# UNIVERSIDAD AUTÓNOMA DE SAN LUIS POTOSÍ

## FACULTAD DE MEDICINA

Centro de Investigación en Ciencias de la Salud y Biomedicina
(CICSaB)

# ASOCIACIÓN DE LA CONCENTRACIÓN SÉRICA DE ZINC TOTAL Y ZINC ALFA 2 GLICOPROTEÍNA CON EL ESTADO NUTRICIO Y PERFIL METABÓLICO EN POBLACIÓN INFANTIL CON SOBREPESO Y OBESIDAD

**TESIS QUE PRESENTA**

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**PARA OBTENER EL GRADO DE DOCTOR EN CIENCIAS BIOMÉDICAS BÁSICAS**

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## CRÉDITOS INSTITUCIONALES

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Tesis que presenta

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# 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 (BMIz)), 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 BMIz without sex exclusion ($r=-0.181$ and $p=0.009$). The boy's population did not show an association between the SZn and BMIz 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 |
| BMIz | Body mass index *z* score |
| TC | Total cholesterol |
| ENSANUT | The National Health and Nutrition Survey |
| FPG | Fasting plasma glucose |
| HDLc | Cholesterol high-density lipoprotein |
| ICP–MS | Inductively coupled plasma mass spectrometry |
| IZiNCG | International Zinc Nutrition Consultative Group |
| LDLc | Cholesterol low-density lipoprotein |
| NW | Normal weight |
| OB | Obesity |
| OW | Overweight |
| SZn | Serum zinc levels |
| TG | Triglycerides |
| WC | Waist circumference |
| Zn | Zinc |

## 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

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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. BMIz was obtained using the children's age, weight, height, and sex, which were classified as NW ($z$ score $\geq -2$ to $<1$), OW ($z$ score $\geq 1$ to $<2$), and OB ($z$ score $\geq 2$), 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 × 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 µg $L^{-1}$) 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 $HNO_3$ 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 $HNO_3$. SZn quantification in samples was performed by an external calibration curve of Zn (10, 25, 50, 75, 100, 200, 500, and 1000 µg $L^{-1}$). 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 $HNO_3$ (Milestone Duopur system Milestonesrl, Italia) and high-purity water with 18 MΩ 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 ug/dL) and one above the cutoff value (> 70 ug/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 BMIz, 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<br>Median (Q1–Q3) | Overweight/obesity<br>Median (Q1–Q3) | *p |
|---|---|---|---|
| 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<br>$n = 103$<br>Median (Q1–Q3) | Overweight/obesity<br>$n = 107$<br>Median (Q1–Q3) | *p* |
|---|---|---|---|
| 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). [a]Mann–Whitney *U* test, [b]Pearson's $X^2$ test, [c]Medians 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 ($r=-0.396$, $p\leq0.001$). The boys' population showed a positive correlation between SZn and TC and LDLc. Moreover, negative correlations were found between SZn and BMIz ($r=-0.277$, $p\leq0.004$), FPG ($r=-0.229$, $p\leq0.019$), and TG ($r=-0.260$, $p\leq0.007$) 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].

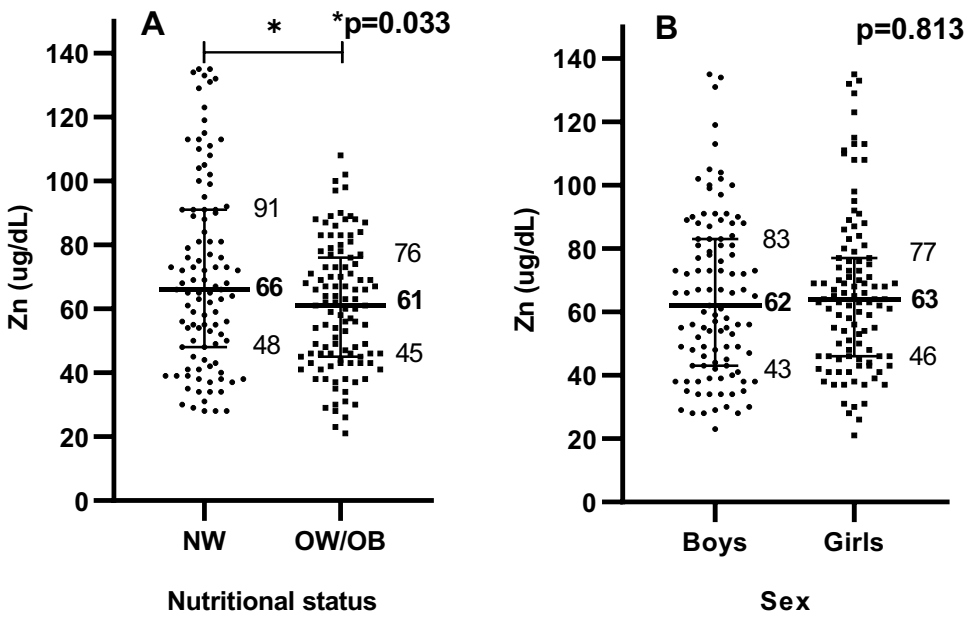



**Fig. 1** Comparison of SZn among the population of Mexican children with respect to nutritional status and sex ($n=210$). **A** There was a difference between the nutritional condition (Mann–Whitney *U* test) **B** There was no difference between the two sex groups (Mann–Whitney U test)

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

| Trait | Zn (μg/dL) | | *p* |
|---|---|---|---|
| | < 70 | > 70 | |
| | *n* = 81 (38.6%) | *n* = 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 [*n* = 210 (%)][a] | 33 (40.7) | 69 (53.5) | 0.114 |
| BMI *z* score[bd] | 0.91 (0.32 to 2.06) | 1.12 (−0.11 to 2.12) | 0.451 |
| BMI *z* 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(μU/mL) | 2.8 (1.99 to 5.53) | 3.8 (2.22 to 6.98) | 0.034 |
| Socioeconomic level [*n* = 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 [*n* = 214 (%)][a] | | | |
| Public | 22 (27.5) | 72 (53.7) | < 0.001 |
| Private | 58 (72.5) | 62 (46.3) | |
| Maternal schooling [*n* = 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 *X*)^2 test, [b]*BMI*: body mass index, [c] World Health Organization, 2007, [d]Mann–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 | 0.6 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 Chernausek [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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# Correlation of Zinc-α-2 glycoproteín and zinc levels with Anthropometrical and Biochemical Parameters in Overweight and Obese Children

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**Competing interests**

We declare no conflict of interest.

**Availability of data and material**

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

**Author Contributions**

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., 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.

**Abstract**

The biological role of Zinc-alpha 2-glycoprotein (ZAG) has been associated with lipid mobilization, although this is not entirely clear. The study's aim was to examine the serum levels of ZAG and zinc (Zn) in a children population with overweight (OW) and obesity (OB), and their relationship with biochemical parameters. Our study was a cross-sectional analysis of a group of Mexican children aged 6–9 (n=72). We analyzed anthropometric data and various biochemical parameters, including fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (TG), total cholesterol (TC), insulin, and homeostatic model assessment insulin resistance

(HOMA-IR). ZAG protein levels were measured using enzyme-linked immunosorbent assay (ELISA), and serum zinc (Zn) levels were quantified using inductively coupled plasma mass spectrometry (ICP–MS). The Zn values indicate a statistically significant difference between normal weight (NW) and overweight/obese (OW/OB) children with Zn concentrations was (91 µg/dL; IQR: 61.7 to 108.8) for NW and (66 µg/dL; IQR: 42.5 to 82.7) for OW/OB. ZAG values did not show significant differences between NW and OW/OB, of (2.1 mg/dL; IQR: 1.6 to 2.6) and (2.3 mg/dL; IQR 1.6 to 2.8), respectively Additionally, the Zn/ZAG ratio was lower in the OW/OB population (2.9 IQR: 1.9 to 4.5, $p$= 0.05) compared to the NW population (3.7 IQR 2.5 to 5.1 , $p$= 0.05) and the correlations were found between fasting plasma glucose (FPG) with Zn ($r$= 0.880, $p$= 0.004) and ZAG ($r$= 0.387, $p$= 0.046) in the boys population, as well as a negative correlation between insulin and Zn in NW children of both sex. HOMA-IR shows correlations between Zn (r=0.499, p=0.008) and ZAG (r=0.473, p=0.010) in the overweight/obese (OW/OB) population of both boys and girls. Additionally, correlations were observed between LDLc, TG, and BMIz with Zn and ZAG in the boys population. In the same way we also found that girls with OW/OB had a Zn/ZAG ratio of -2.32 (95% CI -4.58 to -0.07, p=0.043) compared to normal weight boys. In conclusion, our findings highlight the significant roles of Zn and ZAG in glucose and lipid metabolism. Furthermore, the Zn/ZAG ratio might be a potential indicator for assessing Zn and ZAG levels in nutritional balance and the preventing of metabolic diseases. However, further studies are necessary to validate our results.

**Key words:** zinc alpha-2-glycoprotein, zinc, anthropometric, overweight/obesity, biochemical parameters, children.

**Abbreviations**

| | |
|---|---|
| AKT | Serine-threonine kinase |
| BMI | Body Mass Index |
| BMIz | Body Mass Index z score |
| TC | Total Cholesterol |

| | |
|---|---|
| NHNS | National Survey of Health and Nutrition |
| FPG | Fasting Plasma Glucose |
| GLP-1 | Glucagon-like peptide- 1 |
| HDLc | High Density Lipoprotein Cholesterol |
| ICP-MS | Inductively Coupled Plasma Mass Spectrometry |
| IZiNCG | International Zinc Nutrition Consultative Group |
| LDLc | Low Density Lipoprotein Cholesterol |
| NW | Normal Weight |
| OB | Obesity |
| OW | Overweight |
| PPA2 | Protein phosphatase 2 |
| TC | Total Cholesterol |
| TG | Triglycerides |
| WC | Waist Circumference |
| ZAG | Zinc-α-2-glycoprotein |
| Zn | Zinc |

## Introduction

Zinc-α2 glycoprotein (ZAG) was initially discovered in human plasma in 1961. This protein has a molecular weight of 43 kDa [1] and is found in plasma at concentrations of a few mg/dL (8–12 mg/dL in young individuals and 18–30 mg/dL in adults) [2]. ZAG contains two high-affinity binding sites for zinc, making it a protein dependent on Zn [3]. In vitro studies with murine epididymal adipocytes have shown that ZAG stimulates lipolysis associated with the activation of adenylate cyclase in the plasma membrane, which is GTP-dependent [4]. This process is carried out through the inhibition of lipogenic enzymes such as fatty acid synthase (FAS), acetyl coenzyme A carboxylase (ACC) and diacyl glycerol acyltransferase (DGAT), and also produces an increase in the expression of lipolytic enzymes such as hormone-sensitive lipase (HLS) and adipose tissue triglyceride lipase (ATGL) [5]. Recently, (ZAG) has been identified as a novel anti-inflammatory adipokine associated with OW/OB, playing a role in modulating lipolysis mobilization, adipokine production [6-8], regulating glucose

metabolism [9], and is linked to insulin resistance [10].For this reason, ZAG has come to be considered as a prospect and alternative in the treatment of obesity [11].

Circulating Zn concentrations are crucial for maintaining ZAG activity, as zinc facilitates the binding of ZAG to fatty acids, as demonstrated in certain in vitro experiments [12]. Additionally, it has been observed that changes in Zn metabolism in adults obese may lead to impaired ZAG function [13]. While the complete biological role of ZAG is not yet understood, it has been demonstrated that its expression in adipose tissue is down-regulated in individuals with obesity [14]. On the other hand (Zn), a crucial element in cellular metabolism, functions as a structural component by binding to around 3000 proteins in vivo as well as a catalytic co-factor in more than 300 enzymatic reactions [15-17]. It also acts as a regulatory ion, modulating cellular signal transduction processes [18]. Furthermore, Zn is involved in various biochemical pathways and cellular functions, including the response to oxidative stress, homeostasis, immune responses, cell cycle progression, apoptosis, and aging [19]. Zn also plays a significant role in the growth and development of children and acts as a signaling factor in the function of neurons, reproduction, immunity, skeletal muscle, intestinal, glucolipid metabolism, and reduction of inflammatory cytokines [20]. Moreover, Zn is a trace element with a minor plasma pool and a rapid turnover (70–110 μg/dL) [21], however, Zn is not stored in the body, so a daily intake of Zn is necessary to achieve a steady state. In the case of children, a daily Zn intake between 5–8 mg/day is recommended for children younger than 13 years old [22]. Zinc's role in regulating various metabolic processes and its potential impact on obesity-related pathways become even more pertinent in light of the World Health Organization (WHO) recognizing the global obesity epidemic nearly two decades ago. WHO's 2022 reports on overweight (OW) and obesity (OB) further underscore the escalating prevalence of these conditions, highlighting the urgent need to explore how zinc deficiency and other micronutrient imbalances may contribute to and exacerbate metabolic disorders associated with obesity [23].

