REVISTA CHILENA DE NUTRICIÓN

Sociedad Chilena de Nutrición

Original article

Mineral deficiency and cardiovascular risk in women with obesity

Deficiencia mineral y riesgo cardiovascular en mujeres con obesidad

Loanne Rocha dos Santos[1], Stéfany Rodrigues de Sousa Melo[1], Juliana Soares Severo[1], Kyria Jayanne Clímaco Cruz[1], Emyle Horrana Serafim de Oliveira[1], Thayanne Gabryelle Visgueira de Sousa[1], Jennifer Beatriz Silva Morais[1], Tamires da Cunha Soares[1], Francisco Erasmo de Oliveira[2], Gilberto Simeone Henriques[3], Dilina do Nascimento Marreiro[1]*

1. Department of Nutrition, Federal University of Piaui, Teresina, Brazil
2. Centro de Estudos Filosóficos e Humanísticos, Universidade Católica Portuguesa, Braga, Portugal
3. Department of Nutrition, Federal University of Minas Gerais, Belo Horizonte, Brazil

Reception date: 12/04/2024
Acceptance date: 03/19/2025
Publication date: 30/04/2025

***Correspondence:** Dilina do Nascimento Marreiro. dilina.marreiro@gmail.com.

Abstract

This study aims to test the association between magnesium, selenium, and calcium and the increased cardiometabolic risk in women with obesity. This was a cross-sectional study that involved 130 women divided into a group of women with obesity (n=69) and a control group (n=61). Statistical analysis was performed through the GraphPad Prism program. The results shown that women with obesity have a lower concentration of the minerals magnesium, selenium and calcium in blood, as well increase in the excretion of these minerals in the urine when compared to the control group. Addition, thit group showed high concentrations of total cholesterol, TGC, VLDL-C, LDL-C, non-HDL, IC I, IC II, interleukine-6 and interleukine-8, which suggests increased risk for cardiovascular disease in this group. There was also a positive correlation between urinary mineral concentrations and anthropometric parameters. The results suggest that excess adiposity is associated with deficiency of the minerals analyzed, as well as revealing the association of this deficiency with increased cardiometabolic risk in the population evaluated.

Keywords: Obesity. Magnesium. Selenium. Calcium. Cardiovascular diseases.

Resumen

Este estudio pretende comprobar la asociación entre el magnesio, el selenio y el calcio y el aumento del riesgo cardiometabólico en mujeres con obesidad. Se trató de un estudio transversal en el que participaron 130 mujeres divididas en un grupo de mujeres con obesidad (n=69) y un grupo de control (n=61). El análisis estadístico se realizó mediante el programa GraphPad Prism. Los resultados mostraron que las mujeres con obesidad tienen una menor concentración de los minerales magnesio, selenio y calcio en rubio, así como un aumento en la excreción de estos minerales en la orina en comparación con el grupo control. Además, este grupo mostró concentraciones elevadas de colesterol total, TGC, VLDL-C, LDL-C, no-HDL, IC I, IC II, interleucina-6 e interleucina-8, lo que sugiere un mayor riesgo de enfermedad cardiovascular en este grupo. También se observó una correlación positiva entre las concentraciones urinarias de minerales y los parámetros antropométricos. Los resultados sugieren que el exceso de adiposidad está asociado a la deficiencia de los minerales analizados, así como revelan la asociación de esta deficiencia con un mayor riesgo cardiometabólico en la población evaluada.

Palabras clave: Obesidad. Magnesio. Selenio. Calcio. Enfermedades cardiovasculares.

Introduction

Obesity is a chronic disease, characterized by excess adipose tissue, that favors the manifestation of various comorbidities, such as type 2 diabetes mellitus, breast cancer, and cardiovascular disease, with a relevant impact on increased mortality. Data from the World Obesity Atlas show that in 2020 obesity reached 15 % of the world's population, a total of 764 million people, and the forecast for 2030 is a prevalence of 18 %, representing over one billion people worldwide[1,2].

The literature highlights that the increase in triacylglycerol deposition in adipose tissue, particularly in the visceral region, induces of dysfunction this tissue, characterized by adipocyte hypertrophy, angiogenesis reduction, increase the pro-inflammatory cytokines synthesis such as IL-1β, IL-6, and TNF-α, oxidative stress, insulin resistance, and dyslipidemia, important cardiometabolic risk factors[3].

This setting contributes to the deposition of ectopic fat in other target tissues that participate in the regulation of glucose homeostasis, such as the liver tissue. This reduces

Rev Chil Nutr 2025; 52(2): 13-23
https://doi.org/10.4067/S0717-75182025000200013

the sensitivity of this tissue to insulin and facilitates the production of very low-density lipoproteins (VLDL-C), which increases the incorporation of triacylglycerols (TGC) and Apolipoprotein B. Such lipoprotein suffers triacylglycerol removal by lipoprotein lipase and gives rise to the fraction of low-density lipoproteins (LDL-C), which is deposited in vascular endothelium tissues, contributing to dyslipidemia, endothelial dysfunction and, consequently, increased cardiometabolic risk[4].

To understand the influence of nutrition on cardiometabolic protection, research has investigated the participation of minerals, particularly magnesium, selenium, and calcium, in the control of disorders in individuals with obesity. Magnesium, for example, maintains blood glucose homeostasis, participates in the synthesis and signaling of insulin, and reactions in the glycolytic pathway. It also influences the control of systemic blood pressure and regulates the synthesis of non-esterified fatty acids in hepatocytes[5].

Selenium is also an important nutrient of cardiometabolic protection, as it participates in lipid metabolism, such as in its performance in the activity of HMG-COA enzyme reductase, playing a hypocholesterolemic role. Associated with this, indirectly, selenium also participates in cardiometabolic protection because it has antioxidant and anti-inflammatory action, assists in the stimulation of insulin secretion, and contributes to signal transduction stimulated by the connection of this hormone to its specific receptor. Calcium is a mineral that regulates blood pressure via the renin-angiotensin-aldosterone system, acts to contract vascular smooth muscle, stimulates insulin secretion and signaling, and coordinates processes related to apoptosis and immune function[6].

To this matter, although the various relevant functions performed by magnesium, selenium, and calcium in cardiometabolic protection have been demonstrated, there is still a data gap in the literature that can indicate the relationship between the deficiency of these nutrients and the increased cardiometabolic risk, particularly, in women with obesity. Thus, this study aimed to verify the association between magnesium, selenium, and calcium and the increased cardiometabolic risk in women with obesity.

Materials and method

Study characterization and experimental protocol

This cross-sectional study involved 130 women, aged between 20 and 50 years, and divided into two groups: women with body mass index (BMI) ≥ 35 kg/m² (obese n=69) and women with BMI between 18.5 to 24.9 kg/m²; (eutrophic n=61). The sample was defined by means of convenience sampling and the participants were recruited from clinics located in Teresina - PI, with similar distribution of age and socioeconomic status between the two groups.

