

Review Paper

The Effect of Zinc on Appetite and Nutritional Status in Children: A Systematic Review



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ABSTRACT

Background: Zinc is essential for growth, immune function, and numerous cellular processes. Zinc deficiency—prevalent in over 20% of children in low- and middle-income countries—is associated with stunted growth, cognitive impairment, and increased susceptibility to infections. Low zinc status may also impair taste perception, thereby reducing appetite and exacerbating nutritional deficiencies.

Objectives: This study aimed to evaluate the effects of dietary zinc intake and/or supplementation on appetite and growth in healthy children aged 6 months to 18 years.

Methods: Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, we conducted a comprehensive search of PubMed, Web of Science, and Scopus for observational studies, prospective and retrospective cohort studies, case-control studies, and randomized controlled trials (RCTs) published between April 2015 and January 2024. Reference lists were also reviewed. The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024578984). Studies assessing zinc status or intake (via supplementation or diet) and its relationship with appetite or growth in healthy children were included.

Results: Of the 1,797 initial studies, 23 studies from 14 countries involving 79,319 participants aged 6 months to 18 years met the eligibility criteria and were included. Zinc supplementation doses ranged from 3 to 20 mg/day and were administered for durations between 1 and 24 months. Of the 23 studies, 10 examined zinc supplementation alone, and 7 assessed both dietary zinc intake and supplementation. Appetite was evaluated in nine studies (five RCTs, four observational studies). Five studies (55.6%, all RCTs) reported significant improvements in appetite among zinc-deficient children (level I evidence), whereas four studies (44.4%, two RCTs, two observational studies) reported no significant effect (level I and II evidence). Growth outcomes were assessed in all 23 studies (12 RCTs and 11 observational studies). Sixteen studies (69.6%, nine RCTs and seven observational studies) demonstrated significant improvements in weight-for-age (WAZ) and height-for-age (HAZ) Z-scores (Level I and II evidence), particularly among zinc-deficient or malnourished children. Seven studies (30.4%, three RCTs and four observational studies) reported no significant effect (level I and II evidence). Zinc levels were measured in 18 studies using plasma or serum analysis, and 10 studies used placebo-controlled designs.

Conclusions: Zinc supplementation demonstrates variable but generally positive effects on appetite and growth in healthy children, with stronger benefits in zinc-deficient or malnourished populations. The evidence (primarily level I from RCTs) supports zinc's role in improving appetite and growth in specific contexts; however, inconsistencies across studies highlight the need for further research to optimize supplementation protocols and explore synergistic effects with other micronutrients.

Key Words:

Zinc, Pediatrics,
 Micronutrients,
 Development, Nutrition,
 Supplementation,
 Systematic review

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Introduction

Zinc, an essential trace element, plays a critical role for numerous biological processes in the human body, particularly in supporting cellular growth and differentiation. This role is largely attributed to its involvement in nucleic acid and protein synthesis, as well as its influence on hormonal mediators of growth [1]. Zinc is also integral to the metabolism of proteins, lipids, and nucleic acids and contributes to gene transcription. Its wide range of functions includes roles in supporting reproduction, immune function, and wound repair. At the cellular level, zinc significantly impacts the normal functioning of macrophages, neutrophils, natural killer cells, and the complement system [2]. Furthermore, zinc serves as a structural component or catalyst in zinc metalloenzymes that regulate antioxidant defense, anti-inflammatory responses, immune function, and apoptosis [3].

Zinc deficiency is a major contributor to childhood stunting, particularly during infancy and early childhood, and is associated with several adverse health consequences, including growth retardation [4], delayed wound healing [5], increased susceptibility to infectious diseases [6], and impaired cognitive function [7]. Zinc deficiency is a significant public health issue in nearly all low- and middle-income countries, with an estimated prevalence ranging from 20% to 26% among children [8]. The main causes of zinc deficiency include inadequate consumption of zinc-rich foods, increased requirements or losses, malabsorption, and impaired zinc utilization. In healthy infants, zinc needs are typically met through breast milk during the first 6 months of life. However, beyond this period, complementary foods must provide sufficient zinc to support optimal growth and development, as breast milk alone may no longer be adequate [9]. Zinc is abundant in foods, such as meat, fish, poultry, and oysters; however, its bioavailability is reduced by dietary components, such as phytates—inositol phosphates found in cereals, grains, seeds, and legumes—which form poorly soluble complexes with zinc and inhibit its absorption. Diets high in phytates, common in many low- and middle-income countries, thus increase the risk of zinc deficiency, particularly where access to high-zinc foods is limited [10].

Globally, approximately 17.3% of the population is estimated to be at risk of inadequate zinc intake [11]. This issue is particularly concerning in pediatric populations, where zinc deficiency has been reported in 20–26% of otherwise healthy children, underscoring the need for

enhanced monitoring and intervention strategies [12]. Zinc has been shown to influence appetite by enhancing ghrelin secretion, a hormone that stimulates hunger [13, 14]. Additionally, low zinc status may impair taste acuity and increase stress and anxiety in children, potentially reducing appetite and food intake, thereby exacerbating nutritional deficiencies [12, 15].

