. This supports recent evidence showing that environmental enteric dysfunction, recurrent infections, and persistent inflammation are major contributors to childhood stunting and poor nutritional outcomes, particularly among children in low- and middle-income countries (Sturgeon et al., 2023; Carvalho et al. (2025). Consequently, interventions aimed at improving growth outcomes must address both nutritional deficiencies and inflammatory conditions simultaneously to achieve sustained recovery.

The review further demonstrates that alterations in protein and energy metabolism constitute a central biochemical pathway through which malnutrition impairs growth and development. The observed shift from protein synthesis to accelerated proteolysis reflects a metabolic adaptation designed to maintain essential physiological functions during nutrient scarcity. However, this adaptation ultimately results in negative nitrogen balance, muscle wasting, impaired tissue repair, and reduced structural protein synthesis, all of which compromise normal growth processes.

The distinction between marasmus and kwashiorkor highlighted in the reviewed studies illustrates how different patterns of nutrient deficiency produce distinct biochemical manifestations while converging on the common outcome of growth failure. Similar findings have been documented in previous investigations showing that prolonged energy deficiency promotes muscle catabolism and depletion of lean body mass, whereas severe protein deficiency impairs hepatic protein synthesis, resulting in hypoalbuminemia and oedema. (Ali & Mouzaki, 2024). These metabolic disruptions are particularly important because they affect not only physical growth but also immune competence, cognitive development, and long-term health trajectories. The findings therefore reinforce the concept that adequate protein intake is indispensable for maintaining positive nitrogen balance and supporting the anabolic processes required for normal childhood growth.Furthermore, the observed alterations in

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glucose homeostasis and metabolic regulation suggest that the consequences of undernutrition may extend beyond childhood, with emerging evidence indicating that early nutritional deprivation can produce long-term effects on metabolic regulation, growth trajectories, and overall health outcomes (Carvalho et al., 2025; Sturgeon et al., 2023).

Another important finding of this review is the critical role of micronutrients in regulating biochemical pathways necessary for growth. The evidence demonstrates that deficiencies of iron, zinc, vitamin D, iodine, selenium, and vitamin A disrupt multiple physiological systems involved in growth regulation, including oxygen transport, DNA synthesis, cellular proliferation, thyroid hormone production, antioxidant defense, and skeletal development.This finding aligns with recent evidence indicating that micronutrient deficiencies frequently coexist with protein-energy malnutrition, thereby worsening metabolic dysfunction, increasing disease susceptibility, and delaying nutritional recovery among affected children (Vresk et al., 2025; Sturgeon et al., 2023). Recent evidence indicates that deficiencies in zinc, iodine, and other essential micronutrients remain important contributors to impaired growth, delayed recovery, and adverse rehabilitation outcomes among children with severe malnutrition due to their critical roles in cellular proliferation, endocrine regulation, and metabolic function (Vresk et al., 2025).

Similarly, deficiencies in vitamin D, iron, and other essential micronutrients have been associated with impaired skeletal development, reduced oxygen transport capacity, and compromised metabolic efficiency, all of which negatively affect growth and developmental outcomes in children (Ali & Mouzaki, 2024; Vresk et al., 2025). The observation that multiple micronutrient deficiencies contribute to prolonged catabolism even after caloric rehabilitation underscores the importance of comprehensive nutritional interventions that extend beyond energy replacement. This finding provides further support for integrated therapeutic approaches that combine macronutrient rehabilitation with targeted micronutrient supplementation to improve growth recovery and reduce the risk of long-term developmental deficits.

The findings also underscore the significant contribution of inflammation and immune–metabolic interactions to the pathogenesis of malnutrition-induced growth failure. The reviewed evidence suggests that chronic undernutrition and recurrent infection create a self-perpetuating cycle in which immune dysfunction increases susceptibility to infection, while persistent inflammatory responses divert nutrients away from growth-related processes toward immune defense. This results in increased energy expenditure, suppression of anabolic signaling pathways, impaired nutrient absorption, and sustained catabolic activity. Similar mechanisms have been reported in recent studies demonstrating that persistent inflammatory responses and immune activation suppress growth-promoting pathways, impair

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nutrient utilization, and contribute to growth faltering in children exposed to chronic infectious and environmental challenges (Sturgeon et al., 2023; Carvalho et al., 2025)

The role of environmental enteric dysfunction identified in this review further strengthens recent evidence indicating that chronic intestinal inflammation and enteric infections significantly impair nutrient absorption, growth regulation, and recovery from malnutrition, even when dietary intake is improved (da Cruz Carvalho et al., 2025). These findings suggest that effective management of childhood malnutrition should incorporate measures aimed at reducing infection burden, improving sanitation and hygiene, and addressing chronic inflammatory conditions that compromise nutrient utilization and growth.