The study participants were selected through an interview considering the following exclusion criteria: pregnant or lactating; postmenopausal; participating in another clinical study; presence of comorbidities, such as diabetes mellitus, chronic kidney disease, cancer, and recent infections. Women using vitamin-mineral supplements or medications that could interfere with the nutritional status of minerals, smokers, and those with history of chronic alcohol intake were also excluded.

The project was registered in the Plataforma Brasil, and it was approved by the Research Ethics Committee of the Federal University of Piaui, according to the CNS Resolution 466/12, under Certificate of Presentation for Ethics Appreciation (CAAE) 3.276.485. All participants signed an informed consent form describing the study procedures.

Assessment of nutritional status

For anthropometric assessment, body weight, height, waist circumference, neck, and hip measurements were taken according to the methodology described by the Brazilian Ministry of Health[7]. To assess the nutritional status of the study participants, BMI was calculated by dividing the participant's weight by their height squared[8]. In addition, the waist-to-hip ratio was calculated.

Collection and processing of biological material

20mL blood samples were collected in the morning between 7 and 9 am, with the participants fasting for at least 12 hours. The collected blood was distributed in two separate tubes: (1) a polypropylene tube containing 30 % sodium citrate as an anticoagulant for the analysis of magnesium (2) a vacuette® tube with a clot activator for the determination of the lipid profile, (3) without anticoagulant to analyze serum glucose, serum insulin and markers of inflammation (8 mL of blood), and (4) with ethylenediamine tetra acetic acid (EDTA) anticoagulant to analyze glycated hemoglobin and selenium.

Plasma was separated by centrifugation (CIENTEC® 4K15, São Paulo, Brazil) at 1831 x g for 15 minutes at 4 ºC. Then, it was extracted with an automatic pipette and placed in demineralized polypropylene microtubes which were subsequently kept at -20 °C. For the separation of erythrocytes and subsequent determination of minerals. These comprised washing the erythrocyte mass with 10 mL of an isotonic saline solution (0.9 % NaCl), followed by thorough homogenization by inversion, and subsequent centrifugation at 2493 x g for 10 minutes. This procedure was repeated three times to remove contaminants from the erythrocytes (platelets and leukocytes). After the last centrifugation, the saline solution was aspirated and discarded, and the erythrocyte mass was carefully extracted with the aid of an automatic pipette and transferred to demineralized polypropylene tubes which were kept at –20 °C for further analysis.

For 24-hour urine collection, the demineralized containers were weighed before and after the collection on a semi-analytical scale to determine the urine volume from the density. After this procedure, 20 mL of the urine was removed, distributed between polypropylene microtubes, and stored at -20 °C for later measurement of the mineral's concentration.

Plasma, erythrocyte, and urinary minerals analyses were performed at the Atomic Emission Spectrometry Laboratory - Embrapa (National Corn and Sorghum Research Center), located in Sete Lagoas - Minas Gerais. The elemental analysis of the mineral was performed in an inductively coupled plasma spectrometer - Optical Emission Spectrometry with an axial view configuration and a V-Groove nebulizer

(720 ICP / OES, Varian Inc., California, United States). The detection limits were measured using the equation 3x standard deviation of 10 blank measurements, divided by the slope of the calibration curve. Monoelemental stock solutions of magnesium 1000 mgL^{-1} (Titrisol and Certipur - Merck, Germany) were used for the preparation of the reference solutions for the calibration curve and optimization of the analytical conditions. All aqueous solutions and dilutions were prepared using ultrapure water (18 MΩ.cm -1) obtained using a Milli-Q system (Millipore, Bedford, MA).

Determination of the biochemical parameters of magnesium, selenium and calcium

Analyses of plasma, erythrocyte and urinary mineral concentrations were carried out at the Atomic Emission Spectrometry Laboratory - Embrapa (National Maize and Sorghum Research Centre, Sete Lagoas - MG. The elemental analysis of the minerals was carried out in an Inductively Coupled Plasma-Optical Emission Spectrometer with an axial view configuration and a V-Groove nebuliser (720 ICP/OES, Varian Inc., California, United States).

The reference values adopted were 0.75 to 1.05 mmol /L for plasma magnesium[9], 1.65 to 2.65 mmol /L for erythrocyte magnesium, and 3.00 to 5.00 mmol /24 h for urinary magnesium[10], 80 to 95 µg/L for plasma selenium[11], 0,18 to 0.55 µg/gHb for erythrocyte selenium[12], calculation of clearance for urinary selenium[13] 2.12 to 2.65 mmol/l for plasma calcium[14], and lower values than 4.0 mg/kg/day for urinary calcium[15].

Evaluation of cardiovascular risk parameters

Neck circumference (NC)

The measurement was taken at the midpoint of the cervical spine up to the mid-anterior point of the neck using a Seca® (São Paulo, Brazil) flexible, non-extendable measuring tape, accurate to 0.1 centimeters. The reference value used was greater than 34 cm for mild risk and greater than 36.5 cm for high risk of cardiometabolic diseases[16].

Waist-to-hip ratio (WHR)

The waist-to-hip ratio was calculated from the participant's waist circumference divided by the hip circumference, using as a reference value that recommended by the World Health Organization (WHO)[17].

Conicity index (ICON)

This indicator was determined using weight, height and waist circumference measurements, and is used to assess obesity and body fat distribution. The threshold value for the conicity index associated with the development of obesity-related complications and cardiovascular diseases is 1.18 for women[18].

Determination of lipid profile

Serum concentrations of total cholesterol, HDL-cholesterol, and triacylglycerols were determined according to the colorimetric enzymatic method, using a COBAS INTEGRA automated biochemical analyzer with ROCHE® kits (Roche Diagnostics, Brazil). The LDL-cholesterol fraction was calculated according to the formula of Friedwald et al.[19]: LDL-c = CT - HDL-c - TG / 5, and was considered valid for values of TGC up to 400mg/dL. The reference values for the lipid fractions were those defined in the Update of the Brazilian Dyslipidemia and Atherosclerosis Prevention - 2017[20].

Determination of Castelli I and II indexes

To determine the risk of cardiovascular disease, Castelli I and II indexes were used, and these correspond to the ratio between total cholesterol (TC) and HDL-cholesterol and the ratio between LDL cholesterol and HDL cholesterol, respectively. The reference values are Castelli I (CI) index ≤ 4.3 mg / dL; and Castelli II (CII) index ≤ 2.9 mg / dL[21].

Blood pressure measurement

Blood pressure was measured using a G-Tech model BP3AF1-3 digital pulse device after the participant had been at rest for ten minutes. The reference standard was systolic pressure below 130 mmHg and diastolic pressure below 85 mmHg[22,23].

