Selenium-Related Nutritional Status in Patients With Common Variable Immunodeficiency: Association With Oxidative Stress and Atherosclerosis Risk

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Abstract

Background: Common variable immunodeficiency (CVID) is an innate immunity error, possibly associated with recurrent or chronic infections and autoimmune / inflammatory diseases and neoplasms. It is suggested that these conditions lead to persistent immune stimulation and increased oxidative stress. A positive impact on the survival of patients with an inborn errors of immunity was observed with advanced clinical care protocols, thus raising concerns about the risk of developing other associated chronic diseases, such as atherosclerosis. Studies suggest that selenium (Se) is a protective trace element against damage caused by oxidative stress. Thus, it is postulated that adequate consumption reduces the risk of some chronic diseases.

Results: The median age of CVID patients was 36.8 years, with a female predominance. Low concentrations of GPx, Se and apo A-1 were observed in the patients, besides the presence of dyslipidemia and higher concentrations of adiponectin, us-CRP, and LDLox. There was no association between the concentrations of Se and GPx and the biomarkers of lipid metabolism involved in atherosclerosis risk, except for a positive association with apo A-1 and HDL. The median of polyunsaturated fat was lower in CVID patients and the intake of zinc and retinol was higher among them when compared to controls.

Conclusion: The study showed a higher risk of cardiovascular disease in CVID patients. The presence of low selenium in CVID patients points to the importance of assessing the selenium-related nutritional status in these patients.

Introduction

Selenium (Se) plays a vital role in lipid metabolism due to its antioxidant properties. The protection provided by Se against cardiovascular diseases (CVD) is supported by its role in the antioxidant defense mediated by the glutathione peroxidase (GPx) family. In this context, GPx reduces the formation of hydroperoxides of phospholipids and cholesterol esters, and prevents oxidized low-density lipoprotein (LDL) artery sedimentation and, consequently, slows or prevents the atherosclerotic process [1–3].

The inadequate consumption of Se and the presence of polymorphism in the GPx1 gene are related to this enzyme's lower activity, which can harm the body's antioxidant defense system [4]. Some studies have highlighted the relationship between single nucleotide polymorphism (SNP) in GPx genes with increased risk of CVD and metabolic syndrome [5, 6]. Elevated serum Se concentrations have been associated with increased heart rate and systolic and diastolic blood pressure [2, 3], although no clear relationship has been found between selenium concentrations and hypertension [7].

Common Variable Immunodeficiency (CVID) is a syndrome encompassing a heterogeneous group of diseases, appearing at any age, characterized by changes in the immune function involving T and B cells, inadequate production of antibodies, causing recurrent bacterial infections [8, 9]. Because patients with CVID may have recurrent or chronic infections and autoimmune/inflammatory diseases and neoplasms,

it was suggested that these conditions led to persistent immune stimulation and increased oxidative stress [10, 11].

In this context, a study conducted with CVID patients described higher malondialdehyde (lipid peroxidation marker) concentrations and homocysteine, compared to those observed in healthy controls [12]. Vieira et al. (2015) [13] found increased inflammatory markers and lower high-density lipoprotein cholesterol (HDL-c) and Apoliprotein A-1 (apo A-1) concentrations, suggesting a predisposition to cardiovascular risk in these patients.

A positive impact on the survival of patients with an inborn errors of immunity (IEI) was observed with advanced clinical care protocols, thus raising concerns about the risk of developing other associated chronic diseases, such as atherosclerosis.

This study aims to describe selenium and glutathione peroxidase concentrations in patients with CVID and relate them to lipid profile markers.

Methods

In 2016, patients of both genders aged from 9 to 61 years, diagnosed with common variable immunodeficiency, according to the criteria of the European Immunodeficiency Society [14], were evaluated through a controlled cross-sectional study, conducted in the Discipline of Allergy, Clinical Immunology and Pediatric Rheumatology, Federal University of São Paulo – São Paulo Medicine School (UNIFESP-EPM).

Thirty-two patients with CVID and 37 healthy volunteers were included, paired with patients by gender and age, comparing nutritional status variables, biochemical markers related to cardiovascular risk (CVR), and food intake.

The study followed the guidelines of the Helsinki Declaration of 1975 as revised in 1996 regarding the use of human subjects. The study was approved by The Research Ethics Committee from the Federal University of São Paulo (No. 972812/2015), with funding received by The São Paulo Research Foundation - FAPESP nº 2015/13308-9, and signed informed consents were obtained from all participants (or a responsible guardian in the case of children).

