

Zinc Deficiency and Impact on Lipid Profiles in Malnourished Children in Senegal.

ABSTRACT:

Aims: Zinc is an important element for the body because of the role it plays in the structure but also in the catalytic activity of several metabolic enzymes. The aim of this study is to evaluate the zinc status in malnourished children and its association with lipid profile parameters.

Study design: This is a cross-sectional and prospective analytical study.

Place and Duration of Study: This is a fifteen-month study, conducted at the Diamniadio Children's Hospital. Children under five years of age, malnourished according to the weight/height ratio were selected after parental consent.

Methodology: The study population comprised 176 children with a sex ratio of 1, of whom 49% with severe acute malnutrition, 41% moderately malnourished and 10% undernourished. Zinc was determined using Biosystem's[®] 5 Br PAPS colorimetric method. To compare the groups, we used the Chi-squared test (X²) or the Fisher's exact test. For the comparison of quantitative variables between the targeted groups, we used the ANOVA test. Zinc, total cholesterol (TC), HDL cholesterol (HDLc) and LDL cholesterol (LDLc) were significantly lower in the malnourished. Hypozincemia was found in 66% of children. TC, HDLc and triglycerides (TG) are significantly lower in malnourished patients with hypozincemia with a mean average of 2.99 ± 1.31 mmol/L ($p < 0.001$), 0.56 ± 0.36 mmol/L ($p = 0.007$) and 1.73 ± 0.85 mmol/L ($p = 0.004$), respectively.

There is a positive correlation between zinc and the various lipid profile parameters. TC ($r = 0.314$; $p < 0.001$), HDLc ($r = 0.326$; $p < 0.001$), LDLc ($r = 0.200$; $p = 0.008$) and TG ($r = 0.229$; $p = 0.002$).

Conclusion: The management of hypozincemia is essential within the follow-up of malnourished children. Zinc supplementation can prevent dyslipidemia, which is secondary to malnutrition and serve as a preventive measure against dyslipidemia in malnourished children.

Keywords: Zinc, total cholesterol, HDL-c, LDL-c, triglyceride, malnutrition, children

1. INTRODUCTION

Zinc ranks second after iron, as a metal that is very abundant in the body [1]. It is found throughout the body with a predominance in muscles and bones (85%), 11% in the skin and liver, the rest is distributed in other tissues [2]. It participates in the catalytic activity of about 2000 enzymes as a cofactor, hence its crucial role in several physiological processes such as the metabolism of carbohydrates, lipids and proteins [3].

It is a powerful antioxidant that protects cells from the attack of free radicals and thus slows down their aging [4]. Zinc deficiency is one of the risk factors relating to malnutrition and is responsible for deaths in children under five years of age [3].

The causes of zinc deficiency can be nutritional, iatrogenic, genetic, or result from diseases.

Severe zinc deficiency results in symptoms such as diarrhea, pustular dermatitis, alopecia, weight loss, wound healing problems, immune disorders, and sexual maturation [4].

The objective of this study is to evaluate the zinc status in malnourished children under five years of age and its influence on lipid profile.

2. MATERIAL AND METHODS

This is a prospective cross-sectional study conducted between August 2019 and November 2020. Recruitment was carried out at the Diamniadio Children's Hospital (DCH) and biological analyses were performed at the department of medical biochemistry.

