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REVIEW ARTICLE

Zinc Deficiency and Immune Function in Children from Low- and Middle-Income Countries: A Systematic Review

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ABSTRACT

Zinc is an essential micronutrient required for several metabolic activities. It plays a key role in immune system function, growth, protein and DNA synthesis, and is also needed in the metabolism of over 200 enzymes. Its role in child growth and development cannot be overemphasized. Despite zinc's established immunological benefits, a significant knowledge gap exists regarding the prevalence, consequences, and impact of its deficiency on immunological function among children in low- and middle-income countries (LMICs). This review aims to establish the relationship between zinc deficiency and immune system function among children in LMICs. Literature databases were searched with keywords related to zinc deficiency, children, and immune function. The search included studies focused on children from 0 to 18 years in LMICs, assessing zinc status and immune-related outcomes. The studies should have been published between 2010 and 2024 and published in English. Animal studies and editorials were excluded. Scopus, PubMed, Web of Science, Google Scholar, and Cochrane were searched for eligible articles. Data was extracted by 2 independent reviewers. Information obtained included characteristics of participants, assessments, immune parameters, and interventions. Prevalence of zinc deficiency ranged from 9.5 to 99%. Zinc deficiency in children significantly reduced T-cell counts, impaired cytokine regulation, and elevated inflammatory markers such as CRP AND IL-6. Intervention studies reported that zinc supplementation significantly increases serum zinc concentrations. Supplementation was also found to reduce the incidence of diarrhea and pneumonia. Fortification showed moderate improvements with smaller effect sizes. Zinc deficiency in children remains a significant public health concern in LMICs and is strongly related to impaired function and heightened susceptibility to infections in children. Current evidence supports zinc supplementation and fortification as effective strategies for improving zinc status and immune outcomes.

Keywords: *Zinc, Micronutrients, LMICs, Immune Function, Children*

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INTRODUCTION

Zinc has long been known and used for medicinal purposes. For example, an Egyptian papyrus dating from the year 2000 BCE mentions its use in cream for the skin (Khan et al., 2022). Some appropriately refer to it as a metal of life due to its significance in the physiology and metabolism of both plants and animals (Khan et al., 2022). However, its significance was not fully recognized until centuries after the acknowledgement of the biological role and importance of iron (Hambidge, 2000). Eventually, studies conducted in Egypt by Prasad et al. in 1963 conclusively established zinc as essential for human health (Prasad, 2009). Zinc can be found in all classes of enzymes, including those which catalyze DNA replication, repair, translation, inter and intracellular signaling and maintenance of membrane integrity (Andreini et al., 2006). Evidence points to the fact that zinc also plays a key role in human immunity, neurotransmission, and proper brain function (Frederickson, Koh, & Bush, 2005). It strengthens the defense against oxidative stress and the synthesis, storage, and release of insulin.

In terms of immune function, zinc is necessary for both humoral and cell-mediated immunity (Chasapis et al., 2020). A zinc deficiency can lead to a decline in innate immunity cellular mediators, including neutrophils, macrophages, and natural killer cell activity, as well as cytokine production and complement activity. Zinc deficiency also affects intracellular killing and phagocytosis and negatively impacts T and B cell development and function (Prasad, 2009). Zinc deficiency further causes a decrease in peripheral and thymic T cells, an impaired proliferative response, and a reduction in the function of T helper and cytotoxic T cells (Overbeck, Rink, & Haase, 2008). Moreover, a zinc deficit suppresses the Th1 response, which is critical for infection defense. These immune response deficiencies result in increased vulnerability to infections (Prasad, 2009). The risk of micronutrient deficiency remains high in low and middle-income countries, including those in Sub-Saharan Africa (SSA) and children remain the most vulnerable. Due to the presence of antinutritive factors that inhibit its absorption, Zinc deficiency is especially prevalent in areas where the staple local diet consists of cereals (Prasad, 2017). This of course is the case in many LMICs, besides inadequate dietary intake. The risk of Zinc deficiency during diarrhea increases because zinc is lost through feces and therefore the presence of diarrhea in children exacerbates zinc deficiency. Impaired intestinal integrity affects absorption and increases endogenous zinc loss as well (Sangeetha et al., 2022). In infants and young children, deficiency may also be acquired as a result of low zinc concentration in the mothers' breastmilk.

