Nutritional Status Related to Selenium in Patients With Ataxia-Telangiectasia - A Case Control Study: an Association With Oxidative Stress and Risk of Atherosclerosis

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Abstract

Introduction: Ataxia-Telangiectasia (A-T) is a multi-system disorder that may be associated with endocrine changes, oxidative stress in addition to inflammation. Studies suggest that selenium (Se) is a trace element related to protection against damage caused by oxidative stress; it is postulated that adequate consumption reduces the risk of some chronic diseases.

Objective: To describe the concentrations of Se and glutathione peroxidase (GPx) in patients with A-T, to relate them to markers of the lipid profile.

Methods: We evaluated, through a controlled cross-sectional study, 22 A-T patients matched by sex and age with healthy individuals, conjointly evaluating: nutritional status, food intake, serum selenium, glutathione peroxidase (activity), lipid metabolism biomarkers, inflammation and lipid.

Results: The median age in the A-T group was 12.2 years. A-T patients had greater impairment of lean body mass and GPx activity as well as lower abdominal circumference. A more atherogenic lipid profile was observed with higher concentrations of total cholesterol, non-HDL cholesterol, LDLox, Apo B, Apo B / Apo A-1 and LDL / HDL ratio; while a lower value was observed in the Apo A-1 / HDL ratio. It was also in the A-T group that statistical difference was detected in the three markers of liver function AST, ALT and GGT. In regard to food intake, A-T patients had lower values of carbohydrate, protein, monounsaturated fat, trans fat, and Se.

Conclusion: The study showed cardiovascular risk in A-T patients. A-T patients appear to be at increased risk of reduced nutritional status, impaired liver function, dyslipidemia and inflammation.

Introduction

Selenium (Se) is an essential micronutrient for antioxidant defense that integrates an important part of selenoproteins [1, 2]. The most well-known selenoprotein is Glutathione peroxidase (GPx), which protects cells from damage caused by free radicals amongst reactive oxygen species (ROS) [3, 4]. Selenium, in turn, blocks the activation of the nuclear transcription factor NFkB, a sensitive regulator that modulates the production of inflammatory mediators and adhesion molecules [5].

The trace element also stands out for its participation in immunological competence, particularly in cell-mediated immunity, cognitive function, and protection against cardiovascular diseases (CVDs) [6,7].

Due to its antioxidant properties, Se plays an important role in lipid metabolism; however, the associations between serum Se concentrations and the risk of dyslipidemia are still controversial in the literature [3].

Some scientific evidence has shown that Se deficiency occasionally increases the concentrations of total cholesterol (TC) [7] and triglycerides (TG) [8], elevating the risk of heart disease (HD), such as atherosclerosis, up to three times [9].
Patients with innate immunity errors (EII) have a higher susceptibility to infections, among other characteristics, hence the highest susceptibility to developing malignancies and autoimmunity. The release of inflammatory cytokines is remarkable along with many diseases belonging to this group. Thus, it is inferred that chronic inflammation might be associated with the pathogenesis of atherosclerosis [10-13]. Additional cardiovascular risk factors have been described in these diseases, such as increased oxidative stress and changes in the intestinal microbiota [14, 15].

Ataxia-telangiectasia (A-T) is a rare disease (OMIM 208900) in which incidence ranges from 1: 40,000 to 1: 100,000, and it is caused by a mutation in the ATM gene (ataxia-telangiectasia mutated). The change induces difficulty in repairing ruptures of double-stranded DNA, increases ROS production, mitochondrial dysfunction, with concomitant elevation of oxidative stress and consequent cell apoptosis [16, 17]. DNA damage, combined with oxidative stress, can contribute to the pathogenesis of associated chronic diseases, including atherosclerosis [18, 19].

Due to advances in the care of patients, different studies reveal increasing survival rates, with ensuing concern about the possible appearance of further associated diseases such as cardiovascular [20, 21]. Dyslipidemia, a component of the metabolic syndrome, is one of the greatest risk factors with an impact on atherogenesis, which increases the risk of coronary failure two to three times [9]. To date, no studies are evaluating the risk of atherosclerosis in patients with A-T.