Determination of markers of inflammation

The determination of plasma concentration of cytokines IL-6 and IL-8 was performed using the Cytometric Bead ArrayTM Human Inflammatory Cytokines kit (BD Biosciences, USA), in a FACS CANTO II® (Becton Dickinson) flow cytometer. Following the manufacturer's instructions, capture beads were added to the serum samples, and, after 1.5 h of incubation in the dark, each sample was suspended in 1 ml of wash buffer and centrifuged at 200 × g for 5 min; then, the supernatants were carefully discarded. Human inflammatory cytokine PE detection reagent was added to each sample to resuspend the pellet followed by 1.5 h incubation in the dark. Wash buffer was again added to the samples and centrifuged at 200 × g for 5 min. Finally, the supernatants were carefully discarded, and the pellet was resuspended in 300 µL of wash buffer. The standard curve for all cytokines was initially prepared, and the standard samples were analyzed similarly to the serum samples. Samples and calibration curves were acquired using FACSCantoTM II software (BD Biosciences, USA). FCAP Array Infinite software (Soft Flow®, Hungary) was used to quantify all cytokines in the standards and samples.

Determination of glycemic control parameters

Fasting serum glucose levels were assessed through the utilization of colorimetric enzymatic methodology along with Labtest kits and the biochemical analyzer Labmax 100 (Labtest, Brazil). We considered values between 75 and 99 mg/dl as normal. Serum insulin concentration was determined using the chemiluminescence method, employing the Liaison XL (DiaSorin, Italy) instrument. Normal ranges of insulin were considered for values between 2,3-26 µU/ml. Analysis of glycated hemoglobin was carried out using the ion exchange chromatography method (Variant II Turbo – BIORAD). Were considered values lower than 5.7 % as normal[24].

Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated from fasting serum glucose and

fasting serum insulin. HOMA-IR values greater than 2.71 were classified as insulin resistance[25,26].

Statistical analysis

Data imputation was performed to handle missing data, with the goal of "completing" the bank and enabling the analysis with all individuals in the study, being up to 18 % in the group of women with obesity and 15 % in the control group.

The unique imputation was performed by the Predictive Mean Marching (PMM) method, which is indicated for quantitative variables. It was conducted in three steps, using the function created by Andreozzi: (1) estimation of a regression model, the variable of interest (the imputation) was the response variable and the remaining variables were explanatory; (2) estimation of the value of the variable of interest to the subjects with the omissive data; (3) pairing of the value of the predicted variable of interest, for the subjects with the omitted data, with the nearest adjusted value (made from the calculation of the Euclidean distance). In the case where there was more than one value adjusted with a distance equal to the minimum distance found, the amount to be imputable was randomly chosen, among those who underwent a draw. All these analyses were performed using the R (R Development Core Team) program[27-29].

The data were organized in Excel spreadsheets, to perform descriptive analysis of the observed variables, and were later exported to the GraphPad Prism program (version 9.3) for statistical analysis of the results. Continuous variables were expressed as mean ± SD.

The assumption of normality of the variables was evaluated through the Kolmogorov-Smirnov test. Then, for comparison purposes, a t-test was performed for continuous variables with normal distribution and the Mann-Whitney test for those with nonparametric distribution. For the study of correlations, the Pearson or Spearman correlation coefficient for variables with parametric and non-parametric distribution, respectively. The tests were considered significant when $p < 0.05$.

Results

The mean values and standard deviations of age and anthropometric parameters used to assess the nutritional status of the participants are shown in **table 1**. It was observed that there was a statistically significant difference in the parameters of weight, height, and BMI index ($p < 0.05$), these parameters being higher in women with obesity.

Women with obesity had decrease plasm and erythrocyte's concentration of magnesium, selenium and zinc. Additionally, they had increased values of these minerals in urine compared to the control group (**Table 2**).

Cardiometabolic risk markers revealed statistically significant differences between the obese women and the control group in terms of total cholesterol, triacylglycerols, VLDL-C, LDL-C, HDL-C, non-HDL, Castelli I, Castelli II, Interleukin-6 and Interleukin-8, as shown in **table 3**.

The analysis of simple linear correlation between magnesium, selenium, and calcium concentrations and adiposity parameters of study participants, involving obese and eutrophic women, is shown in **figures 1, 2,** and **3**. The results revealed a significant negative correlation between plasma concentrations and magnesium erythrocytes, selenium, and calcium and anthropometric parameters.

A simple linear correlation analysis between cardiometabolic risk markers and plasma, erythrocyte, and urinary concentrations of women with obesity is presented in **table 4**. There was a positive correlation between magnesium erythrocyte concentrations and a waist-hip ratio, LDL-C, Non-HDL-C, Castelli I index, and Castelli II index, as well as a negative correlation between this biomarker and HDL-C.

Data regarding selenium biomarkers showed a positive correlation between their plasma concentrations and a hip and HOMA-IR waist relationship, as well as a negative correlation between mineral and total cholesterol, LDL-C, non-HDL-C, and interleucine-8. A positive correlation was also verified between the concentrations of urinary selenium

Table 1. Mean values and standard deviations of age, anthropometric parameters of study participants.

Parameteres	Control (n=61) Mean ± SD	Obese (n=69) Mean ± SD	p value
Age (years)	35.07 ± 7.61	32.61 ± 7.74	0.080
Body weight (kg)	55.70 ± 5.27	104.7 ± 11.64	<0.001*
Height (m)	158.2 ± 6.15	160.5 ± 6.24	0.027*
BMI (kg/m^2)	22.26 ± 1.65	40.66 ± 4.03	<0.001*
WC (cm)	73.92 ± 4.90	111.6 ± 9.91	<0.001*
HC (cm)	95.90 ± 4.62	128.8 ± 8.39	<0.001*

*Significantly different values between women with obesity and the control group, Student's t-test or Mann-Whitney test ($p<0.05$). WC=waist circumference; HC=hip circumference; SD=standard deviation; BMI=body mass index.

Table 2. Mean values and standard deviations of the biochemical parameters of minerals of study participants.

Parameteres	Control (n=61) Mean ± SD	Obese (n=69) Mean ± SD	P value
Plasma Mg (mmol/L)	0.92 ± 0.11	0.61 ± 0.10	<0.001*
Erythrocyte Mg(mmol/L)	2.31 ± 0.24	1.51 ± 0.19	<0.001*
Urinary Mg (mmol/day)	3.48 ± 1.72	5.72 ± 2.40	<0.001*
Plasma Se (µg/L)	78.74 ± 9.22	59.60 ± 5.85	<0.001*
Erythrocyte Se (µg/gHb)	0.39 ± 0.07	0.24 ± 0.03	<0.001*
Urinary Se (µg/day)	42.99 ± 5.47	62.38 ± 9.46	<0.001*
Clearence of Se	0.45 ± 0.26	0.93 ± 0.44	<0.001*
Plasma Ca (mmol/L)	2.45 ± 0.19	1.93 ± 0.19	<0.001*
Urinary Ca (mmol/day)	2.99 ± 0.96	4.27 ± 1.24	<0.001*

*Values significantly different between women with obesity and control groups, Student's t test or Mann-Whitney test ($p<0.05$). SD=standard deviation; Mg=magnesium, Se=selenium; Ca=calcium.

Table 3. Mean values and standard deviations of the cardiometabolic risk markers of the study participants.