In addition to its well-known role in appetite regulation and growth, zinc is involved in the modulation of the hypothalamic–pituitary–gonadal axis. Emerging evidence suggests that excessive zinc exposure during sensitive developmental periods may be associated with earlier activation of pubertal pathways. This biological consideration has led to clinical caution regarding routine zinc supplementation before the onset of puberty, particularly in otherwise healthy children [16].

Multiple studies have been conducted to assess the effect of zinc on children's growth; however, their findings are inconsistent, with variations attributed to differences in study populations, intervention types, and settings. Previous systematic reviews on this topic have highlighted significant variability in participant characteristics, intervention protocols, and outcome measures, making it challenging to provide clear, evidence-based conclusions about the efficacy and safety of zinc supplementation for improving linear growth and appetite in children [14]. Therefore, this systematic review aimed to synthesize the available evidence and address the specific question of how zinc intake, through diet or supplementation, impacts appetite and growth in healthy children aged 6 months to 18 years.

Materials and Methods

Protocol and registration

This systematic review followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 guidelines [17] and was registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42024578984). Ethical approval and patient consent were not required because all analyses were based on previously published studies.

Eligibility criteria

Type of studies: We included observational studies (cross-sectional, case–control, and cohort studies), prospective and retrospective studies, and randomized controlled trials (RCTs) assessing zinc intake (dietary or supplemental, including medicinal or food fortification)

and its relationship with appetite or growth in healthy children. The exclusion criteria were letters, conference proceedings, reviews, duplicated data, animal studies, and studies lacking relevant data. To minimize bias, we attempted to obtain full texts through institutional access, interlibrary loans, or author contact; however, 14 studies were excluded due to inaccessible full texts, potentially introducing selection bias.

Study population: Healthy children and adolescents aged 6 months to 18 years were eligible. Studies on infants younger than six months or children with chronic illnesses were excluded to focus on healthy populations.

Outcome parameters: Studies were included if they reported outcomes related to appetite, weight-for-age Z-score (WAZ), height-for-age Z-scores (HAZ), linear growth, weight-for-length Z-scores (WLZ), or body mass index (BMI)-for-age.

Information sources and search

We searched PubMed, Web of Science, and Scopus for studies published from April 2015 to January 2024, using

terms such as “zinc”, “dietary zinc”, “zinc intake”, “serum zinc”, “zinc supplementation”, “zinc supplements”, “poor appetite”, “appetite”, “anorexia”, “nutritional status”, “food intake”, “eating”, “food consumption”, “energy intake”, “growth”, “growth development”, “malnutrition”, “body height”, “body weight”, “body mass index”, “child”, “children”, “toddler”, “pediatrics”, “adolescent”, “infant”. Reference lists of all included papers and relevant reviews were screened for additional citations [18]. The search identified 1,797 articles, which were managed using Endnote 20.0 to remove duplicates. Titles and abstracts of the identified studies were scanned in duplicate to exclude irrelevant references. Titles, abstracts, and full texts were screened independently by two authors to ensure eligibility, with disputes resolved through consensus. Twenty-three studies met the eligibility criteria and were included in the final review (Figure 1).

Search strategy

PubMed

Search terms: (“zinc”[Mesh] OR “dietary zinc” OR “zinc intake” OR “serum zinc” OR “zinc supplementa-