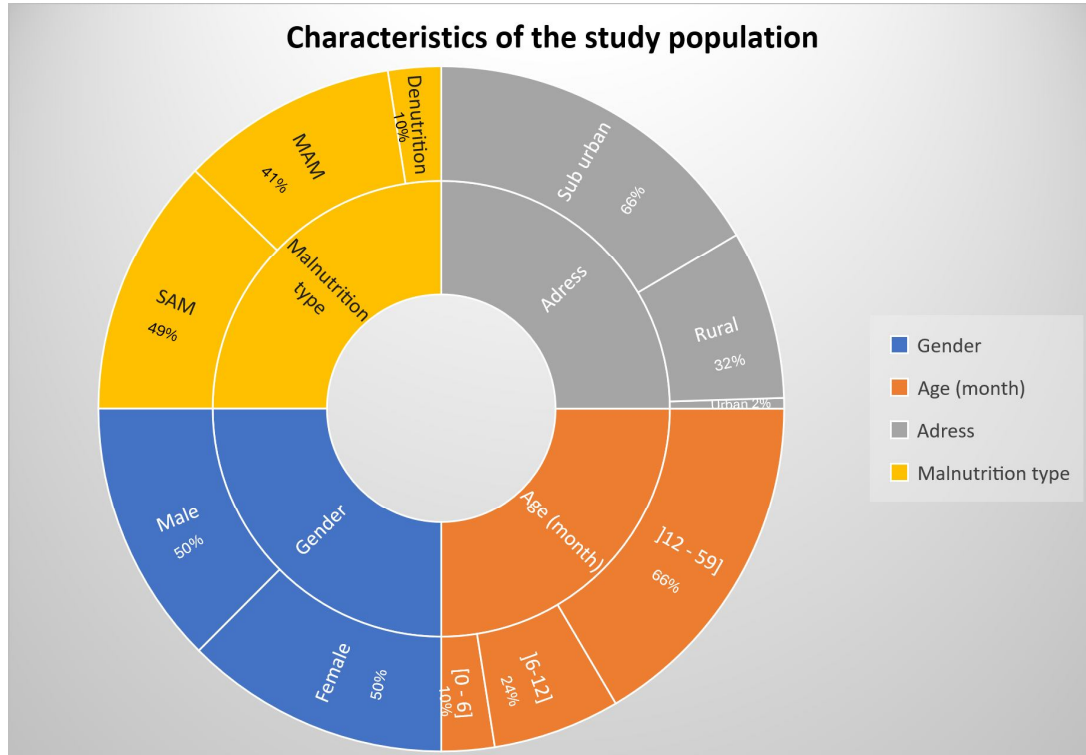
Children under 5 years of age, followed on an outpatient basis or hospitalized for acute malnutrition, were included after parental consent. Children with chronic conditions were not included.

The nutritional status of children was defined using the body mass index (BMI) in relation to the WHO growth standards. Normal nutritional status is defined by a BMI index between -2 and +2 z-score. Moderate acute malnutrition (MAM) is considered to have a BMI index between -2 and -3 z-score and is classified as severe for a BMI index < -3 z-score according to the WHO Child Growth Standards published in 2009 [5].

Zinc and lipid profile parameters were measured on serum with the A25 Biosystem[®] automaton at the medical analysis laboratory of the Diamniadio Children's Hospital. Zinc is determined by a colorimetric method with Biosystem's 2-(5-Bromo-2-pyridylazo)-5-(N-propyl-N-sulfopropylamino)-phenol (5Br-PAPS) with which it forms a red chelated complex.[®] The intensity of this stain, the absorbance of which is measured by spectrophotometry, is proportional to the concentration of total zinc in the sample. Hypozincemia has been defined as a concentration < 70 µg/dl [6].

Statistical analyses were performed with Jamovi software (Version 1.6.22.0). Sociodemographic and clinical data are described by numbers and percentages, while biological parameters are expressed as mean or median depending on the nature of the distribution. The Chi2 test or the exact Fisher test was used to compare the groups. The ANOVA made it possible to compare the quantitative variables of the different groups. A p<0.05 was retained as significant.

3. RESULTS



MAM: Moderate Acute Malnutrition; SAM: Severe Acute Malnutrition
Figure 1: Characteristics of the study population

The distribution of the study population was based on gender (male, female), age in months ([0-6], [6-12] and [12-59]), and type of malnutrition (acute, moderate and undernutrition).

A total of 176 children were included in the study with a sex ratio equal to 1. Nearly 66% were over 12 months old. Most of the population came from the outskirts of Dakar (66%). Only 2% came from the city. Severe acute malnutrition was found in 49% of children (Fig 1).

