EXPLORING THE ROLE OF COMPREHENSIVE NUTRIENT PROFILES OF ANIMAL PROTEINS IN CHILD GROWTH AND DEVELOPMENT, WITH A FOCUS ON ESSENTIAL AMINO ACIDS

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Abstract

Stunting, a condition that can lead to future cognitive and physical disorders in children, remains a significant issue, particularly in developing countries burdened with a high prevalence of stunting. The role of amino acid in reducing stunting is still a subject of debate, contrasting with the previous emphasis on micronutrients, calories, and lipids. This article reviews existing evidence on the benefits of animal proteins, specifically their essential amino acid (EAA) content, in alleviating stunting. It also discusses the potential of animal proteins other than traditional red meat as affordable supplementary foods for children with stunting to support optimal development. When evaluating stunting, EAAs, and animal-source protein, evidence indicate that children with stunting exhibit lower levels of circulating AAs. EAAs influence various growth pathways, such as mTORC1 and GCN2, making them crucial targets for addressing stunting. Animal proteins such as cow's milk, eggs, and fish are rich in EAAs, with cow's milk being particularly abundant in AA content. Additionally, studies have indicated the potential of alternative, low-cost animal protein sources, such as cow's milk, eggs, and fish in reducing the risk of stunting and supporting linear and developmental growth. In summary, it is essential for children in developing countries to consume EAAs from animal proteins to address stunting. Future longitudinal studies and randomized clinical trials are recommended to quantify the metabolomic profiles of children. Feasibility studies and cost analyses on public health approaches and nutritional interventions to increase the consumption of other animal proteins in children are also recommended. These studies will help identify and further validate accessible and low-cost animal proteins as nutritional support for children with stunting, particularly in developing countries.

Keywords: Stunting, Essential Amino Acids, Animal Protein, Child Development, Developing Countries

Introduction

Stunting remains a prevalent issue in the field of paediatrics worldwide, particularly in developing countries. It is a persistent form of malnutrition that affects approximately 150.8 million (22.2%) children under the age of five across the globe, primarily in sub-Saharan Africa and Asia. In 2017, the prevalence rate exceeded 30% in these regions (1). Even in 2020, countries such as Pakistan, Indonesia, India, and Nigeria continued to report stunting rates of over 30% (2). The effects of stunting are long-lasting, beginning prenatally and lasting throughout the individual's lifetime (3). Consequently, it is crucial to maternal and paediatric nutrition within the first 1,000 days after conception (4). Chronic malnutrition can have various adverse consequences, including impaired cognitive and physical development, increased morbidity and mortality rates, as well as diminished educational and productive capacities (5). During infancy, nutritional deficiencies may induce permanent epigenetic changes in metabolism, resulting in poorer long-term health, altered metabolism, and an elevated risk of non-communicable diseases in adulthood. This risk is particularly pronounced in regions where the consumption of calorie-dense, low-nutrient foods is prevalent (6–9). Furthermore, there is evidence to suggest that the effects of stunting may be hereditary, with mothers who have a history of stunting being at risk of giving birth to infants with low birth weight (3). These implications have wider ramifications for the global economy, as studies have indicated a decline of 9-10% in gross domestic product per capita income in Africa and South Asia due to this condition (7).

Stunting is a persistent and future health problem that arises from inadequate environmental conditions (10). Therefore, it is crucial to improve the nutrition, sanitation and healthcare provisions for both mothers and children (9). This improvement should involve parents paying close attention to their child's nutrition during the critical "golden age" of development, which occurs between 6 and 24 months of age, by supplementing their diet with various micronutrients. This intervention has been proven to significantly reduce the risk of stunting (11). In the past, stunting management focused solely on addressing protein malnutrition. However, the current approach emphasizes the consumption of high-quality protein, taking into consideration the essential amino acid (EAA) content, bioavailability and digestibility, rather than just the quantity consumed (12).

The new paradigm of EAA in alleviating stunting is based on molecular evidence of linear human growth regulated by the mechanistic target of the rapamycin complex 1 (mTORC1) pathway, influenced by EAA adequacy (13). It is also supported by recent advances in metabolomics and mass spectrometry, which facilitate the quantification of serum AA and other metabolites in a broader range of studies, revealing the importance of EAA on growth (8). Cross-sectional studies have revealed the importance of proper dietary intake of animal proteins (an undetermined fraction of the required daily intake of 0.85 – 1.2 g/kgBW of protein per day, according to age group, since consuming a balanced mixture of both is considered sufficient) (14), including AA-rich dairy proteins, to prevent stunting due to their abundance of EAA and specific micronutrients, which are more bioavailable than plant proteins (7, 9).

Several preceding studies on stunting have investigated the administration of micronutrients, calories, and lipids on children's growth, as well as EAA, which played an essential role in stunting management (7–9, 15–20). However, few studies have focused on strategies to alleviate stunting by providing accessible and low-cost animal protein to children in developing countries, such as cow milk, eggs, and fish. Therefore, this narrative review aims to discuss the benefits of components of animal protein, especially EAA, in reducing stunting and optimizing child growth and development, particularly in the first 3,000 days of life, through evidence-based nutritional interventions tailored to the socio-economic situation of low- and middle-income countries (LMICs), through a review of existing pre-clinical and clinical evidence on the topic.