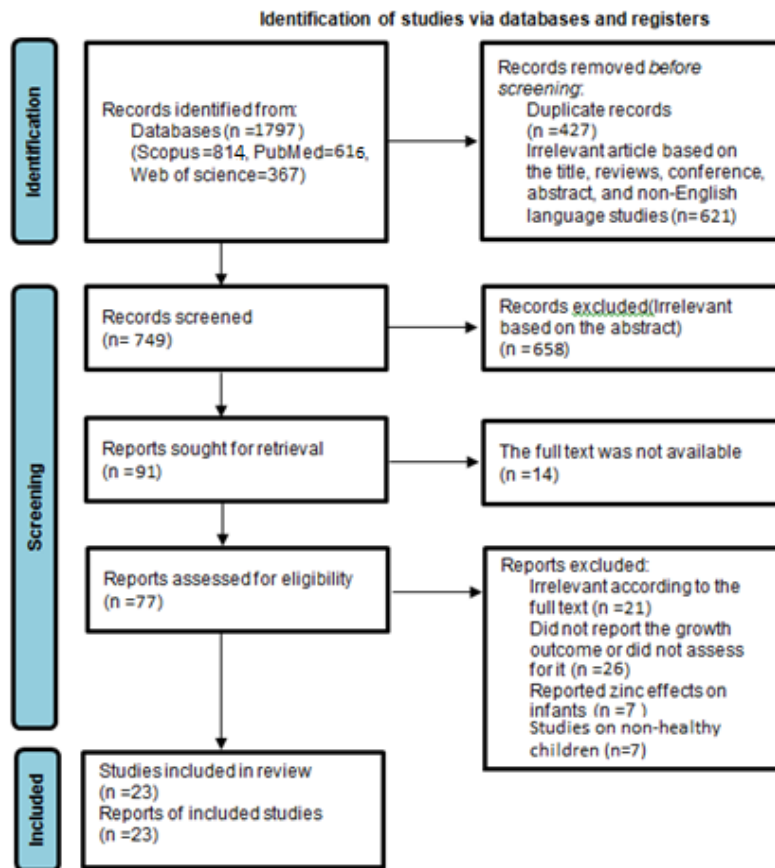


Figure 1. The PRISMA

tion" OR "zinc supplements") AND ("poor appetite" OR "appetite"[Mesh] OR "anorexia"[Mesh] OR "nutritional status"[Mesh] OR "food intake" OR "eating"[Mesh] OR "food consumption" OR "energy intake"[Mesh] OR "growth"[Mesh] OR "growth development"[Mesh] OR "malnutrition"[Mesh] OR "body height"[Mesh] OR "body weight"[Mesh] OR "body mass index"[Mesh]) AND ("child"[Mesh] OR "children" OR "toddler" OR "pediatrics"[Mesh] OR "adolescent"[Mesh] OR "infant"[Mesh]))

Search timeframe: January 2015-January 2024, Total articles identified: 616.

Web of Science

Search terms: TS=("Zinc" OR "dietary zinc" OR "zinc intake" OR "serum zinc" OR "zinc supplementation" OR "zinc supplements") AND

TS=("Poor appetite" OR "appetite" OR "anorexia" OR "nutritional status" OR "food intake" OR "eating" OR "food consumption" OR "energy intake" OR "growth" OR "growth development" OR "malnutrition" OR "body height" OR "body weight" OR "body mass index") AND

TS=("Child" OR "children" OR "toddler" OR "pediatrics" OR "adolescent" OR "infant")

Search timeframe: January 2015-January 2024, Total articles identified: 367.

Scopus

Search terms: (TITLE-ABS-KEY("zinc" OR "dietary zinc" OR "zinc intake" OR "serum zinc" OR "zinc supplementation" OR "zinc supplements") AND

TITLE-ABS-KEY("poor appetite" OR "appetite" OR "anorexia" OR "nutritional status" OR "food intake" OR "eating" OR "food consumption" OR "energy intake" OR "growth" OR "growth development" OR "malnutrition" OR "body height" OR "body weight" OR "body mass index") AND

TITLE-ABS-KEY("child" OR "children" OR "toddler" OR "pediatrics" OR "adolescent" OR "infant"))

Search timeframe: January 2015-January 2024, Total articles identified: 814.

Selection of studies

Two authors independently screened and assessed the eligibility of the studies, extracted relevant data, and assessed the risk of bias for all included studies. Disagreements were resolved through discussion until consensus was reached.

Data collection process

Data were collected independently by two authors, who reviewed and consolidated the data from the included studies.

Assessment of risk of bias

In this review, all studies underwent critical appraisal by one review team member (X) using the Joanna Briggs Institute critical appraisal checklists [19]. This tool was chosen because it can be used to assess descriptive cross-sectional studies as well as randomized controlled trials [20, 21]. A second reviewer (Y) blinded to the first reviewer's (X) assessments checked a random 15% of the included articles for risk of bias, and any differences between the reviewers were discussed and resolved. Figure 2 shows the reviewers' judgments about each risk of bias item for each included study.

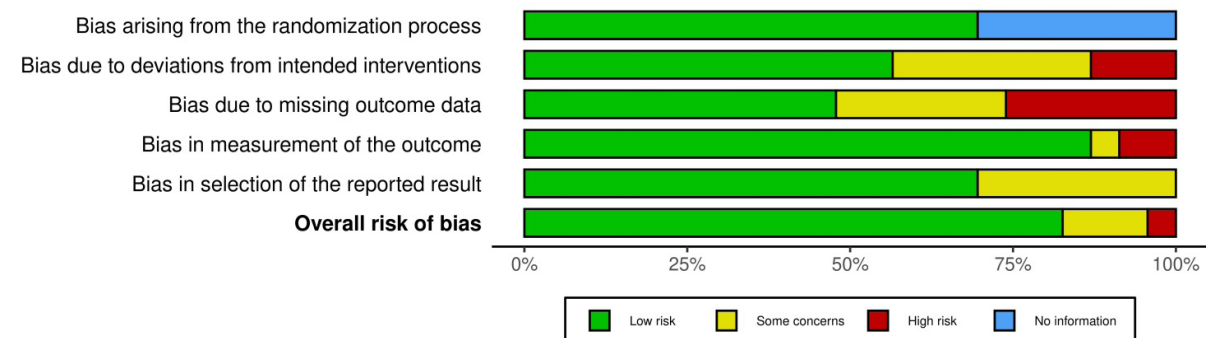


Figure 1. Risk of bias graph: Review authors' judgements about each risk of bias item presented as percentages across all included studies

Synthesis of results

The results were synthesized based on the extracted data, and findings were analyzed to provide insights into the effect of zinc on appetite and growth in children.