A notable contribution of this review is the recognition of oxidative stress as an important but often underappreciated mechanism in malnutrition-induced growth failure. The evidence indicates that deficiencies in antioxidant micronutrients combined with increased reactive oxygen species production during infection and inflammation create a state of oxidative imbalance that damages proteins, lipids, DNA, and cellular membranes. Such damage disrupts intracellular signaling pathways, impairs enzymatic activity, and compromises cellular proliferation required for tissue growth and repair. These findings are consistent with recent evidence demonstrating that oxidative stress contributes to cellular dysfunction, impaired tissue repair, disrupted metabolic regulation, and adverse growth outcomes in children experiencing nutritional deficiencies and chronic inflammatory conditions (Samsonov & Urlacher, 2025; Shahzad et al., 2025).

The identification of oxidative stress as a contributor to growth failure broadens the current understanding of malnutrition pathophysiology and highlights the need to consider antioxidant status during nutritional assessment and rehabilitation. Addressing oxidative imbalance may therefore represent an important complementary strategy for improving growth outcomes and reducing long-term cellular damage associated with chronic undernutrition.

The review also highlights the growing importance of biochemical biomarkers in the diagnosis and monitoring of malnutrition-related growth impairment. Traditional indicators such as serum albumin and anthropometric measurements remain valuable; however, the findings suggest that integrating hormonal markers such as IGF-1 with inflammatory indicators including C-reactive protein and micronutrient assessments may provide a more comprehensive evaluation of underlying metabolic dysfunction.This multidimensional approach reflects recent shifts toward precision nutrition and personalized therapeutic interventions, where treatment decisions are informed by specific biochemical abnormalities rather than anthropometric deficits alone (Vresk et al., 2025).

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The emergence of these biomarkers offers opportunities for earlier detection of growth impairment, improved monitoring of treatment response, and more targeted nutritional rehabilitation strategies. Nevertheless, further studies are needed to establish standardized reference ranges and evaluate the feasibility of incorporating these biomarkers into routine clinical practice, particularly in resource-limited settings where the burden of childhood malnutrition remains highest.

Overall, this review sought to synthesize current evidence on the biochemical mechanisms underlying malnutrition-induced growth failure in children. The findings demonstrate that growth impairment results from the interaction of hormonal dysregulation, protein-energy metabolic disturbances, micronutrient deficiencies, chronic inflammation, and oxidative stress, all of which converge to disrupt normal growth processes. The significance of these findings lies in their contribution to a more integrated understanding of malnutrition as a systemic biochemical disorder rather than a simple deficiency of dietary intake. Future research should focus on longitudinal investigations examining the interaction between endocrine dysfunction, inflammation, and oxidative stress during nutritional rehabilitation, while also exploring novel biomarkers that can improve early diagnosis and treatment monitoring. In addition, intervention studies evaluating combined nutritional, anti-inflammatory, and antioxidant approaches are needed to identify the most effective strategies for restoring normal growth trajectories. The central message emerging from this review is that successful prevention and management of childhood growth failure require a comprehensive approach that addresses the multiple biochemical pathways through which malnutrition impairs growth, development, and long-term health outcomes.

Conclusion

This review demonstrates that malnutrition-induced growth failure is a multifactorial biochemical disorder arising from the convergence of endocrine disruption, metabolic imbalance, micronutrient deficiencies, chronic inflammation, and oxidative stress. Central to this process is impairment of the growth hormone–insulin-like growth factor-1 (GH–IGF-1) axis, particularly the development of growth hormone resistance and reduced IGF-1 synthesis, which collectively compromise linear growth and tissue development. In addition, persistent alterations in protein and energy metabolism lead to catabolic dominance, muscle wasting, and reduced anabolic capacity, further aggravating growth deficits.

The evidence also highlights that micronutrient deficiencies and inflammatory processes act synergistically to worsen growth impairment by disrupting cellular proliferation, hormone production, immune function, and nutrient utilization. Chronic inflammation and environmental enteric dysfunction perpetuate a state of nutrient diversion away from growth processes, while oxidative stress contributes additional cellular and molecular damage that impairs growth plate function and tissue repair. Collectively, these interconnected pathways

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reinforce the understanding that malnutrition is not merely a deficiency state but a systemic biochemical disorder with wide-ranging physiological consequences.

Importantly, the findings emphasize that effective management of growth failure requires a comprehensive and integrated approach that goes beyond caloric supplementation. Nutritional rehabilitation must be combined with strategies targeting inflammation control, infection prevention, and correction of micronutrient imbalances, alongside emerging biomarker-guided assessment tools that can improve early detection and treatment monitoring.

Overall, this review underscores that successful prevention and reversal of malnutrition-induced growth failure depends on addressing its multiple underlying biochemical mechanisms simultaneously. Future research should prioritize longitudinal and interventional studies exploring combined nutritional, anti-inflammatory, and antioxidant strategies, as well as the validation of reliable biomarkers for precision-based management of childhood malnutrition.

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