Review methods

This evidence-based narrative review article was conducted between March and May 2023. A systematic search was performed across three journal databases: Pubmed (n = 19,694), Proquest (n = 73,697), and Google Scholar (n = 29,600). Various keyword combinations, such as "stunting", "essential amino acids" and "animal protein" were used. The search results were filtered based on article titles and abstracts. Due to the excessive number of search results, a decision was made to skim through them instead of comparing for duplicates; we intended to make a narrative review based on available relevant evidence, not generating a systematic review. Inclusion criteria consisted of articles written in English, original research, topical significance, availability of full text, and publication date within the past 23 years (2000 – 2023). The wide range for the publication date was intentional to accommodate the limited amount of research conducted on this subject matter. Articles that did not align with the narrative of this review were then excluded. The selected articles obtained (n = 23) were synthesized into a narrative review. Additional citations were obtained through hand-searching to provide further details for the overall narrative review.

Results and Discussion

The role of amino acids in stunting: a primer

Stunting is defined as having a height-for-age score (HAZ) below two standard deviations (SD) from the World Health Organisation (WHO) Child Growth Standards. In contrast, linear growth faltering is defined as failing to attain linear growth potential (10). Therefore, stunting is a more severe subset of linear growth faltering.

Stunting reflects a child's clinical history, especially their development, but also factors such as food security, caregiver's nutritional and health knowledge, and use and access to health services. The condition also serves as a predictor for future linear growth, developmental milestones, and economic well-being. It encompasses multiple aspects of individuals' future lives, including income, wealth, employment opportunities, access to essential goods and services, social support, and overall life satisfaction (5, 10). It impacts several domains, including development delay, declining work capacity, future chronic health issues, elevated cephalo-pelvic disproportion risk, and unwanted birth outcomes (10). Thus, early nutritional interventions are essential. Appropriate nutrition for children will impact linear growth by providing required macronutrients (9), increasing plasma levels of insulin-like growth factor-1 (IGF-1) (21), and consequently reducing stunting (22). This study discusses nutritional interventions to alleviate these problems, mainly through essential amino acids derived from animal sources.

The reviewed literature indicates that EAA plays a crucial role in multiple growth pathways. Several studies have demonstrated notable distinctions between the EAA profiles of typically developing children and those who are stunted. EAA can be obtained from both plant (in lower bioavailability compared to animal proteins) and animal proteins (7, 9), such as milk, eggs, and fish. Although both plant and animal proteins have the potential to reduce stunting in developing countries, however, in this review, we will focus exclusively on animal proteins.

Status of essential amino acids in children with stunting

Amino acids are building blocks of protein, which includes various hormones essential for the growth and development of children (8, 21, 23). There are more than 20 amino acids involved in protein synthesis, which are categorized into essential, non-essential, and conditionally essential amino acids. EAA is termed as such because the body is incapable of synthesizing them and must acquire them through dietary sources (24).

The quality of protein is evaluated by considering its amino acid composition, digestibility and bioavailability (12). The bioavailability of protein is influenced by its inherent digestibility and the processing methods used. In general, processing enhances the digestibility and bioavailability (25). Deficient digestibility in children may be a plausible explanation for the lack of success in previous nutritional interventions aimed at promoting linear growth (26). Other possible factors that contribute to this include increased intestinal permeability resulting from environmental enteric dysfunction (8), deficiencies in pancreatic enzymes, the presence of intestinal parasites, and anti-nutrient factors (such as tannins and phytates) that diminish the bioavailability of amino acids (26).

EAAs are also present in plant-based food sources, such as legumes, nuts, and soy. However, animal-source proteins are generally considered to be of higher quality than plant-source proteins due to their higher digestible indispensable amino acid score (DIAAS), with most animal-source proteins having a DIAAS value above 90%. In contrast, only soy proteins reach the ideal DIAAS value among all plant-based proteins (12). It is important to note that a food item is regarded as having an "excellent" DIAAS score if the score is above 100, meaning that it fulfils more than 100% of the recommended daily intake of digestible indispensable amino acids. A "good" DIAAS score falls between 75 and 99, while a score below 75 indicates that the food item cannot be claimed as a source of indispensable amino acids (27). Plants generally have a DIAAS value below 75 and may contain natural anti-nutrient factors, such as tannins which can form reversible and/or irreversible complexes with proteins, hindering their breakdown into amino acids), and phytates, which can inhibit digestive enzymes that degrade proteins, and also chelate with essential minerals found in animal protein, among others effects (12, 26, 28). Additionally, plant-based proteins are less easily digested and are highly influenced by food processing (25). Furthermore, animal proteins generally contain higher amounts of iron, including both haem and non-haem iron, whereas plants only provide non-haem iron, which is more difficult to absorb and has lower bioavailability (29).

Amino acids have substantial cognitive and developmental advantages for children, particularly in early childhood. Increased protein intake may stimulate liver secretion of IGF-1, thereby reducing the risk of growth impairment. In addition to the study conducted by Semba et al. (8) which will be elaborated in subsequent sections, the ability of EAAs to mitigate the risk of growth impairment is demonstrated by Maulidiana and Sutjiati, who discovered that children in Malang, East Java, who consumed adequate methionine (an EAA) were 86% less likely to develop growth impairment (30). Consequently, the intake of amino acids is beneficial for children's linear growth, cognition, and psycho-educational performance (31).

Studies have indicated that a deficiency in certain EAAs (particularly tryptophan and lysine) can disrupt lipid and protein synthesis, which are essential for children's linear growth (8). In an experimental investigation (32), supplying growth-related amino acids and ensuring balanced intake was found to be associated with better linear growth in malnourished male rats compared to feeding them diets based on cornmeal and casein. Analyzing the relationship between plasma amino acids and growth is crucial for identifying additional amino acid supplementation to prevent malnutrition, an approach that could be applied to children in underdeveloped countries. Supporting this, Semba et al. (8) recruited 313 Malawian children aged 12–59 months, of whom 194 (62%) were classified as having growth impairment. They demonstrated a significant deficiency of nine EAAs (tryptophan, isoleucine, leucine, valine, methionine, threonine, histidine, phenylalanine, lysine), three conditionally EAAs (arginine, glycine, glutamine), and three non-EAAs (asparagine, glutamate, serine), as well as other metabolites, in children with growth impairment compared to normal children (8). All amino acids exhibited a significant positive correlation with the height-for-age Z-score (HAZ) score.