Approximately 1/8 of the world's population is affected by OB, with 43% of adults experiencing OW and 16% dealing with OB. Furthermore, over 390 million children are affected by OW, and 160 million are dealing with OB. Mexico has a high prevalence of OW/OB and is among the countries with the highest OB rates among children [24]. On the

other hand, OW and OB are linked to excessive adipose tissue in the body, especially in visceral areas, which can result in insulin resistance [25], hyperglycemia [26], dyslipidemia [27], diabetes [28], cardiovascular diseases [29], respiratory issues [30], and hypertension [31], as well as prothrombotic and pro-inflammatory conditions [32].

In this context, the aim of this study was to analyze the levels of ZAG and Zn as well as the Zn/ZAG ratio, and their association with anthropometric and biochemical parameters and homeostatic model assessment of insulin resistance (HOMA-IR)] in mexican children with overweight and obesity, to better understand their roles and potential associations in metabolic health.

## Materials and methods

### *Study design*

The cross-sectional study involved 72 children, with an equal split of [36 boys and 36 girls], aged 6 to 10 years, all residing in the same geographic area of Mexico City. The children were categorized into two groups based on their BMIz (NW and OW/OB). Individuals with underlying medical conditions or those taking medications that could impact their metabolic profile were excluded from the study.

### *Ethical approval*

The study was conducted in compliance with the guidelines set forth in the Declaration of Helsinki and in accordance with articles 14 and 16 of the Regulations of the General Health Law on Health Research in Mexico. The research protocol was approved by the school authorities and the Research, Ethics, and Biosecurity Committee of the Hospital Infantil de México Federico Gómez (approval register: HIM/2013/003). Moreover, written assent and consent were obtained from the children and their parents to participate in the study.

### *Body Mass Index z score*

Anthropometric parameters were measured wearing light clothing and without shoes, standing in the middle of the scale platform, and with arms resting freely by their sides, with their heads in the Frankfurt horizontal plane. 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. WC was measured with a nonelastic flexible measuring tape (Seca 200). The determination of BMIz was carried out using children's age, weight, height, and sex data, these 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 [33].

***Serum sample collection***

A blood sample of 5 mL of peripheral blood was collected by venipuncture after a 12 h fast in a sterile vacutainer tube. Serum separation in the samples was carried out by centrifugation at 3000 × g for 10 min to 4 °C. All serum samples were stored in Eppendorf tubes at −80 °C.

***Analysis of biochemical parameters***

Biochemical parameters analysis of the FPG, TC, HDLc and TG were realized by commercial kits and measures were carried out at LAB 300, Instrumentation Laboratory, Barcelona, Spain. For LDL-C, DeLong's modified Friedwald formula was utilized [34]. Insulin was determined by chemiluminescence immunoassay (IMMULITE 2000, Euro, DPC, Llanberis, UK). HOMA-IR was calculated using the equation by Matthews et al. (1985) [35].

***Analysis of Zn and ZAG***

Total Zn analysis was carried out using an inductively coupled plasma mass spectrometer (ICP–MS iCAP Q, Thermo Scientific, Germany) in Helium Kinetic Energy Discrimination (He KED) mode. The Zn measure was determined using an external calibration curve (10, 25, 50, 75, 100, 200, 500, and 1000 μg $L^{-1}$), and reagent blanks, quality control samples, and serum samples were analyzed. Sample treatment followed the protocol proposed by Rios Lugo et al [36], and the yield recovery of samples was assessed using an internal standard [Indium (In); 10 μg $L^{-1}$]. $HNO_3$ concentrated high-purity (Milestone Duopur system by Milestonesrl, Italia), high-purity water with 18 MΩ cm (Milli-Q® system by Millipore, Mexico), and Zn standards dissolution (High–Purity Standards, North Charleston, USA) were employed in the sample preparation.

ZAG analysis, an enzyme-linked immunosorbent assay (ELISA) was conducted using a commercial kit from Invitrogen (Thermo Fisher, Vienna, Austria, Catalog No. BMS220).

The kit's sensitivity was 0.174 ng $mL^{-1}$, with an analytical range of 0.23-15.0 ng $mL^{-1}$, an inter-assay coefficient of 4.9%, and an intra-assay coefficient of 5.6%. The readings were taken using a spectrophotometer at a wavelength of 450 nm in a BioTek Epoch Instruments Microplate (U.S.A).

### *Data Analysis*

Population characteristics were assessed using measures of central tendency, and multiple linear regression analysis was conducted to adjust weight and height measurements based on age and sex. To enhance statistical stability, the categories of OW and OB were combined. The Kolmogorov-Smirnov test revealed a non-normal distribution of the continuous variables. Subsequently, the interquartile range (IQR) was calculated for non-normally distributed continuous data, and percentages were used for categorical variables. The Mann-Whitney U test was utilized to compare age, anthropometric measurements, serum ZAG, Zn, Zn/ZAG ratio, and biochemical parameters based on nutritional status. Furthermore, a Spearman's rank correlation coefficient was employed to assess the relationship between ZAG, Zn, and BMIz, WC, FPG, TC, TG, LDLc, HDLc, insulin, and HOMA-IR. Like wise age-adjusted quantile regression models was conducted to evaluate association of nutritional status on Zn, ZAG and Zn/ZAG ratio concentrations. The interaction between the sex and the nutritional status, was assessed. The statistical analyses were performed using SPSS® v20.0 (SPSS Inc., Chicago, Illinois), and a significance level of $P < 0.05$ was considered for all analyses.

## Results

### *General characteristics of the study population and anthropometric values*

Our study was cross-sectional in a Mexican children population with median 8 years. Values obtained in the anthropometric and biochemical parameters are shown in Table 1. According to nutritional status, significant differences were found between NW and OW/OB for weight, WC, and BMIz.

### *Biochemical profile*

The biochemical parameters revealed significant differences between the NW and OW/OB children (Table 1). OW/OB children showed higher levels of fasting plasma glucose (87.5

IQR: 84.3 to 93.8, *p*= 0.004), triglycerides (90 IQR: 67 to 120), *p* <0.001), and insulin (4.6 IQR: 2.9 to 7.3, *p*= 0.018), In addition a significant lower concentration of high-density lipoprotein cholesterol (42.5 IQR: 37 to 53, p =0.004).

***Zn, ZAG and Zn/ZAG ratio according to nutritional status***

ZAG values show no significant differences between NW and OW/OB, and the concentration was 2.1 mg/dL (IQR: 1.6 to 2.6) and 2.3 mg/dL ( IQR: 1.6 to 2.8) by NW and OW/OB, respectively. (Figure 1 A). Zn values show a statistically significant difference in NW and OW/OB (*p*= 0.020), where the concentration was 91 µg/dL (IQR: 61.7 to 108.8) by NW and 66 µg/dL (IQR: 42.5 to 82.7) by OW/OB (Figure 1 B). For the population of children with OW/OB a decreased Zn/ZAG ratio (*p*= 0.05) was found concerning children with NW, for the case of the population with OW/OB it was 2.9 (IQR 1.9 to 4.5) while for the children population with NW it was 3.7 (IQR 2.5 to 5.1) [Figure 1C].

***Correlation between Zn and ZAG levels with anthropometric and biochemical profile***

None correlation in the general children population was found. However positive associations were found in the group of boys' with NW population between serum ZAG concentrations and height, TG *r*= 0.802, *p*= 0.017 and *r*= 0.731, *p*= 0.040 respectively). Mean while boys with , OW/OB showed a positive association between ZAG with FPG (*r*= 0.387, *p*= 0.046). In addition, with the Zn levels OW/OB showed , negative associations were found with BMIz (*r*= -0.825, *p*= 0.012) and insulin (*r*= -0.823, *p*= 0.012). Also a positive association was observed with FPG (*r*= 0.880, *p*= 0.004), LDLc (*r*= 0.517, *p*= 0.006) and HOMA-IR (*r*= 0.499, *p*= 0.008). In the case of the girls' population, our results show a negative association between serum Zn concentration with insulin (*r*= -0.786, *p*= 0.021) in NW and a positive association with HOMA-IR in OW/OB (*r*= 0.473, *p*= 0.010).

***Association of nutritional status on Zn, ZAG and Zn/ZAG ratio concentrations by sex***

Overweight and obese boys had -2.09 (95% CI -4.34 to 0.17, p=0.069) in the Zn/ZAG ratio compared to normal weight boys, and overweight and obese girls had -2.32 (95% CI -4.58 to -0.07, p=0.043) in the Zn/ZAG ratio compared to normal weight boys (Table 3).

## Discussion

The current study found a significant positive correlation between ZAG and glucose levels in boys with OW/OB as well as a correlation between ZAG and HOMA-IR in the girls with OW/OB population. These findings contrast with other studies [37,38], where ZAG levels are related to dysglycemia, insulin resistance, and diabetes in the OB population. In addition, a study has suggested that ZAG expression in adipose tissue could serve as a valuable biomarker for predicting insulin sensitivity [10]. It has been reported that the ZAG activates protein phosphatase 2 (PPA2) through the beta-adrenergic receptor 2 (β2-AR), leading to the inhibition of insulin-induced phosphorylation protein serine-threonine kinase (AKT) and, consequently, glucose uptake. Conversely, Yang et al [9], found that hyperglycemia and hyperinsulinemia could negatively regulate ZAG activity. Additionally, we found a positive association between ZAG and TG in the NW population, which is consistent with findings from other population studies [39, 40]. ZAG is recognized as a factor in lipid mobilization due to its connection with key enzymes in lipid metabolism [41].

Additionally, we were able to find a significant correlation between height and serum ZAG levels (Table 2) which has not been reported before, however, considering the known role of ZAG in the metabolism and regulation of adiposity, there may be an indirect connection by influencing the redistribution and localization of adipose tissue, especially in the growth stage [42, 43]. It's worth noting that studies have shown higher expression of ZAG in visceral adipose tissue (VAT) and a reduction in subcutaneous adipose tissue (SAT) in human adipocytes from obese individuals. This was not found to alter serum concentrations. Conversely, in lean individuals, the result were the opposite [44].

On the other hand, serum ZAG levels were higher in the OW/OB population than in the NW population but were not statistically significant (Figure 1A). This corresponds with studies by Stejskal et al, [45] and Balaz et al, [44] which found no significant statistical difference between serum ZAG concentrations in patients with normal body mass versus obese individuals. Serum Zn levels were significantly lower in the OW/OB population (Figure 1B), as reported by other studies in children and adolescents increasing the risk of developing insulin resistance, diabetes mellitus as well as high systolic and diastolic blood pressure [46-48]. However, a gradual decrease in serum Zn levels could restrict the antioxidant capacity

of ZAG, since it is a Zn-dependent metalloprotein, as mentioned by Kumar A. A et al [49] and Zahid et al [50]. We also evaluated the Zn/ZAG ratio, finding a significant decrease in this parameter in the population of children with OW/OB (Figure 1C) compared to the population of children with NW.

Regarding Zn, this study found a negative correlation between serum Zn levels and BMIz (Table 2), aligning with findings in both adult and child populations [51], despite some discrepancies between these studies. In this study, we observed a consistent positive correlation between Zn and glucose, as well as a negative correlation with insulin in boys with NW. These findings are similar to results from other studies [52–56]. Likewise, we identified a correlation between Zn levels and LDLc, and these could be associated with dyslipidemia in the OB population. Moreover, the correlation highlights the antioxidant function of zinc, which may help reduce the risk of atherogenesis [57].

