



Relationship of Serum Zinc Levels with Cardiometabolic Traits in Overweight and Obese Schoolchildren from Mexico City

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Abstract

Zinc (Zn) participates as a cofactor for many enzymes in the cellular metabolism, and its serum levels have been associated with different metabolic diseases, especially obesity (OB). Nevertheless, its associations are not clear in the children population. The objective of this study is to evaluate the association between serum Zn levels (SZn) with overweight/obesity status (OW/OB), as well as its cardiometabolic traits in a population of children in Mexico City. Anthropometrical data (body mass index *z* score (BMI_z)), demographic variables (age and sex), and cardiometabolic traits (total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (TG), fasting plasma glucose (FPG), and insulin) were analyzed in this cross-sectional study. SZn were measured by inductively coupled plasma mass spectrometry (ICP–MS). The population included 210 children from Mexico City (girls (*n* = 105) and boys (*n* = 105)) between ages 6 and 10 years. Normal-weight (NW) schoolchildren had higher SZn concentrations (66 µg/dL; IQR: 48 to 91) compared to OW or OB schoolchildren (61 µg/dL; IQR: 45 to 76). The data showed a significant negative association between SZn and BMI_z without sex exclusion (*r* = −0.181 and *p* = 0.009). The boy's population did not show an association between the SZn and BMI_z compared to the girl's population which showed a significant negative association (*r* = −0.277 and *p* = 0.004). In addition, other associations were found between SZn and TC (boys (*r* = 0.214 and *p* = 0.025), LDLc (boys (*r* = 0.213 and *p* = 0.029), and TG (girls (*r* = −0.260 and *p* = 0.007)). Moreover, 38.6% of the total children in our population study had Zn deficiency (ZnD). NW schoolchildren had higher SZn concentrations compared to OW or OB schoolchildren. A diet low in Zn can be a factor to evaluate in the development of childhood OB in Mexico. However, further studies need to be performed on the children Mexican population to replicate and confirm our findings.

Keywords Serum zinc level · Body mass index *z* score · Overweight/obesity · Cardiometabolic traits · Schoolchildren

Abbreviations

BMI	Body mass index	IZiNCG	International Zinc Nutrition Consultative Group
BMI _z	Body mass index <i>z</i> score	LDLc	Cholesterol low-density lipoprotein
TC	Total cholesterol	NW	Normal weight
ENSANUT	The National Health and Nutrition Survey	OB	Obesity
FPG	Fasting plasma glucose	OW	Overweight
HDLc	Cholesterol high-density lipoprotein	SZn	Serum zinc levels
ICP–MS	Inductively coupled plasma mass spectrometry	TG	Triglycerides
		WC	Waist circumference
		Zn	Zinc

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Introduction

The prevalence of overweight/obesity (OW/OB) in schoolchildren has increased consistently around the world; in recent years, this prevalence has been considered a pandemic in many populations, especially those with high

incomes [1, 2]. However, today has been described that OW/OB are now on the rise in low- and middle-income populations [3].

OB is a multifactorial disease with genetic, environmental, behavioral, and sociocultural characteristics [4, 5]. In this context, many children with OB retain a high body mass index (BMI), which can be maintained or increased in adulthood, contributing to the development of cardiometabolic diseases [6], specifically type 2 diabetes, hypertension, and heart disease [7]. Moreover, OB has recently been associated with severity and mortality among the adult population with the COVID-19 [8, 9].

Mexico has shown a high prevalence of OW/OB in schoolchildren in the last 2 decades, and the National Health and Nutrition Survey found that three out of ten children have OW or OB [10]. The main factors of increases in OB have been the association of frequent intake of foods with high fat and sugar content and a more sedentary lifestyle. Nevertheless, Mexico has implemented new health policies focusing on food labeling as an alternative to prevent OB [11, 12], which are related to food education, lifestyle change, and time increases in daily exercise [13]. In addition, security food and traditional food programs have been carried out to decrease OB in the Mexican population. Some of these programs include the Strategic Project for Food Security between the Secretariat of Agriculture, Livestock, Rural Development, Fisheries and Food (SAGARPA) in collaboration with the FAO; the Sustainable Modernization of Traditional Agriculture program implemented by SAGARPA and the International Maize and Wheat Improvement Centre (CIMMYT) and Education, Health and Food Program (PROSPERA) by Education by the Secretary of Social Development that supports families to acquire and increase the variety and quantity of food [11, 14, 15].