Results

Study selection

A total of 1,797 articles were identified (616 from PubMed, 814 from Scopus, and 367 from Web of Science). After removing 427 duplicates, 1,370 abstracts were screened, and 621 articles unrelated to zinc, growth, or appetite in children were excluded, along with 658 additional irrelevant records. Of the remaining 91 articles, the full texts were reviewed, and 68 were excluded: 14 due to unavailable full texts, 21 for irrelevance, 26 for not reporting growth outcomes or focusing on infants under 6 months, and 7 for including non-healthy children. Twenty-three studies [12, 22-43] were included (Figure 1).

Characteristics of included studies

The 23 studies, conducted in Asia [12, 22-24, 26-30, 32, 34-37, 40-43], Africa [25, 38], and South America [31, 33, 39], involved 79,319 participants aged 6 months to 18 years. Study durations ranged from 1 to 24 months, with zinc supplementation doses of 3–20 mg/day administered via micronutrient powders, zinc sulfate tablets, or syrups (Table 1).

Of the 23 included studies, 16 were interventional studies (12 randomized controlled trials and 4 non-randomized trials), while 7 were observational studies, including 6 cross-sectional studies and 1 case-control study.

Baseline for zinc deficiency

Zinc deficiency was typically defined as serum or plasma zinc concentrations below 65 µg/dL, with some studies adjusting thresholds for age or inflammation according to International Zinc Nutrition Consultative Group guidelines [23, 30, 40].

Zinc level measurement

Zinc levels were measured in 18 studies using plasma or serum analysis, primarily using inductively coupled plasma optical emission spectrophotometry (ICP-OES) or atomic absorption spectrophotometry (AAS). Two studies [24, 28] used hair samples for zinc analysis, and five studies [12, 29, 31, 33, 34] did not measure zinc levels.

Zinc intake assessment

Seven studies assessed both dietary and supplemental zinc intake. For example, Elshemy et al. (2022) measured plasma zinc levels and dietary intake using food frequency questionnaires (FFQs) and 24-hour dietary recalls [25]. Some studies focused solely on supplementation [12, 26, 30, 32, 34, 40], while others relied solely on dietary intake [28].

Zinc's effect on appetite

Five studies (55.6%, including four RCTs and one observational study) reported significant improvements in appetite, particularly in zinc-deficient children [12, 25, 28, 33, 39], while four (44.4%, including three RCTs and one observational study) found no significant effect [22, 24, 26, 42]. No studies reported any negative effects on appetite.

Zinc's effect on growth and nutritional status

All 23 studies (12 RCTs and 11 observational studies) evaluated growth outcomes, focusing on HAZ, WAZ, and WHZ. Sixteen studies (69.6%, including nine RCTs and seven observational studies) reported significant improvements in growth, particularly in zinc-deficient or malnourished children [12, 22-33, 34, 39-40]. Seven studies (30.4%, including three RCTs and four observational studies) found no significant effect [35-38, 41-43].

Zinc supplementation vs placebo

Ten studies (all RCTs) used placebo-controlled designs, with most (e.g. Abdollahi et al. 2019 [30]; Vakili et al. 2015 [34]) showing significant growth improvements in children receiving zinc supplementation compared to those receiving placebo.

Gender-based effects

Males were more likely to exhibit zinc deficiency [23] and showed greater growth responses to supplementation, particularly in HAZ [30, 32, 34]. In another study, boys showed more significant improvements in WAZ and WHZ [24]. Appetite improvements were not consistently gender-specific, but boys with zinc deficiency at baseline were more likely to benefit from supplementation.

Age-based effects

Children under 5 years, especially those aged 6–24 months, showed the most significant growth and appetite improvements [30, 32, 40]. Effects in school-aged children (6–18 years) were less consistent [27]. Appetite improvements were more pronounced in younger children, particularly those with growth faltering [28].

Discussion

This systematic review synthesizes evidence from 23 studies across Asia, Africa, and South America to evaluate the effects of zinc supplementation on appetite and growth in healthy children aged six months to 18 years. The findings reveal a complex relationship between zinc supplementation, appetite stimulation, and growth improvements, with outcomes varying based on baseline zinc status, population characteristics, and study design.

Main findings and implications

Zinc supplementation improved appetite in five of nine studies (all of which were RCTs), particularly in zinc-deficient children. For instance, Rosa et al. (2022) reported significant appetite enhancements in children with growth faltering following zinc supplementation [28]. These effects may stem from zinc's role in promoting ghrelin secretion, a hormone that stimulates hunger, and in enhancing taste acuity, which increases food intake [44]. Ghrelin, released primarily in response to a negative energy balance, regulates appetite by acting on the hypothalamus and limbic system and counteracting appetite-suppressing peptides through the vagus nerve [45–47]. Additionally, zinc supports the production and release of neuropeptide Y (NPY), a key appetite regulator, and zinc deficiency may impair NPY function, potentially reducing appetite and food intake [48–50]. Elshemy et al. (2022) further confirmed that therapeutic doses of zinc sulfate improved appetite in zinc-deficient children [25]. However, four studies (two RCTs and two observational studies) found no significant appetite changes, with Barffour et al. (2023) reporting no effect despite improved plasma zinc concentrations [22]. These inconsistencies suggest that zinc's impact on appetite is most evident in children with severe zinc deficiency or significant malnutrition, particularly in high-prevalence regions like Southeast Asia and Africa.