Parameteres	Control (n=61) Mean ± SD	Obese (n=69) Mean ± SD	P value
NC (cm)	31.57 ± 2.11	39.58 ± 2.69	<0.001*
WHR	0.77 ± 0.05	0.86 ± 0.06	<0.001*
ICON	1.14 ± 0.06	1.27 ± 0.08	0.024*
SBP (mmHg)	116.7 ± 11.23	121.0 ± 15.60	0.176
DBP (mmHg)	80.52 ± 9.79	80.49 ± 9.79	0.782
TC	182.2 ± 20.97	193.1 ± 25.53	0.009*
TGC	112.0 ± 33.49	142.5 ± 46.00	<0.001*
VLDL-c	22.40 ± 6.69	28.49 ± 9.20	<0.001*
HDL-c	54.97 ± 9.34	49.09 ± 11.20	0.003*
LDL-c	104.9 ± 18.60	115.5 ± 24.56	0.007*
non-HDL	127.2 ± 20.91	144.0 ± 25.45	<0.001*
IC I	3.40 ± 0.66	4.19 ± 1.36	<0.001*
IC II	1.98 ± 0.55	2.55 ± 1.03	<0.001*
FPG	80.34 ± 9.44	83.54 ± 12.31	0.231
SI	10.47 ± 3.38	11.64 ± 4.08	0.157
HOMA-IR	2.10 ± 0.78	2.47 ± 1.12	0.081
Hba1C	5.08 ± 0.56	5.12 ± 0.51	0.926
IL-6	3.70 ± 3.45	7.48 ± 5.32	<0.001*
IL-8	23.32 ± 15.89	13.67 ± 7.92	0.012*

*Values significantly different between women with obesity and control groups, Student's t test or Mann-Whitney test ($p<0.05$). SD=standard deviation; NC=neck circumference; WHR=waist-hip ratio; ICON=conicity index; SBP=systolic blood pressure; DBP=diastolic blood; TC=total cholesterol; TGC=triacylglycerols; VLDL=very low density lipoprotein; HDL=high density lipoprotein; LDL=low density lipoprotein; non- HDL=non-high-density lipoprotein; CRI I=Castelli's risk index I; CRI II=Castelli's risk index II; SI=serum insulin; FPG=fasting plasma glucose; HbA1c=glycated hemoglobin; HOMA-IR=homeostasis model assessment insulin resistance; IL=interleukin.

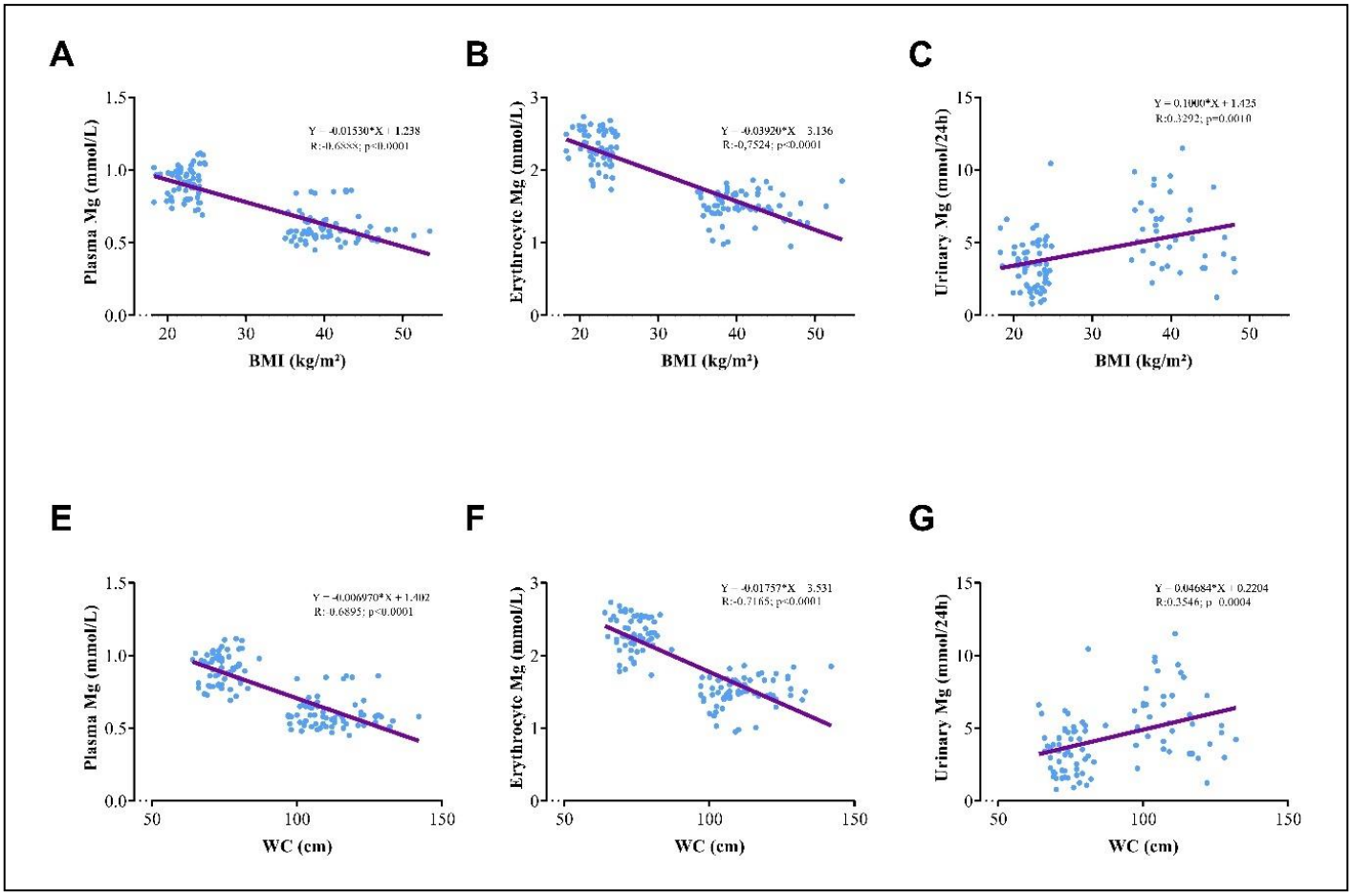

Figure 1. Simple linear correlation analysis between plasma, erythrocyte and urinary magnesium concentrations and adiposity parameters in the study participants.
A: plasma magnesium concentrations and BMI. B: erythrocyte magnesium concentrations and BMI. C: urinary magnesium concentrations and BMI. E: plasma magnesium concentrations and WC. F: erythrocyte magnesium concentrations and WC. G: urinary magnesium concentrations and WC. *Significance was found in A, B, C, E, F and G, with $p < 0.05$. Pearson or spearman correlation was used for R and p values.

and total cholesterol, non-HDL-C, and negative correlation between the marker and diastolic blood pressure. Furthermore, urinary calcium was positively correlated with Castelli indexes I and II. On the other hand, it was negatively correlated with insulin and HOMA-IR.