The present study aims to describe the concentrations of selenium and glutathione peroxidase in A-T patients and to relate them to markers of the lipid profile.

**Methods**

Through the medium of a cross-sectional controlled study, we evaluated 22 A-T patients of both genders, between 3 and 27 years of age, who were diagnosed with A-T according to the criteria of the European Society for Immunodeficiencies (ESID) [22].

Recruited from Primary Health Care Service, the control group was composed of 18 healthy volunteers matched in age and gender, comparing biochemical markers related to cardiovascular risk and food intake.

The study was approved by The Research Ethics Committee from the Federal University of São Paulo, financed 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).

The demographic, clinical, and treatment data were obtained from the patients’ charts. The family history risk of atherosclerosis was assessed for patients and controls.

At the time of sample collection, none of the subjects had an acute infectious disease, nor had they been using corticosteroids for at least 3 months. Howbeit, one patient was using antifungal and five were using antibiotics.
Anthropometric evaluation and food intake

The anthropometric evaluation involved measurements of weight, height, mid-upper arm circumference (MUAC), and skinfold thickness (tricipital, subscapular, bicipital, and sacroiliac) as proposed by the World Health Organization (WHO) and Frisancho (1990) [23, 24]. The patients who were unable to stand upright had their weight measured in the wheelchair, on a specific scale for wheelchair-users (Micheletti - capacity 1100 lbs - serial: 2161058). Recumbent height was measured with the patient lying on a flat and firm surface, using an inextensible tape graduated in millimeters.

To assess the body mass index (BMI) and height for age (H/A) of children and adolescents, expressed as Z-scores, the WHO [25] criteria and the classification proposed by De Onis et al. were adopted [26]. For adults, the cut-off point of the WHO for BMI was chosen instead [23]. The sum of skinfold thickness and MUAC was used to estimate children's body composition [27-29]. While for adults, the estimation of body composition was based on the sum of the four different skinfolds [30]. The body fat percentage was classified according to the method previously described [28, 29].

The pubertal stage was evaluated according to Marshall and Tanner [31].

The assessment of food intake was performed using a 24 h dietary recall (R24hs), applied at 3 times, with an interval of 15 days between them. The calculation of nutrients in the diet was performed by the use of the Software Dietwin ®, comparing the cases to the controls [32, 33].

Considering that food composition tables available in some software do not have complete data on Se content in food, these data were included manually based on the article by Ferreira et al. (2002) [34]. Thereby, only one of A-T patients had feeding tubes.

Biochemical Assessment

After 8-hour fasting, blood was collected by peripheral venipuncture to analyze the selenium, glutathione peroxidase, lipid profile, apolipoproteins A-1 and B (Apo A-1, Apo 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).

Selenium was determined by graphite furnace atomic absorption spectrometry. For classification, the cut-off point ≤ 45 µg/L was adopted for inadequacy. Glutathione peroxidase activity was measured by the enzymatic method.

The lipid profile, including the triglyceride, total cholesterol and high-density lipoprotein cholesterol (HDL-c) was measured with enzymatic-colorimetric tests. Low-density lipoprotein cholesterol (LDL-c) and very-low-density lipoprotein cholesterol (VLDL-c) were calculated using the formula by Friedewald et al. (1972) [35].
For classification, the cut-off points suggested by the American Academy of Pediatrics [36] and the National Cholesterol Education Program (NCEP) [37] were adopted. The presence of dyslipidemia was considered when the TC> 170 mg / dL for children / adolescents and> 200 mg / dL for adults and / or LDL-c> 110 mg / dL for children / adolescents and> 129 mg / dL for adults and / or triglycerides> 100 mg / dL for children / adolescents and> 150 mg / dL for adults and / or HDL-c <35 mg / dL for children / adolescents, <40 mg / dL for women and <50 mg / dL for men.

The non-HDLc (NHDL-c) values were obtained by subtracting the HDL-c rates from the TC levels and thereafter classified according to the work of Bogalusa [38] and NCEP. The following ratios were also calculated: total cholesterol/ HDL-c, Apo B/Apo A-1, LDL-c/Apo B, LDL-c/HDL-c [39], HDL-c/Apo A-1 [40].