Meanwhile, there was no significant difference in the serum levels of proline, tyrosine, alanine, and aspartic acid between children with and without stunting. Additionally, there was a decrease in other proteinogenic amino acids, biogenic amines (such as serotonin), amino acid metabolites, sphingomyelin, and glycerophospholipids compared to non-stunted children ($p < 0.01$). Stunting is also associated with alterations in serum glycerophospholipid concentrations. Therefore, these findings support the hypothesis that children at high risk of stunting may not receive sufficient dietary intake of EAA and choline, which are necessary for the synthesis of sphingolipids and glycerophospholipids (8).

Furthermore, the results of serum biogenic amines and amino acid metabolites (including ornithine, taurine, and asymmetric dimethylarginine) were significantly lower in stunted children compared to non-stunted children (8). However, the levels of alpha-aminoadipic acid (an intermediate molecule in the degradation of lysine), kynurenine (a metabolite of tryptophan), and certain biogenic amines (such as creatinine, spermine, putrescine, symmetric dimethylarginine, and total dimethylarginine) were all similar between the two groups. Moreover, the assessment of height-for-age showed associations between these biogenic amines and blood amino acids, amino acid metabolites, acylcarnitines, and sphingolipids. Therefore, collectively, stunting was found to be associated with reduced levels of three conditionally necessary amino acids, other proteinogenic amino acids, biogenic amines, amino acid metabolites, sphingomyelins, and changes in glycerophospholipids (8).

Looking in more detail at the molecular processes involved in stunting, two molecular pathways—the mammalian target of rapamycin complex 1 (mTORC1) and the general control non-depressible-2 kinases (GCN2) pathways—may explain the connection between amino acids and stunting (33). The GCN2 pathway detects cellular starvation for specific amino acids, thus regulating autophagy and biosynthesis (34, 35). Changes in serum amino acids in stunted children are detected by the mTORC1 nutritional sensor and GCN2 (13, 34, 35), which then suppress protein and lipid synthesis and promote autophagy, leading to slow and stunted growth. These findings were also supported by the cohort study conducted by Semba et al. (8) cohort study, which found reduced concentrations of various lipids in children with stunting as a result of mTORC1 and GCN2-mediated suppression of macronutrient synthesis and promotion of autophagy. Furthermore, the linear growth of children depends on the chondral growth plates (36), which are also regulated by the mTORC1 pathway and the availability of EAAs such as leucine (37), tryptophan, and lysine (38). mTORC1 critically responds to leucine, which has the most robust relationship with the linear growth of children (13, 34, 39). Besides those pathways, another molecule probably interrelated with EAAs is IGF-1, which is essential in regulating children's growth (40). EAA deficiency is widely known to suppress IGF-1 signalling directly and indirectly, precipitating growth retardation (40).

Methionine, a sulfuric amino acid, serves as a precursor for homocysteine, cysteine, and taurine. These compounds are essential in stimulating the expression of genes related to growth hormone and IGF receptor synthesis, and they increase protein turnover in liver cells (15, 41, 42). Unfortunately, soybeans have minimal methionine content, despite being widely consumed as protein sources in developing countries, particularly in the form of processed products such as tempeh and tofu (9). Tryptophan, on the other hand, serves as a precursor for niacin and serotonin, which are neurological mediators primarily found in intestinal enterochromaffin cells (24). Arginine and lysine have a more significant impact on growth hormone synthesis than other amino acids (43). Lysine is also a precursor of carnitine, which is necessary for the structural modification of collagen (24). However, staple carbohydrates like rice have limited lysine content (9). Threonine is the primary component of the secretory mucin that forms the protective mucus layer of the intestine. Histidine is involved in protein methylation, as well as the structure and function of haemoglobin. It also serves as a precursor for histamine and carnosine. Phenylalanine, on the other hand, acts as a precursor for tyrosine, which is a substrate for catecholamine synthesis (8, 24). Arginine serves as a precursor for various compounds such as nitric oxide, creatine, symmetric and asymmetric dimethylarginine, and polyamines. It is also interchangeable with proline and glutamate. Glutamine is crucial for the growth of enterocytes and the functioning of the intestinal barrier. Glycine acts as a neurotransmitter in the central nervous system and plays a role in protein and purine synthesis, bile acid conjugation, and cyto-protection (15).

Evidence indicating that lipogenesis is inhibited by mTORC1 as a result of EAA deficiencies in children with stunted growth can also be observed in low concentrations of sphingomyelin observed in the cohort studied by Semba et al. (8). Among sphingolipids in the trans-Golgi network, endocytic recycling compartments, and the plasma membrane of mammalian cells (up to 20%), sphingomyelin is the most abundant (44). It is also a critical component of the myelin sheath and plays a crucial role in the myelination of the central nervous system during childhood development. This association between sphingomyelin and EAA could explain the strong connection between the mTORC1 pathway and disturbances in neural plasticity in stunted growth (45). Additionally, sphingomyelin is involved in the immune system through the formation of Toll-like receptors and scavenger receptors A and B (44), as well as in cell signalling (24) and T-cell activation and differentiation (42).