Trace elements have an essential role in cellular metabolism, and a deficiency of these elements can lead to the incidence of OW and OB [16–18]. However, these findings do not show conclusive evidence. The main trace elements that have been studied and associated with OW/OB are zinc (Zn) and copper (Cu), followed by magnesium (Mg), chromium (Cr), and selenium (Se) [19–23]. In the case of Zn, this is an essential element present in several enzymes, and it participates in the mechanisms of energy metabolism by carbohydrates, proteins, and lipids [24, 25].

Serum Zn levels (SZn) are altered with OB due to oxidative stress and inflammatory processes [25–28], and Zn levels have been related to OB. However, the relationship between SZn and OW/OB is unclear in the children population. Recently, Fan et al. reported that Zn deficiency (ZnD) is an important cause of morbidity and mortality in the children population [19]. On the other hand, ZnD in children increases the risk of growth retardation [29–33],

insulin resistance [34–36], and neurological disorders [37, 38] and increased susceptibility to infections [39, 40].

The aim of this study was to measure SZn and its association with OW/OB and cardiometabolic traits (total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (TG), fasting plasma glucose (FPG), and insulin) in a population of schoolchildren from Mexico City.

Materials and Methods

Study Design

A cross-sectional study was carried out, and children from 6 to 10 years old were recruited from four elementary schools (two public and two private) selected by convenience in Mexico City and located in the same geographic area. Children with normal weight (NW), OW, or OB were included according to the BMIz [41]. Children with any disease or taking any medication that affected the metabolic profile were excluded.

Ethical Approval

The study was conducted according to the guidelines established in the Declaration of Helsinki and based on the Regulations of the General Health Law on Health Research in Mexico, based on articles 14 and 16. The research protocol was approved by Research, Ethics, and Biosecurity Committees from the Hospital Infantil de México Federico Gómez (approval register: HIM/2013/003) and by school authorities. Likewise, children and parents gave written assent and consent to participate in the study.

Measurements

Sociodemographic Characteristics

The parents answered a questionnaire that was sent to the home, and information was obtained on chronic diseases of the student and the level of education of the mother (secondary education or less, high school or technical school, and university or postgraduate studies). To evaluate the socioeconomic level of the families, information was obtained on the characteristics of the home and possession of goods such as refrigerators, washing machines, heaters, televisions, computers, ovens, internet, automobiles, and landline telephones. Principal component analysis was used, and considering the score obtained, the households were divided into categories of socioeconomic level in tertiles (low, medium, and high) based on the score obtained.

Anthropometry

Anthropometric parameters were registered by two previously trained nutritionists using standardized international anthropometric procedures [42]. Weight was measured with a balance (SECA model-882, SECA Corp., Hamburg, Germany) to the nearest 0.1 kg, and height was measured on a stadiometer (SECA model-225, SECA Corp., Hamburg, Germany) with a precision of 0.1 cm. Waist circumference was measured with a nonelastic flexible measuring tape (Seca 200). The measurements were carried out without shoes and wearing light clothing, standing in the middle of the scale platform or stadiometer, arms resting freely by their sides, with their heads in the Frankfurt horizontal plane. BMI_z was obtained using the children's age, weight, height, and sex, which were classified as NW (z score ≥ -2 to <1), OW (z score ≥ 1 to <2), and OB (z score ≥ 2), according to standards provided by the World Health Organization [43]. Waist circumference was used as a proxy to assess central visceral adiposity, and the waist circumference percentile was calculated considering age, sex, and height using the waist circumference tables of Mexican children [44].

