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Risk factors associated with metabolic syndrome in women with chronic autoimmune thyroiditis

Fatores de risco associados à síndrome metabólica em mulheres com tireoidite crônica autoimune

Factores de riesgo asociados al síndrome metabólico en mujeres con tiroiditis crónica autoinmune

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Marina Destefano Prezotto[1]
Adriana Paula da Silva[2]
Elvi Cristina Rojas Fonseca[3]
Priscila de Melo Franciscon[4]
Maria de Fátima Borges[5]

This is a cross-sectional study with a descriptive design, with two population groups before and after, type, with a quantitative approach of the analytical type with correlation between variables, carried out between 2018 and 2019. It aimed to analyze cardiometabolic, clinical and laboratory risk factors associated with metabolic syndrome in women with chronic autoimmune euthyroid thyroiditis, in pre and post-menopause, followed up in a tertiary service. 109 women participated, 56 with Chronic Autoimmune Thyroiditis in euthyroid status and 53 with no thyroid dysfunction. Of the 56 women, 25 were included in the premenopausal Chronic Autoimmune Thyroiditis group and 31 were included in the postmenopausal group, and of the 53 women with normal thyroid function, 25 were included in the premenopausal comparative group and 28 in the postmenopausal comparative group. The metabolic profile suggested insulin resistance, with higher rates in the pre and post-menopausal thyroiditis group and post-menopausal control group, as well as an unfavorable lipid profile. 36% of the premenopausal affected group and 51.6% of the postmenopausal affected group had metabolic syndrome, against none and 14.3% of the comparative groups, respectively. Whether insulin resistance or obesity resulted from thyroiditis, the study did not allow us to conclude. Patients with thyroiditis should be given attention to their lipid profile.
Descriptors: Thyroiditis, autoimmune; Metabolic syndrome; Insulin resistance; Risk factors.

Este é um estudo de corte transversal com delineamento descritivo, com dois grupos populacionais, tipo antes e depois, com abordagem quantitativa do tipo analítica com correlação entre variáveis, realizado entre 2018 e 2019, com objetivo de analisar fatores de risco cardiometabólicos, clínicos e laboratoriais associados à síndrome metabólica em mulheres com tireoidite crônica autoimune eutireoideas, na pré e pós-menopausa, acompanhadas em serviço terciário. Participaram 109 mulheres, sendo 56 com Tireoidite Crônica Autoimune em *status* eutireoideo e 53 sem disfunção tireoidiana. Das 56 mulheres, 25 foram incluídas no grupo com Tireoidite Crônica Autoimune na pré-menopausa e 31 foram incluídas na pós-menopausa e, das 53 mulheres com função tireoidiana normal, 25 foram incluídas no grupo comparativo na pré-menopausa e 28 no grupo comparativo na pós-menopausa. O perfil metabólico sugeriu resistência insulínica, com taxas mais elevadas no grupo com tireoidite pré e pós-menopausa e grupo controle pós, bem como perfil lipídico desfavorável. Apresentaram síndrome metabólica 36% do grupo afetado pré-menopausa e 51,6% do grupo afetado pós, contra nenhuma e 14,3% dos grupos comparativos, respectivamente. Se resistência insulínica ou obesidade decorreram da tireoidite, o estudo não permitiu concluir. Pacientes com tireoidite devem receber atenção com relação ao perfil lipídico.
Descritores: Tireoidite autoimune; Síndrome metabólica; Resistência à insulina; Fatores de risco.