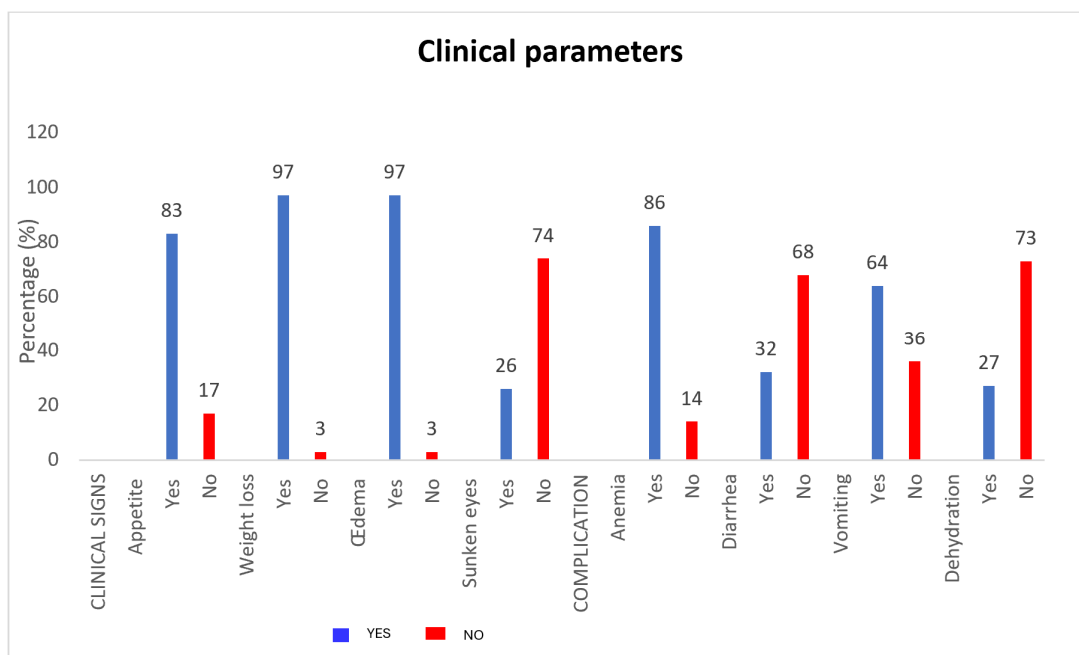


Figure 2: Distribution of the population by clinical parameters and complications observed

The distribution of the study population was based on the presence or absence of clinical signs (appetite, weight loss, oedema and sunken eyes) and the type of complications (anemia, diarrhea, vomiting, dehydration). Lack of appetite and weight loss were strongly observed with a percentage of 83% and 97% respectively. Oedema was found in only 3% of children. Anemia and vomiting were the main complications, 86% and 64% respectively (Fig 2).

Table 1: Change in zinc and lipid profile by type of malnutrition (ANOVA)

Type of malnutrition	Biological parameters				
	Zincemia($\mu\text{g/dl}$)	Total cholesterol (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	TG (mmol/L)
Malnutrition	53.93 \pm 31.81	2.66 \pm 0.93	0.56 \pm 0.15	0.79 \pm 0.43	0.92 \pm 0.35
MAM	65.90 \pm 29.30	3.59 \pm 1.31	0.68 \pm 0.31	1.27 \pm 0.80	0.83 \pm 0.42
MAS	54.68 \pm 27.27	3.10 \pm 1.39	0.61 \pm 0.41	1.09 \pm 0.72	0.92 \pm 0.33
p-value	0.047	0.005	0.097	0.007	0.254

MAM: Moderate Acute Malnutrition; SAM: Severe Acute Malnutrition; HDL-c : Hight Density Lipoprotein; LDL-c: Low Density Lipoprotein; TG: Triglyceride
 Zinc levels were significantly lower in malnourished people and those with SAM ($p = 0.047$). This same trend is observed for cholesterol ($p = 0.005$) and LDL cholesterol ($p = 0.007$).

Table 2: Change in lipid profile by zinc level (ANOVA)

	Group	N	Moy \pm ET	p-value
Cholesterol (mmol/L)	Normal	116	2.99 \pm 1.31	< 0.001
	Hypozincemia	60	3.77 \pm 1.29	
HDL-C (mmol/L)	Normal	116	0.56 \pm 0.36	0.007
	Hypozincemia	60	0.72 \pm 0.31	
LDL-C (mmol/L)	Normal	116	1.06 \pm 0.74	0.052
	Hypozincemia	60	1.29 \pm 0.69	
TG (mmol/L)	Normal	116	1.73 \pm 0.85	0.004
	Hypozincemia	60	2.12 \pm 0.85	

HDL-c : Hight Density Lipoprotein; LDL-c: Low Density Lipoprotein; TG: Triglyceride

Hypozincemia was found in 66% of children and was associated with low values of lipid profile parameters with a significant difference for TC, HDL-c and TG.