Sphingomyelin synthesis is closely related to phosphatidylcholine, particularly in the final step of its biosynthesis. Semba et al. (8) also observed significantly lower levels of phosphatidylcholine in stunted children. Phosphatidylcholine is the most abundant phospholipid in mammalian cell membranes and the predominant circulating phospholipid in plasma (46). It plays an essential role in cellular proliferation, differentiation, and growth, due to its involvement in the composition of the cell membrane (46). Phosphatidylcholine is vital for the assembly and secretion of lipoproteins by the liver (41) and is a major active component of pulmonary surfactant. The effects of EAAs on phosphatidylcholine and sphingomyelin concentrations are crucial to mention because these substances are involved in chondrogenesis, particularly in the growth plates, therefore significantly influencing linear growth (36). Low serum phosphatidylcholine levels can be corrected by increasing the consumption of choline-rich foods, which are mainly derived from animal sources (15).

One limitation of Semba et al. (8) is that it did not focus on molecular assessment at the transcriptomic or proteomic level, making it difficult to truly identify the involvement of the mTORC1 and/or GCN2 pathways as the biological framework for amino acid dependence in normal child development (15, 33). Further research is needed in this regard. Nonetheless, the study supports the hypothesis that EAAs play a vital role in the growth and development of children and that their levels are insufficient in the plasma of stunted children. EAA deficiency may explain the limited improvement observed from supplementation with other nutrients such as micronutrients, calories, and lipids (although these aspects are also necessary) (16–18, 23). In the absence of adequate amounts of amino acids, the growth-regulatory mechanisms of mTORC1 and GCN2 will not allow for effective linear growth in children (13, 34). However, it should be noted that this study is cross-sectional, so, causality cannot always be inferred. A prospective, longitudinal assessment of the effects of serum amino acids on stunting is needed to initiate randomized clinical trials and investigate the causal role of amino acid deficiency in the pathogenesis of stunting.

Importance of animal protein for children with stunting

As previously mentioned, amino acids are constituents of proteins and are classified into essential, conditionally essential, and non-essential types based on the body's innate ability to synthesize them (47). Animal-source proteins are highly diverse and contain EAAs as well as micronutrients, such as sulphur and easily absorbable (haem) iron. This review focuses on the most accessible and cost-effective sources of animal proteins such as cow's milk, eggs, and fish (in countries with maritime resources). The consumption of animal protein leads to three primary outcomes, namely improved linear growth, weight gain, and a decrease in all-cause morbidity. According to a study by Eaton et al. (48), the consumption of animal-source proteins is associated with better scores in HAZ or length-for-age Z (LAZ) with odds ratio (OR): 0.24; 95% CI (95% confidence interval): -0.09 to 0.56, $p < 0.0001$) and weight-for-age Z-score (WAZ) (OR 0.26; 95% CI: 0.00–0.52, $p < 0.0001$). Additionally, the consumption of animal protein is suggested to reduce morbidity rates in children, as observed in participants who experienced at least one episode of illness during the study (48). However, no studies provided data on children's anaemia (48). Three studies included in Eaton et al. (48) reported no significant difference in haemoglobin levels between intervention groups, indicating no effect on iron deficiency. Furthermore, there was no significant difference in developmental outcomes between the two intervention groups: meat (99.1 points, 95% CI: 97.9–100.3, $p = 0.54$) and cereal (99.7 points, 95% CI: 98.8–100.7, $p = 0.54$) (48).

Despite its potential to alleviate stunting, cow's milk and egg allergies are the two most common food allergies in children, with a prevalence of 0.8% among all children and 1.3% in children under five years old (49). Egg allergy has been used as a predictor of atopy and is correlated with a twofold increase in the risk of asthma (49). The underlying mechanism of egg and cow's milk allergies is similar to other food allergies, which is mediated by immunoglobulin E (IgE). This process begins with sensitization, where IgE binds to mast cells, and ends with the release of chemical mediators from mast cell degranulation (50). In the case of egg allergy, the binding of IgE and mast cells also occurs in the gastrointestinal tract, causing smooth muscle contraction and vasodilatation, resulting in vomiting and diarrhoea (50). Allergenic proteins then circulate in the bloodstream, increasing vascular permeability and releasing dermal mast cell granules, resulting in urticaria (50). These allergies can have serious effects such as anaphylaxis and a decline in children's quality of life (49). However, Eaton et al. (48) found no allergic reactions in groups given daily eggs as a nutritional intervention.

It is important to note that animal-source protein intake in children in developing countries tends to be low. For example, in Indonesia, the average protein consumption rate in children under five was 29–40 grams per day in urban areas, and even lower, 21–30 grams per day in rural areas (9, 51). Mauludyani et al. (52) showed that higher household expenses on soybeans and lower expenditures on sugar and oil were significantly associated with a lower risk of wasting and being underweight. The study calculated monthly household expenses by estimating the mean household income per district (52). In this study, high-income households were less likely to consume rice and preferred manufactured complementary foods, which leads to under-nutrition (52). However, low-income households were associated with high sugar and cooking oil consumption, which can also lead to similar outcomes (52). It has also been found that the relative prices of animal-source foods, which are crucial for combating stunting, are higher in developing nations such as in Africa (53, 54). Thus, addressing socioeconomic inequities in complementary feeding is necessary by increasing nutrition education coverage and providing food security and innovations to make nutrient-dense foods available for all. Aligning the health and food sectors is therefore required to achieve much-needed synergy in improving both the demand and supply of healthy diets.

Figure 1 illustrates the correlation between animal-source foods and the incidence of stunting in various countries, particularly in LMICs, where starch-based diets are more prevalent. The visual representation is based on recent data on stunting prevalence in children, using the WHO's child growth criteria of height/length-for-age z-scores ≤ 2 SD (World Health Statistics, 2020, data is presented in a point plot) (2). Additionally, data on meat consumption worldwide, measured in thousand tons of carcass weight and kilograms of retail weight per capita, was obtained from the Organization for Economic Cooperation and Development (OECD) and the Food and Agriculture Organization (FAO) (data is presented in a bar chart) (55). Supplementary Table S1 provides further details regarding this data.

