

Effect of Zinc Supplementation on Changes in Anthropometric Index of Toddler: A Meta-Analysis

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ABSTRACT

Background: Stunting occurs as a result of a long chain of malnutrition burden at every phase of life. Insufficient intake of protein energy in pregnancy and toddler growth has an impact on the risk of stunting under five. In addition, stunting is also considered to be closely related to deficiency of essential micronutrients, especially iron and zinc.

Subjects and Method: This research is a systematic review and meta-analysis study using PRISMA diagrams. The article search was conducted based on the eligibility criteria using the PICO Model. Population: Infants aged 0-59 months, Intervention: Zinc supplementation, Comparison: Placebo, Outcome: Anthropometric index of height for age (HAZ). The articles used were from PubMed, Google Scholar, Science Direct, and Scopus published from 2016 – 2022. The keywords used in the search were “zinc” AND “height” AND “infant” OR “toddler”. The inclusion criteria in this study were full paper articles with Randomized Control Trial, the intervention given was zinc with placebo comparison, research subjects were infants aged 0 – 59 months, and articles were published in English. The final results are presented in Standardized Mean Difference (SMD) in the analysis using the Revman 5.3 application.

Results: Meta-analysis was carried out on 10 articles originating from the continents of Asia, Africa, and America. The results of the analysis showed that zinc supplementation increased the anthropometric index (HAZ) with SMD=0.51 units higher than placebo and statistically significant (SMD=0.51, 95% CI=0.17 to 0.85; p=0.003).

Conclusion: The results of the meta-analysis showed that the administration of zinc supplementation increased the anthropometric index (HAZ) in children under five.

Keywords: zinc, anthropometry, height for age, toddler.

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BACKGROUND

Stunting is a developmental disorder in children aged < 5 years, as a result of poor nutrition, repeated infections, or inadequate psychosocial stimulation. The condition is indicated by the child's height by age less than 2 standard deviations based on the

WHO Child Growth Standard (WHO, 2015).

Stunting has an impact on the quality of long-term human resources or is factually visible in impaired growth and development of toddlers (Ministry of Health, 2018). The long-term consequences, even to the next generation, are a global concern and are

included in the issue of the Sustainable Development Goals (SDGs) targets. In 2020, UNICEF-WHO-WB Joint Child Malnutrition recorded 149.2 million or 22% of children under five in the world suffer from stunting (WHO, 2021). However, the prevalence of stunting in children under five continues to improve compared to 2000 where the incidence rate reached 33.1%. The distribution area is also diverse, dominated by the distribution of stunting toddlers in the Asian continent (53%) and the African continent (41%) (UNICEF, 2021).

The average prevalence of stunting in Indonesia from 2005 to 2017 was 36.4%, ranking the 3rd Southeast Asian country with a high prevalence of stunting after Timor Leste and India (WHO, 2018). Stunting is a chronic nutritional problem caused by socioeconomic factors and family food security, nutritional status and knowledge of mothers during pregnancy, infection in infants and environmental sanitation hygiene, and nutritional deficiencies of infants and toddlers (Helmiyati, 2020).

Insufficient intake of protein energy in pregnancy and toddler growth has an impact on the risk of stunting under five. In addition, stunting was also assessed to be closely related to deficiency of essential micronutrients, especially iron and zinc (Black et al, 2008). The Food and Nutrition Board developed by the Institute of Medicine of the National Academies USA (2001) recommends a maximum zinc intake for children aged 1-6 months of 2 mg per day, 7-36 months a maximum of 3 mg per day, and a maximum of 37-59 months. 5 mg per day. However, the degree of micronutrient deficiency is not well documented, with all populations at risk for micronutrient deficiencies, including zinc. Groups of pregnant women, toddlers, children, and young women are groups that are vulnerable to micronutrient deficiencies (WHO, 2006).

A study by Wessells and Brown (2012) shows a positive correlation between the prevalence of stunting and the availability of zinc in the national food supply in various regions of Sub-Saharan and South Asian countries. Assessment of zinc status can be done individually or in a population by taking into account the confounding variables that contribute to each assessment method (Brown et al., 2004). Nikoyeeh's study (2021) showed an increase in serum zinc in infants given Micronutrient powders (MNPs).