Table 3: Correlation of zinc with lipid profile parameters

Parameters	r	p-value
Total cholesterol	0.314	< 0.001
HDL-c	0.326	< 0.001
LDL-c	0.200	0.008
Triglyceride	0.229	0.002

HDL-c : Hight Density Lipoprotein; LDL-c: Low Density Lipoprotein; TG: Triglyceride

There is a weak positive correlation between lipid profile parameters and zinc.

4. DISCUSSION

Hypozincemia associated with malnutrition is frequently observed in children in developing countries [7,8]. Transient zinc deficiency is common in breastfed infants with a significant or unmet need for feeding or breastfeeding [9]. Our population is mainly made up of children over 6 months of age (Fig 1). This phase corresponds to the end of exclusive breastfeeding with the gradual introduction of semi-solid and then solid foods [10]. Failure to meet nutritional needs, which are high due to growth and functional development, can be the cause of malnutrition [11]. Severe acute malnutrition is observed in 49% of the population (Fig 1). The prevalence of hypozincemia is 66% in our study (Table 2). It was observed in all three groups of malnourished people (Table 1) with a significant difference ($p = 0.047$). Several studies have demonstrated a frequency of hypozincemia in the global population [12,13] particularly in malnourished children. Compared to healthy children, serum zinc levels are consistently higher than those of malnourished children [13, 14]. Zinc homeostasis is dependent on diet and its bioavailability, which are a function of intestinal absorption and losses [15]. Molecules such as phytate found in cereals, the main sources of food at this age, and vegetables can inhibit zinc absorption after reduction [2, 16]. Nearly 32.4% and 26.7% of our cohorts had diarrhea and dehydration, respectively (Fig 2). Zinc deficiency has been shown to reduce the absorption of water and electrolytes in the gut [17]. In their study, the authors, Alam J et al. [18] demonstrated that the association of diarrhea, dehydration, and fever was lower in children supplemented with zinc. In all areas where zinc supplementation interventions were performed in children, all-cause of hospitalizations and diarrhea decreased [19, 20]. According to Walker [21], zinc deficiency was responsible for 14.4% of diarrhea deaths in children aged 6 months to 5 years. weight loss and lack of appetite are the main clinical signs found (Fig 2). In a randomized study [22], zinc supplementation has been shown to increase the appetite of children aged from 6 to 12 months. At the same time, it reduces the incidence of diarrhea by 18% and its duration by 15% [23]. Among the complications observed, anemia and vomiting are mainly found, 86% and 64% respectively (Fig 2). Due to the involvement of zinc as a cofactor of enzymes involved in iron metabolism, hypozincemia is often associated with iron deficiency anemia [24]. The meta-analysis conducted by Rouhani's on randomized clinical trials revealed that zinc supplementation with a dose of 10 mg/d or more zinc supplementation, a maximum of 11 months of supplementation, in children under 5-year has significantly reduced the risk of all-cause mortality [25].

For lipid profile, with the exception of hypohdlmia, all other parameters were within normal limits. Nevertheless, a significant difference was observed between the different groups of malnourished. Total cholesterol, LDL-c, HDL-

c, and triglyceridemia are lower in children with hypozincemia (table 2). They are positively correlated with zincemia (table 3) $r=0.314$ ($p<0.001$); HDL-c, $r = 0.326$ ($p<0.001$), LDL-c, $r = 0.200$ ($p = 0.008$). These results are partly confirmed by the Van Biervliet study [26], which showed that infants with lower serum Zn concentrations had significantly lower cholesterol, LDL-c and apo B levels than those with higher concentrations. However, no such association was observed with HDL-c in older children (1 to 14 years). Similarly, the Fan study [27] of 5404 children and teenagers aged 6 to 19 years showed a positive association between zinc and increased cholesterol in men, while an inverse relationship is observed between serum zinc and HDL-c concentration in both men and women. No effect of zinc supplementation was observed on cholesterol based on the Ceballos Rasgado meta-analysis [28] including three studies conducted in children less than three months of age and more than 12 months of age. However, out of thirteen studies, only four have shown that zinc supplementation increases the incidence of vomiting [28].