Clinical, demographic, and socioeconomic data were collected through a structured and standardized questionnaire. Anthropometric and food consumption assessments and biochemical tests were also performed. At the time of collecting laboratory tests, none of the subjects had an acute infectious disease, clinically identified through the complete blood count, nor had they been using corticosteroids for at least three months.

Anthropometric and food consumption assessment

The anthropometric evaluation included measurements of weight, height, skinfolds (bicipital, tricipital, subscapular, and suprailiac, and abdominal circumference. Weight and height were measured according to the recommendations of the World Health Organization (WHO) [15] and skinfolds, according to Frisancho (1990) [16].

The body mass index-for-age (BMI/A) and height-for-age (H/A) indicators were calculated for the classification of nutritional status, expressed as Z-score, using De Onis (2007) [17] as a reference, for children and adolescents, and the body mass index (BMI), as proposed by the World Health Organization for adults (WHO, 1995). The classification by Freedman et al. [18] was used to assess the waist circumference of children and adolescents, and values above the 90th percentile were considered high. Adults were classified according to the WHO [15]. Body composition was estimated based on the sum of the four skinfolds for adults [19] and the TSF and SSSF for children/adolescents using Slaughter's Eq. (1988) [20]. Body fat percentage was classified as proposed by Deurenberg (1990) [21] and Lohman (1992) [22].

The stage of pubertal development was self-assessed (Saito, 1984) [25], according to Marshall & Tanner (1969) [26].

Food consumption was assessed with the 24-hour food record [27], applied in three stages [28], with a 15-day interval. The surveys were collected on Tuesdays, Thursdays, and Fridays, thus avoiding days after the weekends.

The participants' food intake was calculated with the Dietwin software, comparing cases to controls. Considering that the food composition tables available in some software do not have complete data about the Se content in foods, these data were included manually based on the paper by Ferreira et al. (2002) [29]. Also, the total consumption of energy, lipids, protein per kilogram of body weight, vitamins A and C, copper, and zinc were analyzed.

Biochemical assessment

After a 12-hour fast, a blood aliquot was collected to analyze selenium, glutathione peroxidase, lipid profile, apolipoproteins A-1 and B, oxidized LDL (LDLox), malondialdehyde (MDA), ultra-sensitive C-reactive protein (us-CRP), adiponectin, insulin, glucose, aspartate aminotransferase (AST), alanine transaminase (ALT) and gamma-glutamyl transpeptidase (Gamma GT).

Serum selenium was obtained by atomic absorption spectrophotometry (Graphite Furnace) with Zeeman Corrector. For classification purposes, a cut-off point ≤ 45 µg/L was adopted for inadequacy. Glutathione peroxidase activity was measured by the enzymatic method and the MDA was measured in the serum using the colorimetric method in whole blood.

Enzymatic-colorimetric methods evaluated the lipid profile, including the triglyceride (TG), total cholesterol (TC), and HDL-c parameters. LDL-c and VLDL-c were calculated using the formula by Friedewald et al. (1972) [30]. The cut-off points suggested by the American Academy of Pediatrics [31]

and the National Cholesterol Education Program (NCEP) [32] were adopted for classification purposes. The presence of dyslipidemia was considered when the TC > 170 mg/dL for children/adolescents and > 200 mg/dL for adults, or LDL-c > 110 mg/dL for children/adolescents and > 129 mg/dL for adults, or triglycerides > 100 mg/dL for children/adolescents and > 150 mg/dL for adults, or HDL-c < 35 mg/dL for children/adolescents, < 40 mg/dL for women and < 50 mg/dL for men.

The values of non-HDLc cholesterol (NHDL-c) were obtained by subtracting the HDL-c values from the TC values and classified according to the work of Bogalusa [33] and NCEP. The following ratios were also calculated: total cholesterol/HDL-c, LDL-c/HDL-c [34], Apo B/Apo A-1, LDL-c/Apo B, and HDL-c/Apo A-1 [35].