Based on this background, researchers are interested in conducting a systematic review and meta-analysis to expand the facts from the results of previous primary studies related to the effect of zinc supplementation on changes in the anthropometric index of toddlers.

SUBJECTS AND METHOD

1. Study Design

This research was conducted using a systematic review and meta-analysis method. The articles used were from PubMed, Google Scholar, Science Direct, and Scopus published from 2016 – 2022. The keywords used in the search were “zinc” AND “height” AND “infant” OR “toddler”. The article search process is in accordance with the PRISMA diagram in Figure 1.

2. Steps of Meta-Analysis

Meta-analysis is carried out through 5 steps as follows:

- 1) Formulate research questions in PICO (Population, Intervention, Comparison, and Outcome).
- 2) Searching for primary study articles from various databases including PubMed, Scopus, Science Direct, and Google Scholar.
- 3) Perform screening and conduct critical quality primary studies.

- 4) Perform data extraction and enter the estimated effect of each primary study into the RevMan 5.3 application.
- 5) Interpret the results and draw conclusions.

The assessment of critical criteria is carried out by 2 independents using the Critical Appraisal Skills Program published by the 2018 Critical Appraisal Skills Program which consists of 12 questions. The questions are answered by giving a score. A score of 0 for answers was not carried out in the primary study, and a score of 1 for answers if done. The primary study is carried out if the total is at least 10. Then it is entered into the RevMan 5.3 application.

3. Inclusion Criteria

The inclusion criteria in this study were full paper articles with Randomized Control Trial (RCT), the intervention given was zinc with placebo comparison, research subjects were infants aged 0–59 months, and articles were published in English.

4. Exclusion Criteria

The exclusion criteria in this study were articles published before 2016 and the results of the study did not include the Mean and Standard Deviation values.

5. Operational Definition of Variables

The article search was conducted based on the eligibility criteria using the PICO Model. Population: Infants aged 0-59 months, In-

tervention: Zinc supplementation, Comparison: Placebo, Outcome: Anthropometric index of HAZ or LAZ.

Zinc supplementation is the administration of zinc supplements in liquid or tablet form with a minimum dose containing 5 mg of zinc per day for a minimum duration of 3 months or 12 weeks of intervention.

Anthropometric Index (HAZ) is an assessment of the nutritional status of children based on height according to age (months).

3. Instrument

This study was conducted using the guidelines from the PRISMA diagram and the quality of the articles was assessed using Critical Appraisal for the RCT study.

4. Data Analysis

The results of the study were analyzed using the Review Manager application (Revman 5.3). Forest plots and funnel plots were used to determine effect size and data heterogeneity. The fixed effect model is used to determine homogeneous data, while the random effects model is used for heterogeneous data.

RESULTS

Article searches were conducted through the PubMed, Google Scholar, Science Direct, and Scopus databases. Research articles are sourced from various countries as shown in Figure 2.



Figure 2. Map of Research Locations Effect of Zinc Supplementation on Anthropometric Index of Toddlers

Table 1. Results of quality assessment of rct studies the effect of zinc supplementation on anthropometric index of toddlers