Biochemical Determinations

Serum sample collection

A sample of 5 mL of peripheral blood was collected by venipuncture from each participant after a 12 h fast in a sterile vacutainer tube. Separation of serum was performed in the following steps: (a) total blood sample was allowed to stand for 20 min, (b) separation of serum by centrifugation in glass tubes at $3000 \times g$ for 10 min to 4 °C, and (c) all serum samples were stored in Eppendorf tubes at -80 °C.

Analysis of TC, HDLc, LDLc, TG, and FPG was performed by commercial kits, and measures were carried out at LAB 300, Instrumentation Laboratory, Barcelona, Spain. For LDLc, DeLong's modified Friedwald formula was utilized [45]. Insulin was determined by chemiluminescence immunoassay (IMMULITE 2000, Euro, DPC, Llanberis, UK).

Analysis of Zn by ICP–MS

SZn quantification was performed with inductively coupled plasma mass spectrometry (ICP–MS iCAP Q, Thermo Scientific, Germany) following the protocol proposed by Rios Lugo et al. [46]. Samples were traced with indium (In; $10 \mu\text{g L}^{-1}$) and mineralized with a microwave system (MARS6 CEM, Matthews, North Carolina) before analysis of total Zn with ICP–MS. The mineralization process was realized with 8 mL HNO₃ in two steps (ramp of temperature to 200 °C and holding for 15 min). Finally, samples were recovered

and evaporated to dryness and diluted to 10 mL with 2% v/v HNO₃. SZn quantification in samples was performed by an external calibration curve of Zn (10, 25, 50, 75, 100, 200, 500, and 1000 $\mu\text{g L}^{-1}$). Moreover, contribution contamination in the analysis was considered by calculating SZn in samples (blank reagents), as well as the recovery of an internal standard (In), final volume (10 mL), and sample volume (0.1 mL). Concentrated high-purity HNO₃ (Milestone Duopur system Milestonesrl, Italia) and high-purity water with 18 M Ω cm (Milli-Q® system Millipore, México) were used in the sample preparation. In addition, Zn standards were obtained from the High-Purity Standards (North Charleston, USA).

Data Analysis

Analysis was performed with SPSS® v20.0 (SPSS Inc., Chicago, Illinois). Measures of central tendency were used to describe the baseline characteristics of the study population. Weight and height measurements were adjusted for age and sex using multiple linear regression. For statistical analysis, the categories of OW and OB (OW/OB) were combined and compared to children with NW to balance the sample size and provide greater statistical stability. The normality of the continuous variables was evaluated using the Kolmogorov–Smirnov test, indicating a non-normal distribution of the data. In this case, the medians and interquartile range (IQR) were obtained for continuous data without normal distribution and percentages for categorical variables. The Mann–Whitney U test was used to compare age, anthropometric measurements, SZn, and metabolic parameters according to nutritional status. To determine which variables were related to ZnD, the study population was divided into two groups based on SZn, one below the cutoff value ($<70 \mu\text{g/dL}$) and one above the cutoff value ($>70 \mu\text{g/dL}$) according to the International Zinc Nutrition Consultative Group (IZiNCG) [47]. For age, sex, BMI, waist circumference (WC), and biochemical status, Mann–Whitney U test was used, while socioeconomic variables were analyzed using the Pearson X^2 test. In addition, Spearman linear correlation was carried out to evaluate the correlations between SZn and BMI_z, WC, FPG, TC, TG, LDLc, HDLc, and insulin. P values <0.05 were considered statistically significant for all analyses.

Results

General Characteristics of the Study Population

The general characteristics of the population are shown in Table 1. The median age of the children population was

8.0 ± 1.1 years. Statistically significant differences were found in the anthropometric variables (weight, height, BMIz, and WC) according to nutritional status ($p < 0.05$). In addition, school type in the children population showed a significant statistical difference ($p = 0.025$).