Apo A-1 and Apo B were measured using kits of turbidimetric methods for human Apo A-1 and Apo B (Roche, Indianapolis, IN, USA) and oxidized LDL, (ELISA)PRO (Wuhan Fine Biological Technology Co, Wuhan, China).

Complete blood counts, MDA, and us-CRP were measured by the methods of Colorimetric and Turbidimetric, respectively. The cutoff point used to indicate elevation was us-CRP $\geq 8$.

Glycemia was measured by enzymatic reference method with hexokinase, while insulin was quantified by electrochemiluminescence. Using the fasting glucose and insulin values, the HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) rate was calculated utilizing the following formula: $\text{HOMA-IR} = \frac{\text{fasting glucose (mmol / L)} \times \text{fasting insulin (µU / mL)}}{22.5}$. HOMA-IR was considerably changed> 3.16 [41].

**Statistical Analysis**

The statistical package SPSS 25.0 was used for the analysis. Continuous variables were tested for normality. For comparisons between nonparametric variables, the Mann-Whitney or Kruskal-Wallis test was applied, and, for the parametric variables, the t-Student or ANOVA was the chosen test. To analyze the association between qualitative variables, either the Chi-square test or Fisher’s exact test was used. A significance level of 5% (p < 0.05) was adopted.

**Results**

The classification of nutritional status by BMI of the patients and the controls is summarized in Table 1. Both groups had similar socioeconomic conditions, per capita income, and pubertal stage (data not shown).

The characterization of patients with A-T is in Table 2. Therein is identified the median time since diagnosis of the disease as 7 years and 2 months (0.7-20.2 years). Twelve out of 22 patients (54.5%) received regular intravenous immunoglobulin (IVIG) treatment and vitamin supplement was used by 17/22 (77.3%) convalescents. Over 60.0% patients had dyslipidemia, while 3/22 (13.6%) had
pneumopathy, and 1/22 (5.4%) had constipation. Selenium alterations were found in 9/22 (40.9%) of cases. All patients had an increase in alpha-fetoprotein (AFP) to a normal value of up to 5.8 IU / mL, a pathognomonic characteristic of the disease. Whereas there was no correlation between AFP concentrations and biomarkers associated with the atherosclerosis risk (data not shown in the table).

The biochemical variables that assess nutritional status relative to selenium, inflammation biomarkers, glycemic metabolism, and liver function are presented in Table 3.

A lower total intake of energy, protein, and carbohydrate was observed in A-T group, compared to the control group (Table 4). Although total fat intake did not show any statistical difference between groups, conflictingly results were found the A-T group. The intake of polyunsaturated, monounsaturated and trans fat was lower, as well as that of selenium.

The markers of the lipid profile are shown in Table 5. A more atherogenic lipid profile with higher concentrations of total cholesterol, non-HDL cholesterol, oxidized LDL, Apo B, Apo B / Apo A-1, LDL / HDL and less than Apo A-1 / HDL was observed in the A-T group.

The combined analysis of laboratory variables using the ROC curve (Figure 1) showed that ALT (AUC = 0.854; 95% CI 0.732 to 0.976; p <0.0001) and oxidized LDL (AUC = 0.849; CI 95% 0.725 to 0.973; p <0.0001) were the variables that showed greater discriminatory power between groups.

No studied variable is significantly corresponding to the concentrations of GPx in the A-T group. In turn, selenium concentrations were associated with those of TC / HDL (rho = 0.481; p = 0.024), LDL / HDL (rho = 0.476; p = 0.025) and TG / HDL (rho = 0.434; p = 0.044) (Figure 2).

**Discussion**

The present study showed that selenium concentrations did not differ significantly between patients and controls. However, it must be pointed out that 41% of A-T patients had selenium concentrations below the reference value. and that MDA concentrations and plus activity of GPx were higher and lower in the A-T group compared to controls, respectively. Also, A-T patients had an atherogenic profile (> NHDL-c, >LDLox, >Apo B and <Apo A-1 / HDL-c) and there was a relevant and positive correlation of selenium concentrations with TC/ HDL-c, LDL-c/ HDL-c and TG / HDL-c ratios.