No	Checklist of Questions	Publication (Author and Year)									
		Locks et al. (2016)	Kujinga et al. (2018)	Howie et al. (2018)	Barrffour et al. (2019)	Abdollahi et al (2019)	Cho et al. (2019)	Purnama-ningrum et al. (2020)	Hayman et al. (2021)	Islam et al. (2021)	Mayén et al. (2022)
Part A : Randomized Control Trial Research Design											
1	Does the study clearly answer the research question?	2	2	2	2	2	2	2	2	2	2
2	Was participants randomized to intervention?	2	2	2	2	2	2	2	2	2	2
3	Were all participants recorded and calculated correctly at the conclusion?	2	2	2	2	2	2	2	2	2	2
Part B : Research Methodology											
4	Were the interventions and analyzes done in a blinded manner?	2	2	2	2	2	0	1	1	2	0
5	Were the study groups similar at the start of the test?	2	2	2	2	2	2	2	2	2	2
6	Apart from the experimental intervention, did each test group receive the same treatment?	2	2	2	2	2	2	2	2	2	2
Part C: Research Results											
7	Were the effects of the intervention reported comprehensively?	2	2	2	2	2	2	2	2	2	2
8	Are estimates of the accuracy of the intervention effects reported?	2	2	2	2	2	2	2	2	2	2
9	Are the benefits of research worth the costs and disadvantages?	2	1	2	2	2	2	2	2	2	2
Part D: Application of Research Results											
10	Can the research results be applied to the population?	2	2	2	2	2	2	2	2	2	2
11	Can the research results be considered?	2	2	2	2	2	2	2	2	2	2
Total		22	21	22	22	22	20	21	22	22	20

Note: Score 2=Yes, Score 1=Cant be explained/Hesitant, Score 0=No

Table 2. Summary source of primary studies included in the meta-analysis

Author (Year)	Country	Study Design	Sample Size	P Population	I Intervention	C Comparison	O Outcome
Locks et al. (2016)	Tanzania	Randomized, placebo- controlled, double-blind trial	1,200	Children aged 5 – 7 weeks	Liquid zinc supplement containing 5 mg Zn for 6 months	Placebo	LAZ/ HAZ
Kujinga et al. (2018)	Kenya	Randomized controlled trial	156	Children aged 24 – 59 months	Zinc fortification containing 8 mg Zn for 25 weeks	Placebo	LAZ/ HAZ
Howie et al. (2018)	Gambia	Randomized, parallel group, double-blind, placebo- controlled trial	181	Children aged 2 – 59 months	Tablets containing 10 mg elemental zinc (ZnSo4) for 6 months	Placebo	LAZ/ HAZ
Barrfour et al. (2019)	Laos	Randomized, double-blind, placebo-controlled trial	1,479	Children aged 6 – 23 months	Zinc tablets containing 7 mg Zn for 36 weeks	Placebo	LAZ/ HAZ
Abdollahi et al. (2019)	Iran	Randomized, multicenter, double-blind, parallel group effectiveness trial	580	Children aged 6 – 24 months	5 mL zinc sulfate suspension containing 5 mg elemental zinc for 6 months	Placebo	LAZ/ HAZ
Cho et al. (2019)	South Korea	Randomized pre posttest with control trial	66	Children aged ≤ 24 months	Supplementation containing 5 mg Zn for 6 months	Placebo	LAZ/ HAZ
Purnama-ningrum et al. (2020)	Indonesia	Randomized pre posttest with control trial	70	Children aged 24 – 59 months	Zinc tablets 5 mg for 12 weeks	Placebo	LAZ/ HAZ
Hayman et al. (2021)	Bangladesh	Large randomized, controlled, community-based efficacy trial	72	Children aged 9 – 11 months	10 mg zinc tablets for 24 weeks	Placebo	LAZ/ HAZ
Islam et al. (2021)	Bangladesh	A randomized, partially double-blind, controlled, community-based efficacy trial	894	Children aged 9 – 11 months	Zinc permeable tablets containing 10 mg for 24 weeks	Placebo	LAZ/ HAZ
Mayen et al. (2022)	Guatemala	Randomised controlled trial	917	Children aged 6 – 59 months	Atole fortification containing 9 mg Zn for 18 months	Placebo	LAZ/ HAZ