Discussion

This study examined the levels of magnesium, selenium, and calcium in the blood and urine of women with obesity. The data obtained showed that mineral concentrations exhibited statistically significant differences between the groups, similar to the results found in the study conducted by Morais et al[30].

Regarding magnesium levels, it is worth noting that these findings are supported by previous literature, which highlights that women with obesity tend to have diets with high energy density, low in whole grains and leafy green vegetables, and rich in ultra-processed foods, resulting in a reduced intake of micronutrients, particularly magnesium[31]. In addition to the reduced intake of magnesium by obese individuals, there are also changes in the absorption process of this nutrient in the enterocytes, which may be due to reduction in the concentrations of sodium and calcium, elements that are important in the active transport of the mineral and interact with its receptors. Another important point concerns the high excretion of magnesium in the urine, which may be influenced by increased insulin resistance or leptin concentrations in obesity. These facts may be a relevant contributing factor to the reduction in concentrations seen in the obese women evaluated in this study[32] (**Figure 1**).

The amount of magnesium in erythrocytes was also reduced in women with obesity, which reinforces the condition of deficiency in this mineral, since this biomarker reflects the existence of a possible chronic depletion, suggesting the occurrence of a medium- and long-term deficit[33]. Associated with this, women with obesity had high amounts of magnesium in the urine when compared to the control group, ratifying the state of deficiency in this mineral, as the reduction of renal reabsorption of this nutrient reduces its amount in plasma and erythrocytes.

Literature shows that hypomagnesemia favors the manifestation of low-grade chronic inflammation, characterized by high concentrations of proinflammatory cytokines and by the increase in free radical production, metabolic changes considered important risk factors for the development of hypertension, cardiovascular disease, metabolic syndrome, and diabetes *mellitus*[31].

Selenium concentrations in the plasma of women with obesity had reduced values when compared to the control group, which can also be due to their insufficient dietary intake, as observed in the study conducted by Fontenelle et al[34].

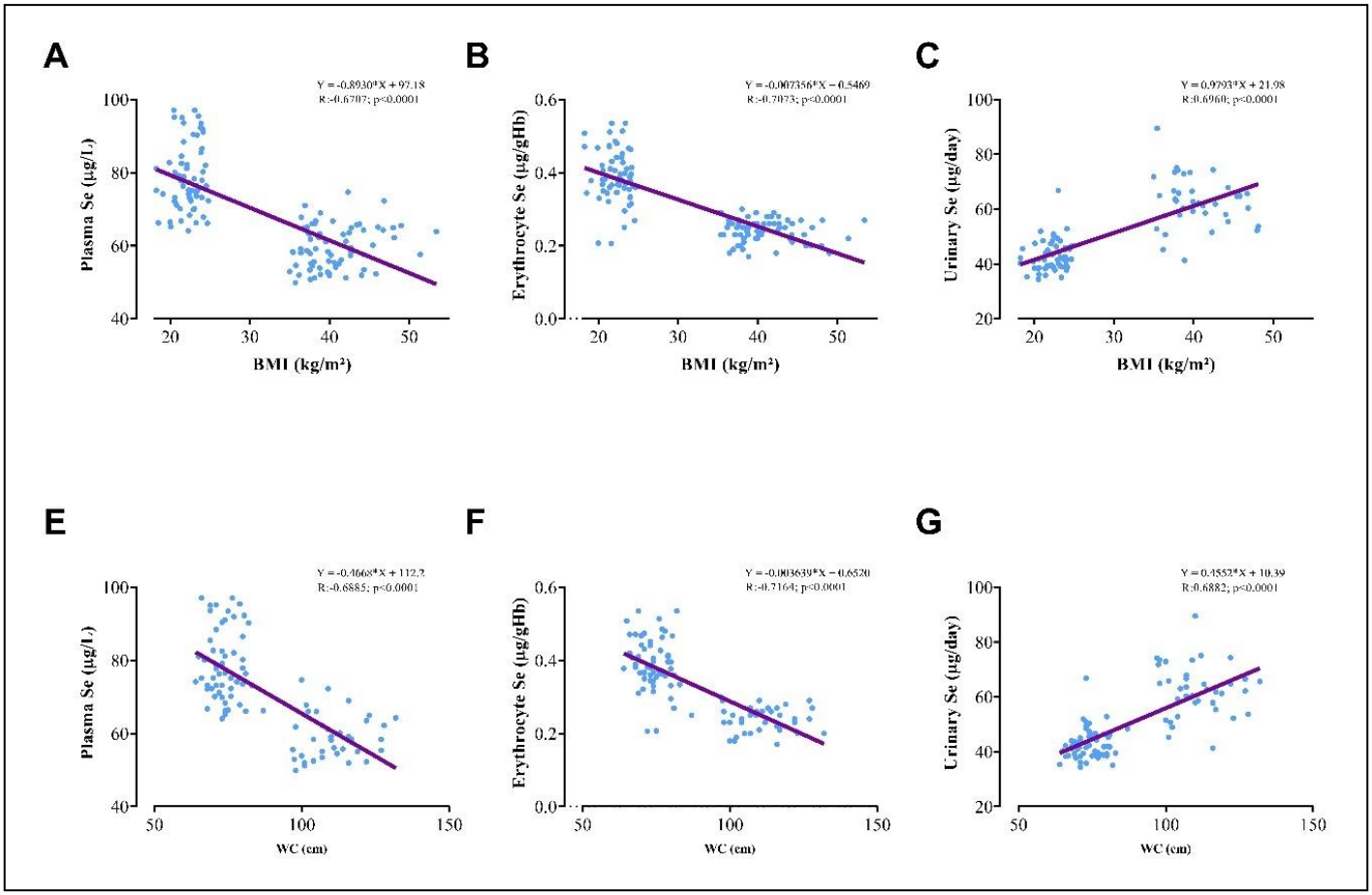

Figure 2. Simple linear correlation analysis between plasma, erythrocyte and urinary selenium concentrations and adiposity parameters in the study participants.
A: plasma selenium concentrations and BMI. B: erythrocyte selenium concentrations and BMI. C: urinary selenium concentrations and BMI. E: plasma selenium concentrations and WC. F: erythrocyte selenium concentrations and WC. G: urinary selenium concentrations and WC. *Significance was found in A, B, C, E, F and G, with $p < 0.05$. Pearson or spearman correlation was used for R and p values.

It is also worth noting that in obesity, high body weight, excess body fat, and the presence of metabolic changes may require amount of selenium quantities of the values established by the recommendation. Thus, when considering the participation of selenium as a cofactor of various antioxidant enzymes, the presence of oxidative stress, for example, can contribute to the reduction in the amount of this micronutrient in the plasma. Associated with this, low-grade chronic inflammation also seems to favor selenium reduction, as inflammatory cytokines inhibit seleno protein P synthesis, the main enzyme involved in selenium transport in plasma[35] (**Figure 2**).