Significant statistical differences were not observed in the serum Zn, ZAG levels and the Zn/ZAG ratio based on sex in our study. This contrasts with the findings of González-Domínguez et al [58], who reported lower levels of Zn and other trace elements in girls, indicating genotypic sex as a potential susceptibility factor in childhood with OB. Moreover, Yeung et al [59] discovered higher serum ZAG levels in men compared to women. Consistent with these findings, adipose tissue distribution is known to significantly influence the risk of developing cardio-metabolic diseases based on gender [60–62]. Furthermore, we found significant statistical differences between the nutrition status with Zn and Zn/ZAG.

The biochemical profile values of FPG, TG, and insulin were more elevated in the OW/OB children population. However, these values fall within the limits established by the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents (NHLBI) for children aged 6 to 11 years [63]. Nevertheless, prospective cohort studies with these values have been related to dyslipidemia, and insulin resistance, as well as to the increase in the risk of atherosclerosis at an early age [64].

Lastly, we identified a significant negative association between the Zn/ZAG ratio in the population of girls with OW/OB, similar to what was observed in the population of boys with OW/OB, although the latter did not reach statistical significance. While no sex-specific differences were found in individual serum Zn and ZAG levels, the Zn/ZAG ratio indicates

a greater susceptibility to zinc depletion and a more pronounced negative impact on ZAG function due to OW/OB in girls compared to boys. This condition is associated with sustained oxidative stress and an elevated risk of developing metabolic diseases.

An important consideration in our study is the limited number of children from Mexico City, which restricts the generalizability of our results to the entire population. To address this, we propose expanding the participant pool and incorporating other adipokines and inflammatory markers that may be associated with the function of ZAG protein and Zn. This would provide a more comprehensive understanding of our findings.

## Conclusions

The accumulation of body fat during childhood and early adolescence could potentially increase the risk of developing chronic degenerative diseases at a young age. Zinc and ZAG play a crucial role in mitigating the harmful effects of obesity, reducing lipotoxicity, and combating oxidative stress, ultimately improving lipid and carbohydrate metabolism through insulin regulation. It's worth noting that the role of ZAG protein during childhood is pivotal in preventing metabolic imbalances, as evidenced by studies in adult populations with conditions like metabolic syndrome, cancer-related cachexia, and anorexia. The Zn/ZAG ratio may serve as a valuable indicator for nutritional status and the risk of metabolic or inflammatory diseases, as well as for assessing the effectiveness of studies investigating zinc supplementation and its impact on health.

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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 and ELISA. E.L.E., O.G.C., I.M.N., M.J.R.L., H.H.M.,

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**Conflict of Interest** The authors declare that they have no conflict of interest.

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## Tables and Figures

Table 1. General Characteristics of the Study population by Nutrition Condition

| **Traits** | **NW n= 16 Median (IQR)** | **OW/OB n= 56 Median (IQR)** | ***p*** |
|---|---|---|---|
| Age[a] (years) | 7.3 (6.5-8.7) | 8.1 (7.1- 9.1) | 0.147 |
| Sex, female, n (%) | 8 (44.4) | 16 (55.2) | 0.631 |
| **Anthropometric status** | | | |
| Weight (Kg)[ac] | 27 (19.5-29.7) | 33 (27-43.5) | **<0.001** |
| Height (cm)[ac] | 124 (112.2-131) | 130 (121-135.8) | 0.083 |
| WC (percentile)[a] | 58.2 (51.5-62) | 67 (62-74.8) | **<0.001** |
| BMIz[a] | 0.01 (-1.2-0.68) | 1.99 (1.53-2.5) | **<0.001** |
| **Biochemical status[a]** | | | |
| FPG (mg/dL) | 81.5 (78-87.25) | 87.5 (84.3-93.8) | **0.004** |
| TC (mg/dL) | 150.5 (141.7-176.5) | 166 (147.3-177) | 0.281 |
| TG (mg/dL) | 51 (43-67.8) | 90 (67-120) | **<0.001** |
| HDLc (mg/dL) | 50.5 (43-59.5) | 42.5 (37-53) | **0.004** |
| LDLc (mg/dL) | 95.9 (77.8-115.3) | 102.3 (87.6-116.3) | 0.560 |
| Insulin (µU/mL) | 2.8 (1.99-4.6) | 4.6 (2.9-7.3) | **0.018** |
| HOMA-IR | 0.85 (0.41-1.19) | 0.91 (0.63-1.58) | 0.090 |

Data are presented as median value interquartile ranges (IQR). [a]U Mann Whitney test, [c]Medians adjusted by age and sex. Abbreviations: *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

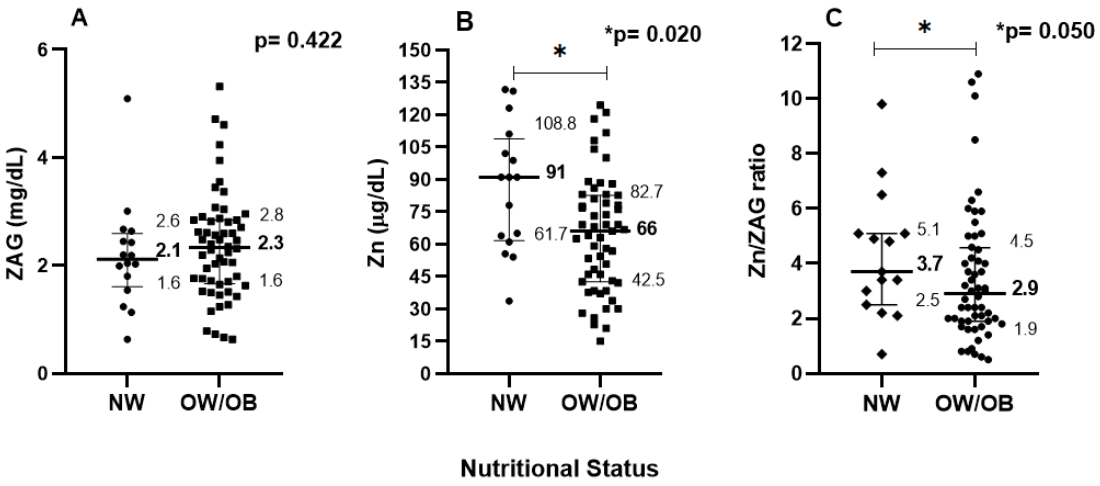



**Figure 1**. Comparing blood serum ZAG and Zn in Mexican children according to nutritional status (n = 72). **A** There was no difference between the nutrition status in ZAG **B**. There was a difference between serum Zn the nutritional status. **C** There was a difference between the nutrition status Zn/ZAG ratio. (Mann–Whitney U test)

Table 2. Correlations between Zn and ZAG with anthropometric and biochemical values in the population of children according to sex. (n=72)

| | **NW** | | **OW/OB** | | **NW** | | **OW/OB** | |
|---|---|---|---|---|---|---|---|---|
| | **boys (n=8)** | | **boys (n=27)** | | **girls (n= 8)** | | **girls (n=29)** | |
| **Traits** | **SZn** | **ZAG** | **SZn** | **ZAG** | **SZn** | **ZAG** | **SZn** | **ZAG** |
| Age | -0.295 (0.478) | 0.599 (0.117) | 0.299 (0.130) | 0.064 (0.752) | -0.132 (0.756) | 0.144 (0.734) | 0.039 (0.842) | -0.014 (0.942) |
| **Anthropometric status** | | | | | | | | |
| Weight | -0.301 (0.466) | 0.659 (0.076) | 0.367 (0.059) | -0.346 (0.077) | -0.061 (0.885) | -0.012 (0.977) | 0.121 (0.533) | -0.011 (0.953) |
| Height | -0.060 (0.887) | **0.802 (0.017) *** | 0.376 (0.053) | -0.121 (0.549) | -0.169 (0.690) | -0.036 (0.932) | 0.152 (0.430) | -0.142 (0.464) |
| WC | -0.309 (0.456) | 0.699 (0.054) | 0.333 (0.090) | -0.251 (0.208) | 0.084 (0.844) | -0.228 (0.588) | 0.013 (0.946) | -0.063 (0.744) |
| BMIz | **-0.825 (0.012) *** | 0.156 (0.713) | 0.322 (0.101) | -0.242 (0.223) | -0.119 (0.779) | 0.024 (0.955) | -0.131 (0.497) | 0.230 (0.230) |
| **Biochemical status** | | | | | | | | |
| FPG | **0.880 (0.004) *** | 0.168 (0.691) | -0.147 (0.464) | **0.387 (0.046) *** | 0.146 (0.729) | -0.537 (0.170) | 0.343 (0.069) | -0.189 (0.326) |
| TC | 0.311 (0.453) | 0.000 (1.000) | 0.376 (0.053) | 0.344 (0.079) | 0.024 (0.955) | -0.119 (0.779) | -0.067 (0.729) | 0.077 (0.693) |
| TG | 0.054 (0.889) | **0.731 (0.040) *** | 0.080 (0.692) | 0.007 (0.973) | -0.084 (0.844) | 0.287 (0.490) | -0.034 (0.859) | 0.007 (0.973) |
| HDLc | 0.024 (0.955) | 0.000 (1.000) | -0.143 (0.476) | 0.185 (0.355) | 0.275 (0.509) | -0.156 (0.713) | -0.034 (0.859) | 0.128 (0.508) |
| LDLc | -0.048 (0.910) | -0.395 (0.333) | **0.517 (0.006) *** | 0.110 (0.585) | 0.071 (0.867) | -0.119 (0.779) | -0.078 (0.689) | -0.030 (0.877) |
| Insulin | **-0.823 (0.012) *** | 0.101 (0.811) | 0.389 (0.055) | -0.183 (0.362) | **-0.786 (0.021) *** | 0.476 (0.233) | 0.160 (0.408) | 0.318 (0.093) |
| HOMA-IR | 0.288 (0.588) | 0.048 (0.911) | **0.499 (0.008) *** | 0.061 (0.762) | -0.500 (0.253) | 0.536 (0.215) | 0.069 (0.720) | **0.473 (0.010) *** |
| Zn | --- | -0.132 (0.756) | --- | -0.154 (0.442) | --- | -0.667 (0.071) | --- | -0.8 (0.682) |

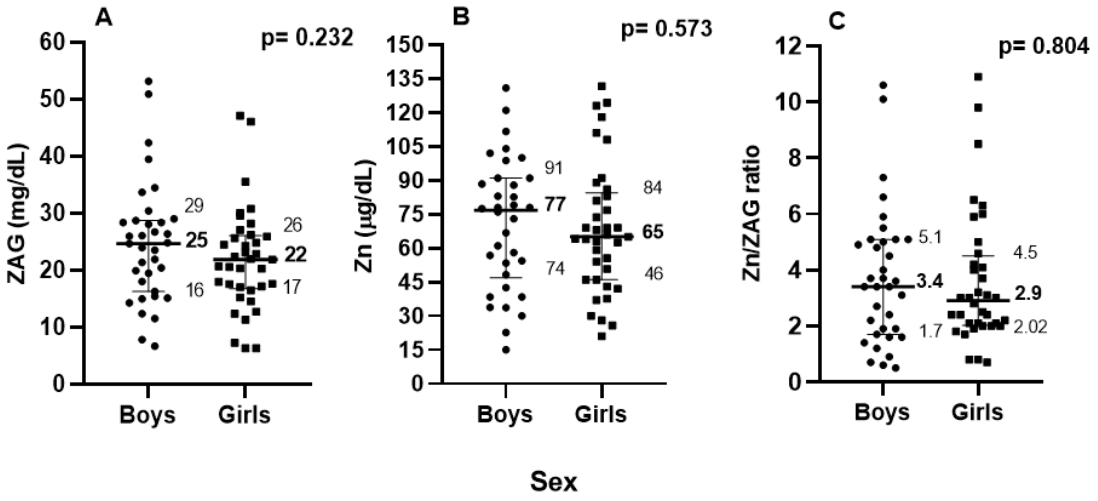
Data are expressed Spearman´s rank correlation coefficient (p-value). *Significant p values ($p < 0.05$). Abbreviations: SZn, serum zinc levels; ZAG, Zinc apha 2 glycoprotein, BMIz, body mass index z-score; WC, waist circumference; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides, HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol

Table 3. Association of sex and nutritional status on Zn, ZAG and Zn/ZAG ratio concentrations (n= 72)

| | **Zn β (95% CI)** | **ZAG β (95% CI)** | **Zn/ZAG ratio β (95% CI)** |
|---|---|---|---|
| **Interaction (sex*nutritional status)** | | | |
| Boys + Normal weight | Reference | Reference | Reference |
| Boys + Overweight/Obesity | -12.5 (-45.3 to 20.2) | 2.1 (-5.6 to 9.9) | -2.09 (-4.34 to 0.17) |
| Girls + Normal weight | 6.4 (-33.7 to 46.6) | -2.8 (-12.4 to 6.7) | -1.1 (-3.91 to 1.62) |
| Girls + Overweight/Obesity | -22.2 (-54.9 to 10.5) | -3.3 (-11.1 to 4.4) | **-2.32 (-4.58 to -0.07)*** |

Age-adjusted quantile regression models. * P value<0.05

## Supplementary figures




**Supplementary figure 1.** Comparison of ZAG and Zn/ZAG ratio in Mexican children according to sex (n = 72). **A** There was not statistical difference in serum ZAG level according to sex. **B** There was not statistical difference in serum Zn levels according to sex. **C.** There was not a difference in Zn/ZAG ratio according to sex.. (Mann–Whitney U test)

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## Serum levels of anti-inflammatory/proinflammatory adipocytokines, and copper levels in overweight and obese women in an adult Mexican population

Original Article | Published: 21 August 2023

Volume 22, pages 647–654, (2023) Cite this article

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### Abstract

#### Background

An imbalance between adipokines and micronutrient concentrations, such as those of copper (Cu), has been linked to dysregulation of energy homeostasis leading to weight gain and the development of other comorbidities; however, information on this issue remains limited. Our aim was to investigate the correlation between Cu status and serum adipokine levels and their relationship in normal-weight, overweight, and obese adult women.

#### Methods

Sixty patients were evaluated and classified according to their body mass index (BMI) and biochemical parameters; adipokines and Cu were measured at fasting.

#### Results

Leptin (Lep) and resistin (Res) levels were elevated, whereas adiponectin (Adpn) and ghrelin (Ghr) values were decreased in overweight and obese women ($p = 0.001$). The mean Adpn/Lep ratio was <0.5 in overweight and obese subjects, while the Lep/Ghr ratio increased significantly in relation to weight gain, suggesting an inverse link between the ratios of these hormones in the regulation of obesity. The analysis revealed a positive association between BMI and Cu levels in obese women. Moreover, a negative association between Cu and Res in normal-weight subjects was found.

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# Relationship Between Serum Levels of Arsenic, Cadmium, and Mercury and Body Mass Index and Fasting Plasma Glucose in a Mexican Adult Population

Published: 31 January 2022

Volume 200, pages 4916–4923, (2022) Cite this article

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Héctor Hernández-Mendoza, Héctor Edmundo Álvarez-Loredo, Elizabeth Teresita Romero-Guzmán, Darío Gaytán-Hernández, Consuelo Chang-Rueda, Israel Martínez-Navarro, Bertha Irene Juárez-Flores & María Judith Rios-Lugo

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## Abstract

In Mexico, few studies have analyzed the associations between toxic elements and metabolic diseases. In the present study, we analyzed the associations between serum arsenic (As), cadmium (Cd), and mercury (Hg) levels and body mass index (BMI) and fasting plasma glucose (FPG) in a Mexican adult population. Anthropometric data corresponding to 86 Mexican healthy adults (59 females and 27 men) were analyzed. FPG was analyzed by an enzymatic colorimetric method, and serum As, Cd, and Hg levels were analyzed by inductively coupled plasma–mass spectrometry (ICP–MS). The data show that the median serum As, Cd, and Hg levels were relatively higher in females (As = 1.78 ng $mL^{-1}$, Cd = 1.00 ng $mL^{-1}$, Hg = 0.96 ng $mL^{-1}$) than those in males (As = 1.22 ng $mL^{-1}$, Cd = 0.91 ng $mL^{-1}$, Hg = 0.95 ng $mL^{-1}$). However, these differences were not statistically significant ($p \geq 0.097$). We also found that the median level of As significantly increased with an increase in the body weight categories (normal weight = 1.08; overweight = 1.50; obesity = 2.75; $p < 0.001$). In addition, a positive association between serum As levels and FPG before and after adjustment for BMI was demonstrated ($Rho_{Unadjusted} = 0.012$; ($RhoA_{djusted} = 0.243$, $p = 0.032$). Serum As levels are positively associated with BMI and FPG in the adult population of Mexico. Nevertheless, these results need to be replicated and confirmed with a larger sample size.

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About this article

Article | Published: 14 May 2024

# Mediation effect of body mass index on the association between serum magnesium level and insulin resistance in children from Mexico City

María Judith Rios-Lugo, Jesús Isimar Serafín-Fabián, Héctor Hernández-Mendoza, Miguel Klünder-Klünder, Miguel Cruz, Estefania Chavez-Prieto, Israel Martínez- Navarro, Jenny Vilchis-Gil ✉ & Miguel Vazquez-Moreno ✉

*European Journal of Clinical Nutrition* (2024) | Cite this article

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A Correction to this article was published on 17 July 2024

This article has been updated

## Abstract

### Background/Objectives

Reduced serum magnesium (Mg) levels have been associated with obesity, insulin resistance (IR), type 2 diabetes, and metabolic syndrome in adults. However, in the children population, the evidence is still limited. In this cross-sectional study, we aimed to analyze the association of serum Mg levels with the frequency of overweight and obesity and cardiometabolic traits in 189 schoolchildren (91 girls and 98 boys) between 6 and 12 years old from Mexico City.

### Subjects/Methods

Anthropometrical data were collected and biochemical parameters were measured by enzymatic colorimetric assay. Serum Mg level was analyzed by inductively coupled plasma mass spectrometry (ICP-MS). The triglyceride-glucose (TyG) index was used as a surrogate marker to evaluate IR.

### Results

Serum Mg level was negatively associated with overweight (Odds ratio [OR] = 0.377, 95% confidence interval [CI] 0.231–0.614, $p < 0.001$) and obesity (OR = 0.345, 95% CI 0.202–0.589, $p < 0.001$). Serum Mg level resulted negatively associated with body mass index (BMI, $\beta = -1.16 \pm 0.26$, $p < 0.001$), BMI z-score ($\beta = -0.48 \pm 0.10$, $p < 0.001$) and TyG index ($\beta = -0.04 \pm 0.04$, $p = 0.041$). Through a mediation analysis was estimated that BMI z-score accounts for 60.5% of the negative association of serum Mg level with IR (Sobel test: $z = 2.761$; $p = 0.005$).

### Conclusion

Our results evidence that BMI z-score mediate part of the negative association of serum Mg level and IR in Mexican schoolchildren.

Journal of Trace Elements in Medicine and Biology
Volume 72, July 2022, 126984

# Serum lead levels and its association with overweight and obesity

Héctor Hernández-Mendoza [a b], María Judith Rios-Lugo [c d] ✉,
Héctor Edmundo Álvarez-Loredo [d], Elizabeth Teresita Romero-Guzmán [e],
Darío Gaytán-Hernández [c], Israel Martínez-Navarro [d], Bertha Irene Juárez-Flores [a],
Consuelo Chang-Rueda [f]

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## Abstract

### Background

Lead (Pb) exposure has been associated with cardiovascular diseases and metabolic syndrome, nevertheless its association with obesity, type 2 diabetes, and dyslipidemia markers has been little explored in Mexico. Therefore, we evaluated the association of serum Pb levels (Pb-S), with body mass index (BMI), fasting plasma glucose (FPG), total cholesterol (TC), and triglycerides (TG).

### Methods

A cross-sectional study was performed on 85 Mexican adults (57 women and 28 men). BMI was calculated, while FPG, TC, and TG were measured by the enzymatic colorimetric method. Total Pb-S levels were measured using inductively coupled plasma mass spectrometry (ICP-MS).

### Results

The study population was 20.3±1.9 years old, showed an average of Pb-S of 0.0982±0.068μgdL$^{-1}$, and presented a frequency of overweight (OW) and obesity (OB) of 50.5% and 18.8%, respectively. Men had higher average FPG than women (Women= 83.930±5.662 vs Men= 84.953±6.495; p=0.037). When we analyzed anthropometric and clinical variables, Pb-S and frequency of OW and OB were observed to increase within the categories of Pb-S tertiles (<0.001). The averages of Pb-S were 0.051±0.035μgdL$^{-1}$, 0.107±0.067μgdL$^{-1}$, and 0.151±0.063μgdL$^{-1}$ for individuals with normal weight (NW), OW, and OB, respectively. In addition, an analysis adjusted for age and sex shows Pb-S is positively associated with BMI (β=2.76±0.498, p=<0.001).

### Conclusion

Our results evidence a significant association between Pb-S and the increase of BMI in Mexican adults and highlight the important health impact that may represent environmental Pb exposure.

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# Overweight and Obesity Are Positively Associated with Serum Copper Levels in Mexican Schoolchildren

Published: 11 August 2022

Volume 201, pages 2744–2749, (2023) Cite this article

Miguel Vazquez-Moreno, Marián Sandoval-Castillo, María Judith Rios-Lugo, Miguel Klünder-Klünder, Miguel Cruz, Israel Martínez-Navarro, Elizabeth Teresita Romero-Guzmán, Claudia Inés Victoria-Campos, Jenny Vilchis-Gil & Héctor Hernández-Mendoza

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## Abstract

Due to its relationship with oxidative stress and inflammation responses, obesity and its cardiometabolic implications have been related with serum copper (Cu). Hence, we analyzed the association of overweight (OW) and obesity (OB) status and cardiometabolic traits with serum Cu level in Mexican schoolchildren. Anthropometrical data and cardiometabolic traits were analyzed in this cross-sectional study. Serum Cu level was measured by inductively coupled plasma mass spectrometry. The study involved 191 schoolchildren (93 girls and 98 boys) with a mean age of 8.054 ± 1.170 years. Children with OW and OB had higher serum Cu levels than children with normal weight (NW) (mean difference: OW vs NW = 51.85 μg $dL^{-1}$, OB vs NW = 47.22 μg $dL^{-1}$, $p < 0.001$). In a multiple linear regression model, OW and OB status were positively associated with serum Cu levels ($\beta_{OW} = 49.85$, 95% confidence interval (95% CI) 35.84–63.87, $p < 0.001$; $\beta_{OB} = 44.38$, 95% CI 27.70–61.05, $p < 0.001$). We did not identify any significant association between cardiometabolic traits and serum Cu level. In conclusion, our results show an association of the presence of OW and OB with higher serum Cu levels, for the first time in Mexican schoolchildren. However, further functional studies are needed to better understand the role of Cu in the pathophysiology of obesity.

Journal of Trace Elements in Medicine and Biology
Volume 73, September 2022, 127002

# Serum zinc levels are associated with obesity and low-density lipoprotein cholesterol in Mexican adults

Héctor Hernández-Mendoza [a b], Israel Martínez-Navarro [c], Edduin Hernández-Ochoa [a d], Marisol Espinoza-Ruiz [d], Angel Lugo-Trampe [e], Karina del C. Trujillo-Murillo [e], Maximiliano Arahon López-García [e], María Judith Rios-Lugo [c f] ✉, Consuelo Chang-Rueda [d] ✉

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## Abstract

### Purpose

Little is known about the association between serum zinc (Zn) levels and obesity in the Mexican population. Therefore, we tested the association between serum Zn levels, obesity status, and serum lipid levels in a sample of Mexican adults.

### Methods

Anthropometric data and serum levels of total cholesterol, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively), and triglycerides were analyzed in 96 Mexican adults. Serum Zn was measured with inductively coupled plasma mass spectrometry. An individual data meta-analysis of the association between serum Zn, overweight, and obesity status was performed in 172 adults from two different provinces in Mexico.