Glycemia was measured using a GLUC3/Roche kit (Indianapolis, IN - USA), using an enzymatic reference method with hexokinase, and insulin using an Elecsys Insulin/Roche kit (Indianapolis, IN-USA), using electrochemiluminescence. The fasting blood glucose and insulin values calculated the HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) using the following formula: HOMA-IR = fasting glucose (mmol/l) x fasting insulinemia (μU/ml)/22.5. HOMA-IR was considered changed > 3.16 [36].

Alanine transaminase was measured by an ALTL/Roche kit (Indianapolis, IN-USA), using the enzymatic-kinetic method; aspartate aminotransferase by ASTL/Roche kit (Indianapolis, IN-USA), using the enzymatic-kinetic method, and the gamma-glutamyl transpeptidase range by the GGT2/Roche kit (Indianapolis, IN-USA), using the enzymatic colorimetric method. The complete blood count was performed in whole blood using the cytochemical/isovolumetric method.

The dry tubes directed to the Clinical Analysis Laboratory of the ABC Medical School were centrifuged at 10,000 rpm for 10 minutes. The serums obtained after centrifugation were stored at -80 °C and used to determine the non-classic markers of lipid metabolism: quantity and quality of Apo A-1, Apo B, LDLox and of inflammation biomarkers: us-CRP and adiponectin. All analyses were performed in duplicate. These biomarkers have no benchmark values in the pediatric age group.

The determination of Apo A-1 was performed using the Apo A-1 ver.2/Roche kit (Indianapolis, IN-USA) by the turbidimetry method; that of Apo B, by the Apo B kit ver. 2/Roche (Indianapolis, IN-USA) using the turbidimetry method; that of oxidized LDL, by the Human OxLDL/Wuhan Fine Biological Technology Co kit (Wuhan, China), by the ELISA method.

The CRPLX/Roche kit (Indianapolis, IN-USA) measured the ultrasensitive C-reactive protein using the turbidimetry method. Adiponectin was measured by the Adiponectin Human ELISA kit/ABCAM kit (San Francisco, USA), with the ELISA method. The cutoff point used to indicate elevation was us-CRP ≥ 8.

Statistical Analysis

The SPSS 25.0 (IBM®) program was used for statistical analysis. Categorical variables were shown as absolute numbers and percentages, compared using the Chi-square test. The continuous variables were evidenced in the median and interquartile range and compared using the Mann-Whitney test. The

Spearman test was used to assess the correlation between continuous variables and glutathione peroxidase and selenium levels.

Results

The classification of the nutritional status of patients with CVID and the control group is summarized in Table 1. Except for income, where the controls had a higher income than the patients, there was no difference between the groups regarding gender, age, pubertal stage, family cardiovascular risk, and BMI (data not shown). The presence of dyslipidemia was found in 24/32 (75.0%) of the patients.

Table 1
Demographic and anthropometric data of CVID patients and the control group.

Variables	**CVID Patients** (*n = 32*)	**Control group** (*n = 37*)	**p***
Age, median (IQ_{25-75})	36.8 (27.9–45.2)	34.7 (20.7–44.3)	0.481[2]
Gender			
Male %	14 (43.8)	16 (43.2)	0.972[1]
BMI, kg/m^2			
Underweight, %	2 (6.2)	1 (2.8)	0.704
Eutrophy, %	15 (46.9)	18 (48.6)	
Overweight, %	15 (46.9)	18 (48.6)	
[1] Chi-square and [2] Mann-Whitney tests; level of significance $p < 0.05$			

The characterization of patients with CVID is shown in Table 2. The median age was 36.8 years (min-max 9.6–61.4 years) in the CVID group; there was one child, four teenagers, and the remaining were adults. The mean time since diagnosis was five years and six months (min-max 0.5–16.4 years). Of the 32 patients, fourteen (43.8%) had a chronic pulmonary disease (CPD) and were on continuous use of antibiotics, while 5/32 (15.6%) had chronic diarrhea. All patients received regular immunoglobulin infusion, and only 7/32 (21.9%) used vitamin or food supplements regularly (data not shown).

Regarding laboratory variables, dyslipidemia was observed in the CVID vs. control group, respectively, in 24 (75.0%) vs. 21 (77.8%); p = 0.525. In this same group, there was also a higher percentage of inadequacy in Se concentrations 16 (50.0%) vs. 6 (22.2%); p = 0.036, whereas there was no statistically significant difference between groups for the adequacy of GPx 4 (12.5%) vs. 7 (25.9%); p = 0.315.

Table 2
Characterization of CVID patients.