The obese group showed reduced concentrations of selenium in the erythrocytes when compared to the control group, similar to the data obtained by Oliveira et al[36]. This data reinforces the finding of mineral deficiency in the case group. The results also showed greater excretion of the mineral in the group of women with obesity when compared to the control group, which can be explained by the fact that, according to the literature, chronic low-grade inflammation reduces the synthesis of selectoprotein by hepatocytes, and selenide, a substrate used for the synthesis of this protein, is directed to urinary excretion, which contributes to the reduction in the bioavailability of this mineral in obesity[37,38].

In this study, there were reduced calcium concentrations in plasma and high mineral excretion in urine, which may be due to the scarce amount of this nutrient in the diets consumed by the obesity group. Similar data were found in studies conducted by Zohal et al.[39]. It is reinforced that proper plasma calcium concentrations are important to maintain the regulation of lipid metabolism, pancreatic insulin and glucagon secretion, and insulin sensitivity[40] (**Figure 3**).

This study explored the association between the levels of these micronutrients and cardiometabolic risk markers in research participants, and the results revealed a positive correlation between reduced magnesium values in red blood cells and concentrations of LDL-C, non-HDL-C, Castelli index I and II, hip/waist ratio and ICON. In addition, the results revealed a negative correlation between reduced magnesium concentrations in erythrocytes and HDL-C values. These findings demonstrate the possible negative influence of reduced magnesium concentrations on women's erythrocytes evaluated on lipid metabolism, since this mineral acts on the regulation of the quantities of lipid fractions found in the bloodstream, by modulating the activity of important enzymes such as lipase Lipoprotein (LPL), lecithin-cholesterol aCillransferase (LCAT) and 3-hydroxy-3-methyl-glutaril-coenzyme to reductase (HMG-COA reductase)[33].

Magnesium regulates the homeostasis of lipid fractions by stimulating lipoprotein lipase activity, which participates in the regulation of the number of triacylglycerol values and contributes to increased HDL-C. In addition, it

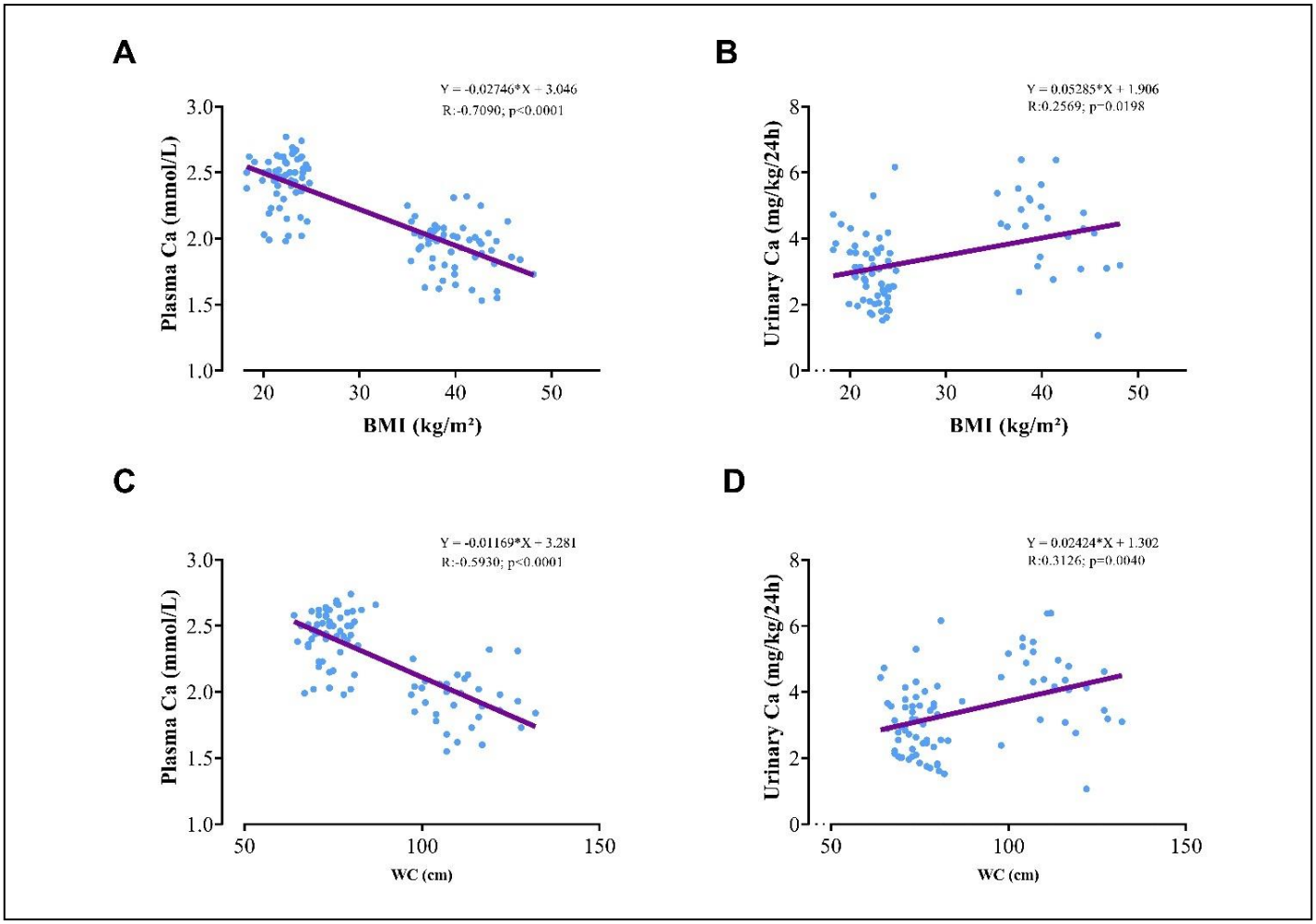

Figure 3. Simple linear correlation analysis between plasma and urinary calcium concentrations and adiposity parameters in the study participants. A: plasma calcium concentrations and BMI. B: urinary calcium concentrations and BMI. C: plasma calcium concentrations and WC. D: urinary calcium concentrations and WC. *Significance was found in A, B, C and D with $p < 0.05$. Pearson or spearman correlation was used for R and p values.

activates LCAT, an enzyme involved in maintaining lipoprotein balance in the body. On the other hand, under conditions of deficiency in this mineral, there is increased activity of HMG-COA reductase, which can increase the concentrations of lipid fractions and an increased proportion of saturated fatty acids to unsaturated[33].

Considering the positive correlation between selenium concentrations in plasma and lipid fractions (total cholesterol, LDL-c, non-HDL-c) in obese women, it should be noted that reduced concentrations of this mineral in plasma may contribute to inadequate control of HMG-CoA reductase expression, leading to increased cholesterol concentrations in the bloodstream. These findings are complemented by the positive correlation between the amount of selenium excreted in urine and the concentrations of total cholesterol and non-HDL-C in the present study, reinforcing that the increased loss of this mineral through the kidneys limits its physiological functions, particularly in controlling cholesterol concentrations in plasma[6,41].