The analysis suggests that developing countries including Ethiopia, India, Nigeria, Indonesia, and Pakistan are the top ten nations with the lowest meat consumption (2, 55). Interestingly, these countries also have high rates of stunting, with prevalence rates of 35%, 31%, 35%, 32%, and 37%, respectively. On the other hand, developed nations, such as the United States of America and Australia are ranked as the top meat consumer nations. This observation may indicate an inverse relationship between meat consumption and stunting rates. However, it is important to note that this correlation at the country level does not provide scientific evidence of a causal relationship.

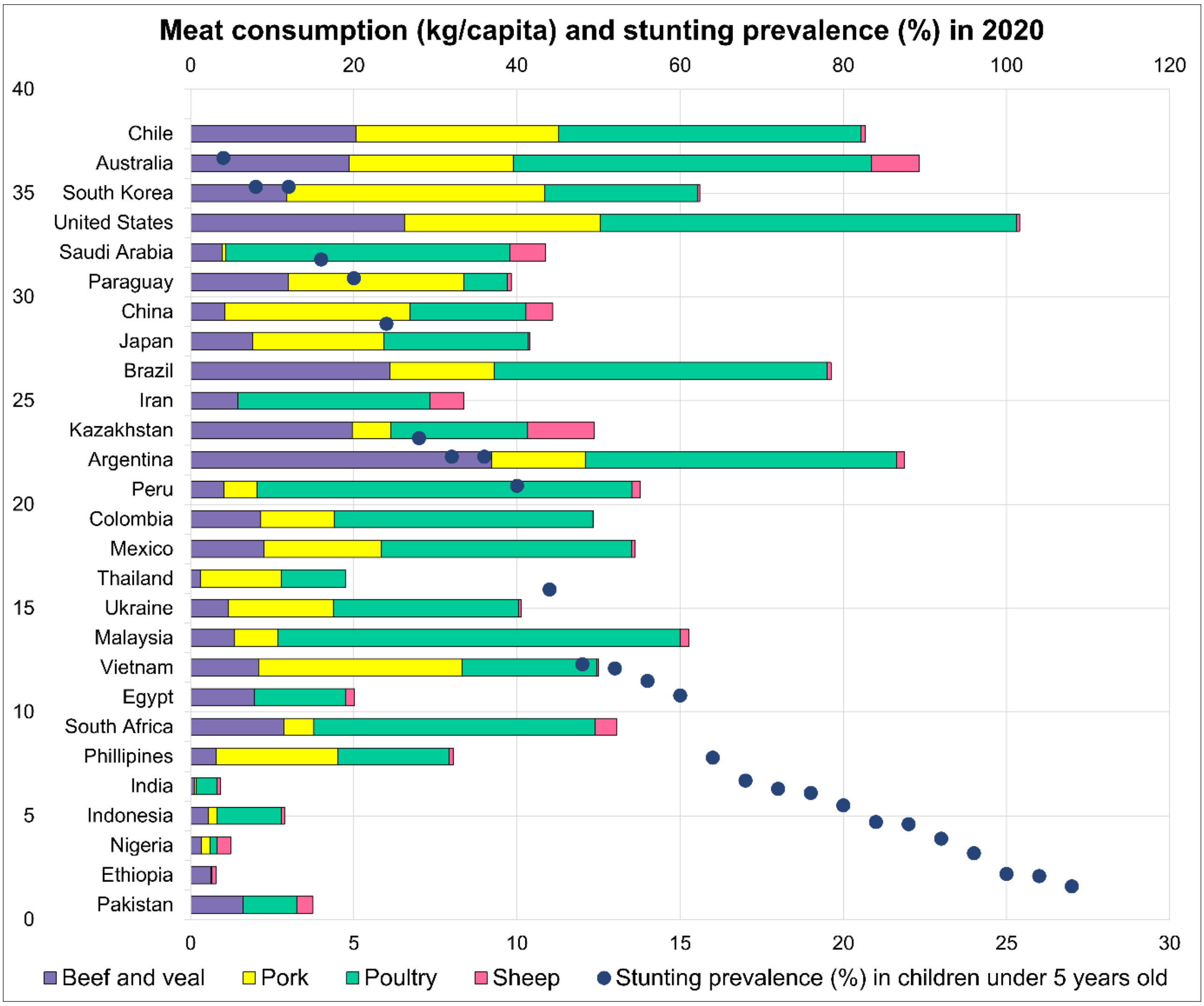

Figure 1: Levels of consumption of animal meat in various countries and its relationship with stunting (2, 55). Bar graph indicating an inverse relationship between meat consumption and stunting prevalence in 2020. Data for stunting and meat consumption were respectively obtained from World Health Statistics (2), and the Organization for Economic Cooperation and Development (OECD) (55). The lowest rates of meat consumption and highest stunting prevalences were seen in developing countries, such as Pakistan, Ethiopia, Nigeria, and Indonesia. In contrast, the highest meat consumption rate and lowest stunting prevalences were seen in developed countries, including the United States of America and Australia.

Nevertheless, it supports previous meta-analyses (56, 57) that have proposed a hypothesis that animal-source diets have a positive impact on child growth. Further research is needed in various settings, including experimental, observational, and clinical studies at the individual level. Additionally, it is essential to explore other indicators such as dietary diversity and meal frequency to thoroughly examine the dietary quality and its association with child linear growth (58).