Variables (*n = 32*)		**N (%)**
Age	9–19 years	5 (15.6)
	20–61 years	27 (84.4)
Abdominal	Adequate	20 (62.5)
circumference	High	12 (37.5)
Lipid profile	High total cholesterol	7 (21.9)
	High LDL-c	6 (18.8)
	High triglycerides	4 (12.5)
	Low HDL-c	18 (56.3)
	High NHDL-c	12 (37.5)
Selenium	Adequate (> 46 µg/L)	16 (50.0)
Glutathione peroxidase	Adequate	28 (87.5)
N (%)		
Captions: LDL-c low-density lipoprotein, HDL-c high-density lipoprotein, NHDL-c Non-HDL cholesterol		

The comparison of laboratory variables is shown in Table 3. Lower Se and GPx concentrations were found in the CVID group. While the median of us-CRP was higher in the CVID group, there was no statistically significant difference between the groups. However, a trend towards a higher percentage of inadequacy in the CVID group 8 (36.4%) vs. 2 (11.1%); p = 0.082 was observed when the us-CRP was stratified according to its cutoff point.

Table 3
Comparison of biochemical variables between CVID patients and control group.

Variables	**CVID Patients** (*n = 32*)	**Control group** (*n = 37*)	**p***
	Median (IQ_{25-75})	Median (IQ_{25-75})	
Glutathione peroxidase U/L	7,682 (6,548-8,446)	9,284 (8,440 – 10,720)	**0.002**
Selenium µg/L	45.6 (37.3–56.2)	57.8 (46.0–66.0)	**0.004**
Malondialdehyde nmol/mL	3.5 (3.1–3.9)	3.2 (2.4-4.0)	0.514
Us-CRP mg/L	6.3 (0.9–17.7)	1.8 (0.8–1.8)	0.124
Glucose mg/dL	85.5 (81.0–92.0)	85.0 (77.0–95.0)	0.813
Insulin	6.6 (2.6–10.8)	8.1 (5.2–13.8)	0.155
HOMA-IR	1.2 (0.5–2.2)	1.6 (0.9–2.9)	0.177
AST U/L	19.0 (15.5–24.0)	18.0 (15.0–19.0)	0.116
ALT U/L	10.0 (8.0–14.0)	12.0 (9.0–17.0)	0.108
GGT U/L	14.0 (10.3–25.8)	16.3 (10.7–21.5)	0.519
Mann-Whitney test; level of significance $p < 0.05$			
Captions: HOMA-IR = Homeostatic Model Assessment for Insulin Resistance; GGT Gamma-Glutamyl Transpeptidases.			

Regarding dietary intake, we observed that the CVID group had a lower intake of polyunsaturated fat and a higher intake of zinc and retinol (Table 4) than the control group.

Table 4
Comparison of the median of macro and micronutrients between CVID patients and control group.

Variables	CVID Patients N = 32	Control group N = 37	
	Median (IQ_{25-75})		P*
Energy (Kcal)	1,747.0 (1,568.1-1,960.7)	1,736.9 (1,416.3-2,214.1)	0.485
Carbohydrate (g)	233.8 (205.9-285.2)	238.5 (200.4-342.2)	0.894
Protein (g)	80.5 (64.7–101.0)	72.8 (58.4–96.8)	0.258
Total fat (g)	53.7 (42.5–56.8)	46.6 (33.8–58.1)	0.323
Saturated fat (g)	18.4 (14.8–21.7)	15.3 (11.4–20.1)	0.074
Monounsaturated fat (g)	14.7 (9.8–18.5)	12.4 (9.2–15.2)	0.197
Polyunsaturated fat (g)	6.4 (4.7–8.7)	9.4 (6.3–11.4)	**0.006**
Trans fat (g)	0.7 (0.4–1.4)	0.9 (0.6–1.4)	0.335
Copper (µg)	0.7 (0.5-1.0)	0.6 (0.5–0.9)	0.434
Selenium (mg)	66.3 (56.7–79.3)	66.2 (60.8–72.3)	0.682
Zinc (mg)	7.8 (6.0-9.7)	6.8 (4.6–7.8)	**0.028**
Retinol (µg)	269.9 (152.1-419.3)	199.9 (150.5-243.8)	**0.026**
Ascorbic acid (mg)	75.0 (49.4-110.6)	59.4 (50.8–99.9)	0.571
Mann-Whitney test; level of significance $p < 0.05$			

The lipid profile markers are shown in Table 5. Higher concentrations of oxidized LDL (45.3 mg/dL vs. 33.3 mg/dL; p = 0.016) and lower concentrations of Apo A-1 (98.5 mg/dL) vs. 117.0 mg/dL; p = 0.008) were observed in the CVID group compared to the control.