Biochemical Profile

The girls' metabolic profile showed statistically significant differences between girls with normal weight and those with OW/OB (Table 2). Girls with OW/OB had higher concentrations of FPG ($p = 0.043$), TC ($p = 0.001$), TG ($p < 0.001$), LDLc ($p < 0.001$), and insulin ($p < 0.001$), while HDLc was higher in girls with NW ($p = 0.004$). Boys with OW or OB had higher concentrations of FPG ($p = 0.001$), TG ($p < 0.001$), and insulin ($p < 0.001$), while boys with NW also had higher concentrations of HDLc ($p = 0.02$) in comparison to boys with OW and OB.

Zn Levels According to Nutritional Status and Sex

SZn levels in the children according to nutritional status and sex are shown in Fig. 1. SZn showed significant differences between the schoolchildren with NW and the schoolchildren with OW/OB ($p = 0.033$), where SZn values in OW/OB had a median of 61 µg/dL (IQR: 45 to 76) versus those in NW who showed a concentration of 66 µg/dL (IQR: 48 to

Table 2 Biochemical parameters in schoolchildren according to nutritional status

Traits	Normal weight	Overweight/obesity	* p
	Median (Q1–Q3)	Median (Q1–Q3)	
Boys			
FPG (mg/dL)	85 (80 to 89.2)	90 (86.2 to 93.7)	0.001
TC (mg/dL)	160 (146 to 180)	166 (149 to 178)	0.432
TG (mg/dL)	58 (44.5 to 81)	67 (59.2 to 108.5)	<0.001
HDLc (mg/dL)	54 (48 to 66)	52 (40 to 54)	0.02
LDLc (mg/dL)	94 (80.2 to 115.2)	97 (80.7 to 113.5)	0.273
Insulin (µU/mL)	2.1 (2.0 to 3.2)	2.8 (2.6 to 6.5)	<0.001
Girls			
FPG (mg/dL)	83 (80 to 89)	87 (81.7 to 91)	0.043
TC (mg/dL)	152 (138 to 172)	167 (157.2 to 187)	0.001
TG (mg/dL)	57 (47.5 to 87)	75 (68 to 120.7)	<0.001
HDLc (mg/dL)	51 (43 to 57.5)	47 (36.7 to 52.2)	0.004
LDLc (mg/dL)	92 (80 to 103)	99 (92.7 to 121)	<0.001
Insulin (µU/mL)	2.6 (1.9 to 4.5)	3.9 (3.8 to 10.6)	<0.001

Data are presented as median value and interquartile ranges (Q1, Q3). *Mann–Whitney U test. Abbreviations: FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol

Table 1 General characteristics of the study population by nutritional status

Traits	Normal weight	Overweight/obesity	p
	$n = 103$	$n = 107$	
	Median (Q1–Q3)	Median (Q1–Q3)	
Age ^a (years)	7.8 (6.9 to 8.8)	8.2 (7.4 to 9.2)	0.018
Sex, female, n (%)	45 (43.7)	60 (56.1)	0.168
Weight (kg) ^{ac}	30.8 (27 to 36)	33.8 (29 to 38)	0.017
Height (cm) ^{ac}	125.8 (121 to 132)	129.2 (124 to 135)	0.018
BMI z score ^a	−0.11 (−0.82 to 0.54)	1.88 (1.4 to 2.5)	<0.001
WC (percentile) ^a	55.2 (52 to 59)	67.9 (62 to 74)	<0.001
Socioeconomic level [$n = 193$ (%)] ^b			
Lower	30 (32)	22 (22.2)	0.141
Medium	36 (38.3)	34 (34.4)	
Higher	28 (29.7)	43 (43.4)	
School (%) ^b			
Public	40 (40)	61 (55.5)	0.025
Private	60 (60)	49 (44.5)	
Maternal schooling [$n = 201$ (%)] ^b			
Secondary or less	17 (17.7)	11 (10.5)	0.362
High school or technical school	37 (38.5)	37 (35.2)	
College career or postgraduate	42 (43.8)	57 (54.3)	

Data are presented as median value and interquartile ranges (Q1, Q3). ^aMann–Whitney U test, ^bPearson's X^2 test, ^cMedians adjusted by age and sex. Abbreviations: BMI, body mass index; WC, waist circumference

91). These results were independent of sex. In addition, our study did not find statistically significant differences in SZn according to sex ($p=0.813$). In the case of ZnD, the results showed that 38.5% of the children were below the cutoff value established according to the IZiNCG.