For practical reasons, many parents in underdeveloped nations opt to provide their children with processed meats, such as meatballs, sausages, and nuggets, instead of fresh meat (9). This practice can have detrimental effects due to the limited nutritional value found in processed meat as compared to fresh meat (9). Conversely, offering cost-effective fresh (unprocessed) animal-source protein as a form of nutritional intervention may prove to be more advantageous. A recent randomized study conducted in Ecuador suggests that providing one egg per day to toddlers aged 6 and 9 months for a period of one year resulted in a reduction of stunting by 47% and low body weight by 74%, which are indicators of chronic and acute malnutrition, respectively. Furthermore, this dietary habit did not appear to trigger allergies (19). It is also worth considering other easily accessible sources of protein, such as fish (20, 59).

Coincidentally, Sjarif et al. (9) also underscored their discovery that the consumption of red meat products (including processed meats such as sausages, corned beef, and meatballs) five times per week was considered a risk factor for stunting. The unadjusted OR was found to be 3.70 (95% CI: 1.17–11.74, $p = 0.026$), while the adjusted OR was 3.64 (95% CI: 1.00–13.26, $p = 0.05$). This suggests a

364% increased risk of stunting occurrence. These findings may indicate that the red meat products commonly consumed by the participants in the study are of poor quality, characterized by low red meat content and higher levels of starch and salt (9). Processed red meat products are frequently consumed and practical, but they cannot be considered a reliable source of animal protein with high nutritional value due to their inconsistent composition. Therefore, it is imperative to re-evaluate and regulate their nutritional quality.

Globally, there has been a significant increase in the consumption of unprocessed red meat, by 88.1% between 1990 and 2018. This increase is primarily driven by Southeast and East Asia, Latin America, and the Caribbean (60). In contrast, processed meat consumption has risen by 152.8% worldwide (60). It is important to note that unprocessed meat is associated with cardiovascular disease, diabetes mellitus, and certain types of cancer. Therefore, it is crucial to consume unprocessed meat only within safe limits (60). It is recommended to incorporate other protein alternatives, such as cow's milk, white meats like poultry and fish, and eggs into one's diet. In addition to the increase in unprocessed meat consumption, there has also been a rise in the consumption of seafood (109.4%), eggs (141.4%), and milk (98.6%) (60). However, it is worth mentioning that seafood consumption is lower among children and populations with lower education or who reside in rural areas (60). While excessive animal protein consumption may have potential drawbacks in high-income countries, it is suggested that children in LMICs may benefit from it, as they are at risk of under-nutrition, particularly during the complementary feeding period, in the first place (61).

Table 1 presents the requirement of EAA and protein amounts for children based on their age, as well as the compositions of such EAA in various proteins. These statistical data were obtained from a study by Uauy et al. (31) and the Food and the recommended dietary allowances provided by the Food and Nutrition Board Commission on Life Sciences National Research Council (62). Generally, human milk and animal protein (such as cow's milk, chicken, eggs, and beef) contain the nine EAAs necessary for the human body. Furthermore, the demand for EAA is higher during early childhood compared to later stages of life. This indicates the significance of supplying EAA during early life to prevent stunted growth. Consequently, multiple studies conducted worldwide have established a correlation between linear growth in children and protein intake, particularly from animal sources (63).

Table 1: Essential amino acids requirements in children and their composition in animal-source foods (31, 62).

Essential amino acids	Composition of protein in animal-source foods (in mg/g protein/day)[a]				Essential amino acid requirements by age (years) (in mg/kg body weight/day)[b]					
	Human milk	Cow's milk	Chicken eggs	Beef	0–1	1–2	3–10	11–14	15–18	>18
Histidine	26	27	22	34	22	15	12	12	11	10
Isoleucine	46	47	54	48	36	27	23	22	21	20
Leucine	93	95	86	81	73	54	44	44	42	39
Lysine	66	78	70	89	64	45	35	35	33	30
Methionine + cysteine	42	33	57	40	31	22	18	17	16	15
Phenylalanine + tyrosine	72	102	93	80	59	40	30	30	28	25
Threonine	43	44	47	46	34	23	18	18	17	15
Tryptophan	17	14	17	12	9.5	6.4	4.8	4.8	4.5	4.0
Valine	55	64	66	50	49	36	29	29	28	26
Protein for maintenance (g/kg body weight/day)					0.66	0.66	0.66	0.66	0.66	0.66
Protein for growth (g/kg body weight/ day)					0.46	0.20	0.07	0.07	0.04	0.0

[a,b:] Data on EAA requirements in children and their compositions in animal-source proteins were obtained from two studies (31, 62). Affordable sources of animal protein (human milk, cow's milk, chicken eggs, and beef) contain nine types of EAA, with eggs being the richest. A greater demand for EAA was found in the first year of life and declines with age.

Use of cow milk in stunting elimination

The efficacy of cow milk in promoting linear growth in children surpasses that of other sources of animal-based (meat, poultry, and eggs) or plant-based (soy, nuts, and oats) proteins (9). A study conducted in Denmark revealed that a daily consumption of approximately 200–600 mL of milk by toddlers was associated with a 30% increase in circulating IGF-1 (21). Similarly, research carried out in Vietnam demonstrated that the consumption of formula milk among school-aged children could reduce the incidence of underweight and stunting, enhance micronutrient status, and improve learning outcomes and quality of life (22).

Another advantage of animal protein consumption is the presence of essential micronutrients, such as highly bioavailable haem iron. Sjarif et al. (9) conducted a study involving 41 stunted Indonesian children aged 12–36 months, which resulted in recommendations for optimal food sources to prevent stunting in Indonesia, one of which is milk derived from animal sources. The study used the Ironcheq questionnaire, utilized in this study to assess the risk of iron deficiency in toddlers, which consists of five questions related to the daily intake of iron sources, including milk for growth, red meats, liver, processed red meat products (e.g., meatballs), and eggs. Iron, a vital micronutrient, is commonly found in animal proteins. However, it is worth noting that this questionnaire did not evaluate other commonly consumed animal protein sources, such as fish. Outcomes from the Indonesian study (9) demonstrated a significant association between two protein sources (i.e., growing-up milk (GUM) and processed red meat products) and the mitigation of stunting, with GUM proving beneficial and processed red meats showing detrimental effects.