To our knowledge, there are no current publications evaluating the association between selenium concentrations and GPx activity with those of lipid metabolism biomarkers in A-T patients. Additionally, in vitro A-T cells are under a constant state of oxidative stress and have an abnormal response to agents inducing this state [42]. Oxidative stress is a central mechanism in the pathogenesis of the disease, especially neurodegeneration [43] and other morbidities associated with the disease, such as liver disorders and dyslipidemias [44, 45].

An experimental study by Mercer et al. (2010) [46] demonstrated that ATM protein deficiency accelerates the atherosclerotic process via systemic effects (regulation of NF-κB expression) and on the vascular
endothelium. The authors concluded that damage to mitochondrial DNA, increased production of free radicals and reduced oxidative phosphorylation, in which effects are directly related to changes in lipid and glucose metabolism as well as presented in A-T patients.

Nonetheless, Squadrone et al (2015) [47] evaluated the concentrations of trace elements, including selenium and the antioxidant enzymes, associated with them in 16 individuals with A-T and controls. The essayists also found no differences in selenium concentrations, similarly to what we have observed before, between patients and controls. They described a break in trace element homeostasis with an increase in copper concentrations and a reduction in zinc volume with a consequent reduction in the expression of SOD1 and SOD2 and an increase in the risk of cell apoptosis in A-T patients. GPx activity did not differ between groups. During oxidative stress, selenoprotein P binds to the endothelium of inflamed tissues and it is mobilized to other compartments to exercise its antioxidant function. There is a reduction in its hepatic synthesis, induced by inflammatory cytokines. The synthesis and activity of glutathione, in turn, can be reduced when there is malnutrition, hyperglycemia, corticotherapy, skeletal muscle inactivity; situations frequently observed in A-T patients [48]. Some hypotheses may explain the higher MDA values and the lower GPx activity, pointing to an exacerbation of oxidative stress in our patients: a) older age (median 12.2 years) b) a significant change in liver enzymes, malnutrition level, and impaired lean mass (not mentioned in the study by Squadrone et al.).

Individuals with A-T demonstrated changes in lipid metabolism biomarkers compatible with an atherogenic profile, with an emphasis on elevating NHDL-c and LDLox. LDL-c is easily susceptible to oxidation under conditions of oxidative stress, revealed in our study by the elevation of MDA (lipid peroxidation marker) and reduction of GPx in A-T convalescents, which results in LDLox, and has some atherogenic characteristics. A recent meta-analysis and systematic review described, based on observational studies, the association between LDLox concentrations and the development of atherosclerotic cardiovascular diseases [49].

The findings of lower selenium consumption in the A-T group combined with about 40% of serum concentrations below the reference value may reflect on neurodegeneration. Se is vital for the central nervous system and it is involved in various functions, such as motor performance, coordination, memory and cognition. The role of Se and selenoproteins in neurotransmission goes beyond their antioxidant properties and involves the regulation of inflammation, influencing the phosphorylation of proteins and ion channels, modifying calcium homeostasis, and cholesterol metabolism in the brain. Furthermore, it plays a direct role in signaling by means of selenoprotein P and its interaction with 2 synaptic post receptors of Apolipoprotein (ApoER2) [50]. Future studies evaluating the role of selenium in neurodegeneration-related outcomes in A-T patients appear promising.

Regarding the association of selenium with total cholesterol and LDL-c, some studies show a direct association in the general population [51, 52], while others display a negative correlation [53, 54] or no association at all [55]. This inconsistency may be due to the sample size or even the lack of adjustment for confounding variables. In our study, there was a significant and positive connection between selenium
and the TC/ LDL-c, LDL-c/ HDL-c, and TG/ HDL-c ratios. Therefore, caution should be exercised when proposing selenium supplementation in A-T patients with an open view to distinct outcomes.

In conclusion, the presence of selenium below the reference value by nearly 40% and lower GPx activity in individuals with A-T reinforces the importance of assessing the nutritional status of selenium in those patients. Particularly due to the positive correlation between the lipid profile ratios related to cardiovascular risk and selenium concentrations. Consequently, it is thus possible to deduce that A-T patients are most prone to present increased risk of other morbidities by reason of impaired nutritional status, impaired liver function, dyslipidemia and oxidative stress.