Este es un estudio transversal con diseño descriptivo, con dos grupos poblacionales, tipo antes y después, con enfoque cuantitativo de tipo analítico con correlación entre variables, realizado entre 2018 y 2019, con el objetivo de analizar los factores de riesgo cardiometabólicos, clínicos y de laboratorio asociados al síndrome metabólico en mujeres con tiroiditis crónica autoinmune eutiroidea, pre y postmenopáusicas, monitoreadas en un servicio terciario. Participaron 109 mujeres, 56 con Tiroiditis Crónica Autoinmune en estado eutiroideo y 53 sin disfunción tiroidea. De las 56 mujeres, 25 se incluyeron en el grupo con Tiroiditis Crónica Autoinmune en la premenopausia y 31 en la posmenopausia, y de las 53 mujeres con función tiroidea normal, 25 se incluyeron en el grupo de comparación en la premenopausia y 28 en el grupo de comparación en la posmenopausia. El perfil metabólico sugirió resistencia a la insulina, con tasas más elevadas en el grupo con tiroiditis pre y posmenopáusica y en el grupo de control posmenopáusico, así como un perfil lipídico desfavorable. El 36% del grupo afectado premenopausia y el 51,6% del grupo de afectado posmenopausia tenían síndrome metabólico, frente a ninguna y el 14,3% de los grupos de comparación, respectivamente. El estudio no pudo concluir si la resistencia a la insulina o la obesidad eran consecuencia de la tiroiditis. Los pacientes con tiroiditis deben recibir atención respecto a su perfil lipídico.
Descriptores: Tiroiditis autoinmune; Síndrome metabólico; Resistencia a la insulina; Factores de riesgo.

1. Nutritionist. Specialist in Sports Nutrition and Obesity. Master in Health Care. Uberaba, MG, Brazil. ORCID: 0000-0003-1114-5355 E-mail: nutrimarinaprezotto@hotmail.com
2. Nutritionist. Specialist in Public Health Education. Master in Health Care. PhD in Health Sciences. Nutritionist at the Hospital de Clínicas of the Universidade Federal do Triângulo Mineiro (UFTM), Uberaba, MG, Brazil. ORCID: 0000-0001-5275-9981 E-mail: adrianapaulanutri@gmail.com
3. Doctor. Specialist in Endocrinology and Metabolism. Master in Tropical Medicine and Infectology. PhD in Health Sciences. Hospital de Clínicas (HC) of UFTM, Uberaba, MG, Brazil.ORCID: 0000-0003-2049-1719 E-mail: elvicristina@terra.com.br
4. Doctor. Specialist in Endocrinology and Metabolism. Master in Health Sciences. Department of Internal Medicine, HC/UFTM, Uberaba, MG, Brazil. ORCID: 0000-0003-0148-1697 E-mail: priscilafranciscon@hotmail.com
5. Doctor. Master and PhD in Endocrinology. HC/UFTM, Uberaba, MG, Brazil.ORCID: 0000-0002-2294-848X E-mail: borgmf@uol.com.br

INTRODUCTION

Chronic Autoimmune Thyroiditis (AIT), also called Hashimoto's Thyroiditis (HT) or Chronic Lymphocytic Thyroiditis, represents the most common cause of hypothyroidism in areas with iodini sufficiency[1,2]. It has an estimated prevalence of 5% of the adult population, with a prevalence five times higher in women than in men; and its incidence has increased in the last 50 years, especially between 45 and 65 years[3,4].

Thyroid autoimmunity develops as a result of loss of immune tolerance and reactivity to autoantigens. The attack on the immune system is manifested by the infiltration of the thyroid by T lymphocytes, production of anti-thyroglobulin (anti-TG) and anti-thyroperoxidase (anti-TPO) antibodies, which can be presented in two clinical forms: atrophic and goiter[1-3]. There are several factors associated with the breakdown of immunological tolerance, such as infections, genetic predisposition, medications and environmental factors such as concentrations of iodine, selenium and others[1,5].

Metabolic Syndrome (MS) is a complex disorder, consisting of a set of cardiometabolic risk factors. It is characterized by the accumulation of abdominal fat, dyslipidemia (low HDL and hypertriglyceridemia), insulin resistance and systemic arterial hypertension (SAH)[6,7]. It confers a 2.5 times greater predisposition to cardiovascular diseases, increasing overall mortality by approximately 1.5 times[7,8].