Table 5
Family cardiovascular risk and biomarkers of the atherogenic lipid profile for CVID patients and control group.

Variables	**CVID Patients** (*n = 32*)	**Control group** (*n = 37*)	**p***
	Median (IQ_{25-75})	Median (IQ_{25-75})	
Family CVR Yes	13 (40.6)	16 (43.2)	0.826
Lipid profile biomarkers			
Total cholesterol mg/dL	166.0 (138.5–185.0)	179.0 (164.0-213.0)	0.085
LDL-c mg/dL	100.1 (86.0-116.6)	108.8 (84.2–139.0)	0.237
Triglycerides mg/dL	91.0 (78.5–104.0)	91.0 (75.0-121.0)	0.995
HDL-c mg/dL	43.0 (34.5–52.5)	48.0 (37.0–56.0)	0.210
NHDL-c mg/dL, %	118.0 (104.0-138.0)	135.0 (108.0-161.0)	0.226
VLDL-c mg/dL	18.2 (15.6–20.8)	18.2 (15.0-24.2)	0.990
Remnant cholesterol mg/dL	18.5 (15.6–20.8)	18.2 (15.0-22.8)	0.909
Oxidized LDL mg/dL	45.3 (26.8–65.7)	33.3 (23.7–42.2)	**0.016**
Apo A-1 mg/dL	98.5 (81.5-112.5)	117.0 (92.0-130.0)	**0.008**
Apo B mg/dL	94.0 (81.0-111.5)	102.0 (90.0-119.0)	0.215
Apo B/ Apo A-1	0.9 (0.7–1.1)	0.8 (0.6-1.0)	0.238
Total cholesterol/HDL-c	4.0 (3.0–4.0)	4.0 (3.0–4.0)	0.484
LDL-c/ Apo B	1.0 (0.9–1.2)	1.0 (0.9–1.2)	0.976
LDL-c/ HDL-c	2.0 (2.0–3.0)	2.0 (2.0–3.0)	0.442
TG/ HDL-c	2.0 (2.0–3.0)	2.0 (1.0–3.0)	0.516
Apo A-1/ HDL-c	2.3 (1.9–2.5)	2.3 (1.2–2.6)	0.392
Chi-square or Fisher's exact test			
CVR cardiovascular risk, LDL-c low-density lipoprotein, HDL-c high-density lipoprotein, NHDL-c non-HDL cholesterol, VLDL-c very low-density lipoprotein			

No variable studied correlated in a statistically significant way with GPx concentrations in the CVID group. In turn, selenium concentrations were associated with those of Apo A-1 (Fig. 1).

Discussion

This study showed lower Se concentrations and lower GPx activity in patients with CVID. There was a significant and positive correlation between the concentrations of Se and those of Apo A-1, a negative reactive acute-phase protein, and the main protein component of the HDL cholesterol fraction.

According to our knowledge, this study is a pioneer in assessing the association between selenium concentrations and GPx activity with biomarkers of lipid metabolism in individuals with CVID. A recent paper evaluating 124 men with human immunodeficiency virus (HIV) infection described serum selenium deficiency in 65.9% of individuals. There was a significant and negative correlation between the concentrations of Se and pro-inflammatory cytokines (IL-1beta, IL-6, and TNF-alpha). The authors emphasized that Se deficiency has been associated with increased morbimortality and other adverse outcomes in HIV + individuals [37].

Patients with primary immunodeficiencies or who are currently called with Innate Immunity Errors have different clinical characteristics, especially recurrent infections linked to incompetence in regulating different homeostatic processes, with an increased risk of the development of tumors and autoimmune diseases [38, 39]. Furthermore, in predominantly humoral deficiencies, patients are exposed to extracellular bacteria and have severe and recurrent sinopulmonary infections requiring hospitalization and frequent antibiotics use. Bacterial infections are associated with a reduction in serum selenium concentrations, and supplementation studies show favorable results.