These findings align with prior research indicating that children with low serum zinc levels experience greater appetite improvements with supplementation [15]. However, the lack of effect in some studies highlights

the need to identify specific populations and conditions where zinc supplementation is most effective. Factors, such as baseline zinc status, dietary intake, and coexisting micronutrient deficiencies, may influence outcomes.

Zinc's effect on growth

The evidence for zinc's effect on growth was mixed, with 16 of 23 studies (nine RCTs and seven observational studies) reporting significant improvements in growth outcomes, such as HAZ and WAZ Z-scores, particularly in zinc-deficient or malnourished children. Khan et al. (2023) observed significant increases in WAZ and WHZ after 12 months of zinc supplementation via micronutrient powders [24], while Abdollahi et al. (2019) reported enhanced height and weight gains in children receiving zinc sulfate for six months [30]. These benefits likely stem from zinc's role in protein synthesis and its mediation of insulin-like growth factor 1 (IGF-1) bioavailability, a critical growth hormone regulator [51, 52]. Zinc also supports immune function, reducing infection-related growth setbacks, and contributes to bone development, essential for linear growth [53–56].

However, seven studies (three RCTs and four observational studies) found no significant growth effects. For example, Barffour et al. (2023) and Hinnouho et al. (2020) reported no impact on linear growth or weight gain, despite improved zinc status [22, 36]. These discrepancies may reflect variations in baseline zinc deficiency, supplementation dosage, duration, or population-specific factors, such as dietary adequacy or socioeconomic conditions. The mixed results underscore the importance of tailoring interventions to populations with confirmed zinc deficiency.

Subgroup and regional variations

Subgroup analyses indicated that children with baseline zinc deficiency or stunting benefited most from supplementation. Lu et al. (2023) found that stunted children showed greater appetite and growth responses to zinc supplementation, particularly among males, who exhibited higher deficiency rates [23]. Similarly, Khan et al. (2023) reported more significant growth improvements in boys for WAZ and WHZ [24]. These findings highlight the need to target supplementation to high-risk subgroups, such as malnourished or zinc-deficient children.