Zn Cutoff Value and Anthropometric, Biochemical, and Socioeconomic Variables

We did not find a relationship between age or sex with SZn using the cutoff value, nor did we find statistically significant differences with BMIz. Notably, those children with higher WC were related to SZn levels below the cutoff value ($p=0.038$). Regarding biochemical measures, we found that children with ZnD had lower LDLc and insulin levels compared to children without ZnD ($p<0.05$). Moreover, the results obtained did not reveal statistically significant differences from the other biochemical parameters (Table 3). This last finding was reinforced when we evaluated the type of school, where the highest deficiency was found in children attending private schools. Finally, focusing only on the population below the cutoff value, we found a higher ZnD in children whose mothers had a higher level of education.

Associations Between Zn Levels and BMIz and Biochemical Profile

The results obtained for the correlations between SZn, BMIz, and cardiometabolic traits are shown in Table 4. Our study found a negative correlation between Zn levels and BMIz ($r=-0.181$, $p=0.009$). In addition, the BMIz showed positive correlations with WC, FPG, TC, TG, LDLc,

and insulin without difference by sex, except for HDLc ($r=-0.396$, $p\leq 0.001$). The boys' population showed a positive correlation between SZn and TC and LDLc. Moreover, negative correlations were found between SZn and BMIz ($r=-0.277$, $p\leq 0.004$), FPG ($r=-0.229$, $p\leq 0.019$), and TG ($r=-0.260$, $p\leq 0.007$) in the female population.

Discussion

Our work determined SZn levels in a population of children in Mexico City and showed that more than one-third of the study population had ZnD according to the cutoff established by IZiNCG [47, 48]. Our finding is consistent with other studies on the Mexican children, which have shown that the Mexican children have ZnD [49–52]. Likewise, other studies performed on the Latin American population showed similar results [53–57]. On the other hand, our results did not show significant differences in the age and sex distribution between the population studied with and without ZnD. Nevertheless, the study by Pullakhandam et al. mentioned that ZnD is higher in adolescents than in children because the requirements increase in the development stage [58].

Studies have shown evidence about the SZn and its relationship with OW and OB in humans [46, 59–62], but the data has not even been clear. Our study found a statistically significant difference between the population of children with OW/OB and NW (Fig. 1). These results are consistent with other performed studies on populations from Egypt, Korea, and India [63–65]. In contrast, Weisstaub et al. reported the absence of a relationship between SZn and OW/OB in a population of Chilean preschool children [66].

Fig. 1 Comparison of SZn among the population of Mexican children with respect to nutritional status and sex ($n=210$). **A** There was a difference between the nutritional condition (Mann–Whitney U test) **B** There was no difference between the two sex groups (Mann–Whitney U test)