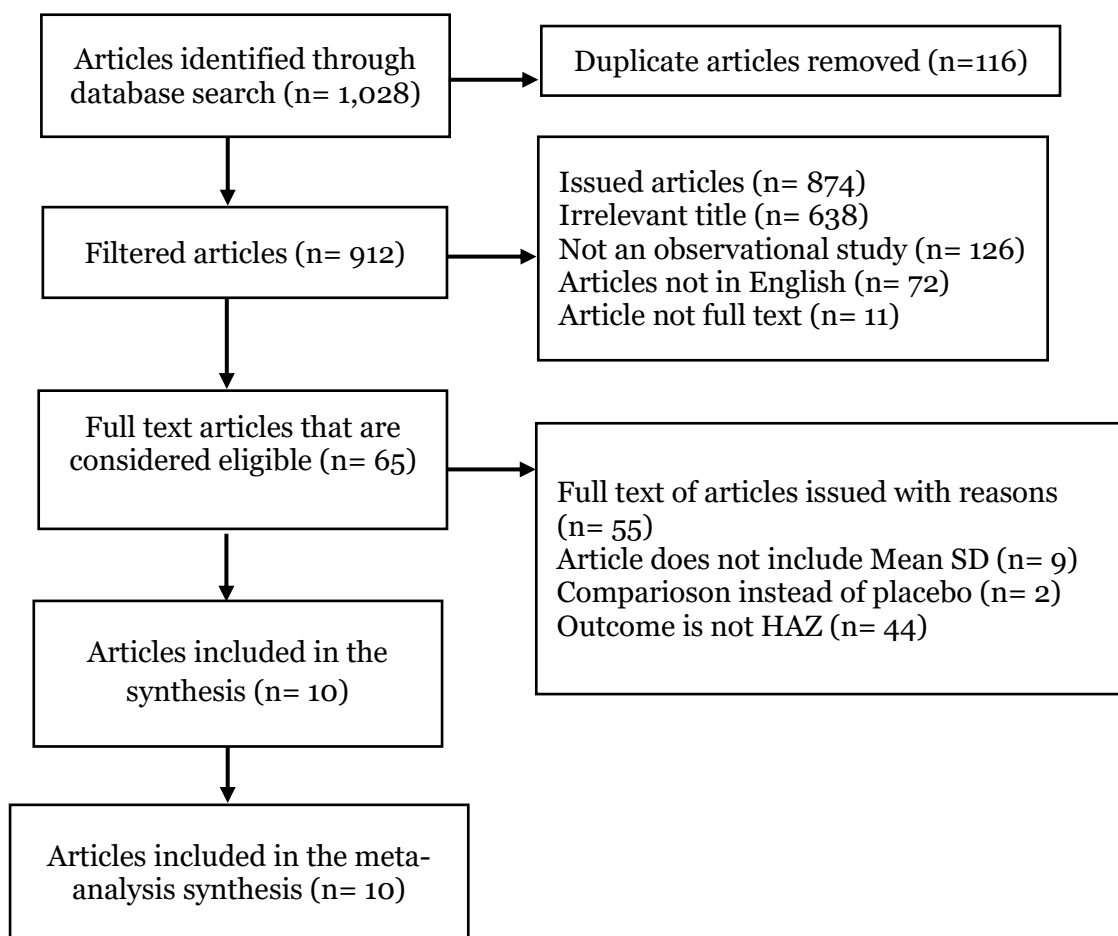


Figure 1. PRISMA Flow Diagram

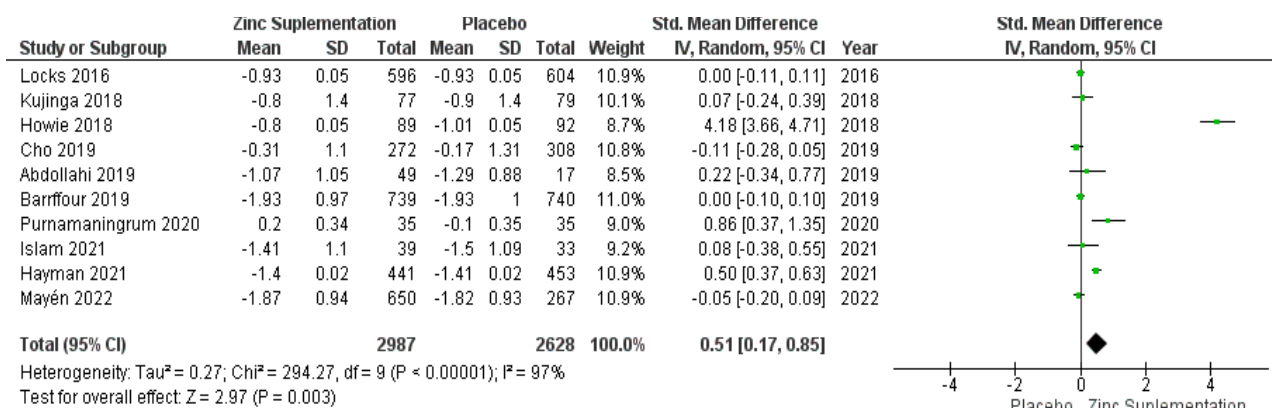


Figure 3. Forest Plot Effect of Zinc Supplementation on Anthropometric Index of Toddlers

The forest plot in Figure 3 shows that there are 10 articles reporting that zinc supplementation is an alternative to increase the anthropometric index of toddler growth. Based on the results of the analysis, there was

a high heterogeneity between experiments (I²=97%, p<0.001), so Random Effect Model (REM) analysis was used. Zinc supplementation was able to increase the anthropometric index (HAZ) with SMD=0.51 units higher

than placebo and statistically significant (SMD= 0.51, 95%CI= 0.17 to 0.85; p=0.003).