The negative correlation revealed between the concentrations of selenium in plasma and LDL-C in the obesity group, particularly, suggests the possible performance of this nutrient as a 5'-en-type deiodinase cofactor, an enzyme that participates in the synthesis of the triiodothyronine hormone, which contributes to the expression of the LDL-C receiver, a molecular substrate that acts by promoting the influx of LDL-C to intracellular space, reducing its concentration in the bloodstream. In addition, reduced selenium concentrations in the blood compromise the performance of selenoprotein P, an important amino acid in reducing LDL-C oxidation by neutralization of hydroperoxides[42].

Correlation analysis was performed to determine the relationship of selenium to the chronic inflammatory process present in obesity, a negative correlation between the mineral in erythrocytes and interleukin-8 being verified. About this result, data in the literature suggest that indirectly reducing selenium favors inflammation because it limits antioxidant defense, which consequently accentuates chronic inflammation[43].

The results of this study revealed a negative correlation between the urinary calcium excretion and the insulin concentrations and of HOMA-IR values. This finding can be explained by the fact that calcium performs important functions in the insulin secretion route, acting as the second cell messenger in the endocrine system exocytosis processes and regulating hormone signaling in the endoplasmic reticulum[44,45].

In addition, the results show the correlation between urinary calcium and Castelli I and II rates suggest that the loss of this mineral compromises the body's ability to protect these indicators of cardiometabolic risk. Thus, adequate

Table 4. Simple linear correlation between plasma, erythrocyte and urinary concentrations of magnesium, selenium and calcium and markers of cardiometabolic risk in women with obesity.

Parameters	Plasma Mg r	Erythrocyte Mg r	Urinary Mg r	Plasma Se r	Erythrocyte Se r	Urinary Se r	Plasma Ca r	Urinary Ca r
NC (cm)	-0.146	0.052	-0.012	0.060	0.097	0.027	0.129	-0.325*
WHR	0.009	0.261*	-0.056	0.268*	0.150	-0.075	0.089	-0.887
ICON	-0.020	0.298*	-0.146	0.140	0.165	-0.014	0.110	0.174
SBP (mmHg)	0.097	-0.114	0.033	-0.180	-0.059	-0.285	-0.183	-0.065
DBP (mmHg)	0.165	-0.116	0.220	-0.124	-0.132	-0.372*	-0.205	0.039
TC	0.017	0.191	-0.174	-0.415*	0.318*	0.455*	0.187	0.013
TGC	-0.058	0.139	0.092	0.132	-0.053	0.227	0.071	0.001
VLDL-c	-0.058	0.139	0.092	0.132	-0.053	0.227	0.071	0.001
HDL-c	-0.116	-0.267*	0.022	-0.048	-0.088	0.013	-0.038	0.265
LDL-c	0.067	0.259*	-0.173	-0.414*	0.350*	0.299	0.138	0.122
non-HDL	0.035	0.357*	-0.128	-0.355*	0.378*	0.430*	0.210	0.111
IC I	0.126	0.399*	-0.028	-0.105	0.236	0.195	0.089	0.299*
IC II	0.133	0.351*	-0.039	-0.178	0.237*	0.170	0.050	0.298*
FPG	0.190	0.098	-0.110	0.127	0.104	0.006	-0.135	-0.056
SI	0.005	-0.232	-0.004	0.183	-0.083	-0.168	-0.235	-0.399*
HOMA-IR	0.049	-0.210	0.014	0.243*	-0.062	-0.172	-0.236	-0.370*
Hba1C	0.110	0.103	-0.010	0.027	0.163	-0.040	-0.159	0.239
IL-6	0.057	-0.026	-0.142	-0.139	-0.041	0.079	0.026	-0.010
IL-8	0.090	-0.025	0.066	-0.342*	-0.222	-0.192	-0.014	0.291

* Pearson's or spearman's linear correlation coefficient ($p<0.05$). NC: neck circumference; WHR= waist-hip ratio; ICON= conicity index; SBP= systolic blood pressure; DBP= diastolic blood; TC= Total cholesterol; TGC= triacylglycerols; VLDL = very low density lipoprotein; HDL = high density lipoprotein; LDL = low density lipoprotein; non- HDL= non-high-density lipoprotein; CRI I = Castelli's risk index I; CRI II = Castelli's risk index II; SI= Serum insulin; FPG= Fasting plasma glucoseHbA1c = glycated hemoglobin; HOMA-IR = Homeostasis Model Assessment Insulin Resistance; IL= interleukin.

calcium concentrations contribute to the regulation of lipid fractions, since this nutrient participates in lipolysis, inhibits lipogenesis, and reduces lipid storage[46].

Despite the growing body of evidence supported by this study, it is important to mention some of its limitations. For example, the cross-sectional nature of the study, which does not make it possible to assess causality, as well as the sample size of the groups and the absence of data related to dietary intake. In addition, the use of other molecular markers to assess the impact of mineral deficiency on cardiometabolic risk parameters in this study could have contributed to a better understanding of the action of minerals in protecting against this risk in the population evaluated.

Conclusions

Women with obesity have a lower concentration of the mineral's magnesium, selenium and calcium in their blood, as well as a higher risk of cardiovascular disease and more inflammation when compared to the control group.

In addition, the data from this study suggest that increased adiposity is associated with altered nutritional status of magnesium, selenium and calcium in obesity, and that deficiency of these minerals is associated with increased cardiovascular risk in this population, reinforcing the need for interventions through the use of specific nutrients for the prevention of cardiovascular disease in this group.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors report there are no competing interests to declare.