### Results

Serum Zn was negatively associated with body mass index (BMI, $\beta=-0.034\pm0.013$, $p=2.0\times10^{-6}$) and obesity (odds ratio [OR]= 0.990, 95% confidence interval [CI]= 0.980–0.999, $p=3.4\times10^{-5}$). The association between Zn level and obesity in Mexican adults was confirmed with an individual data meta-analysis (OR= 0.977, 95% CI= 0.966–0.988, $p=3.4\times10^{-5}$). In addition, a significant interaction effect between serum Zn level and sex was observed on LDL-C level ($\beta=7.010\pm3.295$, $p=0.037$). Serum Zn was negatively associated with LDL-C levels in women ($\beta=-0.188\pm0.074$, $p=0.016$).

### Conclusion

Our results confirm the negative association of serum Zn level with obesity. For the first time, we show a sex-specific association between serum Zn and LDL-C levels in a Mexican population. However, further studies are needed in larger and more varied Mexican cohorts to replicate and confirm our findings.

Universidad Autónoma de San Luis Potosí
Posgrado en Ciencias Biomédicas Básicas
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**Asociación de la concentración sérica de Zinc total y Zinc alfa 2 glicoproteína con el estado nutricio y perfil metabólico en población infantil con sobrepeso y obesidad**

**M.C. Israel Martínez Navarro**

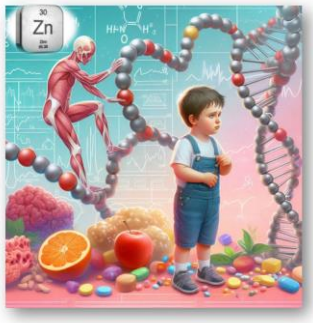
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Dra. Othir Gidalti Galicia Cruz, Dr. Héctor Hernández Mendoza
**Asesor externo:** Dra. Jenny Vilchis Gil

1

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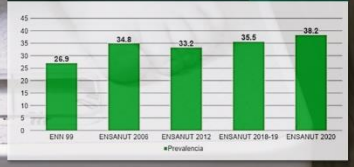



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## 1. Introducción

- La **obesidad** es una enfermedad debida a una acumulación de grasa anormal o **excesiva** que presenta un **riesgo para la salud**.
- Es de etiología **multifactorial** en la que interactúan factores individuales y contextuales tales como: **genéticos, metabólicos, ambientales y socioeconómicos**

Antecedentes: prevalencia de sobrepeso + obesidad en niños escolares 1999-2020



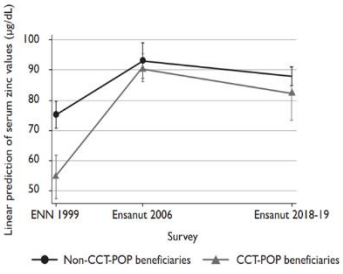

- México aumentó del **35.5 %** en el 2018 al **38.2%** en el 2020

*(OMS, 2018, Carrero, 2020, Salazar D, 2019, CDC, 2020, ENSANUT 2020)*

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## 1. Introducción

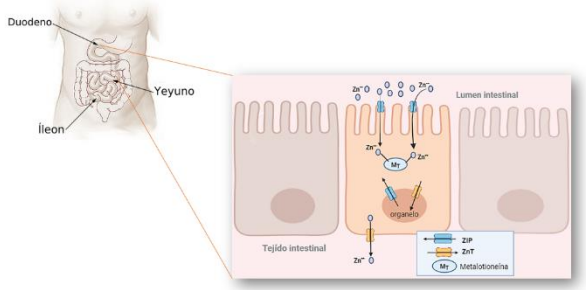
- La **carencia de Zinc (Zn)** afecta unos **2,200 millones de personas** alrededor del mundo
- Ha sido clasificada por la OMS como el **11° factor de riesgo global de mortalidad.**
- En 2019 en México se reportó un **18.6% de deficiencia de Zn (DZn)** en niños en edad escolar.
- De acuerdo con la **FAO** el riesgo para la **DZn** se considera elevado para la salud pública cuando la prevalencia de la concentración es **>20%.**




*(Rivera J, 2009;* De la Cruz-Góngora, 2019)

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## 2. Antecedentes



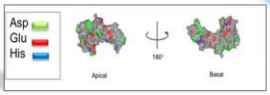

(NIH 2019, CDC, 2005, Krebs NF 2014, Fukunaka A 2018, Marger I. 2014, López de Romaña 2010, Roméo A,2020 )

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## Zinc Alpha 2 glicoproteína



- Es una glicoproteína de 43 kD que es soluble en el plasma.
- Se ha determinado 2 sitios de unión fuerte y 15 débiles a Zn.
- Se sintetiza en el hígado, así como en el tejido adiposo
- **Factor de movilización de lipidos en el adipocito**
- **Actúa de manera autócrina y parácrina**

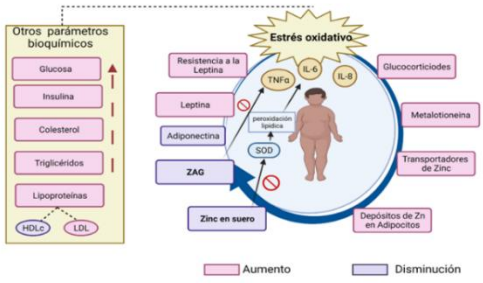



- Los niveles plasmáticos oscilan entre unos pocos mg/dL en un feto, **8 a 12 mg/dL en personas jóvenes** y **18 a 30 mg/dL en adultos** sanos y hombres mayores.

(Zahid et al.,2016 , Kumar AA et al., 2013, Mracek T et al., 2010, Cabassi A, et al., 2013)

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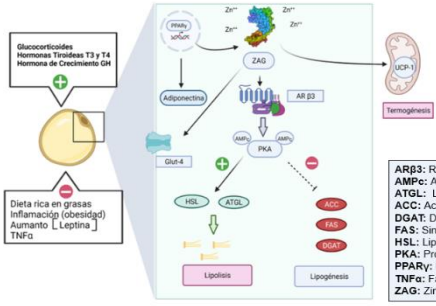
## Zn-ZAG, la obesidad y el estrés oxidativo




(Modificado de Severo JS, 2020, Araki,T,1988 , Zahid H, 2016, Created with BioRender.com)

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## Zn-ZAG, la obesidad y el estrés oxidativo




**ARβ3:** Receptor adrenérgico beta 3
**AMPc:** Adenosín monofosfato cíclico
**ATGL:** Lipasa de triacilglicéridos del tejido adiposo
**ACC:** Acetil coenzima A carboxilasa
**DGAT:** Diacilglicerol aciltransferasa
**FAS:** Sintasa de ácidos grasos
**HSL:** Lipasa Sensible a hormonas
**PKA:** Proteín cinasa A
**PPARγ:** Receptor gama de proliferación de peroxisomas
**TNFα:** Factor de Necrosis tumoral Alpha
**ZAG:** Zinc alfa 2 glicoproteína

(Modificado de Severo JS, 2020, Araki,T,1988 , Zahid H, 2016, Created with BioRender.com)

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**Tabla 1. Zn y su relación con la obesidad en niños, adolescentes y adultos**

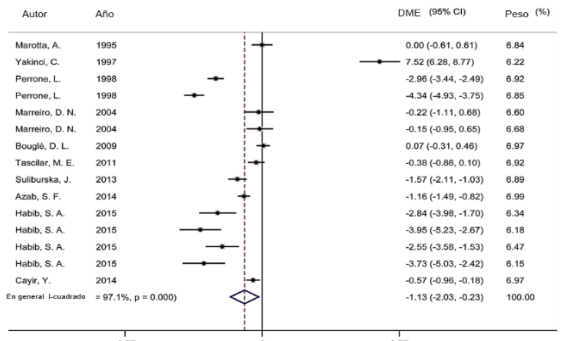
| Población | n | Genero | Asociación | Correlación | Otras asociaciones y correlaciones | Referencia |
|---|---|---|---|---|---|---|
| Rep. de Monte negro | 202 | EX | **Negativa** | −0.048 p <0.221 | En niños con sobrepeso y obesidad correlación positiva PCR y Cu (r = 0.305, p = 0.011 y r = 0.440, p = 0.013, respectively), and TAS and RBP (r = 0.528, p < 0.001 and r = 0.434, p = 0.015, respectively) | Jacksic *et al.*, 2019 |
| India | 173 | H M | **Negativa** | −0.331, p = 0.01 | Negativa entre colesterol y Cu en sangre completa (r = −0.376, p = 0.01) así como la razon entre Cu/Zn (r = −0.278, p = 0.05). | Malik V.S. et al., 2020 |
| México | 76 | EX | **Negativa** | -0.663 p <0,001 | TG . Positiva (r = 0,493, p <0,001). | Rios-Lugo *et al.*, 2020 |
| Iraq | 160 | M | **Negativa** | - | Encontramos un nivel de zinc significativamente atenuado en el suero de todas las pacientes obesas (p< 0,001) en comparación con los controles sanos fe-masculinos. | Amin, M. N., et al., 2020 |
| España | 78 | Ex | **NR** | - | En toda la serie, el 69% de los participantes mostraron una ingesta de zinc inferior a la recomendada y podrían estar en alto riesgo de sufrir una deficiencia de zinc. | Escobedo-Monge, M. F., et al., 2021 |

H: Hombre, M: Mujer, EX: Exclusión de géneros HDLc: Colesterol de alta densidad, LDLc: Colesterol de baja densidad, HOMA-IR: Índice de resistencia a la insulina, TG: Triglicéridos, PCR: Proteína C Reactiva TAG: Estado antioxidante total

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**Tabla 1. Zn y su relación con la obesidad en niños**




(Gu, K 2019)

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**Tabla 2. ZAG y su relación con la Obesidad**

| Título | Analito | Población | Asociaciones | Fuente |
|---|---|---|---|---|
| La zinc-a2-glicoproteína interviene en la regulación del peso corporal mediante la inhibición de enzimas lipogénicas en el tejido adiposo | Suero | H y M 16 NP 28 SP/OB | Peso (r=-0.62, p<0.001) IMC (-0.64, p<0.001) CC (-0.68, p<0.001) Cadera (-0.60. p<0.001) | Gong F-Y et al.,2015 |
| La zinc-α2-glucoproteína está asociada con la obesidad en chinos y ratones obesos inducidos por HFD | Suero | Hombres, Ratones | SAT: (r = −0.407 P<0.01) DC: (r=-0.688 P<0.01) | Liu M et al.,2018 |
| Los niveles séricos de ZAG y adiponectina y su relación con la Obesidad y en la población china | Sangre | 225 hombres y mujeres | Glucosa (r=-0.206, p<0.01) HOMA-IR (r=-0.172, p<0.01) CT (r=0.447, p<0.01) WC (r= -0.321, p<0.01) | Liu M, J et al., 2020 |
| Niveles séricos de ZAG (Zinc-Alpha 2 glicoproteína) en niñas con anorexia nerviosa | Suero | 87 niñas | IMC (r = -0.848 p < 0.0001) HDLc (r=0.514, p<0.0001) TAG (r= -0.278, p=0.009) Cortisol (r= 0.482, p<0.0001) Insulina (r=-0.731, p<0.0001) HOMA-IR (r=-0.74. p<0.0001) | Anna, J, 2022 |

NP: Normo peso, SP: Sobrepeso, OB: Obesidad, SAT: Tejido adiposo subcutáneo, VAT: Tejido adiposo visceral W: Peso corporal, IMC: Índice de masa corporal, DC: diámetro de cintura, % Reducción de peso. CT: Colesterol total, TG: Triglicéridos, HDLc: Lipoproteínas de alta intensidad, LDLc: Lipoproteínas de baja densidad.