Micronutrient deficiencies in general are highly costly and include loss of productivity, direct medical cost and cost due to disability-adjusted life-years (DALYs). To put this into context, it is also estimated that addressing micronutrient deficiencies may save 35 trillion dollars for the world economy (Dimkpa & Bindraban, 2016). The effect among children, particularly in low- and middle-income countries, is dire. According to one estimate, globally, approximately 50% of all childhood deaths under the age of 5 years occur because of micronutrient deficiency (Bailey, West Jr, & Black, 2015). Estimates by (Wessells & Brown, 2012) indicated that Zinc deficiency may have contributed to as many as 453,207 deaths including 4.4% of paediatric deaths and 1.2% of the disease burden, which includes 3.8% of children aged 0.5 to 5 years and corresponds to 16 million disability-adjusted life years. Despite the documented importance of zinc for immune health, there is a lack of comprehensive current literature of the extent and impact of zinc deficiency on immunological function specifically among children in LMICs. This review aimed to map the existing literature on zinc deficiency and its effects on immune function in children within these regions, identify research gaps and provide a foundation for future studies and interventions.

METHODS

Review Design

This review followed the methodological framework outlined by (Arksey & O'Malley, 2005) and (Levac, Colquhoun, & O'brien, 2010). The review was guided by the research question:
"What is the current state of knowledge on zinc deficiency and immune function among children in LMICs?"

Eligibility Criteria

The review included studies that were conducted on children ≤18 years and published between January 2010 and July 2024. Studies were included if they were published in English. Qualitative, quantitative and studies with mixed methods were included. Articles were excluded if they were editorials or opinion pieces and did not meet the inclusion criteria.

Data Sources and Databases

Thorough literature search was done in the following databases; Cochrane, PubMed, Scopus, Medline, CINAHL, Google Scholar, Embase and Web of Science.