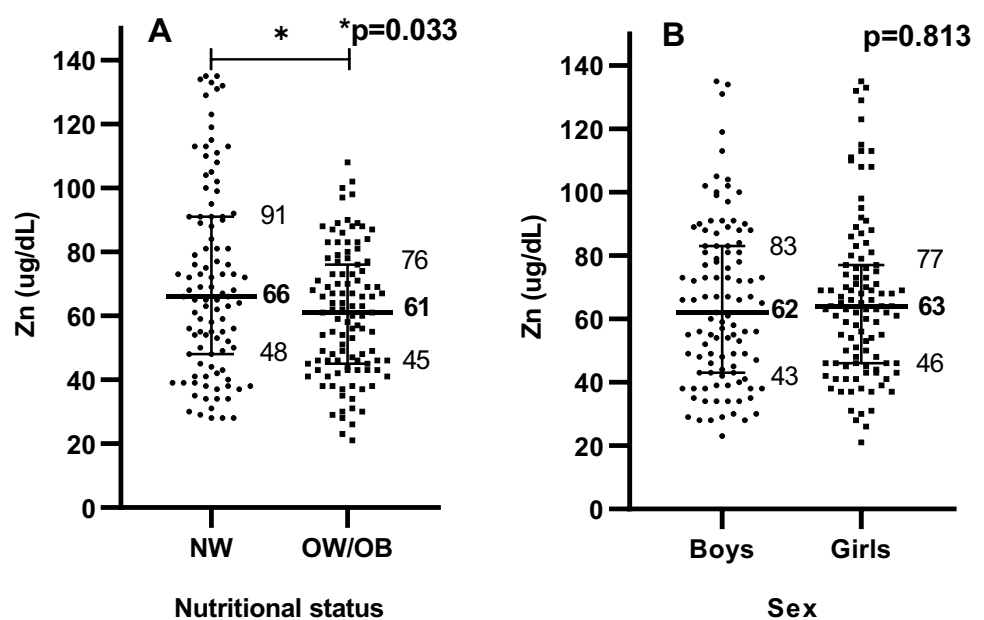


Table 3 Comparison between serum Zn cut value and anthropometric, biochemical, and socioeconomic variables

Trait	Zn ($\mu\text{g/dL}$)		<i>p</i>
	< 70	> 70	
	<i>n</i> = 81 (38.6%)	<i>n</i> = 129 (61.4%)	
	(27.85–66.43)	(71.91–133)	
Age (years) ^d	8.0 (6.8 to 8.9)	8.0 (7.1 to 9.06)	0.323
Sex, female [<i>n</i> = 210 (%)] ^a	33 (40.7)	69 (53.5)	0.114
BMI <i>z</i> score ^{bd}	0.91 (0.32 to 2.06)	1.12 (–0.11 to 2.12)	0.451
BMI <i>z</i> score (%) ^{bc}			
NW	32 (45.1)	51 (40.5)	0.945
OW/OB	39 (54.9)	75 (59.5)	
WC (percentile) ^d	61.9 (54 to 68.8)	61.5 (54.2 to 68.5)	0.038
Biochemical status ^d			
FPG (mg/dL)	87 (81 to 90)	86 (81 to 91)	0.86
TC (mg/dL)	160 (143 to 173)	167 (150 to 186)	0.093
TG (mg/dL)	69.5 (49.5 to 105.5)	73 (54 to 98)	0.631
HDLc (mg/dL)	48.5 (39 to 54.7)	49 (41 to 56.3)	0.925
LDLc (mg/dL)	93.7(80.65 to 113.7)	101.8 (87 to 117.1)	0.033
Insulin($\mu\text{U/mL}$)	2.8 (1.99 to 5.53)	3.8 (2.22 to 6.98)	0.034
Socioeconomic level [<i>n</i> = 196 (%)] ^a			
Lower	19 (27.6)	32 (25.2)	0.767
Medium	23 (33.3)	48 (37.8)	
Higher	27 (39.1)	47 (37.0)	
School [<i>n</i> = 214 (%)] ^a			
Public	22 (27.5)	72 (53.7)	<0.001
Private	58 (72.5)	62 (46.3)	
Maternal schooling [<i>n</i> = 204 (%)] ^a			
Secondary or less	17 (22.7)	12 (9.3)	0.011
High school or technical school	30 (40.0)	47 (36.4)	
College career or postgraduate	28 (37.3)	70 (54.3)	

Data are presented as two groups one below the cutoff value. ^a(Pearson χ^2) test, ^bBMI: body mass index, ^c World Health Organization, 2007, ^dMann–Whitney *U* test. Abbreviations: NW normal weight, OW overweight, OB obesity, WC waist circumference, BMIz body mass index *z* score, FPG fasting plasma glucose, TC total cholesterol, TG triglycerides, HDLc, high-density lipoprotein cholesterol, LDLc low-density lipoprotein cholesterol

Likewise, Jaksic et al. found no association between SZn levels and BMIz in a population of Montenegro children [67].

