Asian Journal of Biochemistry, Genetics and Molecular Biology

Volume 16, Issue 11, Page 44-52, 2024; Article no.AJBGMB.125887
ISSN: 2582-3698

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

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/ajbgmb/2024/v16i11416

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/125887

Original Research Article

Received: 16/08/2024
Accepted: 30/10/2024
Published: 05/11/2024

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***Cite as:** Coly, Najah Fatou, Basse I, Kane EHI, Ka P A, Thiam S, Samba A, Ndiaye A, Soumah IY, Diedhiou F, Cissé F, Diouf N N, Djité M, Barry N O K, Kandji PM, Gueye PM, Diagne Gueye ND R, and Agne F D. 2024. "Zinc Deficiency and Impact on Lipid Profiles in Malnourished Children in Senegal". Asian Journal of Biochemistry, Genetics and Molecular Biology 16 (11):44-52. https://doi.org/10.9734/ajbgmb/2024/v16i11416.*

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.
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 ($r=0.314$; < 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.

ABBREVIATIONS

TC : Total Cholesterol
HDLC : Hight Density Lipoprotein Cholesterol
LDLC : Low Density Lipoprotein Cholesterol
MAM : Moderate Acute Malnutrition)
SAM : Severe Acute Malnutrition
WHO : World Health Organisation
ZN : Zinc

1. INTRODUCTION

Zinc ranks second after iron, as a metal that is very abundant in the body (Saper and Rash 2009). 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 (Kogan et al. 2017). 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 (Read et al. 2019).

It is a powerful antioxidant that protects cells from the attack of free radicals and thus slows down their aging (Kouame et al. 2012). Zinc deficiency is one of the risk factors relating to malnutrition and is responsible for deaths in children under five years of age (Read et al. 2019).

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 (Kouame et al. 2012).

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. MATERIALS 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 (World Health Organisation 2009).

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-Nsulfopropy lamino)-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 (Schneider et al. 2007).

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

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).

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).

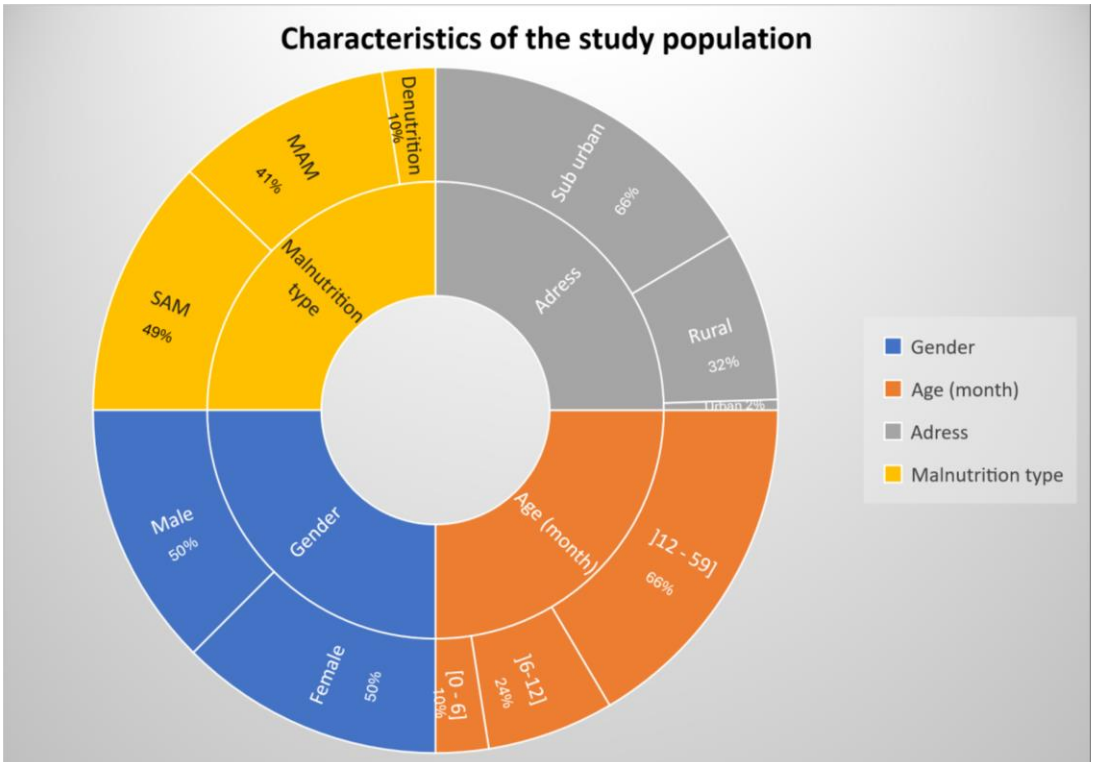

Fig. 1. Characteristics of the study population

MAM: Moderate Acute Malnutrition; SAM: Severe Acute Malnutrition

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).