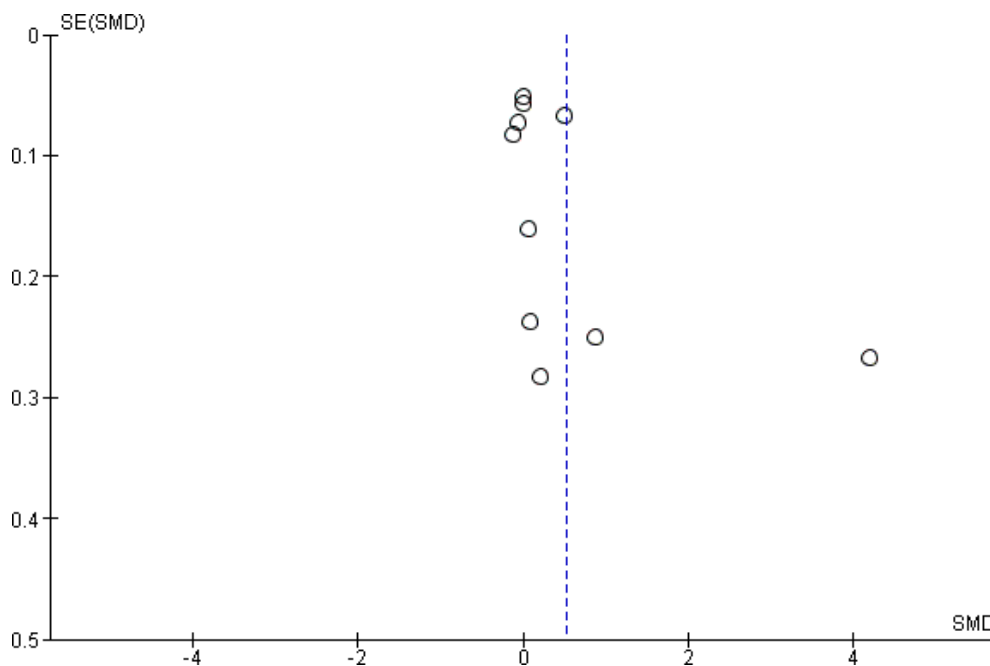


Figure 4. Funnel Plot Effect of Zinc Supplementation on Toddler Anthropometric Index

The funnel plot in Figure 4 shows an asymmetric distribution of effect estimates to the right and left of the mean vertical line of the estimate, indicating publication bias. This is based on the distribution of the estimated effect on the funnel plot, which is more on the left than the right of the vertical line, while the average estimated effect on the forest plot is located on the right of the null hypothesis vertical line, so publication bias underestimates the zinc effect. actually, against HAZ.