Table 1. Summarization of main results of individual studies

Author(s), Year Country	Sample Size Details	Sex (Male %)	Age in Months (Year)	Study Design (Duration, Months)	Zinc Analy- sis	Appetite Mea- sure- ment	Growth Analysis	Effect of Zinc on Growth	Effect of Zinc on Ap- petite	Comment
1. Barffour et al. 2023 [22], Laos	2,943 children in four groups: preventive zinc (n=112, 7 mg/day), MNP (n=141, 10 mg zinc + micronu- trients), therapeutic zinc (n=851, 20 mg/10 days), placebo (n=155)	Preven- tive zinc (48.3%), MNP (52.4%), placebo (54.8%)	6–23 (0–2)	RCT (9)	Plasma zinc via ICP-OES; deficiency <65 µg/dL, adjusted for inflam- mation (BRINDA)	NA	WHO child growth standards for LAZ, WAZ, WLZ; stunting (LAZ ≤2 SD), under- weight (WAZ ≤2 SD)	PE	NA	Zinc improved growth in children with high growth potential, poten- tially via IGF-1 bioavailability.
2. Lu et al. 2023 [23], China	64,850 children from 150 sites across 31 provinces	50%; males at higher risk of deficiency (OR=1.552)	72–200 (6–18)	Cross- sectional (12)	Serum zinc via ICP-MS; deficiency <70 µg/dL (girls), <74 µg/dL (boys) per IZiNCG	NA	Chinese standards for stunting, wasting, overweight, obe- sity (WS/T 456–2014, WS/T 586–2018)	PE	NA	Males, anemic, and stunted chil- dren had higher zinc deficiency risk.
3. Khan et al. 2023 [24], Pakistan	111 children; intervention (n=58, MNP with 4.1 mg zinc every other day), control (n=53)	48.3%	24–59 (2–5)	Non-ran- domized cluster- controlled trial (12)	Plasma zinc via AAS; dietary intake via question- naire	NA	WHO 1982 protocol for height, weight; WAZ, WHZ	PE	NA	MNP supplemen- tation improved plasma zinc, hemoglobin, and growth (WAZ, WHZ).
4. Elshemy et al. 2022 [25], Egypt	50 children; normal zinc (3–5 mg/day zinc sulfate), defi- cient (0.5–1 mg/ kg/day)	Normal zinc (44%), deficient (46%)	36–60 (3–5)	RCT (6)	Plasma zinc via lab tests; dietary in- take via FFQ and 24-hour recall	FFQ and 24-hour recall for dietary assessment	Anthro- pometric measurements and cognitive function	PE	PE	Zinc supplementa- tion improved growth and appetite, likely via increased protein intake.
5. Islam et al. 2022 [26], Bangladesh	2,886 children in six groups: standard MNP (4.1 mg zinc), HiZn LoFe MNP (10 mg zinc), zinc tablets, placebo	49.9– 50.1%	9–11 (0–1)	Prospect- ive (24)	Serum zinc at baseline and 24 weeks	Pre- tested question- naires on appetite	WHO 2006 standards for LAZ, WAZ, WLZ	PE	No effect	HiZn LoFe MNP slightly improved linear growth; no significant ap- petite effect.
6. Sugawara et al. 2022 [27], Japan	63 short-statured children (height SDS ≤2)	Not reported	24–59 (2–5)	Retrospec- tive (24)	Serum zinc via colori- metric assay (SRL Co., Ltd.)	NA	Height, weight, BMI SDS compared to Japanese norms	PE	NA	Serum zinc corre- lated with weight SDS and BMI SDS, not height SDS.
7. Rosa et al. 2022 [28], Indonesia	70 children, excluding severe conditions	42.9%	12–36 (2–3)	Cross- sectional (12)	Hair zinc via AAS; dietary intake via SQ-FFQ	VAS for appetite (parent- reported)	WHO Z-scores for weight, height	PE	PE	Zinc supplementa- tion improved ap- petite and weight in growth-failure children.
8. Nuryanti et al. 2020 [29], Indonesia	32 children; experi- mental (n=16, 5 mL zinc syrup daily), control (n=16, weekly)	Experimen- tal (63%), control (50%)	6–24 (0–2)	Comparative (1)	NA	NA	Weight, body status pre- and post-test	PE	NA	Daily zinc syrup significantly in- creased toddler body weight.
9. Abdollahi et al. 2019 [30], Iran	580 children; in- tervention (n=308, 5 mg zinc sulfate/ day), placebo (n=272)	Not reported	6–24 (0–2)	RCT (6)	Serum zinc via flame spectrom- etry	NA	Monthly anthro- pometric measurements	PE	NA	Zinc supplementa- tion improved growth and length increment.
10. Kusumastuti et al. 2018 [12], Indonesia	68 children in four groups: placebo, zinc (10 mg/day), iron, zinc + iron	45.6%	6–23 (0–2)	Pre-post test (3)	NA	Eating frequen- cy, total energy intake	WHO 2005 anthro- pometry for WAZ, HAZ	PE	PE	Zinc and iron supplementation increased appetite and WAZ.