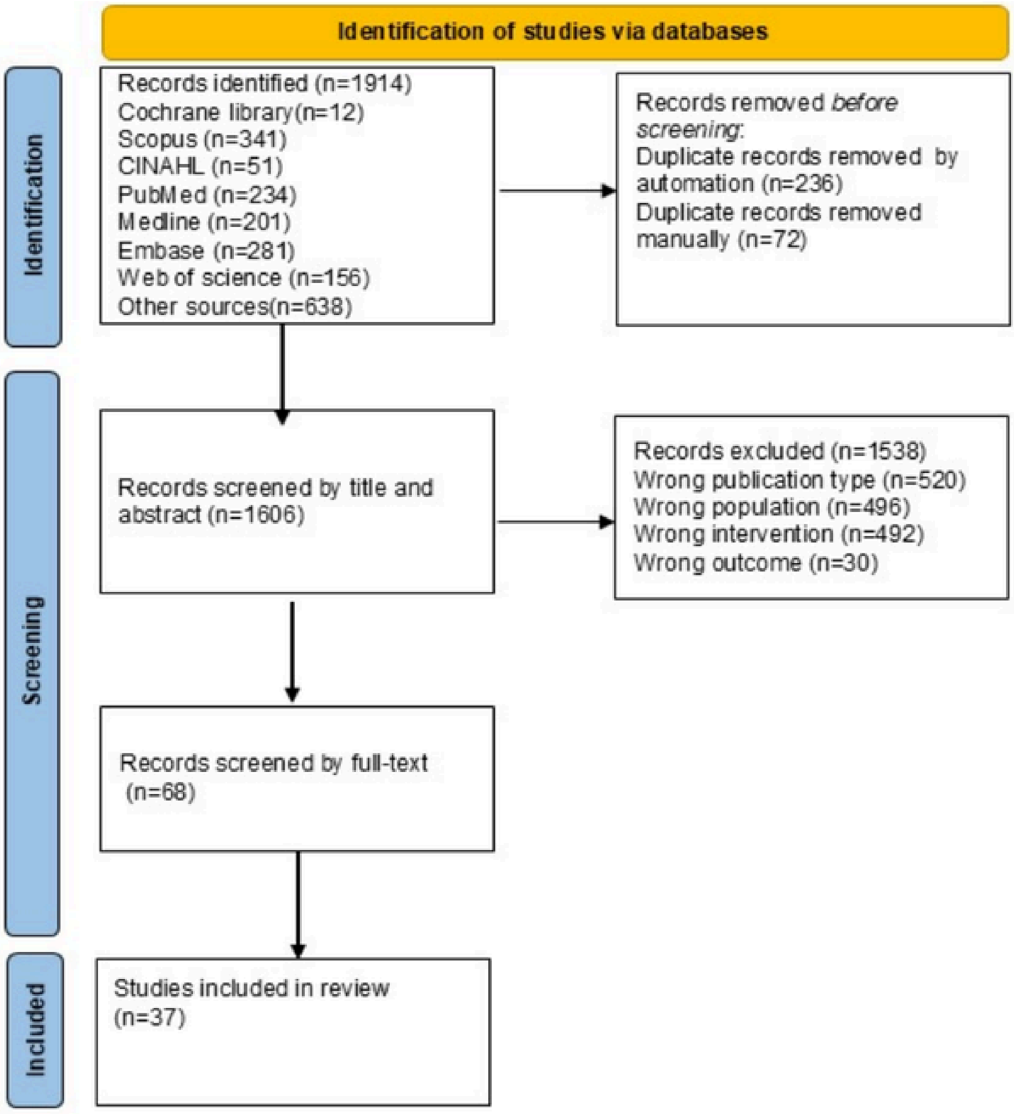
Study Selection Process

The following keywords and MeSH terms were used to obtain information; ("zinc deficiency" OR "zinc inadequacy") AND ("immune function" OR "immunological function" OR "immune response") AND ("children" OR "childhood" OR "pediatric" OR "adolescent") AND ("low-income countries" OR "middle-income countries" OR "developing countries" OR "LMICs"), ("zinc deficiency"[Mesh] OR "zinc inadequacy") AND ("immune function"[Mesh] OR "immunological function" OR "immune response") AND ("child" [Mesh] OR "childhood" OR "pediatric" OR "adolescent") AND ("low-income countries"[Mesh] OR "middle-income countries" OR "developing countries" OR "LMICs").

Data Extraction, Quality Assessment, Synthesis and Analysis

Data Extraction was done with Microsoft word using a standardized data extraction form to capture relevant information. Extracted data were organized and summarized using thematic analysis. References were managed using EndNote X9. Two independent investigators (FI and AAM) extracted and reviewed the data. Discrepancies were checked and resolved by a third investigator (FH). Data obtained were further synthesized and analyzed following the procedures outlined by Arksey & O'Malley (2005) and Levac et al. (2010).

Figure 1:
Boxplot showing the distribution of mothers' age according to the total number of children.



Ethical Considerations

The review did not collect primary data and so institutional review board approval was not obtained. However, it was ensured that all data included in the primary studies had ethical approval.

RESULTS

The review focused on zinc deficiency in children living in LMICs and tackled the following areas; prevalence of deficiency, deficiency causes, dietary patterns and zinc, immune function and zinc, growth and development as well as accurate assessment of zinc. A total of 1606 articles were obtained from different bases. After removal of duplicates and articles with only abstracts and those that did not meet inclusion criteria, 37 full text articles were included in the review.

Table 1 provides information on prevalence and causes of zinc deficiency in LMIC. The studies showed zinc deficiency as a major public health problem in LMIC among children. Prevalence ranged from 9.5% in semi-urban Nigeria among school children to 40.5% among Ghanaian children aged 2-10 years. Extreme levels of deficiency (99%) were also recorded in Nigeria. Broader reviews showed over 20% of children being zinc deficient in at least 23 countries while an overall prevalence of about 24% was observed among children below five years of age. Poor dietary diversity, high consumption of phytate rich cereals and legumes, low socioeconomic status and metabolic conditions that impair zinc absorption. Findings on intervention showed that reducing phytate-rich cereals and legumes in the diet improves absorption of zinc in malnourished children. This underscores the role of diet quality and bioavailability in improving zinc status.

Table 1:

Prevalence and Causes of Zinc Deficiency

Title of Study	Study Type	Population	Study Period	Key Findings	Reference
Zinc in Human Health and Infectious Diseases	Review	General population / children	2022	Overview of zinc biology and deficiency prevalence	Maywald & Rink (2022)
Risk of Zinc deficiency among children aged 0-59 months in sub-Saharan Africa	Review	Children 0–59 months	2023	Estimated 24% prevalence among African children under 5	Dembedza (2023)
Zinc deficiency in low- and middle-income countries: prevalence and approaches for mitigation	Review	Children in LMICs	2020	Prevalence and mitigation strategies across LMICs	Gupta et al. (2020)
Preventing & Controlling Zinc Deficiency across the life course: A Call to Action	Policy review	All ages/children	2024	≥20% deficiency in 23 LMICs where data exist	Lowe et al. (2024)
Prevalence of Zinc Deficiency Among School Children in Rural setting in North-Central Nigeria	Cross-sectional	School children	2015	Reported 99% zinc deficiency; lower zinc in poorer children	Abah et al. (2015)
Relationship between zinc levels and anthropometric parameters and socio-demographic status among primary school pupils in a semi-urban community in Nigeria	Cross-sectional	Primary school pupils	2023	9.5% zinc deficiency; lower zinc in poorer socioeconomic groups	Oladibu et al. (2023)
Prevalence of vitamin A, zinc, iodine deficiency and anaemia among 2–10-year-old Ghanaian children	Cross-sectional	Children 2–10 years	2012	40.5% zinc deficiency reported	Egbi (2012)
Dietary phytate reduction improves zinc absorption in Malawian children recovering from tuberculosis but not in well children	Intervention	Children recovering from TB	2000	Low-phytate diets improved zinc absorption in recovering children	Manary et al. (2000)

Table 2 reports on the immune function of zinc. Zinc deficiency is found to be strongly associated with compromised immune function among children. Zinc was found to be primarily vital for T-cell activity, cytokine production, integrity of the epithelial barrier and overall immune competence. Children with zinc deficiency were found to have reduced T-cell proliferation and weakened mucosal barriers, therefore increasing their risk of infections. Inadequate zinc status increased susceptibility to pneumonia, diarrhea, malaria and other gastrointestinal and respiratory infections.