In recent years, some studies have shown an association between thyroid dysfunction, development of metabolic disorders and cardiovascular diseases[6,9], while other studies have reported an association between free T4 concentrations, occurrence of insulin resistance and dyslipidemia even in euthyroid individuals[10]. Thyroid hormones act in several metabolic pathways related to carbohydrates and lipids, influencing the regulation of hepatic gluconeogenesis, lipogenesis and lipolysis[10]. Therefore, it is to be expected that thyroid dysfunctions that interfere with specific metabolic pathways predispose to MS and increase cardiovascular risk factors[11].

The metabolic changes that occur in hypothyroidism are similar to those present in MS, in addition to sharing risk factors such as age and menopause, increasing the probability of simultaneous occurrence of the two conditions[11]. Thus, this study aims to analyze cardiometabolic, clinical and laboratory risk factors associated with metabolic syndrome in women with chronic autoimmune euthyroid thyroiditis, in pre and post-menopause, followed up in a tertiary service.

METHODS

This is an observational, cross-sectional study with a descriptive design, with two population groups, before and after, with a quantitative analytical approach with correlation between variables, developed at the Thyroid Clinic of the Discipline of Endocrinology and Metabolism, Universidade Federal do Triângulo Miner (UFTM).

The study sample was a convenience sample through the care file book, selecting all women who met the inclusion criteria: women aged between 21 and 66 years, divided into four groups, two groups with AIT in pre-menorapuse (G1) and in postmenopausal women (G2) and their respective comparative groups, with the comparative group in pre-menopausal (CG1) and the comparative group in post-menopausal (CG2), paired for age and pre or post-menopausal status and with thyroid function normal.

The inclusion criteria for G1 were: being female, aged 18 years or over, regular menstrual cycles, therefore being in pre-menopausal status, having a previous diagnosis of AIT (the previous diagnosis must have taken into account the presence of the following alterations: elevated TSH, normal or reduced T4 levels, positive anti-thyroid antibodies or ultrasound and/or cytological alterations suggestive of AIT), being under treatment with thyroid hormone and presenting hormonal dosages compatible with the adequate control of the disease.

Inclusion criteria for G2 were: being female, aged 40 years or older, no longer having menstrual cycles and being in post-menopausal status, having a previous diagnosis of AIT and being treated with thyroid hormone and presenting hormonal dosages compatible with disease control.

The inclusion criteria for CG1 were: being female, being 18 years old or older, not having a diagnosis of thyroid-related diseases, having regular menstrual cycles and being in pre-menopausal status.

Inclusion criteria for CG2 were: being female, aged 40 years or over, not diagnosed with thyroid-related diseases, no longer having menstrual cycles, and postmenopausal status. Pregnant women, with menstrual irregularities and other chronic diseases capable of interfering with thyroid function were excluded.

Data were collected from February 2018 to June 2019. A semi-structured questionnaire, two outpatient systems used to view laboratory tests, patient charts and care records were used. Patients with AIT and the volunteers in the comparative groups underwent clinical evaluation, assessment of anthropometric and laboratory parameters. Two consultations were carried out for each group: in the first consultation, the semi-structured questionnaire was applied, the request for exams was submitted and the return consultation was scheduled. At the return visit for the four groups, the results of the exams were analyzed and an individualized meal plan was delivered to each participant.

In the clinical evaluation, weight, height, skinfolds (triceps, biceps, suprailiac and subscapular) were measured, waist circumference determined at the midpoint between the lower costal margin and the iliac crest, blood pressure measurement and classified according to the 7th Brazilian Guidelines on Hypertension (2016)[12] and calculated the Body Mass Index (BMI) and the percentage of body fat.

The laboratory evaluation consisted of plasma determinations of fasting glucose, total cholesterol, fractions and triglycerides, uric acid, glycated hemoglobin, TSH, T4 levels, Anti-TPO and Anti-TG antibodies and basal insulin. In addition, the Homeostasis model assessment insulin resistance index (HOMA-IR)[13] was calculated according to the formula:

HOMA-IR = fasting blood glucose (mmol/L*) x fasting insulin (μUI/mL) / 22.5

To convert glucose from mg/dL to mmol/L, the value in mg/dl is multiplied by 0.0555 (Directives of the Brazilian Society of Diabetes, 2019-2020)[13].