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## Estudio de ZAG en humanos

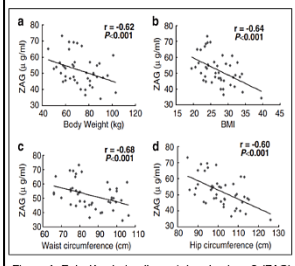
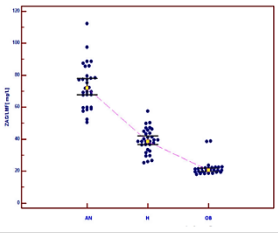



Figura 1. Relación de la glicoproteína de zinc-a2 (ZAG) en suero con el peso corporal (a), índice de masa corporal (IMC) (b), perímetro de cintura (c) y perímetro de cadera (d) en sujetos delgados y con sobrepeso u obesidad.




| | AN Mean ± 1.96 SEM (Range) | H Mean ± 1.96 SEM (Range) | OB Mean ± 1.96 SEM (Range) |
|---|---|---|---|
| ZAG (mg/L) | 73.43 ± 4.96 [a,c] (50.5–112.3) | 39.18 ± 2.77 (25.3–57.6) | 21.96 ± 1.91 [b] (18.1–38.9) |

AN—the group of subjects with anorexia nervosa, H—the group of healthy girls, OB—the group of girls with simple obesity. [a] $p < 0.05$ AN vs. H; [b] $p < 0.05$ OB vs. H; [c] $p < 0.05$ AN vs. OB.

(Gong F-Y, 2009; Anna, J, 2022)

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## 3. Planteamiento del problema

La prevalencia de obesidad infantil ha aumentado considerablemente en México, donde Zinc y ZAG han sido asociados de **manera negativa en población adulta** con el estado nutricio (IMC) y el perfil metabólico. Razón por la cual, el trabajo se enfoca en investigar la relación que guardan el Zinc y ZAG en la malnutricion debida al sobrepeso y obesidad en **población infantil.**

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## 4. Pregunta de investigación

¿Existe alguna asociación entre las concentraciones séricas de Zn total y ZAG con el estado nutricio y perfil metabólico, en población infantil con sobrepeso y obesidad?

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## 5.Hipótesis

**Hipótesis alterna 1 ($H_1$)**

❖Las concentraciones séricas de Zn total y ZAG serán menores en la población infantil con sobrepeso y obesidad.

**Hipótesis alterna 2 ($H_2$)**

❖Las correlaciones entre las concentraciones séricas de Zn total y ZAG serán negativas en población infantil con sobrepeso y obesidad.

**Hipótesis alterna 3 ($H_3$)**

❖ La correlación entre el colesterol total, LDLc, triglicéridos e insulina, **será negativa,** tanto con Zn total como con ZAG; mientras que glucosa y HDLc presentará una **correlación positiva**, en población infantil con sobrepeso y obesidad.

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## 6. Objetivo general

Evaluar la asociación entre las concentraciones séricas de Zn total y ZAG con el IMCz y perfil bioquímico metabólico, en población infantil con sobrepeso y obesidad.

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## Objetivos específicos

1. Determinar las concentraciones séricas de Zn total y ZAG en población infantil con normopeso sobrepeso y obesidad.

2. Evaluar si existen diferencias significativas del perfil lipídico y bioquímico sérico (glucosa, triglicéridos, colesterol, LDLc, HDLc, insulina) de acuerdo al estado nutricio, a partir de una base de datos secundaria.

3. Determinar la correlación entre Zn total y ZAG en población infantil con sobrepeso y obesidad.

4. Determinar la correlación entre los indicadores bioquímicos metabólicos (glucosa, triglicéridos, colesterol, LDLc, HDLc, insulina, leptina y adiponectina) con Zn total y ZAG, respectivamente en población infantil con sobrepeso y obesidad.

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## 8. Tipo de estudio

Analítico transversal

## 9. Metodología

**Criterios de Inclusión**

- ❑ Expedientes con datos completos.
- ❑ Muestras séricas cuyos padres hayan firmado el consentimiento por escrito.
- ❑ Muestras séricas de niños y niñas que hayan firmado el asentimiento por escrito.
- ❑ Muestras séricas con un volumen como mínimo de 150 µL para los análisis.

**Criterios de No inclusión**

- ❑ Niños con enfermedades.
- ❑ Asma, reumatológicas, diabetes, síndrome de intestino irritable.
- ❑ Toma de suplementos y medicamentos.

**Criterios de exclusión**

- ❑ Muestras con datos incompletos.
- ❑ Muestras con hemólisis.

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## 9. Metodología

**Banco de muestras de suero niños y niñas**
4 escuelas primarias de la CDMX (por conveniencia)
1° a 4° grado

n=217 (7 muestras eliminadas)

Estudio de Zn
n=210

Valor z del IMC

Normopeso | Sobrepeso | Obesidad

- Glucosa
- Colesterol
- Triglicéridos
- HDLc
- LDLc
- Insulina

Datos de parámetros bioquímicos | Cuantificación de Zn Total

Ensayo comercial de la marca SIEMENS. | ICP-MS (i-CAP Thermo Fisher Scientific Alemania).

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## 9. Metodología

Estudio de Zn
n=210

Muestreo por conveniencia

Estudio de ZAG
n=72

Valor z del IMC

Normo peso (16) | Sobrepeso (28) | Obesidad (28)

- Glucosa
- Colesterol
- Triglicéridos
- HDLc
- LDLc
- Insulina

Datos de parámetros bioquímicos | Cuantificación de Zn Total | (Ensayo comercial Human ZAG ELISA ) Marca invitrogen Thermofisher scientific

Ensayo comercial de la marca SIEMENS. | ICP-MS (i-CAP Thermo Fisher Scientific Alemania).

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## Protocolo de digestión de muestras



Acondicionamiento de las muestras

100 µL de suero +100 µl $HNO_3$ ultrapuro + 100uL Patrón interno (In) 1 ng/L NIST para cuantificación de Zn



Digestión ácida por horno de microondas
MARS 6 marca CEM
De 12 tubos de reacción
Tiempo: 40 min

| Paso | Tiempo (min) | Temp (°C) | Power (W) |
|---|---|---|---|
| 1 | 15 | 200 | 1200 |
| 2 | 15 | 200 | 1200 |



Desecación de las muestras (Punto crítico)

- Realizada en placa de calentamiento
- 150-180 °C
- Vasos de teflón de 100 mL
- Tiempo de procesamiento 30 min



Recuperación de muestras (Aforar a 10 mL con $HNO_3$ al 2%)

- Matraces volumétricos aforados a 10 mL
- Transvase a tubos Falcon®
- Tiempo 30 min

(Davis KL, 2020, Laur N, Kinscherf R, 2020)

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## Consideraciones éticas

- El estudio se realizó de acuerdo a los lineamientos **Declaración de Helsinki.**
- El Reglamento de la **Ley General de Salud** con base en los artículos 14 y 16.
- El protocolo de investigación fue aprobado por los Comités de Investigación, Ética y Bioseguridad. del Hospital Infantil de México Federico Gómez (registro de aprobación: **HIM/2013/003)** y por autoridades escolares.
- Los padres firmaron el **consentimiento** y los niños el **asentimiento.**




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## Curva de Calibración y lectura de muestras ICP-MS

Calibración

Objetivo: Disminución de interferencias como óxidos y especies con doble carga

Preparación de curva de calibración

Introducción de la muestra

Bomba peristáltica

Nebulización y Atomización de la muestra

Interfase

Zona de vacío

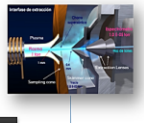
Lentes de iones

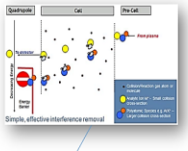
Celda de reacción/Colisión

Cuadruopolo

Detector

Resultados

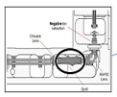






Patrones marca hps en $HNO_3$ al 2% con trazabilidad NIST





(Vanhaecke F,2002, Herrero E & Vigil A, 2003)

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## Protocolo para la cuantificación de ZAG



Acondicionamiento de las muestras

Se tomaron 10 µL de muestra y 190 µL de solución diluyente.

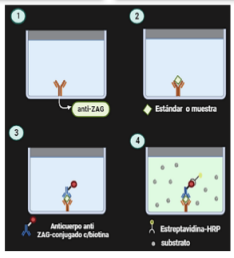
Realización de la curva de calibración




1 — 100 µL de la dilución de muestra 50 µL del conjugado de biotina a cada pozo y se incubó (18°-25°C) durante 2 h

2 3 — 100 µL de la dilución de estreptavidina-HRP y se incubó (18°-25°C) durante 1 h

4 — 100 µL de la solución (TMB) y se incubó durante 30 min, 100 µL de solución stop y se leyó con espectrómetro a 450 nm




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## 10. Análisis de datos

variables

Kolmogorov – Smirnov
n>50 muestras

**No cumplen con normalidad**
- Edad
- Zinc
- ZAG
- Triglicéridos
- HDLc
- Insulina

**Cumplen con normalidad**
- IMCz
- Glucosa
- Colesterol
- LDLc

**Pruebas no paramétricas**
- Kruskal Wallis
- U de Mann Whitney
- Correlación de Spearman
- Regresión por cuantiles

- Para equilibrar el tamaño de muestra entre la población de normopeso, sobrepeso y obesidad y dar una mayor estabilidad estadística se decidió conjuntar éstas dos últimas.

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## 11. Resultados

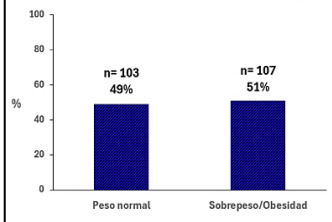



**Figura 3.** Comparativo del porcentaje de población infantil con normopeso vs sobrepeso/Obesidad (n=210)

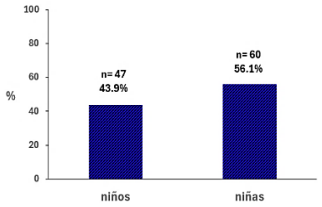



**Figura 4.** Comparativo del porcentaje de población con sobrepeso/Obesidad por sexo (n=107)

- **(INEGI 2020)** Informó que la Ciudad de México, junto con su Zona Metropolitana se ubican en las prevalencias más altas de sobrepeso para niños de 5 a 11 años con un **28%** y en jóvenes de 12 a 19 años de edad **(32%).**
- **(Ensanut 2020)** refirió una prevalencia combinada de **(38.2%)** con sobrepeso y obesidad en niños entre 5 a 11 años.

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**Tabla 3. Características generales de la población de estudio de acuerdo con el estado nutricional.**

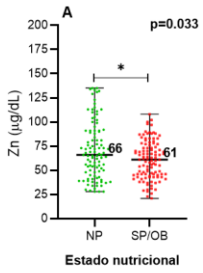
| Variables | Peso Normal n = 103 Media (RIQ) | Sobre peso/Obesidad n = 107 Media (RIQ) | *p* |
|---|---|---|---|
| Edad[a] (years) | 7.8 (6.9 a 8.8) | 8.2 (7.4 a 9.2) | **0.018** |
| Sexo, femenino, n (%) | 45 (43.7) | 60 (56.1) | 0.168 |
| Peso (kg)[ac] | 30.8 (27 a 36) | 33.8 (29 a 38) | **0.017** |
| Talla (cm)[ac] | 125.8 (121 a 132) | 129.2 (124 a 135) | **0.018** |
| IMCz [a] | -0.11 (-0.82 a 0.54) | 1.88 (1.4 a 2.5) | **<0.001** |
| DC (percentile)[a] | 55.2 (52 a 59) | 67.9 (62 a 74) | **<0.001** |
| **Nivel Socioeconómico** [n = 193; (%)] [b] | | | |
| Bajo | 30 (32) | 22 (22.2) | |
| Medio | 36 (38.3) | 34 (34.4) | 0.141 |
| Alta | 28 (29.7) | 43 (43.4) | |
| **Escuela** (%) [b] | | | |
| Publica | 40 (40) | 61 (55.5) | **0.025** |
| Privada | 60 (60) | 49 (44.5) | |
| **Escolaridad materna** [n = 201;(%)] [b] | | | |
| Secundaria o menos | 17 (17.7) | 11 (10.5) | |
| Prepararia or escuela tecnológica | 37 (38.5) | 37 (35.2) | 0.362 |
| Universidad o posgrado | 42 (43.8) | 57 (54.3) | |

Los das se presentan como valor de la media y rangos intercuartiles (RIQ). a Prueba U de Mann-Whitney, b Prueba $X^2$de Pearson, c Medianas ajustadas por edad y sexo. Abreviaturas: IMCz, Índice de Masa Corporal z; DC, diámetro de cintura