**List Of Abbreviations**

- AFP alpha-fetoprotein
- ALT alanine transaminase
- Apo B apolipoproteins B
- Apo-A1 apolipoproteins A-1
- AST aspartate aminotransferase
- A-T Ataxia-telangiectasia
- ATM ataxia-telangiectasia mutated
- BMI body mass index
- CVDs cardiovascular diseases
- EII innate immunity errors
- FAPESP São Paulo Research Foundation
- GGT gamma-glutamyl transpeptidase
- GPx Glutathione peroxidase
- H/A height for age
- HD heart disease
- HDL-c high-density lipoprotein cholesterol
- HOMA-IR Homeostasis Model Assessment of Insulin Resistance
- IVIG intravenous immunoglobulin
- LDL-c Low-density lipoprotein cholesterol
- LDLox oxidized LDL
- MDA malondialdehyde
- MUAC mid-upper arm circumference
- NCEP National Cholesterol Education Program
- NFkB nuclear transcription factor
- NHDL-c non-HDLc
- ROS reactive oxygen species
- Se Selenium
- 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 à collected, analyzed and interpreted data from patients A-T and the control group and was a major contributor in writing the manuscript.

FISS à analyzed and interpreted data from patients A-T and the control group and contributed to the correction of the manuscript writing.

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

CSAL à analyzed and interpreted data from patients A-T and the control group and contributed to the correction of the manuscript writing.
ROSS analyzed and interpreted data from patients A-T 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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Tables

Table 1. Demographic and anthropometric data in AT patients and healthy controls
| Variables          | A-T patients (n=22) | Controls (n=18) | p value |
|-------------------|---------------------|-----------------|---------|
| Age, median (IQ_{25-75}) | 12.2 (8.5-20.9) | 15.8 (9.8-22.8) | 0.615² |
| Gender            |                     |                 |         |
| Male %            | 16 (72.7)           | 13 (72.2)       | 0.972¹  |
| BMI, kg/m²        |                     |                 |         |
| Underweight, %    | 9 (40.9)            | 2 (11.1)        |         |
| Normal, %         | 11 (50.0)           | 14 (77.8)       | 0.146¹  |
| Overweight, %     | 2 (9.1)             | 2 (11.1)        |         |
| WC, cm            |                     |                 |         |
| Median (IQ_{25-75}) | 60.0 (53.0-64.0) | 68.8 (61.0-79.0) | 0.004² |
| Lean body mass , kg |                    |                 |         |
| Median (IQ_{25-75}) | 24.8 (20.2-29.8) | 41.8 (31.0-50.4) | 0.001² |

Significance level of the Chi-square test (¹), Fisher’s exact test (²); p<0.05

**Table 2.** Characterization of A-T patients.
| Variable (n=22)                   | N (%) |
|----------------------------------|-------|
| Age                              |       |
| 3-15 years                       | 10 (45.5%) |
| 16-27 years                      | 12 (54.5%) |
| Length (n=15)                    |       |
| Low                              | 5 (33.3%) |
| Adequate                         | 10 (66.7%) |
| Mid-upper arm muscle circumference|       |
| Low                              | 10 (45.5%) |
| Adequate                         | 12 (54.5%) |
| Lipid profile                    |       |
| High total cholesterol           | 13 (59.1%) |
| High LDL-c                       | 12 (54.5%) |
| High triglyceride                | 5 (22.7%) |
| Low HDL-c                        | 4 (18.2%) |
| High NHDL-c                      | 13 (59.1%) |
| HOMA-IR                          |       |
| High (> 3.16)                    | 6 (27.3%) |
| Selenium                         |       |
| Adequate (> 46 µg/L)             | 13 (59.1%) |
| Glutathione peroxidase           |       |
| Adequate                         | 20 (90.9%) |
| ALT                              |       |
| > 40 U/L                         | 5 (22.7%) |
| AST/ALT                          |       |
| > 1                               | 17 (77.3%) |

N (%)