Author(s), Year Country	Sample Size Details	Sex (Male %)	Age in Months (Year)	Study Design (Duration, Months)	Zinc Analysis	Appetite Measurement	Growth Analysis	Effect of Zinc on Growth	Effect of Zinc on Appetite	Comment
11. Carrero et al. 2018 [31], Bolivia	80 children in three groups: vitamin A (n=25), zinc (n=26, 12.5 mg/day), vitamin A + zinc (n=29)	Vitamin A (44%), zinc (46%), vitamin A + zinc (34%)	6–23 (0–2)	RCT (12)	Plasma zinc; dietary intake via 24-hour recall	NA	Venezuela Project Charts for WAZ, HAZ, WHZ	PE	NA	Zinc group showed increased weight and height gains.
12. Rerksupphaphol et al. 2018 [32], Thailand	70 children; zinc bisglycinate (15 mg/day, n=35), placebo (n=35)	Zinc (51.5%), placebo (48.4%)	36–60 (3–5)	RCT (6)	NA	NA	Thai child growth standards for WAZ, HAZ	PE	NA	Zinc enhanced linear growth but not other parameters.
13. de Medeiros Rocha et al. 2015 [33], Brazil	40 children; zinc (10 mg/day oral + IV, n=20), placebo (n=20)	Zinc (60%), placebo (55%)	96–108 (8–9)	RCT (3)	Serum zinc via AAS; dietary intake via NutWin software	3-day food record	WHO BMI-for-age curves	PE	PE	Zinc increased energy, protein, fat intake, and growth.
14. Vakili et al. [34] 2015, Iran	200 children; zinc sulfate (10 mg/day, n=100), placebo (n=100)	50%; males showed greater HAZ increase	6–23 (0–2)	RCT (6)	NA	NA	Height, weight, BMI, WAZ, HAZ at 0, 2, 4, 6 months	PE	NA	Zinc significantly increased linear growth and weight.
15. Mehta et al. [35] 2022, India	223 children; FeZnPM (5.6 mg zinc/100 g, n=111), CPM (1.56 mg zinc/100 g, n=111)	FeZnPM (47.3%), CPM (48.6%)	12–18 (1–2)	Pre-post test (9)	Plasma zinc via FAAS; dietary intake via weighed records, 24-hour recalls	NA	Length, weight, MUAC, skinfold thickness	No effect	NA	Zinc-biofortified millet did not improve growth.
16. Hinnouho et al. [36] 2020, Laos	1,204 children in four groups: preventive zinc (7 mg/day, n=303), MNP (10 mg zinc, n=294), therapeutic zinc (20 mg/10 days, n=322), placebo (n=285)	Preventive zinc (53%), MNP (50.3%), therapeutic zinc (54.4%), control (44.3%)	6–59 (0–5)	RCT (24)	NA	NA	WHO 2006 standards for LAZ, WAZ, WLZ; MUAC	No effect	NA	Zinc supplementation had no effect on growth or EED markers.
17. Barffour et al. [37] 2019, Laos	3,470 children in four groups: preventive zinc (7 mg/day, n=738), MNP (10 mg zinc, n=701), therapeutic zinc (20 mg/10 days, n=764), placebo (n=740)	Preventive zinc (50.1%), MNP (50.8%), therapeutic zinc (51.3%)	6–23 (0–2)	RCT (9)	Plasma zinc via ICP-OES; deficiency <65 µg/dL	NA	WHO standards for LAZ, WAZ, WLZ; MUAC	No effect	NA	Zinc improved plasma zinc but not linear growth or weight gain.
18. Tessema et al. [38] 2019, Ethiopia	1,171 children from ENMS with serum zinc; 1,776 with anthropometric data	Zinc deficient (26%), stunting (41%)	6–59 (0–5)	Cross-sectional (1)	Serum zinc via FAAS; deficiency <65 µg/dL	NA	WHO 2006 standards for HAZ, WHZ	No effect	NA	Serum zinc not associated with linear growth.
19. Lopes et al. [39] 2015, Brazil	62 children; zinc (10 mg/day, n=31), placebo (n=31)	51.6%	96–108 (8–9)	RCT (3)	Serum zinc via AAS; dietary intake via NutWin software	3-day food record	WHO growth curves for 5–19 years	PE	PE	Zinc increased height, energy, and nutrient intake via improved appetite.
20. Chao et al. [40] 2018, Taiwan	761 children from ENMS with anthropometric and serum zinc data	51.2%	12–119 (2–10)	Pre-post-test (6)	Serum zinc via FAAS; deficiency <69.8 µg/dL	7-day food diary for caloric intake	Taiwanese growth standards for HAZ, WAZ, BMI-for-age	PE	PE	Zinc improved growth and appetite in undernourished children with low zinc.

Author(s), Year Country	Sample Size Details	Sex (Male %)	Age in Months (Year)	Study Design (Duration, Months)	Zinc Analy- sis	Appetite Mea- sure- ment	Growth Analysis	Effect of Zinc on Growth	Effect of Zinc on Ap- petite	Comment
21. Han et al. [41] 2016, South Korea	56 children; zinc- deficient (n=23, zinc sulfate for 2 weeks), non-defi- cient (n=33)	Zinc- deficient (47%), non- deficient (54.5%)	12–179 (1–15)	Pre-post- test (32)	Serum zinc (<80 µg/dL); hair zinc via mass spec- trometry	Clinical assess- ment of appetite, meal intake	Ko- rean 2007 growth charts for height, weight, BMI	No ef- fect	No effect	Zinc supplementa- tion improved appetite in some deficient children but not signifi- cantly.
22. Pour- mirzaiee et al. [42] 2018, Iran	175 children; zinc supplement (n=68), no supplement (n=67)	64.4%	24–95 (2–8)	Case-con- trol (24)	Serum zinc via AAS; di- etary intake via FFQ	Children's Eating Behavior Question- naire (CEBQ)	Anthropo- metric mea- surements, BMI	No ef- fect	No effect	No significant differences in zinc levels, appetite, or growth.
23. Yazbeck et al. [43] 2016, Lebanon	161 children; cases (nutritional evalu- ation), controls (normal growth)	Cases (52.6%), controls (50.6%)	12–120 (1–10)	Case-con- trol (24)	Plasma zinc via AAS; di- etary intake via 3-day recall	NA	CDC 2000 growth charts	No ef- fect	NA	No significant zinc concentration differences; higher low zinc in cases.

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Abbreviation: RCT: Randomized controlled trial; WAZ: Weight-for-age Z-score; HAZ: Height-for-age Z-score; WLZ: Weight-for-length Z-scores; MNP: Micronutrient powder; LAZ: Length for age Z-score; BRINDA: Biomarkers reflecting inflammation and nutritional determinants of anemia; IGF-1: Insulin-like growth factor 1; OR: Odd ratio; ICP-MS: Inductively coupled plasma mass spectrometry; IZINCG: International zinc nutrition consultative group; AAS: Atomic absorption spectrophotometry; FFQ: Food frequency questionnaire; SDS: Standard deviation score; BMI: Body mass index; IV: Intravenous; ENMS: Edinburgh neuropsychological motor scale; FAAM: Flame atomic absorption spectrometry; FeZnPM: Iron–zinc pairwise model; ICP-OES: Inductively coupled plasma optical emission spectrophotometry; CPM: Complementary food mix; VAS: Visual analogue scale; EED: Environmental enteric dysfunction; PE: Positive effect; NA: Not available.