Table 2:

Immune Function and Infection Studies

Title of Study	Study Type	Population	Study Period	Key Findings	Reference
Zinc and the immune system	Review	General population	2000	Zinc's role in inflammation and immunity	Rink (2000)
Estimating the global prevalence of zinc deficiency: results based on zinc availability in national food supplies and the prevalence of stunting	Epidemiological analysis	Children / populations	2012	Deficiency linked to higher risk of infectious diseases (diarrhea, pneumonia, malaria)	Wessells & Brown (2012)
Maternal and child undernutrition and overweight in LMICs	Review	Children	2013	Undernutrition (including zinc deficiency) increases infection risk	Black et al. (2013)
Zinc supplementation and growth in Tanzanian children	Intervention trial / analysis	Children	2012	Discusses zinc, absorption and growth outcomes	Dewey et al. (2012)
Preventive zinc supplementation for children, and the effect of additional iron: a systemic review and meta-analysis	Systematic review	Children <5 years	2011	Zinc supplementation reduced pneumonia and diarrhea incidence	Mayo-Wilson et al. (2014)
Effect of zinc supplementation on T cell immunity	Experimental study	Malnourished children	2018	Low zinc associated with reduced T-cell proliferation and altered cytokines	Ali et al. (2018)
Zinc deficiency compromises mucosal immunity	Cross-sectional	Children	2018	Disruption of tight junctions and compromised mucosal barriers	Hossain et al. (2018)
Increased risk of infectious disease associated with zinc deficiency in children	Cross-sectional	Children in developing countries	2020	Low serum zinc associated with higher diarrhea and pneumonia rates	Nussenzweig & Sclafani (2020)

Table 3 reports on some Intervention trials and supplementation of zinc. Across the various studies, zinc supplementation was found to result in 20-30% reduction in diarrhea, improved immunity among HIV positive children, decreased severity and duration of diarrhea, 15-20 % reduction in incidence of pneumonia and reduction in the risk of sepsis.

Table 3:

Intervention Trials and Supplementation of Zinc

Title of Study	Study Type	Population	Study Period	Key Findings	Reference
Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses	Meta-analysis	Children	2007	20–30% reduction in diarrhea incidence with zinc	Aggarwal et al. (2007)
Oral zinc for treating diarrhea in children	Cochrane review	Children	2016	Zinc reduced diarrhea duration and incidence	Lazzerini & Wanzira (2016)
Zinc supplementation and immune function in children with HIV	Randomized trial	HIV-positive children	2005	Zinc improved some immune parameters	Bobat et al. (2005)
Zinc supplementation and inflammation in treated HIV	Trial	Children with HIV	2019	Zinc associated with reduced inflammatory markers	Dirajlal-Fargo et al. (2019)
Zinc supplementation and prevention and treatment of sepsis in young infants: a systematic review and meta-analysis	Systematic review & meta-analysis	Infants	2022	Zinc associated with reduced sepsis outcomes	Irfan et al. (2022)
Zinc deficiency and risk of sepsis in children	Systematic review & meta-analysis	Children	2018	Low zinc increased sepsis risk	Li et al. (2018)
Effect of routine zinc supplementation on pneumonia in children aged 6 months to 3 years: randomized controlled trial in an urban slum	Randomized controlled trial	Children 6 months–3 years	2002	Routine zinc supplementation reduced pneumonia incidence (15–20% in some trials)	Bhandari et al. (2002)
Zinc and immune function in children: observational findings	Observational study	Children	2008	Zinc deficiency linked to lower immune cell counts and cytokine changes	Bhandari et al. (2008)
Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials	Randomized controlled trial	Children with diarrhea	2019	Daily zinc reduced duration and severity of diarrhea	Bhutta et al. (2019)
Effect of zinc supplementation in Children less than 5 years on Diarrhea attacks: A randomized controlled trial	Randomized controlled trial	Children <5 years	2022	Zinc supplementation reduced diarrhea attacks	Abd El-Ghaffar et al. (2022)

Table 4 shows information of studies highlighting zinc's essential role in growth, cognitive development and neurobehavioral outcomes. Some of the studies highlight the essential role zinc plays in cognitive development, neurobehavioral outcomes and growth. Its deficiency has been linked to reduced attention, delayed puberty, stunting and impaired cognitive performance. Technical and policy reports underscore the necessity for reliable biomarkers, endorsing collective use of dietary, biochemical and functional indicators at the population level. Biofortification, food fortification and community-based education approaches improve zinc intake and caregiver practices.