Legend: LDL-c low density lipoprotein cholesterol, HDL-c high density lipoprotein cholesterol, NHDL-c Non-HDL-c, ALT alanine aminotransferase, and AST/ALT aspartate aminotransferase/alanine aminotransferase
Table 3. Comparison of the variables in A-T group and control group.

| Variables               | A-T patients (n=22) | Controls (n=18) | p value |
|------------------------|---------------------|-----------------|---------|
|                        | Median (IQ_{25-75}) | Median (IQ_{25-75}) |         |
| Glutathione peroxidase U/L | 7300 (6683-8267)   | 8686 (7967-9449) | **0.005** |
| Selenium µg/L           | 47.6 (43.2-57.0)    | 54.6 (45.2-62.6) | 0.242   |
| Malondialdehyde nmol/mL | 3.8 (3.0-4.0)       | 2.8 (2.4-3.6)    | **0.029** |
| High us- CRP n, %       | 8 (36.4)            | 2 (11.1)         | 0.082   |
| Adiponectin mg/dL       | 156.9 (125.5-234.6) | 180.4 (173.1-183.9) | 0.355 |
| Glucose n, %            | 21 (95.5)           | 17 (94.4)        | 1.000   |
| Insulin                | 6.1 (2.5-11.6)      | 7.4 (3.6-10.6)   | 0.870   |
| HOMA-IR                | 1.1 (0.4-3.4)       | 1.2 (0.7-2.0)    | 0.891   |
| AST U/L                | 31.0 (25.0-47.0)    | 17.0 (14.0-19.0) | <**0.001** |
| ALT U/L                | 21.0 (13.0-32.0)    | 9.5 (9.0-13.0)   | <**0.001** |
| GGT U/L                | 27.7 (14.3-66.7)    | 14.6 (10.1-17.4) | **0.011** |

Significance level of the Chi-square test, Fisher’s exact test or Mann-Whitney test; p<0.05

Legend: HOMA-IR homeostasis model assessment of insulin resistance; GGT gamma-glutamyl transpeptidase

Table 4. Family risk for cardiovascular disease and atherogenic lipid profile for A-T patients and control groups.
| Variables         | A-T patients (n=22) | Controls (n=18) | p value |
|-------------------|---------------------|-----------------|---------|
|                   | Median (IQ_{25-75}) | Median (IQ_{25-75}) |         |
| Family CVR        | Yes                 |                 | 0.119   |
|                   | 8 (36.4%)           | 11 (61.1%)      |         |
| Lipid profile biomarkers |               |                 |         |
| Total cholesterol | mg/dL 188.5 (168.0-228.0) | 164.0 (124.0-172.0) | 0.005   |
| LDL-c             | mg/dL 124.4 (105.4-166.0) | 89.5 (67.0-105.6) | <0.001  |
| Triglycerides     | mg/dL 90.5 (66.0-115.0) | 77.5 (63.0-94.0) | 0.231   |
| HDL-c             | mg/dL 47.5 (42.0-61.4) | 46.0 (35.0-56.0) | 0.549   |
| NHDL-c            | n, % 136.5 (120.0-182.0) | 108.0 (79.0-125.0) | 0.001   |
| VLDL-c            | mg/dL 18.1 (13.2-23.0) | 15.5 (12.6-18.8) | 0.231   |
| Remnant cholesterol | mg/dL 18.2 (13.2-23.0) | 15.6 (12.6-18.8) | 0.221   |
| Oxidized LDL      | mg/dL 72.6 (42.6-137.0) | 25.8 (21.1-40.7) | <0.001  |
| Apo A-1           | mg/dL 99.0 (87.0-117.0) | 122.0 (92.0-138.0) | 0.070   |
| Apo B             | mg/dL 109.5 (96.0-138.0) | 91.0 (78.0-101.0) | 0.002   |
| Apo B/ Apo A-1    | 1.1 (0.7-1.5) | 0.7 (0.5-0.8) | 0.001   |
| Total cholesterol/HDL-c | 4.0 (3.0-5.0) | 3.0 (3.0-4.0) | 0.080   |
| LDL-c/ Apo B      | 1.1 (1.0-1.2) | 1.1 (0.9-1.1) | 0.549   |
| LDL-c/ HDL-c      | 2.5 (2.0-4.0) | 2.0 (1.0-2.0) | 0.021   |
| TG/ HDL-c         | 2.0 (1.0-3.0) | 1.0 (1.0-3.0) | 0.279   |
| Apo A-1/ HDL-c    | 1.9 (1.8-2.1) | 2.5 (2.2-2.7) | 0.008   |