DISCUSSION

Stunting is a complex problem that is closely related to nutritional intake. However, nutrition in children is not the only causative factor that can be immediately resolved, it is necessary to identify sensitive and specific causes of stunting (Wahyuni, 2021). The stunting intervention framework is not only focused on meeting macronutrients, but also meeting the adequacy of micronutrients. Po-

licies from the central to the regional levels have also been taken, one of which is through the collaboration between the Government of Indonesia and Scaling Up Nutrition (SUN), which is a specific and sensitive nutrition intervention framework to intervene in stunting problems in Indonesia.

The micronutrient zinc is a catalytic metal ion found in the cytoplasm of cells and is one of the group II B metals with a molecular weight of 65.4 (Mann et al, 2014). Zinc plays an important role in supporting body functions, namely as a cofactor in the activity of more than 300 enzymes involved in the synthesis and degradation of carbohydrates, fats, proteins, and nucleic acids (Almatsier, 2009). The role of zinc in hormone activity, such as Human Growth Hormone, gonadotropins, sex hormones, prolactin, thyroid, and corticosteroids, which makes the rationale that the fulfillment of zinc micronutrients will be able to optimize the growth of children. Zinc deficiency is

generally caused by inadequate intake, increased demand, malabsorption, increased risk of zinc loss, and impaired utilization (Roohani et al., 2013).

Many studies have considered the use of zinc in optimizing the anti-inflammatory role of zinc and reducing the risk of diarrhea, so that zinc supplements are only given to toddlers with indications of diarrhea. However, in addition to its role in repairing damaged cells, zinc also has a role in the activation of bone-forming elements and cell proliferation. Anindita's research (2012) found that zinc deficiency has a 5.94 times greater risk of experiencing stunting.

This study is a systematic review and meta-analysis that aims to find conclusions from the results of various similar studies that tested the administration of zinc supplementation in increasing the anthropometric index of HAZ in children under five in various countries, so that general conclusions can be obtained that can be used as one of the considerations for giving supplementation. zinc in toddlers. The results of the analysis are presented in the form of forest plots and funnel plots.

Research related to the effect of zinc supplementation on the anthropometric index of toddlers consists of 10 primary study articles from Tanzania, Kenya, Gambia, Laos, Iran, South Korea, Indonesia, Bangladesh, and Guatemala. Based on the primary study conducted by the analysis, it was found that the research similarities, namely the research subjects were toddlers or infants/ children aged 0 to 59 months, the intervention given was zinc with a placebo comparison. The primary study was collected from various samples, the smallest amounting to 66 subjects and the largest amounting to 1,479 subjects. The results showed that zinc supplementation could increase the anthropometric index of HAZ in under-five growth by 0.51 units compared to

placebo (SMD= 0.51, 95% CI= 0.17 to 0.85; $p= 0.003$).

This study is in line with Das et al. (2020), which states that fortification of foods containing a single micronutrient on the concentration of micronutrients in serum in mothers and children. Research Hossain et al. (2021) have identified changes in the nutritional status and morbidity of children under five in Dhaka Hospital, where children who were given zinc and iron supplementation, as well as multivitamins for 3 months showed weight gain, increased mid-upper arm circumference, and changes in anthropometric index.

The study results are in line with the characteristics of zinc which has a unique chemical structure due to its regulatory and catalytic functions (Yuniastuti, 2014). The availability of zinc increases Insulin like Growth Factor I (IGF I) which accelerates bone growth. IGF I will activate growth hormone which plays a role in growth promoting factor. Zinc deficiency will reduce immunity, thereby increasing the risk of disease infection and increasing energy requirements (Soekirman, 2000). Assessment of children's growth and nutritional status is based on anthropometric index results as an indication of nutritional problems, including stunting (Kiik and Nuwa, 2020).

AUTHOR CONTRIBUTION

Desif Upix Usmaningrum as the main character of the research who chooses the topic, conducts searches and collects data in this study. Eti Poncorini Pamungkasari and Bhisma Murti played a role in conducting data analysis and reviewing research documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTERESTS

There is no conflict of interest in this study.

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