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## Resultados




*U de Mann Whitney (p<0.05)*

**Figura 5.** Comparación de los niveles de Zn entre la población infantil con normopeso y sobrepeso/obesidad (n=210).

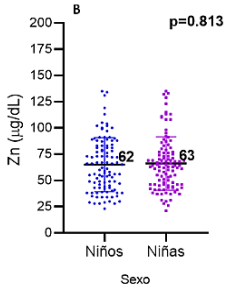
**Tabla 4. Valores séricos de Zn en poblaciones infantil con normopeso y obesidad.**

| País | Normopeso (µg/dL) | Obesidad (µg/dL) | Estudio |
|---|---|---|---|
| Egipto | 75 | 57 | Azab S. F., et al 2014 |
| Korea | 145.4 | 135.2 | H.Kim et al., 2016 |
| India | 152.8 | 85.1 | Malik V.S. et al., 2020 |

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*U de Mann Whitney (p<0.05)*

**Figura 6.** Comparación de los niveles séricos de Zn en población infantil de acuerdo con el sexo (n=210).

**.Tabla 5. Valores séricos de Zn en niños y niñas**

| País | Niños (µg/dL) | Niñas (µg/dl) | Estudio |
|---|---|---|---|
| Venezuela | 88 | 86 | Acosta G et al., 2017 |
| Brasil | 60 | 64.6 | Albuquerque F. M. et al., 2018 |
| Cuba | 49 | 50 | Carrero G et al., 2020 |

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**Tabla 7. Comparación entre el valor de corte sérico Zn y variables antropométricas, bioquímicas y socioeconómicas.**

| Variable | Zn (µg/dL) <70 n = 81 (38.6%) (27.85 a 66.43) | Zn (µg/dL) >70 n = 129 (61.4%) (71.91 a 133) | *p* |
|---|---|---|---|
| **Edad (años)** [d] | 8.0 (6.8 a 8.9) | 8.0 (7.1 a 9.06) | 0.323 |
| **Sexo, femenino [n= 210; (%)]** [a] | 33 (40.7) | 69 (53.5) | 0.114 |
| **IMC z** [bd] | 0.91 (0.32 a 2.06) | 1.12 (-0.11 a 2.12) | 0.451 |
| IMC z (%) [bc] | | | |
| NP | 32 (45.1) | 51 (40.5) | 0.945 |
| SP/OB | 39 (54.9) | 75 (59.5) | |
| **DC (percentil)** [d] | 61.9 (54 a 68.8) | 61.5 (54.2 a 68.5) | **0.038** |
| **Perfil Bioquímico** [d] | | | |
| GPA (mg/dL) | 87 (81 a 90) | 86 (81 a 91) | 0.86 |
| CT (mg/dL) | 160 (143 a 173) | 167 (150 a 186) | 0.093 |
| TG (mg/dL) | 69.5 (49.5 a 105.5) | 73 (54 a 98) | 0.631 |
| HDLc (mg/dL) | 48.5 (39 a 54.7) | 49 (41 a 56.3) | 0.925 |
| LDLc (mg/dL) | 93.7(80.65 a 113.7) | 101.8 (87 a 117.1) | **0.033** |
| Insulina (µU/ml) | 2.8 (1.99 a 5.53) | 3.8 (2.22 a 6.98) | **0.034** |
| **Nivel Socioeconomico** [n = 196; (%)] [a] | | | |
| Bajo | 19 (27.6) | 32 (25.2) | |
| Medio | 23 (33.3) | 48 (37.8) | 0.767 |
| Ala | 27 (39.1) | 47 (37.0) | |
| **Tipo de Escuela** [n = 214; (%)] [a] | | | |
| Publica | 22 (27.5) | 72 (53.7) | **<0.001** |
| Privada | 58 (72.5) | 62 (46.3) | |
| **Escolaridad Materna** [n = 204; (%)] [a] | | | |
| Secundaria o menor | 17 (22.7) | 12 (9.3) | |
| Preparatoria o técnica | 30 (40.0) | 47 (36.4) | **0.011** |
| Universidad o posgrado | 28 (37.3) | 70 (54.3) | |

- De la población total, **81 niños (38.6%)** presentaron concentraciones por debajo del valor de corte (<70ug/dL) estableciendo una DZn de acuerdo con la OMS, UNICEF, IAEA y el Grupo Consultivo Internacional de Nutrición de Zinc (IZiNCG).

IZiNCG

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**Tabla 6. Comparación de valores séricos de ZAG en poblaciones con normopeso y obesidad.**

| País | Normopeso (mg/dL) | Obesidad (mg/dL) | Estudio |
|---|---|---|---|
| Rep. Checa | 2.4 | 2.7 | Stejskal et al;2007 |
| Eslovaquia | 4.4 | 4.9 | Balaz et al; 2014 |
| Polonia | 3.9 | 2.1 | Anna, J; 2022 |
| Pekin | 5.7 | 4.9 | Gong F-Y 2009 |

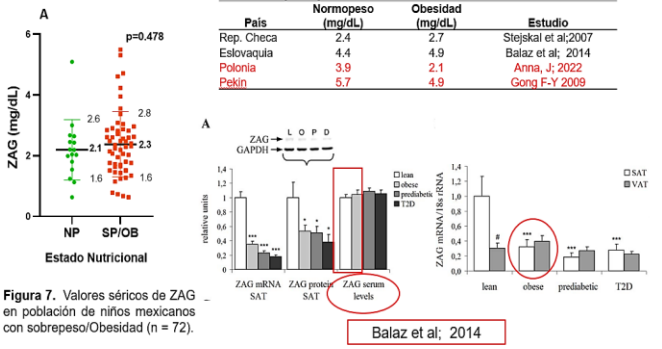



**Figura 7.** Valores séricos de ZAG en población de niños mexicanos con sobrepeso/Obesidad (n = 72).

Balaz et al; 2014



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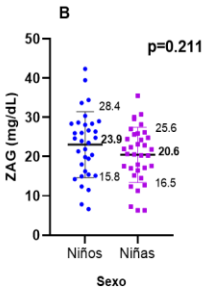



**Figura 8.** Comparación de los niveles séricos de ZAG en población infantil de acuerdo con el sexo (n=72).

**.Tabla 8. Valores séricos de ZAG en niños y niñas**

| País | Hombres (mg/L) | Mujeres (mg/L) | Estudio |
|---|---|---|---|
| Hong Kong China | 17.6 | 10.2 | Yeung, D. C. et al., 2009 |



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**Tabla 4. Diferencias en el perfil bioquímico en población infantil con normopeso y sobrepeso/Obesidad (n= 210).**

| Variables | Peso Normal Mediana (RIQ) | Sobrepeso/Obesidad Mediana (RIQ) | p |
|---|---|---|---|
| **Niños** | | | |
| Glucosa (mg/dL) | 85 (80-89.2) | 87 (86.2-93.7) | **0.001** |
| Colesterol (mg/dL) | 160 (146-180) | 166 (149-178) | 0.432 |
| Triglicéridos (mg/dL) | 58 (44.5-81) | 67 (59.2-108.5) | **<0.001** |
| HDLc (mg/dL) | 54(48-66) | 52 (40-54) | **0.02** |
| LDLc (mg/dL) | 94(80.2-115.2) | 97(80.7-113.5) | 0.273 |
| Insulina (µU/mL) | 2.1 (2.0-3.2) | 2.8 (2.6-6.5) | **<0.001** |
| **Niñas** | | | |
| Glucosa (mg/dL) | 83 (80-89) | 86 (81.7-91) | **0.043** |
| Colesterol (mg/dL) | 152 (138-172) | 167 (157.2-187) | **0.001** |
| Triglicéridos (mg/dL) | 57 (47.5-87) | 75 (68-120.7) | **<0.001** |
| HDLc (mg/dL) | 51(43-57.5) | 47 (36.7-52.2) | **0.004** |
| LDLc (mg/dL) | 92 (80-103) | 99 (92.7-121) | **<0.001** |
| Insulina | 2.6 (1.9-4.5) | 3.9 (3.8-10.6) | **<0.001** |

*Prueba U de Mann Whitney p<0.05; (RIQ) Rango inter cuartil; HDLc: Lipoproteínas de alta densidad; LDLc: Lipoproteínas de baja densidad*

**Tabla 5. Valores bioquímicos aceptables en niños de 6 a 11 años.**

| Variable | Aceptable (mg/dL) |
|---|---|
| Glucosa | 90-180 |
| CT | <170 |
| TG | <90 |
| LDLc | <110 |
| HDL | >45 |
| Insulina (µU/ml) | <15 |

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**Tabla 6. Estudios relacionados con la obesidad y cambios en el perfil lipídico.**

| País | Estudio |
|---|---|
| Italia | Di Martino G, et al; 1993 |
| Italia | Costarelli, L, et al., 2010 |
| Polonia | Olechnowicz, J et al., 2018 |
| Colombia | Aguillón J, et al., 2018 |
| España | Noreña-Peña A, et al., 2021 |



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**Tabla 8. Correlación entre Zn, IMCz, perfil lipídico, glucosa e insulina en población infantil.**

| *Variable* | IMCz | | Glucosa | | Colesterol | | TG | | HDLc | | LDLc | | Insulina | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | r | p | r | p | r | p | r | p |
| **Zn total** | -0.181 | **0.01** | -0.033 | 0.637 | 0.036 | 0.601 | -0.092 | 0.183 | 0.064 | 0.359 | 0.067 | 0.334 | -0.021 | 0.758 |
| **IMCz** | | | 0.265 | **<0.001** | 0.197 | **0.004** | 0.43 | **<0.001** | -0.396 | **<0.001** | 0.265 | **<0.001** | 0.491 | **<0.001** |
| **Glucosa** | | | | | 0.13 | 0.057 | 0.123 | 0.072 | -0.004 | 0.956 | 0.125 | 0.066 | 0.26 | **<0.001** |
| **Colesterol** | | | | | | | 0.314 | **<0.001** | 0.276 | **<0.001** | 0.92 | **<0.001** | 0.164 | 0.015 |
| **niños (n= 105)** | | | | | | | | | | | | | | |
| **Zn total** | -0.084 | 0.395 | -0.026 | 0.795 | 0.214 | **0.028** | 0.051 | 0.605 | 0.035 | 0.724 | 0.213 | **0.029** | 0.105 | 0.285 |
| **IMCz** | | | 0.318 | **<0.001** | 0.159 | 0.097 | 0.418 | **<0.001** | -0.37 | **<0.001** | 0.221 | **0.02** | 0.415 | **<0.001** |
| **Glucosa** | | | | | 0.076 | 0.431 | 0.168 | 0.079 | -0.051 | 0.6 | 0.098 | 0.31 | 0.279 | **0.003** |
| **Colesterol** | | | | | | | 0.312 | **<0.001** | 0.244 | **0.01** | 0.912 | **<0.001** | 0.113 | 0.238 |
| **niñas (n= 105)** | | | | | | | | | | | | | | |
| **Zn total** | -0.277 | 0.004 | -0.229 | **0.019** | -0.117 | 0.235 | -0.26 | **0.007** | 0.6 | 0.54 | -0.04 | 0.686 | -0.098 | 0.319 |
| **IMCz** | | | 0.136 | 0.162 | 0.254 | **0.008** | 0.477 | **<0.001** | -0.421 | **<0.001** | 0.315 | **<0.001** | 0.562 | **<0.001** |
| **Glucosa** | | | | | 0.056 | 0.564 | -0.051 | 0.602 | 0.081 | 0.405 | 0.043 | 0.66 | 0.101 | 0.229 |
| **Colesterol** | | | | | | | 0.314 | **<0.001** | 0.308 | **<0.001** | 0.93 | **<0.001** | 0.201 | **0.038** |

*Prueba de Rho de Spearman p<0.05; HDLc: Lipoproteínas de alta densidad; LDLc: Lipoproteínas de baja densidad; TG: Triglicéridos*

**Tabla 9. Correlación entre Zn sérico IMC y otros parámetros bioquímicos**

| Autores | País | IMC | Glucosa | CT | TG | HDLc | LDLc | Insulina |
|---|---|---|---|---|---|---|---|---|
| García O.P. et al.,2013 | México | + | + | + | + | + | + | - |
| Azab S.F. et al., 2014 | Egipto | - | NP | - | - | + | - | NP |
| Jaksic M. et al., 2019 | Montenegro | - | NP | NP | NP | NP | NP | NP |
| Malik V.S. et al., 2020 | India | - | NP | NP | NP | NP | NP | - |
| **Nuestro estudio** | **México** | - | - | + | - | NP | + | NP |