No significant differences were found between BMIz and WC by sex in our children's population. Our study found that a higher WC percentile had lower SZn despite having a normal BMIz. This indicates that BMIz and WC should be taken into account in the evaluation of trace element deficiency as has been reported by Zohal et al. [68] and Kim et al. [69]. These authors reported that low SZn levels and other trace elements are related to increases in WC and BMIz.

Childhood OB can cause metabolic and hormonal changes [70, 71]. In this way, the prevalence of OW/OB was > 50% in our population, where the prevalence was higher in girls. Our results exceeded the values reported by government institutions from Mexico [72, 73]. Nevertheless,

these results differ from those reported by Del Monte et al. [74], where a higher prevalence of OW/OB was indicated in the child population. Moreover, our results showed significant differences between public and private schools for the values of BMIz and SZn.

Low socioeconomic status and low maternal education are associated with an increase in OW/OB in the child population [75–77]. However, the findings have been unclear because, in the Asian population, a relationship was reported between a high maternal education level and a higher prevalence of OW/OB in the child population [78–80]. In contrast, in the Western population, maternal education level was negatively associated with the prevalence of OW/OB [81, 82]. In this case, our study did not show significant differences between the maternal education level and the socioeconomic level.

Table 4 Correlations between Zn, BMIz, WC, and biochemical variables and insulin in the schoolchildren

Variable	BMIz		WC		FPG		TC		TG		HDLc		LDLc		Insulin	
	r*	p*	r*	p*	r*	p*	r*	p*	r*	p*	r*	p*	r*	p*	r*	p*
SZn	-0.181	0.009	-0.085	0.217	-0.033	0.637	0.036	0.601	-0.092	0.183	0.064	0.359	0.067	0.334	-0.021	0.758
BMIz			0.761	< 0.001	0.265	< 0.001	0.197	0.004	0.43	< 0.001	-0.396	< 0.001	0.265	< 0.001	0.491	< 0.001
WC					0.272	< 0.001	0.207	0.002	0.340	< 0.001	-0.307	< 0.001	0.267	< 0.001	0.504	< 0.001
FPG							0.13	0.057	0.123	0.072	-0.004	0.956	0.125	0.066	0.26	< 0.001
TC									0.314	< 0.001	0.276	< 0.001	0.92	< 0.001	0.164	0.015
Boys (n = 105)																
SZn	-0.084	0.395			-0.026	0.795	0.214	0.028	0.051	0.605	0.035	0.724	0.213	0.0029	0.105	0.285
BMIz					0.318	< 0.001	0.159	0.097	0.418	< 0.001	-0.370	< 0.001	0.221	0.020	0.415	< 0.001
FPG							0.076	0.431	0.168	0.079	-0.051	0.600	0.098	0.310	0.279	0.003
TC									0.312	< 0.001	0.244	0.01	0.912	< 0.001	0.113	0.238
Girls (n = 105)																
SZn	-0.277	0.004			-0.229	0.019	-0.117	0.235	-0.26	0.007	0.600	0.54	-0.040	0.686	-0.098	0.319
BMIz					0.136	0.162	0.254	0.008	0.477	< 0.001	-0.421	< 0.001	0.315	< 0.001	0.562	< 0.001
FPG							0.056	0.564	-0.051	0.602	0.081	0.405	0.043	0.660	0.101	0.229
TC									0.314	< 0.001	0.308	< 0.001	0.93	< 0.001	0.201	0.038

Data are expressed Spearman's rank correlation coefficient (p-value). *Significant p values (p < 0.05). Abbreviations: SZn, serum zinc levels; BMIz, body mass index z-score; WC, waist circumference; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides, HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol

Cardiometabolic traits have been linked to SZn in animal models [83, 84] and humans population with OW/OB [25, 85–88]. However, the available information is not yet conclusive. In our study, the female population showed significant differences in all cardiometabolic traits between NW and OW/OB. These results could have been due to the hormonal changes that have been reported by Arslan et al. [89] and Wisniewski and Chernausk [90]. In the case of the male population, significant differences were found between BMIz and cardiometabolic traits. In addition, we found statistically significant differences for LDLc and insulin with the cutoff established by IZiNCG. Our results agree with the study by Acosta García et al., which was performed on a Mexican children's population [91].