Table 4:
Cognitive/Physical Development, Biomarkers & Policy Studies

Title of Study	Study Type	Population	Study Period	Key Findings	Reference
Human zinc deficiency: discovery to translation	Review	Children / general	2013	Zinc deficiency linked to cognitive impairment and developmental issues	Sandstead (2013)
Preventive zinc supplementation among infants, preschoolers, and older prepubertal children	Review	Infants and children	2009	Preventive zinc associated with growth benefits and reduced morbidity	Brown et al. (2009)
Discovery of human zinc deficiency: Its Impacts on Human Health and Disease	Review	General	2013	Historical impacts of zinc deficiency including growth and immunity	Prasad (2013)
Undernutrition as underlying cause of malaria morbidity and mortality in children	Review	Children	2014	Stunting and nutritional deficiencies linked to disease burden and DALYs	Caulfield et al. (2014)
Conclusions of Joint WHO/UNICEF/IAEA/IZiNCG Meeting on Zinc Status Indicators	Technical report	Populations	2007	Recommended biochemical, dietary and functional indicators for zinc status	de Benoist et al. (2007)
Zinc supplementation for preventing mortality, morbidity, and growth failure in children ages 6-12 years	Cochrane review	Children 6 months–12 years	2023	Evidence synthesis supporting supplementation programs	Imdad et al. (2023)
Impact of Infant and young child feeding (IYCF) Nutrition interventions on Breastfeeding practices	Systematic review	Infants and young children	2020	Nutrition interventions improve breastfeeding and growth outcomes	Lassi et al. (2020)
Large-Scale Food Fortification and Biofortification in Low- and Middle-Income Countries: A Review of Programs, Trends, Challenges, and Evidence Gaps.	Review / policy analysis	Populations in LMICs	2018	Fortification and biofortification shown to improve micronutrient status	Osendarp et al. (2018)
Promotion of zinc tablets with ORS through child health weeks improves caregiver knowledge, attitudes, and practice on treatment of diarrhoea in Nigeria	Implementation study	Caregivers/children	2015	Promotion increased caregiver knowledge and zinc use	Kung'u et al. (2015)
Putting consumers first in food systems analysis: identifying interventions to improve diets in rural Ghana	Field study	Rural households	2022	Identified interventions to improve diets including zinc-rich foods	Aberman et al. (2022)
Putting consumers first in food systems analysis: identifying interventions to improve diets in rural Ghana	Cross-sectional	Households	2022	Community initiatives influenced food access and nutrition	Nkegbe & Mumin (2022)

DISCUSSION

Prevalence and Statistics on Zinc Deficiency in Children in LMICs

It is well established that Zinc is the second most abundant micronutrient in the human body, second only to iron (Martina Maywald & Lothar Rink, 2022). Zinc is also widely available in most foods such as beef, poultry, seafood, grains, legumes, cereals and nuts. The wide range of dietary sources notwithstanding, zinc deficiency is one of the most common forms of micronutrient deficiency globally (Abdulahi, Fretheim, Argaw, & Magnus, 2021; Dembedza, 2023; Gupta, Brazier, & Lowe, 2020; Lowe et al., 2024). Prevalence of zinc deficiency (24%) has been reported among African children under 5 years old (Dembedza, 2023). Although data from most low-and-middle-income-countries (LMIC) is scarce, zinc prevalence of ≥ 20% is reported in about 23 LMIC where data is available (Lowe et al., 2024). Among school children in rural Nigeria, 99% had zinc deficiency. Serum zinc levels were significantly lower among those from lower socioeconomic background compared to middle and upper socioeconomic class (Abah, Okolo, John, & Ochoga, 2015). Among school children in a semi urban population in Nigeria, 9.5% were found to be zinc deficient. Serum zinc was lower among children from poorer socioeconomic backgrounds compared to those from high socioeconomic backgrounds (Oladibu, Kofoworade, Onigbinde, Ojedokun, & Alabi, 2023). A prevalence of 40.5% was reported among 2–10-year-old Ghanaian children, (Egbi, 2012)