The present study adopted the criteria established by the International Diabetes Federation (IDF) (2006)[14] for the diagnosis of Metabolic Syndrome and the Global Risk Score (GRS) to estimate the probability of occurrence of myocardial infarction (heart attack) or death from coronary heart disease in the period of 10 years, calculated according to the Brazilian Society of Cardiology (2017)[15].

To test the data, assumptions of normality were verified by the Kolmogorov-Smirnov test and homogeneity of variances by the Levene test. The variables were transformed by:

$\sqrt{x}$, or $\sqrt{x + 0{,}5}$, or $log\ x$, or $log\ x + 1$,

or by boxcox, when normality assumptions were not met or had heterogeneity of variances.

Comparison of frequencies of occurrences of cardiometabolic risk factors between groups was performed using the chi-square test. ANOVA or Kruskal Wallis test were applied for comparisons between 3 or more groups, followed by Tukey's test or Dun's test for multiple comparisons, respectively. To verify the correlation between variables, Pearson or Spearman coefficients were used. A significance level of 5% was adopted.

The ethical aspects were based on Resolution CNS 466/12 on research involving human beings and was approved by the Research Ethics Committee of the Universidade Federal do Triângulo Mineiro under CAE No. 51789915.5.0000.5154. The participants signed the Informed

Consent Form (ICF), guaranteeing their anonymity and the right to withdraw from the research at any time.

RESULTS

109 women participated, 56 with AIT in euthyroid status and 53 without thyroid dysfunction. Of the 56 women, 25 were included in the premenopausal AIT group (G1) and 31 were included in the postmenopausal AIT group (G2), and of the 53 women with normal thyroid function, 25 were included in the comparative group in pre-menopausal (CG1) and 28 in the post-menopausal comparative group (CG2).

In Tables 1 and 2, clinical and biochemical data were represented. There were no differences in terms of BMI (p=0.372), as well as in terms of frequencies according to nutritional status (p=0.215). Age was significantly higher in groups G2 and GC2.

The AC in G2 was significantly higher than in CG1 (p=0.004), and the frequency of participants with altered AC was also higher in G2 (p=0.002). Likewise, in relation to the %BF, a significant difference was detected between the groups (p=0.016), with CG2 being greater than GC1 (p=0.04), and, in relation to frequencies, GC1 had a higher frequency of participants with an average %BF compared to CG2 (p=0.044) (Tables 1 and 2). No significant differences were observed when comparing the SBP means between the groups, and, for DBP, the Kruskal Wallis test indicated differences between the groups (p=0.027), but the DUN multiple comparisons test did not reveal between which groups were different (Table 1). The frequencies of normal and altered SBP did not differ between groups (p= 0.105) and, in relation to DBP, this comparison was not made, as all participants had normal DBP (Table 2).

When comparing fasting blood sugar (mg/dL) between groups of women with AIT and comparatives, significant differences were observed between groups, with G2 being significantly higher than G1 (p<0.0001), GC1 (p<0 .0001) and GC2 (p<0.0001), and GC2 significantly higher than G1 (p<0.0001), and GC1 (p<0.0001) (Table 1). Frequencies of altered FBS among participants were significantly higher in group G2 compared to all groups, while the frequency of women with normal FBS was significantly higher in CG1 (Table 2).

There was a significant difference when comparing HbA1c between groups (p<0.0001), with G1 being higher than GC1 (p<0.0001); G2 greater than GC1 (p<0.0001) and GC2 greater than GC1 (p<0.02) (Table 1). The frequency of women with normal HbA1c in CG1 was significantly higher than the frequency of women in CG1 with altered HbA1c (p=0.047) (Table 2).

Likewise, a significant difference was observed when comparing insulin concentrations (µUI/mL) between groups (p=0.008), with GC2 being significantly higher than GC1 (p=0.003) and G2 (p=0.01) (Table 1). Normal and altered insulin frequencies between groups did not show statistical significance (p=0.115) (Table 2).