The consumption of 300 mL/day of GUM (not exceeding 600 mL) derived from animal-source protein was found to be a protective factor against stunting, with an unadjusted OR of 0.36 (95%CI: 0.17–0.73, p = 0.005) and adjusted OR 0.28 (95%CI: 0.13–0.63, p = 0.002) (9). This amount was adapted to adhere to the recommendations of the WHO for managing moderate acute malnutrition. A study indicated that 25–33% of protein sources should come from dairy protein due to its positive impact on weight gain and linear growth (64). Another study by Park et al. (11) suggested that supplementation of micronutrients (such as iron, folic acid, and other micronutrients) during the complementary feeding period increased HAZ score, while the consumption of fortified food supplements reduced the risk of stunting. The growth milk used in the 2016 study by Sjarif et al. (9) for children aged 1 to 3 years is fortified with the necessary micronutrients for toddlers, including iron, zinc, and vitamins, as regulated by CODEX STAN 72-1981 (9).

It is important to note that Sjarif et al. (9) have found that stunted children often come from families with low levels of parental education and low socioeconomic status. This is associated with limited purchasing power for animal-source protein foods and milk. Therefore, it is necessary to explore new formulas for more affordable GUM or to consider the combined use of other animal proteins to address stunting in the future.

The studies discussed in this section thus far have utilized modified (“formula”) whole milk powder. These powders have typically undergone various processing steps, such as cold storage, heat treatment, standardization, and homogenization). Additionally, the milk is further modified to adjust its macronutrient composition before being transformed into a powdered form. Despite these processes, including treatment with ultra-high temperatures, pasteurization, and other standardized treatments, the protein and EAA levels in processed milk remain optimal. Generally, there is no change in protein concentration between whole milk and skimmed milk (which has had its fat content removed). However, there is a lack of studies that review or empirically investigate the changes in EAA composition in various dairy products (65).

Eggs as a practical source of animal protein

Eggs, whether from chicken or other poultry species, are rich in EAAs. Various quantities of all EAAs including arginine, histidine, isoleucine, lysine, methionine, cysteine, phenylalanine, tyrosine, threonine, and valine) were found in various quantities within both chicken eggs from different commercial sources in Saudi Arabia (which can fulfil 17.4–26.7% of the recommended daily intake of EAAs) (66), and in the egg whites of various poultry species, such as chicken, duck, geese, turkey, quail, and pigeon (67). Egg yolks consist of low-density lipoprotein (LDL), high-density lipoprotein (HDL), phosvitin, and livetin (68). On the other hand, egg whites contain ovalbumin (54%), ovotransferrin (12%), ovomucoid proteins, and flavoproteins (68). Eggs are also high in choline, which has been associated with growth in animal models (15). Additionally, choline plays a vital role in the production of phospholipids, the maintenance of cell membrane integrity, and the promotion of brain function and development. It also significantly affects chondrogenesis and linear growth (19). Eggs also contain vitamin B12 and docosahexaenoic acid (DHA), an essential fatty acid necessary for growth and development (19).

A randomized controlled trial conducted by Iannotti et al. (19) demonstrated that providing one egg per day for six months to 7-month-old children significantly promotes growth compared to children who did not receive eggs (19). The group that consumed eggs exhibited a 0.63-fold increase in LAZ and a 47% reduction in stunting (19). Furthermore, this study found no evidence of egg allergy within the cohort, suggesting that eggs serve as a safe source of amino acids (19). A subsequent study by Iannotti et al. (69) further confirmed that the intervention group synthesised higher levels of choline and DHA. Another investigation by Headey et al. (56) revealed that egg consumption in children aged 6–23 months significantly lowers stunting rates and may reduce the risk of stunting in children aged 18–23 months (56). Regrettably, global data indicate that only 22.4% of children aged 6–23 months consume eggs (56). Additionally, a study encompassing 46 countries found that egg consumption could reduce stunting by 1.7-fold (70). This is noteworthy given that poultry, particularly chicken is relatively inexpensive to raise in a scavenging system where food is self-gathered by free-ranging chickens. Poultry is also known for its rapid and efficient protein production, ease of care, and relatively short production cycle compared to mammals (71).

Fish as a viable source of animal protein

Fish is a potential source of animal protein that is readily available and efficient in LMICs. Research has shown that fish is preferable to support growth and development than other meats (72) because it contains a greater variety of EAAs necessary for growth. These include arginine, leucine, methionine, glutamic acid, tryptophan, histidine, lysine, threonine, and isoleucine (70). It also contains 1–20% unsaturated fatty acids, eicosapentaenoic acid (EPA) and DHA, beneficial for cell regeneration and growth (73). Unfortunately, fish consumption among children aged 6–23 months worldwide is inadequate, with only 19.6% meeting recommended levels (56).

According to Headey et al. (56), there is a significant correlation between fish consumption and lower rates of stunting in children aged 18–23 months (56). Bolton (70) demonstrated a 5.6-fold reduction in stunting among children aged 6–23 months in Latin America & the Caribbean who consumed fish and a 4.3-fold decrease in West Asia and Middle Asia (70). These findings are further supported by research conducted by Ngaisyah and Rohman (73) in Gunung Kidul, Yogyakarta, which revealed that children with low levels of fish consumption had a six-fold higher risk of stunting compared to children with adequate fish consumption (73). Another study by Suhaimi in the Panggang Lake Region, Kalimantan, showed that fish consumption led to a decrease in stunting (74).