Significance level of the Chi-square test or Fisher’s exact test

CVR cardiovascular risk, LDL-c low-density lipoprotein cholesterol, HDL-c high-density lipoprotein cholesterol, NHDL-c non-HDL cholesterol

**Table 5.** Comparison of the means of energy, macronutrients, and micronutrients intake in A-T group and control group.
| Variable                  | A-T patients | Control A-T | P*   |
|--------------------------|--------------|-------------|------|
|                          | N=22         | N=18        |      |
| Median (IQ_{25-75})      |              |             |      |
| Energy (Kcal)            | 1522.4 (1233.8-1673.1) | 1744.1 (1431.0-2333.2) | 0.031 |
| Carbohydrate (g)         | 211.1 (187.8-249.6)  | 255.4 (218.4-354.3)  | 0.029 |
| Protein (g)              | 60.3 (51.2-68.2)   | 76.8 (60.3-93.2)    | 0.010 |
| Total Fat (g)            | 42.5 (37.2-47.3)   | 44.1 (38.4-60.1)    | 0.127 |
| Saturated Fat (g)        | 13.9 (10.8-16.7)   | 17.1 (12.4-23.7)    | 0.068 |
| Monounsaturated fat (g)  | 10.3 (6.3-11.6)    | 12.2 (11.2-15.4)    | 0.007 |
| Polyunsaturated fat (g)  | 5.6 (4.0-7.6)      | 9.8 (6.6-13.5)      | 0.001 |
| Trans Fat (g)            | 0.5 (0.3-0.7)      | 0.9 (0.7-1.9)       | 0.006 |
| Copper (µg)              | 0.6 (0.5-0.8)      | 0.6 (0.5-0.8)       | 0.913 |
| Selenium (mg)            | 56.1 (43.2-66.0)   | 68.8 (63.0-80.1)    | 0.016 |
| Zinc (mg)                | 7.1 (5.9-8.9)      | 6.0 (4.5-7.1)       | 0.074 |
| Retinol (µg)             | 249.5 (176.8-395.0) | 208.9 (150.5-247.2) | 0.772 |
| Ascorbic Acid (mg)       | 74.6 (57.3-100.7)  | 57.6 (52.4-77.2)    | 0.142 |
Significance level of the Mann-Whitney test; $p<0.05$

| Variables                        | Area Under Curve | CI 95% | Valor-p |
|----------------------------------|------------------|--------|---------|
| Apo A-I/HDL                      | 0.227            | 0.049  | 0.406   | 0.006   |
| Glutathione peroxidase (GPx)     | 0.247            | 0.075  | 0.418   | 0.011   |
| Selenium                         | 0.364            | 0.172  | 0.555   | 0.173   |
| Malondialdehyde (MDA)            | 0.661            | 0.463  | 0.858   | 0.108   |
| LDL/HDL                          | 0.700            | 0.527  | 0.872   | 0.046   |
| Total cholesterol (TC)           | 0.713            | 0.544  | 0.881   | 0.034   |
| Gama-GT (GGT)                    | 0.742            | 0.579  | 0.905   | 0.016   |
| Non-HDL cholesterol (NHDL)       | 0.755            | 0.598  | 0.912   | 0.011   |
| Apo B/Apo A-I                    | 0.789            | 0.641  | 0.937   | 0.004   |
| LDL-c                            | 0.791            | 0.644  | 0.937   | 0.004   |
| Oxidized LDL (LDLox)             | 0.849            | 0.725  | 0.973   | 0.000   |
| ALT                              | 0.854            | 0.732  | 0.976   | 0.000   |

**Figures**
Figure 1

Discriminatory analysis using the ROC curve of the laboratory variables evaluated in A-T patients and the control group.
Figure 2

Correlation matrix between selenium concentrations and the lipid profile of A-T patients. Significance level of Spearman correlation ($p < 0.05$)