Causes of Zinc Deficiency in Children in LMICs

The primary cause of zinc deficiency has been identified as malnutrition (Maywald & Rink, 2022). The absence of available reserve or store for zinc in the human body, coupled with the involvement of the nutrient in numerous human biological functions, puts a high demand on the nutrient, and mandates its constant adequate provision primarily through dietary intake. This may partly explain the high prevalence of zinc deficiency, especially in low- and middle-income countries where food insecurity and poverty threaten the adequacy of dietary zinc intake. Zinc is a versatile nutrient and plays many roles in human health and development including ensuring normal growth, reproduction, being a part of various enzymatic activities and immune defense (Dembedza, 2023; Maywald & Rink, 2022). Zinc deficiency is thus characterized by multiple immune and metabolic disorders as well as infections (Maywald & Rink, 2022). The ubiquitous involvement of zinc in most life processes elucidates the characteristic multiple functional consequences of zinc deficiency (Gupta et al., 2020). Evidence from previous studies have associated zinc deficiency to metabolic and chronic diseases such as diabetes and cancer; neurodegenerative diseases such as Alzheimer's disease; intestinal diseases such as inflammatory bowel disease and irritable bowel syndrome and infectious diseases such as malaria, HIV, tuberculosis, measles and COVID-19 pneumonia (Bitirim, 2021; Jones et al., 2022; MacKenzie & Bergdahl, 2022; Wan & Zhang, 2022).

Zinc homeostasis is largely dependent on intestinal absorption, mostly through the duodenum and jejunum. Intestinal zinc absorption depends on certain factors which determine the bioavailability of dietary zinc. For example, adequate amounts of zinc in the diet are necessary to ensure intestinal zinc absorption (King et al., 2015). The richest dietary sources of zinc are red meat, offal, oysters, shellfish, fortified cereals, and whole-grain products with oysters reporting the highest zinc content per serving (Meyers, Hellwig, & Otten, 2006). Egg, milk and milk products are also good sources of zinc (Ross, 2012). Most of these are not a usual part of the diets of most low and middle income (Abdulahi et al., 2021) populations, partly due to economic and cultural reasons or because of lack of accessibility. Additionally, most families in LMIC may not be able to afford adequate amounts of these ingredients in the diets due to poverty and low socioeconomic states. Low amounts of zinc in the diet affect intestinal zinc absorption leading to zinc deficiency.

The composition of diet also affects zinc absorption (Ross, 2012). Meals prepared from legumes or unrefined cereals and those that contain certain indigestible plant components such as lignin and phytates form insoluble complexes with zinc, preventing intestinal absorption (Hunt, Beiseigel, & Johnson, 2008; Lönnerdal, 2000; Ross, 2012; Wan & Zhang, 2022). Cereals, legumes and nuts are rich sources of phytate, a major inhibitor of intestinal zinc absorption. Diets of most LMI populations have cereals and legumes being their principal components. From early childhood, most weaning foods are prepared with unrefined cereals and legumes. For adults, cereals and legumes form the main component of most staples, thus increasing phytate levels and potentially contributing to zinc deficiency in these populations. In a cohort of Malawian children recovering from tuberculosis who were fed a low phytate diet, zinc absorption was observed to increase (Manary et al., 2000). Micronutrients like copper, calcium, iron and calcium also compete with intestinal zinc absorption (Maywald & Rink, 2022).

Zinc Deficiency and Immune Function

Zinc is involved in the activation of various immune cells, including T-cells, natural killer cells, lymphocytes, neutrophils, and macrophages. These cells collectively coordinate the body's immune response against pathogens and help regulate the production of cytokines, essential proteins such as antibodies that combat infections. A deficiency in zinc can result in a diminished antibody response, thereby increasing susceptibility to infections (Shankar & Prasad, 1998). Additionally, zinc possesses anti-inflammatory properties that are pivotal in mitigating the severity of infections (Rink, 2000).

Inadequate zinc levels may lead to chronic inflammation, elevating the risk of prevalent infectious diseases such as diarrhea, pneumonia, malaria, and respiratory tract infections (Wessells & Brown, 2012), which are major causes of morbidity and mortality in LMICs (Black et al., 2013). In these countries, zinc deficiency is often exacerbated by suboptimal dietary intake, malabsorption issues, and frequent infections. Insufficient access to zinc-rich foods like animal products, legumes, and nuts can contribute to deficiencies. Malabsorption resulting from conditions such as diarrhea, celiac disease, or other gastrointestinal disorders can also precipitate zinc deficiency (Dewey, Engle-Stone, & Haselow, 2012). Moreover, the increased zinc requirements due to recurrent infections can further predispose individuals to deficiencies (Black et al., 2013).

A systematic review conducted by Mayo-Wilson et al., (Mayo-Wilson, Imdad, & Herzer, 2011) delved into the effects of zinc supplementation on childhood infections. The findings revealed a significant reduction in the incidence of pneumonia and diarrhea in children under five years of age following zinc supplementation. This evinces the significance of zinc in enhancing immunity and lowering infection rates. Deficiency in zinc among children can result in various immune dysfunctions.