The potential for fish consumption to address protein needs, particularly in low to as a solution to fulfil protein needs, especially in low-to-medium-income families, is undeniably influenced by geography and cultural perceptions of food. In Southeast Asia, fish (both freshwater and marine) is an important and preferred source of protein, especially among families with lower socioeconomic status. Fish plays a crucial role as a protein source in rural and insular regions, as well as larger families with limited economic resources, particularly in countries with maritime geography or coastal areas. Both saltwater and freshwater fish appear to satisfy protein needs in the region (75, 76). Globally, the use of fish as a protein source is appealing due to its adequate protein content, relatively low cost, and ease of reproduction. However, challenges such as varying proximity to waterways, susceptibility to spoilage without proper preservation techniques (such as cold storage or additives), and differing food preferences discourage widespread fish consumption.

Recommendations and Conclusions

In light of various societal circumstances, we aimed to present scholarly literature on the impact of animal protein on stunting. We examined both the pre-clinical realm, where deficits in animal protein consumption have been linked to stunting through convincing pathophysiology, and the clinical realm, where low-cost and feasible nutritional interventions utilizing animal proteins have been shown to offer an easily accessible strategy for alleviating stunting in the community. We provided ample evidence on the role and benefits of EAAs in child linear growth and development, as well as strategies for preventing stunting through interventions that involve affordable animal proteins containing EAAs for growth (i.e., relatively low-cost and applicable to the settings of an LMIC). However, it is important to acknowledge the limitations of this review, particularly in terms of the scope of the research reviewed. Most of the studies included in this article were cross-sectional, which means that causality cannot always be determined. Furthermore, there is a dearth of high-level evidence, such as randomized controlled trials (RCTs), meta-analyses, systematic reviews, and cohort studies, on this topic. Some studies had limited sample sizes, which may render the result statistically insignificant and not necessarily representative of the actual situation. Consequently, future research should focus on longitudinal studies and RCTs that quantify metabolomic profiles, as well as feasibility trials of public health policies. These studies are necessary to generate recommendations for growth milk with specific formulas that are rich in EAAs and available at affordable prices, as well as low-cost and accessible nutritional interventions that provide affordable animal protein to address stunting in children in need.

The effects of stunting on children's development, particularly in developing countries, are significant. Therefore, it is crucial to consider effective strategies to combat this issue. EAAs, which are primarily found in animal proteins and are most easily absorbed by the body, have been found to help reduce stunting. They provide the necessary building blocks for protein synthesis and prevent autophagous mechanisms at a molecular level. Studies have shown that children with stunting have lower EAA concentrations compared to those without stunting. Animal proteins are superior to plant proteins in this regard as they contain more EAAs, have higher bioavailability, and provide other beneficial micronutrients such as haem and non-haem irons, and vitamins. EAA is found to significantly increase linear growth and weight gain, lower all-cause morbidity, enhance developmental outcomes in children, and have minimal side effects.

The use of accessible animal proteins such as milk, eggs, and fish have been found to improve nutritional status and decrease the risk of stunting, as they offer a comprehensive profile of EAAs and fortified micronutrients including iron, zinc, vitamins, and long-chain fatty acids. Therefore, it is essential to emphasize the need for collaboration between healthcare providers and stakeholders from various sectors to address the extensive problem of stunting. Global and national efforts should be made to provide high-quality protein sources, implement impactful nutritional interventions, and conduct further studies on this topic.

Acknowledgements

None.

Competing interests

The authors declare that they have no competing interests.

Ethical Clearance

Ethical clearance is not needed for this article.

Financial support

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors in the making of this work.

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Supplementary File 1: Data on stunting burden and protein consumption worldwide in 2020 (2, 55).

Country	Meat consumptions				Stunting prevalence (%) in children under five years old
	Beef and veal	Pork	Poultry	Sheep	
Pakistan	6.4	0.0	6.6	2.0	36.7
Ethiopia	2.5	0.0	0.1	0.5	35.3
Nigeria	1.3	1.1	0.8	1.7	35.3
Indonesia	2.2	1.0	7.9	0.4	31.8
India	0.5	0.2	2.5	0.5	30.9
Philippines	3.1	1.9	13.7	0.5	28.7
South Africa	11.4	3.7	34.5	2.6	23.2
Egypt	7.8	0.0	11.2	1.1	22.3
Vietnam	8.3	25.0	16.5	0.2	22.3
Malaysia	5.4	5.3	49.3	1.1	20.9
Ukraine	4.6	12.9	22.7	0.3	15.9
Thailand	1.2	9.9	7.9	0.0	12.3
Mexico	9.0	14.4	30.6	0.5	12.1
Colombia	8.6	9.0	31.7	0.1	11.5
Peru	4.1	4.0	46.0	1.0	10.8
Argentina	36.9	11.5	38.1	1.0	7.8
Kazakhstan	19.8	4.7	16.8	8.2	6.7
Iran	5.8	0.0	23.5	4.2	6.3
Brazil	24.4	12.8	40.8	0.5	6.1
Japan	7.6	16.1	17.7	0.2	5.5
China	4.2	22.7	14.2	3.3	4.7
Paraguay	12.0	21.5	5.3	0.5	4.6
Saudi Arabia	3.9	0.4	34.8	4.4	3.9
United States	26.2	24.0	51.0	0.4	3.2
South Korea	11.8	31.6	18.7	0.3	2.2
Australia	19.4	20.2	43.8	5.9	2.1
Chile	20.3	24.8	37.1	0.5	1.6

Supplementary File 2: The visual abstract presenting this article