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**Tabla 10. Correlaciones entre SZn, ZAG con variables antropométricas y bioquímicas de acuerdo con el sexo y el estado nutricional (n=72)**

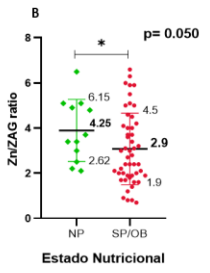
| Variables | Normo peso Niños (n=8) | | Sobre peso/ Obesidad Niños (n=27) | | Normo peso Niñas (n= 8) | | Sobre peso/ Obesidad Niñas (n=29) | |
|---|---|---|---|---|---|---|---|---|
| | SZn | ZAG | SZn | ZAG | SZn | ZAG | SZn | ZAG |
| Edad | -0.295 (0.478) | 0.599 (0.117) | 0.299 (0.130) | 0.064 (0.752) | -0.132 (0.756) | 0.144 (0.734) | 0.039 (0.842) | -0.014 (0.942) |
| **Antropométricos** | | | | | | | | |
| Peso | -0.301 (0.4668) | 0.659 (0.076) | 0.367 (0.059) | -0.346 (0.077) | -0.061 (0.885) | -0.012 (0.977) | 0.121 (0.533) | -0.011 (0.953) |
| Talla | -0.060 (0.887) | **0.802 (0.017)** | 0.376 (0.053) | -0.121 (0.549) | -0.169 (0.690) | -0.036 (0.932) | 0.152 (0.430) | -0.142 (0.464) |
| DC | -0.309 (0.456) | 0.699 (0.054) | 0.333 (0.090) | -0.251 (0.208) | 0.084 (0.844) | -0.228 (0.588) | 0.013 (0.946) | -0.063 (0.744) |
| IMCz | **-0.825 (0.012)** | 0.156 (0.713) | 0.322 (0.101) | -0.242 (0.223) | -0.119 (0.779) | 0.024 (0.955) | -0.131 (0.497) | 0.230 (0.230) |
| **Bioquímicos** | | | | | | | | |
| Glucosa | **0.880 (0.004)** | 0.168 (0.691) | -0.147 (0.464) | **0.387 (0.046)** | 0.146 (0.729) | -0.537 (0.170) | 0.343 (0.069) | -0.189 (0.326) |
| Colesterol total | 0.311 (0.453) | 0.000 (1.000) | 0.376 (0.053) | 0.344 (0.079) | 0.024 (0.955) | -0.119 (0.779) | -0.067 (0.729) | 0.077 (0.693) |
| Triglicéridos | 0.054 (0.889) | **0.731 (0.041)** | 0.080 (0.692) | 0.007 (0.973) | -0.084 (0.844) | 0.287 (0.490) | -0.034 (0.859) | 0.007 (0.973) |
| HDLc | 0.024 (0.955) | 0.000 (1.000) | -0.143 (0.476) | 0.185 (0.355) | 0.275 (0.509) | -0.156 (0.713) | -0.034 (0.859) | 0.128 (0.508) |
| LDLc | -0.048 (0.910) | -0.395 (0.333) | **0.517 (0.006)** | 0.110 (0.585) | 0.071 (0.867) | -0.119 (0.779) | -0.078 (0.689) | -0.030 (0.877) |
| Insulina | **-0.823 (0.012)** | 0.101 (0.811) | 0.389 (0.055) | -0.183 (0.362) | **-0.786 (0.021)** | 0.476 (0.233) | 0.160 (0.408) | 0.318 (0.093) |
| Zn | - | -132 (0.756) | - | -0.154 (0.442) | - | -0.667 (0.071) | - | -0.8 (0.682) |

**Tabla 9. Correlación entre ZAG sérico y parámetros antropométricos bioquímicos**

| Autores | País | IMC | DC | Glucosa | CT | TG | HDLc | LDLc | Insulina |
|---|---|---|---|---|---|---|---|---|---|
| Yeung, D. et al., 2009 | China | + | + | + | NP | + | + | - | + |
| Olofsson, L. Eet al., 2010 | Suecia | NP | NP | NP | + | + | NP | NP | NP |
| **Nuestro estudio** | **México** | **NP** | **NP** | **+** | **NP** | **+** | **NP** | **NP** | **NP** |

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## Resultados



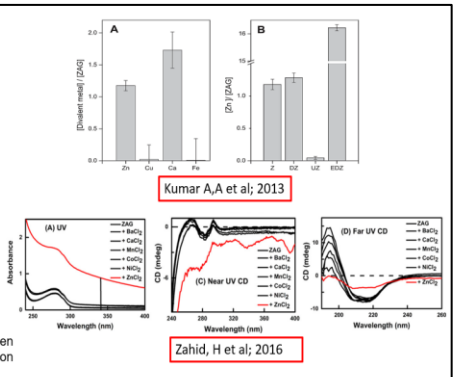




**Figura 9.** Relación Zn/ZAG en población de niños mexicanos con sobrepeso/Obesidad (n = 72).

(Severo, J. S eta al 2020)



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**Table 11. Asociación del sexo y el estado nutricional con las concentraciones de Zn, ZAG y la relación Zn/ZAG (n= 72)**

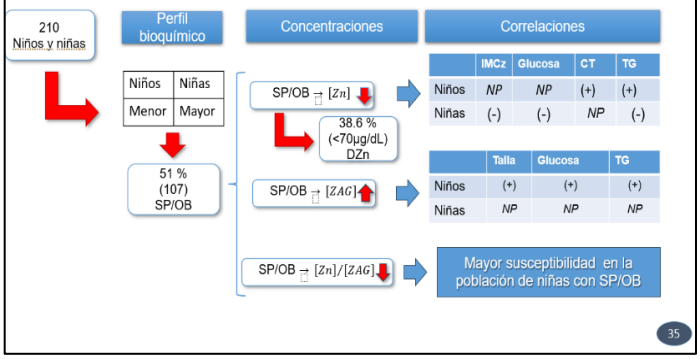
| | Zn β (95% CI) | ZAG β (95% CI) | Zn/ZAG ratio β (95% CI) |
|---|---|---|---|
| **Interacción (sexo* estado nutricional)** | | | |
| Niños + Peso Normal | Referencia | Referencia | Referencia |
| Niños + Sobre Peso/Obesidad | -12.5 (-45.3 to 20.2) | 2.1 (-5.6 to 9.9) | -2.09 (-4.34 to 0.17) |
| Niñas + Peso Normal | 6.4 (-33.7 to 46.6) | -2.8 (-12.4 to 6.7) | -1.1 (-3.91 to 1.62) |
| Niñas + Peso Normal/Obesidad | -22.2 (-54.9 to 10.5) | -3.3 (-11.1 to 4.4) | **-2.32 (-4.58 to -0.07)*** |

Modelo de regresión cuantil ajustados por edad. * Valor P<0,05

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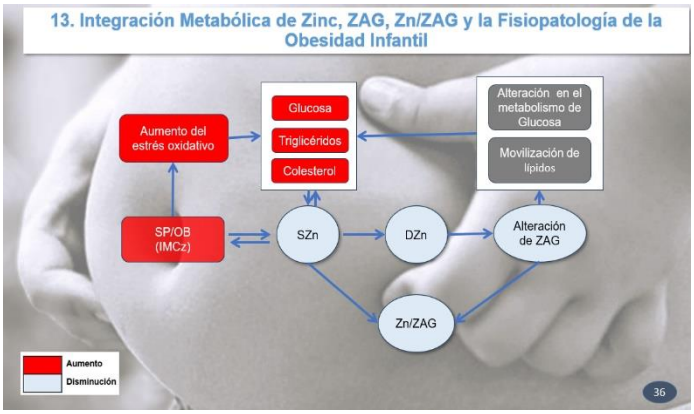
## 12. Resumen de resultados




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## 13. Integración Metabólica de Zinc, ZAG, Zn/ZAG y la Fisiopatología de la Obesidad Infantil




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## 14. Conclusión

La **deficiencia de Zinc** y la disfunción en **la relación Zn/ZAG** reflejan desbalances metabólicos en obesidad infantil, exacerbados por la inflamación y la alteración en el metabolismo de glucosa y lípidos, especialmente en la población de niñas por lo que la investigación de **nuevos biomarcadores como** lo son **Zn y ZAG pueden contribuir** a comprender su relación junto con otras variables socioculturales, antropométricas tales como el **IMC y el CC,** alertando del **riesgo metabólico** y asi tomar medidas de **intervención** con un impacto en el sector salud para evitar complicaciones en la edad adulta.

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## 15. Limitaciones

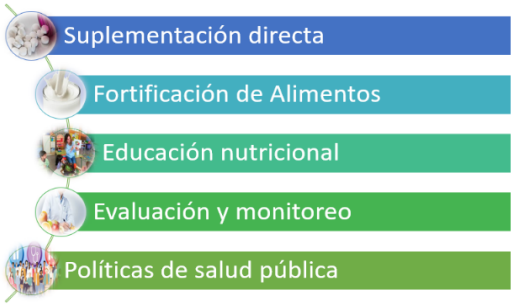
Este estudio tuvo limitaciones metodológicas que deben ser consideradas en la generalización de los resultados a otras poblaciones tales como el tamaño de la muestra entre Zinc y ZAG. Además, la ausencia de biomarcadores inflamatorios que puede restringir nuestra capacidad para explorar mecanismos inflamatorios profundos asociados a los niveles de Zinc y ZAG en relación con el estado nutricional.

A pesar de estas limitaciones, los hallazgos proporcionan información valiosa sobre la asociación entre Zinc, ZAG y obesidad infantil.

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## 16. Estrategias contra la DZn




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## 17. Consideraciones a futuro

- Realizar estudios con muestras más amplias y variadas de niños de diferentes edades, entornos socioeconómicos (urbano-rural), y regiones para validar los hallazgos iniciales y hacerlos más generalizables.
- Realizar análisis longitudinales de los niveles de Zinc y ZAG: Para evaluar cómo los niveles de estos biomarcadores se relacionan con el desarrollo de obesidad o enfermedades metabólicas en la adolescencia o adultez.
- Desarrollar programas de educación y promoción de una dieta rica en Zinc en escuelas con niños en riesgo de obesidad.






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## Participación en congresos y foros:

1. LatinXChem twitter conference 2021 on Sept 20, 2021 with the poster #BIO028 entitled: Analysis of serum Zinc levels in obese Child population

2. TERCER CONGRESO INTERDICIPLINARIO DEL STEAM A LA PRÁCTICA CLÍNICA
Ponencia: Principales Oligoelementos y su relación con la enfermedad y métodos de cuantificación actual celebrado el 23 de junio del 2023

3. Foro de investigación en Enfermería y Nutrición " Un encuentro para el desarrollo académico y cientpífico 2024. Ponencia: Asociación de los niveles de zinc y vitamina A (Retinol) en muestras séricas con el estado nutricional de niños en edad escolar" celebrado los días 6 y 7 de Junio del 2024

4. 24° Verano de la Ciencia de la Región Centro "Evaluación de los niveles séricos de elementos traza en población adulta mexicana"

5. Participación en trabajos finales de servicio social de alumnos de la facultad de Medicina de la Universidad Autónoma de Baja California con el cartel " Valoración del estado nutricional, dieta, composición corporal y parámetros bioquímicos en niños en edad escolar" Como parte de la estancia de trabajo en la Ciudad de Mexicali Baja California Septiembre-Noviembre del 2023

6. Participación en la LII Presentación de conclusiones, avances y nuevas propuestas de investigación del IIZD con el tema: ASOCIACIÓN DE LA CONCENTRACIÓN SÉRICA DE ZINC TOTAL Y ZINC ALFA 2 GLICOPROTEÍNA CON EL ESTADO NUTRICIO Y PERFIL METABÓLICO EN POBLACIÓN INFANTIL CON SOBREPESO Y OBESIDAD, presentado el 15 de Julio del 2024



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