A study by Ali et al. (Ali, Kazi, & Kumar , 2018) investigated the impact of zinc deficiency on T-cell functionality. The research demonstrated that children with low zinc levels exhibited diminished T-cell proliferation and altered cytokine production. Such impairments in T-cell function can lead to suboptimal immune responses to infections, rendering deficient children more susceptible to illnesses. Zinc influences the integrity of the epithelial barriers in the respiratory and gastrointestinal tracts, which serve as the primary defense against pathogens.

In a current study by Hossain et al. (2018), it was shown that zinc deficiency compromises mucosal immunity by disrupting tight junctions in epithelial cells. Consequently, children with inadequate zinc levels are at an increased risk of gastrointestinal and respiratory infections, as the barriers fail to prevent pathogen invasion effectively. In addition to the biological mechanisms, epidemiological evidence supports the relationship between zinc deficiency and susceptibility to infections in children. A cross-sectional study by Nussenzweig et al., (2020) evaluated the zinc status of children in developing nations and identified a robust association between low serum zinc levels and heightened rates of infectious diseases such as diarrhea and pneumonia. The researchers concluded that addressing zinc deficiency in these populations could serve as an effective strategy to enhance child health outcomes.

Impact of Zinc Deficiency on Physical and Cognitive Development

Zinc is important for brain development, it is required for neurotransmitter function, and deficiency can lead to cognitive impairment, reduced attention span, and decreased learning capacity (Sandstead, 2013). Zinc is also needed for the regulation of hormones, including the production of growth hormones. Insufficient zinc levels have been linked to stunted growth and reduced height and delayed puberty (Brown, Peerson, Baker, & Hess, 2009; Prasad, 2013). Zinc contributes significantly to brain development as it is indispensable for neurotransmitter function. A deficiency in zinc can result in cognitive impairment, reduced attention span, and diminished learning capacity (Sandstead, 2013). Zinc is also associated with the regulation of hormones and the production of growth hormones. A lack of zinc can lead to stunted growth, decreased height, and even delay puberty (Brown et al., 2009; Prasad, 2013). Long-term health implications of zinc deficiency include growth retardation and increased risk of chronic diseases, such as cardiovascular disease and diabetes. As earlier mentioned, zinc deficiency can lead to stunted growth, which can have long-term consequences on cognitive development, school performance, and economic productivity (Caulfield, de Onis M, Blössner, & Black, 2014).

Intervention Strategies to Address Zinc Deficiency

The evidence supporting the use of zinc supplementation in preventing infections in children is robust, with numerous studies consistently demonstrating the efficacy of zinc in reducing both the occurrence and duration of such infections. A systematic review showed a 20-30% reduction in diarrhea incidence with zinc supplementation (Aggarwal, Sentz, & Miller, 2007). A similar review corroborated these findings revealing that zinc supplementation led to a decrease in the rates of diarrhea and pneumonia among children under 5 years of age (Lazzerini & Wanzira, 2016). Another study highlighted the enhancement of immune function in children with HIV through zinc supplementation (Bobat, Coovadia, & Stephen , 2005; Dirajlal-Fargo et al., 2019). Notably, zinc supplementation has also been proven to lower the risk of sepsis in children (Irfan, Black, Lassi, & Bhutta, 2022; Li, Wang , & Zhang , 2018). A randomized controlled trial among Indian children further supported these results by demonstrating a 15-20% decrease in pneumonia incidence due to zinc supplementation (Abd El-Ghaffar, Shouman, Hakim, El Gendy, & Wahdan, 2022; Bhandari et al., 2002). Other research findings have indicated that children deficient in zinc exhibit decreased levels of immune cells and cytokines, rendering them more susceptible to infections like diarrhea, pneumonia, and malaria (Bhandari, Bahl, & Taneja, 2008). Furthermore, zinc deficiency can impede the response to vaccinations, thereby heightening children's vulnerability to infections (Bhandari et al., 2008). Furthermore, a randomized controlled trial has provided compelling evidence of the efficacy of zinc supplementation in reducing infection rates among children. For instance, a recent study by Bhutta et al (Bhutta, Black, & Brown, 2019) demonstrated that daily zinc supplementation in children with diarrhea significantly lessened both the duration and severity of the illness. This study emphasized the potential of zinc as a therapeutic intervention to enhance clinical outcomes in pediatric infections.