4. DISCUSSION

Hypozincemia associated with malnutrition is frequently observed in children in developing countries (Willoughby and Bowen 2014, Fischer Walker et al. 2009). Transient zinc deficiency is common in breastfed infants with a significant or unmet need for feeding or breastfeeding (El Fékih et al. 2011). 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 (Lemoine 2021). Failure to meet nutritional needs, which are high due to growth and functional development, can be the cause of malnutrition (Matonti et al. 2020). 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 (Cediel et al. 2015, Ahsan et al. 2021). particularly in malnourished children. Compared to healthy children, serum zinc levels are consistently higher than those of malnourished children (Ahsan et al. 2021, Gautam et al. 2008). Zinc homeostasis is dependent on diet and its bioavailability, which are a function of intestinal absorption and losses (Krebs et al. 2013). Molecules such as phytate found in cereals, the main sources of food at this age, and vegetables can inhibit zinc absorption after reduction (Kogan et al. 2017, Ackland and Michalczyk 2016). 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 (Qadir et al. 2013). In their study, the authors, (Alam J et al. 2023) 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 (Black and Walker 2012, Brown et al. 2009). According to (Walker et al. 2009) 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 (Umeta et al. 2000) 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% (Walker and Black 2004). 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 (Ergul et al. 2018). 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 (Rouhani Parisa et al. 2022).

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

Type of malnutrition	Biological parameters				
	Zincemia (µg/dl)	Total cholesterol (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	TG (mmol/L)
Malnutrition	53.93 ± 31.81	2.66 ± 0.93	0.56 ± 0.15	0.79 ± 0.43	0.92 ± 0.35
MAM	65.90 ± 29.30	3.59 ± 1.31	0.68 ± 0.31	1.27 ± 0.80	0.83 ± 0.42
MAS	54.68 ± 27.27	3.10 ± 1.39	0.61 ± 0.41	1.09 ± 0.72	0.92 ± 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).

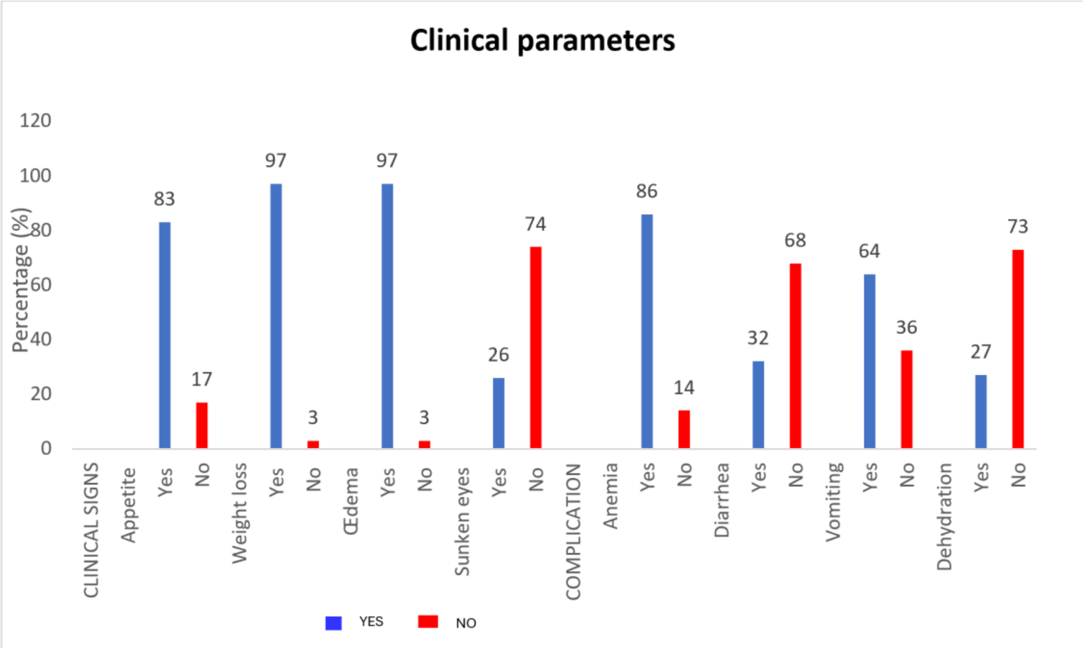

Fig. 2. Distribution of the population by clinical parameters and complications observed

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

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

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) ct, 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 (Van et al. 2003) 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 (Fan et al. 2017) 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 (Ceballos-Rasgado et al. 2022) 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 (Ceballos-Rasgado et al. 2022).

For adults, (Partida-Hernandez 2006) demonstrated that zinc supplementation in diabetics improved HDL-c and LDL-c concentrations and reduced those of TC and TG. The (Övermöhle study 2023) 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 2010) 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 (Ranasinghe et al. 2015) 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 2022) 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 (Hininger-Favier et al. 2007).

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, hypozincemia 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 hypozincemia is then necessary to prevent secondary hypolipidemia. However, in our context, zinc could play an important role in the prevention of atherogenic dyslipidemia.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

All children were included after written consent from their parents.

ETHICAL APPROVAL

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

ACKNOWLEDGEMENTS

We would like to thank the Research and Innovation Support Fund (FARI) of the Iba Der Thiam University of Thiès which financed the project.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/125887