For adults, Partida-Hernandez [29] demonstrated that zinc supplementation in diabetics improved HDL-c and LDL-c concentrations and reduced those of TC and TG. The Övermöhle study [30] conducted in the general population in northern Germany also demonstrated that LDL-c concentrations were much higher in group 3 which had high zinc levels compared to the other groups. On the other hand, the meta-analysis by Foster [31] including 20 studies found that zinc supplementation did not have a conclusive effect on most plasma lipoproteins except for HDL-c, which showed a decrease in their concentrations, which is a risk factor for the occurrence of cardiovascular disease. Five years later, Ranasinghe's study [32] confirmed this hypothesis demonstrating that zinc supplementation reduces total cholesterol, LDL cholesterol and triglycerides in subjects with metabolic diseases such as diabetes, kidney failure and myocardial infarction.

Hernandez-Mendoza [33] demonstrated an association between serum Zn and LDL-c levels as a function of sex. Indeed, his results showed that serum Zn is negatively associated with LDL-c but only in women. Regarding triglycerides, higher Zn consumption was associated with elevated TGs [34].

With reference to all these results, we can say that the effect of zinc on lipid profile is a function of age, sex and the clinical context of the study population.

5. CONCLUSION

Our study showed that the prevalence of hypozincemia is very high in malnourished children under five years of age. With the exception of LDL-c,

hypo-zincemia is significantly associated with a decrease in other lipid profile parameters. This result is supported by the weak positive correlation observed between zinc and the latter. In malnourished children, monitoring for hypo-zincemia is then necessary to prevent secondary hypolipidemia. However, in our context, zinc could play an important role in the prevention of atherogenic dyslipidemia.

DEFINITIONS, ACRONYMS, ABBREVIATIONS

TC : TOTAL CHOLESTEROL

HDLC : HIGH DENSITY LIPOPROTEIN CHOLESTEROL

LDLC : LOW DENSITY LIPOPROTEIN CHOLESTEROL

MAM : MODERATE ACUTE MALNUTRITION)

SAM: SEVERE ACUTE MALNUTRITION

WHO: WORLD HEALTH ORGANISATION

ZN: ZINC

COMPETING INTERESTS

The authors state that they have no conflicts of interest.

CONSENT (WHEREVER APPLICABLE)

All children were included after written consent from their parents.

ETHICAL APPROVAL (WHEREVER APPLICABLE)

The ethics committee of Cheikh Anta Diop University Ref approved the study: CER/UCAD/AD/MSN/015/2020.

Disclaimer (Artificial intelligence)

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REFERENCES

1. Saper RB and RASH R. Zinc: An Essential Micronutrient. Am Fam Physician. 2009; 79 (9): 768. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2820120/>
2. Kogan S, Sood A and Garnick MS. Zinc and Wound Healing: A Review of Zinc Physiology and Clinical Applications. Wounds. 2017; 29 (4): 102-106. Available: <https://pubmed.ncbi.nlm.nih.gov/28448263/>
3. Read SA, Obeid S, Ahlenstiel C and Ahlenstiel G. The Role of Zinc in Antiviral Immunity. Adv Nutr. 2019; 10 (4): 696-710. Available: <https://doi.org/10.1093/advances/nmz013>.
4. Kouame KSA, Verga ME, Pittet A, Rey-Bellet CG, Gehri M, Fontaine O and al. Zinc et diarrhées chez les enfants de moins de cinq ans : les recommandations de l'OMS applicables en Suisse ? Rev Med Suisse. 2012, 344 (22): 1244-1247. DOI: 10.53738/REVMED.2012.8.344.1244. French
5. World Health Organisation. WHO child growth standards : growth velocity based on weight, length and head circumference : methods and development. 2009. Available: <https://www.who.int/tools/child-growth-standards/standards>.
6. Schneider JM, Mary LF, Lamp CL, Lönnerdal B and Zidenberg-Cherr S. The Prevalence of Low Serum Zinc and Copper Levels and Dietary Habits Associated with Serum Zinc and Copper in 12- to 36-Month-Old Children from Low-Income Families at Risk for Iron Deficiency. Journal of