Many bacteria can also synthesize selenocysteine, suggesting that selenoproteins may play a role in bacterial physiology. Simultaneously, the composition of the host's microbiota is also regulated by the diet’s Se. Therefore, pathogenic bacteria, microbiome, and cells of the host’s immune system may be competing for a limited supply of selenium, which is of even more significant concern in patients with CVID [40–42].

A significant and direct correlation was observed between selenium and Apo A-1 concentrations. The literature has shown that Apo A-1 and other HDL-c functionality markers are superior to HDL-c concentrations in predicting risk for cardiovascular disease [43].

Selenium suppresses the activation of pro-inflammatory pathways by chelating free radicals and blocking the nuclear transcription factor NF-kB activation. Changes in the composition and concentration of lipoproteins that occur in inflammation can alter these particles’ function, making them pro-inflammatory. Thus, besides the quantitative alterations, significant changes are also observed in the composition of these lipoproteins, especially in the case of HDL-c that loses its major Apo A-1 protein component, which is replaced by an acute-phase protein, namely, serum amyloid A, which during inflammation, represents 90% of proteins found in HDL-c. Selenium deficiency can contribute to the disruption of inflammation, contributing to the generation of dysfunctional HDL-c, that is, a pro-inflammatory particle [44–45].

A significant change is expected in the microbiota of patients with CVID characterized by reduced intra-individual bacterial diversity due to antibiotic use. Some studies suggest a link between

immunodeficiency, systemic immune activation, and altered intestinal microbiota [46]. Thus, we can conclude that recurrent infections, inflammation, and changes in the microbiota contribute to high oxidative stress, insulin resistance, and consequent elevated risk of dyslipidemia [47].

The group with CVID has a pro-inflammatory state, suggested in this study by the high concentrations of UsCRP and LDLox (LDL fraction of oxidized cholesterol) and low selenium concentrations than healthy controls. Specific LDLox receptors called LOX-1 and SR-PSOX have been isolated. The expression of LOX-1 is found in endothelial cells, smooth muscle cells, and macrophages, while SR-PSOX is expressed in macrophages. LDLox can be produced due to the increased production of reactive species by the mitochondria during oxidative stress and inflammation [48]. Such findings reinforce the atherosclerotic risk of patients with CVID.

Publications assessing CVD risk and its interface with Se are scarce in the literature. In a study of 20 patients with CVID and 16 healthy controls, Aukrust et al. (1997) [12] reported high concentrations of malondialdehyde (lipid peroxidation biomarker) and reduced homocysteine in the group of patients, suggesting the existence of oxidative stress. Future studies are required to assess the effect of selenium supplementation on CVD risk in patients with CVID.

In conclusion, this study showed a CVD risk in patients with CVID. The presence of low Se and reduced GPx activity point to the importance of assessing the Se-related nutritional status in these patients.

List Of Abbreviations

ALT	alanine transaminase
Apo B	apolipoproteins B
Apo A1	apolipoproteins A-1
AST	aspartate aminotransferase
BMI	body mass index
CVDs	cardiovascular diseases
CVID	Common Variable Immunodeficiency
CVR	cardiovascular risk
FAPESP	São Paulo Research Foundation
GGT	gamma-glutamyl transpeptidase
GPx	Glutathione peroxidase
H/A	height for age
HDL-c	high-density lipoprotein cholesterol
HIV	Human immunodeficiency virus
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
IEI	Inborn errors of immunity
LDL-c	Low-density lipoprotein cholesterol
LDLox	oxidized LDL
MDA	malondialdehyde
NCEP	National Cholesterol Education Program
NFkB	nuclear transcription factor
NHDL-c	non-HDLc
Se	Selenium
SNP	Single nucleotide polymorphism
TC	total cholesterol
TG	triglycerides
us-CRP	ultra-sensitive C-reactive protein
VLDL-c	very-low-density lipoprotein cholesterol
WHO	World Health Organization

Declarations

Ethics approval and consent to participate

The study was approved by The Research Ethics Committee from the Federal University of São Paulo (CEP/UNIFESP - 972.812 11/03/2015) and signed informed consents were obtained from all participants (or a responsible guardian in the case of children).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

IGAA → collected, analyzed and interpreted data from CVID patients and the control group and was a major contributor in writing the manuscript.

FISS → analyzed and interpreted data from CVID patients and the control group and contributed to the correction of the manuscript writing.