Cardiometabolic parameters were found to be higher in the groups of schoolchildren OW or OB compared to children with NW, showing that from these ages, there are already clear differences that could remain or increase in adulthood, according to the criteria established by the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, and National Heart, Lung, and Blood Institute (NHLBI 2011) [92]. On the other hand, the dietary intake of Zn has been related to cardiometabolic traits in populations with OW/OB [86–88]. Costarelli et al. [93] mentioned that a lower dietary intake of Zn presents a deeper inflammatory state, an altered lipid profile, and higher production of insulin relative to OB individuals with a normal dietary intake of Zn. Additionally, El-Ashmony et al. reported that zinc supplementation could lower TC, LDLc, and TG and increase HDLc [94]. Moreover, other experimental studies have found a significant decrease in Zn in adipose tissue and a negative correlation with insulin, HOMA-IR, and TNF- α values in OB animals [95, 96] and humans [97].

The relationship between SZn and BMIz is not clear [27]. Our study demonstrated a negative association between SZn and BMIz regardless of sex, which was maintained in the female population (Table 4). The results found in our study were similar to those of other studies that reported this association [25, 27, 59, 62, 63, 65, 68]. However, the study by Sugawara et al. [98] contrasts with our results, as they reported a positive correlation between SZn and BMIz, while other studies have reported the absence of an association between Szn and BMIz [66, 99]. Likewise, the children population showed positive correlations of TC, TG, and LDLc with SZn (boys with TC and LDLc and girls with TG). These results are consistent with the study by Zavala G et al. [100]. However, the study of Azab et al. reported negative correlations between SZn and FPG and TG [63].

The relationship between the decrease in SZn with OW/OB has been evaluated through oxidative stress at the level of adipose tissue [97, 101, 102]. To date, the molecular mechanisms are not clear, but it has been shown that under

these conditions of OW/OB, the increase in visceral fat due to OW and OB contributes to the secretion of cytokines such as IL-6, IL-8, and TNF- α , as well as an increase in the cortisol synthesis. This in turn induces the expression of metallothionein and Zip14 in adipose and hepatic tissue, contributing to the decrease in SZn levels [27, 100, 103].

Within the limitations of the study is that it is a sample of school children from elementary schools in Mexico City selected for convenience, so the findings found in this study cannot be generalized to all Mexican children. In addition, the Tanner stage of the schoolchildren was not measured; however, information was collected on the age of the schoolchildren, which is a proxy variable for said stage, and taking this into account when doing the analysis, no difference was found in the age between deficient and non-deficient school children of SZn. Finally, inflammation markers that could affect serum zinc levels were not obtained either, and studies are needed to complement these findings, since the studies are still inconsistent.

Conclusions

Schoolchildren with NW had higher SZn concentrations compared to schoolchildren with OW or OB. ZnD is a public health problem that can be underestimated in OW and OB, especially during childhood and adolescence, where Zn plays important roles in development and growth as well as in lipid and carbohydrate metabolism. Therefore, this type of study helps to understand its relationship with other variables that alert an early metabolic risk using parameters such as BMIz and WC. Together with the lipid profile, these should be considered to evaluate in a more comprehensive way a population at risk such as children, and thus avoid complications in adulthood.

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Author Contribution I.M.N., M.J.R.L., H.H.M., J.V.G., and P.E.C.T. designed the study, perform the statistical analysis, wrote the manuscript, and designed tables and figures. I.M.N., H.H.M., M.K.K., and J.V.G. collect the data. I.M.N., M.J.R.L., and H.H.M. samples treatment and analysis by ICP-MS. E.L.E., O.G.C., I.M.N., M.J.R.L., H.H.M., M.K.K., J.V.G., and P.E.C.T. critically reviewed the manuscript. All authors read and approved the final manuscript.

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Data Availability The data set of this study is available from the corresponding authors on reasonable request.

Declarations

Competing Interests The authors declare no competing interests.

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