- the American Dietetic Association. 2007; 107 (11): 1924-29. Available: <https://doi.org/10.1016/j.jada.2007.08.011>.
7. Willoughby JL and Bowen CN. Zinc deficiency and toxicity in pediatric practice. *Current Opinion in Pediatrics*. 2014, 26 (5): 579. <https://doi.org/10.1097/MOP.000000000000132>.
 8. Fischer Walker CL, Ezzati M and Black R. E.Global and Regional Child Mortality and Burden of Disease Attributable to Zinc Deficiency . *Eur J Clin Nutr*. 2009, 63 (5) ; 591–97. <https://doi.org/10.1038/ejcn.2008.9>.
 9. El Fékih N, Monia K, Schmitt S, Dorbani I, Küry S and Kamoun M R. Transient symptomatic zinc deficiency in a breast-fed infant: Relevance of a genetic study. 2011, *Nutrition* 27 (10): 1087-89. <https://doi.org/10.1016/j.nut.2011.06.002>.
 10. Lemoine A. Diversification de l'alimentation du nourrisson. *La Revue Du Praticien*. 2021, 71 (10): 1080-83. Available : <https://www.larevuedupraticien.fr/article/diversification-de-l'alimentation-du-nourrisson>. French
 11. Matonti L, Blasetti A and Chiarelli F. Nutrition and Growth in Children. *Minerva Pediatrica*, 2020, 72 (6): 462-71. <https://doi.org/10.23736/S0026-4946.20.05981-2>.
 12. Cediél G, Olivares M, Brito A, Cori H and De Romaña DL. Zinc Deficiency in Latin America and the Caribbean ». *Food and Nutrition Bulletin*. 2015; 36 (2 Suppl): S129-138. <https://doi.org/10.1177/0379572115585781>.
 13. Ahsan AK, Sameer ST, Sangi R, Kamran A, Zaidi ZA, Haque T and al. Zinc Micronutrient Deficiency and Its Prevalence in Malnourished Pediatric Children as Compared to Well-Nourished Children: A Nutritional Emergency. *Global Pediatric Health*. 2021; 8 : 1-6. <https://doi.org/10.1177/2333794X211050316>.
 14. Gautam B, Deb K, Banerjee M, Ali MS, Akhter S, Shahidullah SM and Hoque MR. Serum Zinc and Copper Level in Children with Protein Energy Malnutrition. *Mymensingh Medical Journal*. 2008; 17 (2 Suppl): S12-15. Available: <https://pubmed.ncbi.nlm.nih.gov/18946444/>
 15. Krebs NF. Update on Zinc Deficiency and Excess in Clinical Pediatric Practice. *Ann NutrMetab*. 2013; 62 (1): 19-29. <https://doi.org/10.1159/000348261>
 16. Ackland ML, Michalczyk AA. Zinc and infant nutrition ». *Arch BiochemBiophys*. 2016, 611:51-57. <https://doi.org/10.1016/j.abb.2016.06.011>.
 17. Qadir MI, Arshad A, Ahmad B. Zinc: Role in the management of diarrhea and cholera. *World J Clin Cases*. 2013, 1(4): 140-142. <https://doi.org/10.12998/wjcc.v1.i4.140>.
 18. Alam J, Nuzhat S, Billal S Md, Ahmed T, Khan AI and Iqbal Hossain Md. Nutritional Profiles and Zinc Supplementation among Children with Diarrhea in Bangladesh. *Am. J. Trop. Med. Hyg*. 2023, 108(4); 837–43. <https://doi.org/10.4269/ajtmh.22-0532>.