FLAF → performed the analysis of laboratory tests and contributed to the correction of the manuscript writing.

CSAL → analyzed and interpreted data from CVID patients and the control group and contributed to the correction of the manuscript writing.

ROSS → analyzed and interpreted data from CVID patients and the control group and was a major contributor in writing the manuscript.

All authors read and approved the final manuscript.

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Conflict of interest statement: Nothing to declare (all authors)

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Figures

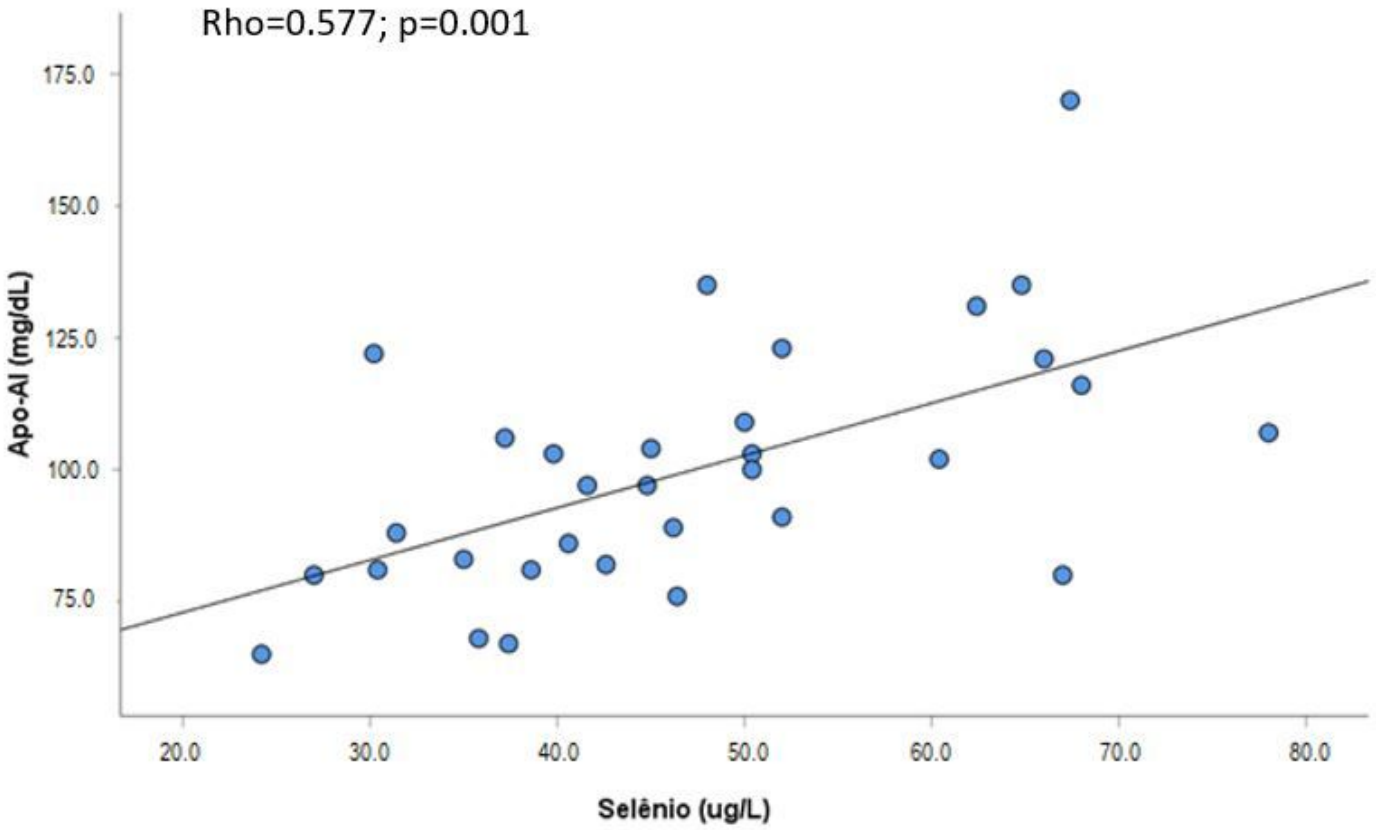

Figure 1

Correlation of selenium concentrations with Apolipoprotein A-1 in CVID patients. Level of significance of Spearman's correlation Caption: Selenium (ug/L)