Geographical variations also influenced outcomes. Studies in Southeast Asia and Africa, where zinc deficiency prevalence is higher (20–26%), generally reported stronger effects on appetite and growth [8]. For instance, studies in Bangladesh and Pakistan reported positive effects on growth outcomes [24, 26]. In contrast, studies in regions with lower deficiency rates, such as parts of South America, often reported less pronounced effects. These regional differences emphasize the importance of context-specific interventions, particularly in areas with limited access to zinc-rich foods, such as meat and fish, where phytate-rich diets can further reduce zinc absorption [10].

Zinc deficiency and measurement methods

Most studies defined zinc deficiency as serum or plasma zinc concentrations below 65 µg/dL, consistent with the International Zinc Nutrition Consultative Group (IZINCG) guidelines, although some studies adjusted the cut-off values for age or inflammatory markers [57, 58]. Eighteen studies used reliable techniques, such as ICP-OES or AAS, to measure zinc levels, ensuring robust assessment. Rosa et al. (2022) employed hair analysis as a non-invasive alternative to evaluate long-term zinc status, offering a complementary approach [28]. These standardized measurement methods strengthen the reliability of zinc status assessments across studies.

Placebo-controlled studies

Ten studies utilized placebo-controlled RCT designs, providing high-quality evidence (level I). Abdollahi et al. (2019) and Vakili et al. (2015) demonstrated significant improvements in growth in zinc-supplemented groups compared to placebo, particularly in children aged 6–24 months [30, 34]. These findings reinforce zinc's potential to address growth faltering and appetite suppression in deficient populations. The use of placebo controls also minimizes bias and enhances the validity of the results.

Conclusion

In conclusion, the evidence synthesized in this systematic review demonstrates that zinc supplementation has a significant and clinically relevant impact on appetite regulation and growth outcomes in children, particularly among those with underlying zinc deficiency, stunting, or malnutrition. The consistent positive effects observed in these high-risk subgroups underscore the role of zinc as a critical micronutrient in childhood growth and nutritional rehabilitation. Importantly, the findings indicate that zinc supplementation is most effective when implemented as a targeted intervention rather than a universal strategy.

For malnourished and zinc-deficient children, zinc supplementation should be considered an essential component of comprehensive nutritional programs designed to improve appetite, linear growth, and overall nutritional status. In contrast, for healthy children with adequate dietary intake, routine supplementation is likely unnecessary, and emphasis should be placed on ensuring sufficient zinc intake through diversified diets rich in animal-source foods.

Despite the demonstrated benefits, substantial heterogeneity across studies—particularly regarding dosage, duration, baseline nutritional status, and co-supplementation with other micronutrients—hinders the formulation of uniform clinical guidelines. This underscores the need for well-designed, standardized RCTs to define optimal supplementation protocols and clarify the mechanisms linking zinc status to appetite and growth regulation. Overall, these findings reinforce the importance of context-specific, evidence-based zinc interventions as a strategic tool to combat childhood malnutrition and support healthy growth and development, especially in regions with a high prevalence of zinc deficiency.

Limitations and future directions

Several limitations should be acknowledged. Variability in study design, zinc dosages (3–20 mg/day), and population characteristics complicates direct comparisons. While 16 studies reported positive growth effects, seven found no impact. This discrepancy may reflect the influence of confounding factors, such as dietary intake, caloric adequacy, or baseline health status, which were not fully addressed in many studies. The exclusion of some studies due to lack of access to full texts may introduce potential selection bias, although efforts were made to mitigate this limitation through interlibrary loans and author contact.

Also, the findings of the present review should be interpreted in light of the potential influence of zinc on pubertal timing. One possible explanation for the inconsistency observed across studies is variation in participants' baseline pubertal status. Studies, including pre-pubertal children, may yield heterogeneous results due to ethical and physiological limits on zinc supplementation during this developmental period. This factor may partially account for the divergent outcomes reported in the literature and underscores the need for future trials to stratify analyses by pubertal stage.

Future research should prioritize long-term RCTs with standardized protocols to clarify optimal zinc supplementation strategies, including dosage, duration, and delivery methods (e.g. tablets vs micronutrient powders). Studies should also explore the synergistic effects of zinc with other micronutrients, such as iron or vitamin A, to enhance nutritional interventions [31]. Additionally, assessing dietary zinc bioavailability in phytate-rich diets, and its impact on supplementation efficacy could inform strategies in low- and middle-income countries [10]. Targeting interventions to high-risk subgroups, such as children younger than five years or those with confirmed deficiency, will maximize benefits.

Ethical Considerations

Compliance with ethical guidelines

This article is a systematic review with no human or animal sample.

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Authors contributions

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Conflicts of interest

The authors declared no conflict of interest.

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