19. Black RE, Walker CF. Role of Zinc in Child Health and Survival. Nestle Nutr Inst Workshop Ser. 2012;70:37-42. <https://doi.org/10.1159/000337393>.
20. Brown KH, Peerson JM., Baker SK and Hess SY. Preventive Zinc Supplementation among Infants, Preschoolers, and Older Prepubertal Children. Food and Nutrition Bulletin. 2009;30 (1 Suppl): S12-40. <https://doi.org/10.1177/15648265090301S103>.
21. Walker CLF, Ezzati M, Black R E. Global and regional child mortality and burden of disease attributable to zinc deficiency. Eur J Clin Nutr. 2009; 63, 591–597. <https://doi.org/10.1038/ejcn.2008.9>.
22. Umeta, M., C. E. West, J. Haidar, P. Deurenberg, et J. G. Hautvast. « Zinc Supplementation and Stunted Infants in Ethiopia: A Randomised Controlled Trial ». Lancet (London, England).2000; 355 (9220): 2021–26. [https://doi.org/10.1016/S0140-6736\(00\)02348-5](https://doi.org/10.1016/S0140-6736(00)02348-5).
23. Walker CF and Black RE. Zinc and the Risk for Infectious Disease. Annual Review of Nutrition. 2004; 24 (1): 255–75. <https://doi.org/10.1146/annurev.nutr.23.011702.073054>.
24. Ergul AB, Turanoglu C, Karakukcu c, Karaman S and Torun YA. Increased Iron Deficiency and Iron Deficiency Anemia in Children with Zinc Deficiency. The Eurasian Journal of Medicine. 2018; 50 (1): 34–37. <https://doi.org/10.5152/eurasianjmed.2017.17237>.
25. Rouhani Parisa, Kelishadi M R, Saneei P. Effect of zinc supplementation on mortality in under 5 year children: a systematic review and meta analysis of randomized clinical trials. Eur J Nutr. 2022, 61(1):37-54. doi: 10.1007/s00394-021-02604-1.
26. Van Biervliet S, Van Biervliet JP, Bernard D, Vercaemst R and Blaton V. Serum Zinc in Healthy Belgian Children. Biol Trace Elem Res. 2003;94 (1): 33–40. <https://doi.org/10.1385/BTER:94:1:33>.
27. Fan Y, Zhang C,Bu J. Relationship between Selected Serum Metallic Elements and Obesity in Children and Adolescent in the U.S. Nutrients.2017;9 (2): 104. <https://doi.org/10.3390/nu9020104>.
28. Ceballos-Rasgado M, Lowe NM, Mallard S, Clegg A, Moran VH, Harris C, and al. Adverse Effects of Excessive Zinc Intake in Infants and Children Aged 0-3 Years: A Systematic Review and Meta-Analysis. Adv Nutr. 2022;13:2488–2518. <https://doi.org/10.1093/advances/nmac088>.
29. Partida-Hernández G, Arreola F, Fenton B, Cabeza M, Román-Ramos R and Revilla-Monsalve MC. Effect of Zinc Replacement on Lipids and Lipoproteins in Type 2-Diabetic Patients. Biomedicine & Pharmacotherapy. 2006; 60 (4): 161–68. <https://doi.org/10.1016/j.biopha.2006.02.004>.
30. Övermöhle C, Rimbach G, Waniek S, Strathmann EA, Liedtke T, Stürmer P and al. Association of Plasma Zinc and Copper with Body Composition, Lipids and Inflammation in a Cross-Sectional General Population Sample

from Germany. *Nutrients*.2023; 15 (20): 4460.
<https://doi.org/10.3390/nu15204460>.

31. Foster M, Petocz P and Samman S. Effects of Zinc on Plasma Lipoprotein Cholesterol Concentrations in Humans: A Meta-Analysis of Randomised Controlled Trials. *Atherosclerosis*. 2010, 210 (2): 344-352. doi:10.1016/j.atherosclerosis.2009.11.038.
32. Ranasinghe P, Wathurapatha WS, Ishara MH, Jayawardana R, Galappatthy P, Katulanda P and al. Effects of Zinc supplementation on serum lipids: a systematic review and meta-analysis. *Nutrition & Metabolism*. 2015; 12 : 26. <https://doi.org/10.1186/s12986-015-0023-4>.
33. Hernández-Mendoza H, Martínez-Navarro I, Hernández-Ochoa E, Espinoza-Ruiz M, Lugo-Trampe A, Trujillo-Murillo KDC and al. Serum Zinc Levels Are Associated with Obesity and Low-Density Lipoprotein Cholesterol in Mexican Adults. *Journal of Trace Elements in Medicine and Biology*. 2022;73 :127002. <https://doi.org/10.1016/j.jtemb.2022.127002>.
34. Hininger-Favier I, Andriollo-Sanchez M, Arnaud J, Meunier N, Bord S, Graham S and al. Age- and Sex-Dependent Effects of Long-Term Zinc Supplementation on Essential Trace Element Status and Lipid Metabolism in European Subjects: The Zenith Study. *The British Journal of Nutrition*. 2007; 97 (3): 569-578. <https://doi.org/10.1017/S0007114507432974>.