References

1. Pereira ES, et al. Brazilian guide to nutrition in bariatric and metabolic surgery. Langenbecks Arch Surg 2023; 408(1).
2. World Obesity Federation, World Obesity Atlas. Available in: https://data.worldobesity.org/publications/?cat=19. 2023.
3. Morais JBS, Da Silva Dias TM, Pereira Cardoso BE, De Paiva Sousa M, Visgueira de Sosa TG, Cardoso de Araújo DS, et al. Adipose tissue dysfunction: impact on metabolic changes? Horm Metab Res 2022;54(12):785-94.
4. Rocha Dos Santos L, Rodrigues de Sousa Melo S, Soaers Severo J, Silva Morais JB, Dias da Silva L, De Paiva Sousa M, et al. Cardiovascular diseases in obesity: what is the role of magnesium? Biol Trace Elem Res 2021;199(11):4020-7.
5. Dastgerdi AH, Rad MG, Soltani N. The therapeutic effects of magnesium on insulin secretion and insulin resistance. Adv Biomed Res 2022;11:54.
6. Hasani M, Djalalinia S, Sharifi F, Varmaghani M, Zarei M, Abdar ME, et al. Effect of selenium supplementation on lipid profile: a systematic review and meta-analysis. Horm Metab Res 2018;50(10):715-27.
7. Ministério da Saúde (Brasil). Orientações para a coleta e análise de dados antropométricos em serviços de saúde: Norma Técnica do Sistema de Vigilância Alimentar e Nutricional. 2011.
8. World Health Organization. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. 2000.
9. Topf JM, Murray PT. Hypomagnesemia and hypermagnesemia. Rev Endocr Metab Disord 2003; 4(3):195-206.
10. Tietz NW. Clinical guide to laboratory tests. 3rd ed. Philadelphia: W.B. Saunders Company; 1995.
11. Thomson CD. Assessment of requirements for selenium and adequacy of selenium status: A review. Eur J Clin Nutr 2004;58(3):391-402.
12. Vitoux D, Arnaud J, Chappuis P. Are copper, zinc, and selenium in erythrocytes valuable biological indexes of nutrition and pathology? J Trace Elem Med Biol 1999;13(1):113-28.
13. Oster O, Prellwitz W. The renal excretion of selenium. Biol Trace Elem Res 1990;24(2):119-46.
14. Madeo B, Kara E, Cioni K, Vezzani S, Trenti T, Santi D, et al. Serum calcium to phosphorous (Ca/P) ratio is a simple, inexpensive, and accurate tool in the diagnosis of primary hyperparathyroidism. JBMR Plus 2018;2(2):109-17.
15. Hodgkinson A, Pyrah LN. The urinary excretion of calcium and inorganic phosphate in 344 patients with calcium stone of renal origin. Br J Surg 1958; 46(10):1-10.
16. Ben-Noun L, Laor A. Relationship between changes in neck circumference and changes in blood pressure. Am J Hypertens 2004;17(5):409-14.
17. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation on Obesity. 1998.
18. Pitanga FJG, Lessa I. Sensibilidade e especificidade do índice de conicidade como discriminador do risco coronariano de adultos em Salvador, Brasil. Rev Bras Epidemiol 2004;7(3):287-94.
19. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18(6):499-502.
20. Faludi AA, Izar MCO, Kerr Saraiva JF, Tria Bianco H, Marte Chacra AP. Atualização da diretriz brasileira de dislipidemias e prevenção da aterosclerose. Arq Bras Cardiol 2017;109(2):1-76.
21. Castelli WP, Abbott WD, McNamara PM. Summary estimates of cholesterol used to predict coronary heart disease. Circulation 1983;67:730-4.
22. Andrade JP, Nobre F. VI Diretriz brasileira de hipertensão. Arq Bras Cardiol 2010;95(1):1-51.
23. Barroso WKS, et al. Diretrizes brasileiras de hipertensão Arterial – 2020. Arq Bras Cardiol 2021; 116(3):516-658.
24. American Diabetes Association. Classification and diagnosis of diabetes: standards of Care in Diabetes - 2023. Diabetes Care 2023;46:S19–S40.

25. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1988;28(4):412-9.
26. Geloneze B, Junqueria Vasques AC, Camargo Stabe CF, Pareja JC, Frandsen Paez de Lima Rosado LE, De Queirzo EC, et al. HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and metabolic syndrome: Brazilian metabolic syndrome Study (BRAMS). Arq Bras Endocrinol Metab 2009;53(3): 281-7.
27. Little RJ. A test of missing completely at random for multivariate data with missing values. J Am Stat Assoc 1988;83(404):1198-202.
28. Andreozzi VL. R Function. 2013. Available from: https://aleskaandreozzi.weebly.com/scripts-in-r.html.
29. R Development Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2022.
30. Morais JBS, Climaco Cruz KJ, Soares de Oliveira AR, Pereira Cardoso BE, Da Silva Dias TM, Rodrigues de Sousa Melo S, et al. Association between parameters of cortisol metabolism, biomarkers of minerals (zinc, selenium, and magnesium), and insulin resistance and oxidative stress in women with obesity. Biol Trace Elem Res 2023;201(12):5677-91.
31. Piuri G, Zocchi M, Della Porta M, Ficara V, Ferramosca A, Rizzo AM. Magnesium in obesity, metabolic syndrome, and type 2 diabetes. Nutrients 2021;13(2):320.
32. DiNicolantonio JJ, O'Keefe JH, Wilson W. Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. Open Heart 2018;5(1):e000668.
33. Pelczyńska M, Moszak M, Bogdański P. The role of magnesium in the pathogenesis of metabolic disorders. Nutrients 2022;14(9):1714.
34. Fontenelle LC, de Oliveira ARS, Cardoso BEP, Morais JBS, Lima SCVC, Marreiro DN. Relationship between selenium nutritional status and markers of low-grade chronic inflammation in obese women. Biol Trace Elem Res 2023;201(2):663-76.
35. Cardoso BEP, de Oliveira ARS, Climaco Cruz KJ, Lima SCVC, Marreiro DN. Selenium biomarkers and their relationship to cardiovascular risk parameters in obese women. Biol Trace Elem Res 2024;202(3): 866-77.
36. Hariharan S, Dharmaraj S. Selenium and selenoproteins: their role in regulation of inflammation. Inflammopharmacology 2020;28(3):667-95.
37. Oliveira ARS, Cardoso BEP, Climaco Cruz KJ, de Sousa Melo SR, Marreiro DN. Selenium status and oxidative stress in obesity: influence of adiposity. Eur J Clin Invest. 2021;51(9):e13538.
38. Burk RF, Hill KE. Regulation of selenium metabolism and transport. Annu Rev Nutr 2015;35:109-34.
39. Burk RF, Hill KE, Motley AK, Winfrey VP, Kurokawa S, Mitchell SL, et al. Deletion of selenoprotein P upregulates urinary selenium excretion and depresses whole-body selenium content. Biochim Biophys Acta Gen Subj 2006;1760(12):1789-93.
40. Sherlock LG, Hill KE, Winfrey VP, Mitchell SL, Combs GF, Burk RF. Hepatic-specific decrease in the expression of selenoenzymes and factors essential for selenium processing after endotoxemia. Front Immunol 2020;5:595282.
41. Zohal M, Hosseinzadeh-Attar MJ, Hajifaraji M, Ahmadi A, Eshraghian MR. Association between selected trace elements and body mass index and waist circumference: a cross-sectional study. Diabetes Metab Syndr 2019;13(2):1293-7.
42. Harahap IA, Landrier JF, Suliburska J. Interrelationship between vitamin D and calcium in obesity and its comorbid conditions. Nutrients 2022;14(15):3187.
43. Chen JM, Yeh WT, Lee HY, Lee M, Lee LT, Lin WY, et al. Association of the serum calcium level with metabolic syndrome and its components among adults in Taiwan. Arch Endocrinol Metab 2023;67(5):e000632.
44. Engin A. The pathogenesis of obesity-associated adipose tissue inflammation. Adv Exp Med Biol 2017;960:221-45.
45. Zhang Q, Yan J, Liu S, Gong Z, Zhu Y, Li Y, et al. Effects of oral selenium and magnesium co-supplementation on lipid metabolism, antioxidative status, histopathological lesions, and related gene expression in rats fed a high-fat diet. Lipids Health Dis 2018;17:165.
46. Traulsen H, Steinbrenner H, Stuhlmann D, Sies H. Selenoprotein P protects low-density lipoprotein against oxidation. Free Radic Res 2004;38(2):123-8.