Outcomes and Effectiveness of Interventions

Zinc supplementation and fortification have been shown to be effective in reducing the risk of zinc deficiency and its associated health consequences. For example, zinc supplements have been shown to increase intake among vulnerable populations (Aggarwal et al., 2007), especially during periods of increased demand, like pregnancy and lactation. This can help bridge the gap in zinc intake. A systematic review of 32 studies found that zinc supplementation improved immune function and reduced infection incidence (Mayo-Wilson et al., 2011). Promoting consumption of zinc-rich foods such as animal products, legumes, and nuts can also help address deficiency (Dewey et al., 2012). Zinc fortification of staple foods has also been shown to improve zinc status (Dewey et al., 2012) and reduce morbidity and mortality (Brown et al., 2009) in vulnerable populations. Addressing poverty, poor sanitation, and inadequate health care can also go a long way to reduce the risk of zinc deficiency (Black et al., 2013).

Common Biomarkers for Measuring Zinc Levels

Despite the high prevalence of zinc deficiency among children in most LMIC, efforts to reduce the prevalence have shown limited success partly due to the lack of sensitive and specific methods to assess human zinc status (Lowe et al., 2024). Different indicators for assessment of zinc status and risk of zinc deficiency at the population level have been recommended;- (1) the percentage of the population with plasma (serum) zinc concentrations below an appropriate cut-off, (2) the prevalence of usual dietary zinc intakes below the Estimated Average Requirement (EAR), and (3) the percentage of children less than five years of age with height-for-age Z scores less than -2 SD with respect to the WHO child growth standards (Wessells & Brown, 2012). A joint World Health Organization/Food and Agriculture Organization/United Nations International Children's Emergency Fund/ International Atomic Energy Agency / International Zinc Nutrition Consultative Group (WHO/FAO/UNICEF/IAEA/IZiNCG) meeting reviewed and categorized indicators of population zinc status assessment into biochemical, dietary and functional (de Benoist, Darnton-Hill, Davidsson, Fontaine, & Hotz, 2007).

Serum/plasm zinc status though considered an objective and quantitative means of assessing zinc status and populations that are suitable targets for intervention, serum zinc is limited in reflecting an individual’s zinc status and predicting their functional response to supplementation (de Benoist et al., 2007). Dietary intake indicators are suitable for identifying groups at risk of zinc deficiency and may help to identify dietary patterns associated with zinc adequacy or inadequacy and potential vehicles for zinc supplementation. However, dietary indicators may not be appropriate for defining an individual’s zinc status but rather for predicting their risk of zinc deficiency. For diagnosing zinc deficiency, dietary indicators must be used in combination with a biochemical indicator (de Benoist et al., 2007). The methodological implications, cost and logistical challenges, coupled with the existence of limited valid biomarkers, have undermined efforts to assess zinc deficiency at the national level in most LMICs (Wessells & Brown, 2012).

Conclusion

Zinc deficiency continues to be a major public health problem among children in LMICs and strongly linked to adverse growth and development, increased susceptibility to infections and impaired immunity. Current evidence shows that poor dietary diversity, inadequate intakes, recurrent infections and consumption of high phytate source foods contribute significantly to low zinc status. Food fortification and supplementation consistently improve serum levels of zinc, reduce pneumonia infection, diarrhea and other infections. Strengthening assessment methods, improvement of dietary quality and scaling of effective intervention strategies are crucial to decreasing the burden of zinc deficiency and improvement of child health across LMICs.

Future directions and recommendations

Efficiently addressing deficiency of zinc and its impact on immunity of children in LMICs entails coordinated research, implementation efforts and policy.

Research Recommendations

Further research studies should assess the long-term effects of zinc supplementation and fortification on cognitive outcomes, growth and immunity through randomized controlled trials and thoroughly designed longitudinal studies. Priority should be given to improving bioavailability of zinc by reducing phytates in foods and exploring food processing techniques. More sensitive biomarkers in combination with dietary indicators will improve the assessment of the population. Development of more sensitive biomarkers in combination with dietary and biochemical indicators will strengthen the assessment of zinc status on the population level.

Policy Recommendations

Policies to combat zinc deficiency should promote diversification of diet, scaling up of zinc fortification of staple foods. and integration of zinc supplementation into routine child health welfare programs. Scaling up public education on zinc-rich foods and improvement of access to supplements, especially in underserved communities, will help decrease population-level deficiencies.

Implementation Strategies

Community based interventions including training of health workers, improvement of food availability through the markets, and provision of household nutrition education should be adopted for a sustainable impact. Partnerships with local and government agencies as well as international agencies can enhance the delivery of supplements and fortified foods, while strong monitoring systems will safeguard program effectiveness. Addressing poverty, sanitation, and healthcare gaps remains critical to reducing zinc deficiency and improving child health outcomes across LMICs.

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Conflict of Interest

The authors declare no conflict of interest.

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