Regarding the Homa-IR index, it was observed that GC2 was significantly higher than GC1 (p=0.04), and no difference was observed between G1 and G2 (Table 1). Normal and altered HOMA-IR frequencies between groups did not show statistical significance (p=0.281) (Table 2).

No significant differences were observed when comparing the means of the TSH, T4 and uric acid variables between the groups (Table 1). The frequencies of normal and altered uric acid between groups did not show statistical significance (p=0.107) and, in relation to TSH and T4, they were not calculated, as all participants had concentrations within the values considered normal (Table 2).

The comparison of the lipid profile variables between the groups showed that the mean concentrations of HDL-c (mg/dL) were significantly higher in CG1 (p=0.04) and CG2 (p=0.012) compared to G1. differences between the other groups (Table 1). The frequencies of normal and altered HDL-c between groups did not show statistical significance (p=0.251) (Table 2).

Mean LDL-c (mg/dL) in groups GC1 and GC2 were significantly lower than in G2 p=0.008, p=0.039, respectively. As for normal and altered frequencies, there was no difference between groups (p=0.357).

Means of ñ-HDL-c were not different between G1 and G2 (Table 1), but mean concentrations in G2 were significantly higher than in GC2 (p=0.025), and the percentage of women with altered ñ-HDL-c was greater than the normal percentage in group G2 (p=0.005).

There was no statistical significance when comparing the means of TC and TG between groups (Table 1), as well as in relation to the frequencies of normal and altered, they also showed no differences (Table 2).

According to guidelines reported in the update of the V Brazilian Guideline on Dyslipidemia and Atherosclerosis (2017), the global risk score (GRS) was calculated in patients over 30 years of age. In G1, the GRS was calculated in 16 patients, and it was considered high in two, average in two and low in the others. In CG1, the GRS calculated in 15 patients was low in all. In G2, it was high in one, average in 16 and low in the others. In CG2, it was average in four, low in the others and the comparison of GRS between groups did not show any statistical difference (p= 0.107) (Table 1).

Table 1. Clinical and biochemical characteristics between groups, Uberaba, 2020.

Variables	G1	GC1	G2	GC2	*p-Value*
Age	33.7 ± 7.5	33.5 ± 7.6	57.1 ± 6.0	56.2 ± 5.9	***<0.0001**[c*]*
BMI (kg/m²)	27.1 ± 5.3	24.9 ± 5.1	26.7 ± 3.3	26.2 ± 4.7	*0.372*[c]
AC (cm)	84.0 (70 – 116)	78.0 (64 – 106)	89.5 (72 – 107)	81.0 (69 – 118)	***0.004**[d*]*
% BF	33.3 (20.1 – 38.6)	31.9 (18.6 – 39.6)	34.3 (22.7 – 41.0)	35.8 (28.1 – 39.3)	***0.016**[d*]*
SBP (mmHg)	120 (90 – 140)	120 (110 – 130)	120 (90 – 140)	120 (110 – 130)	0.597[d]
DBP (mmHg)	80 (60 – 80)	80 (70 – 80)	80 (60 – 80)	80 (80 – 80)	**0.027**[d*]
FBS (mg/dL)	90.6 ± 7.2	85.6 ± 5.9	96.1 ± 12.3	91.0 ± 4.7	**<0.0001**[c*]
HbA1c (%)	5.2 (4.3 – 9.6)	4.8 (3.9 – 5.4)	5.4 (4.9 – 7.4)	5.1 (4.2 – 6.3)	**<0.0001**[d*]
Insulin (µUI/mL)	10.1 (4.1 – 65.3)	9.2 (4.7 – 25)	9.9 (3.7 – 29)	13.1 (7.3 – 19.8)	**0.008**[d*]
HOMA-IR	2.2 (0.8 – 14.5)	1.9 (1.0 – 5.9)	2.2 (0.8 – 6.0)	2.9 (1.6 – 5.0)	**0.026**[d*]
TSH (mUI/L)	2.2 ± 1.3	1.9 ± 0.8	1.6 ± 1.0	1.8 ± 0.8	0.150[c]
T4 (mUI/L)	1.1 (0.8 – 1.4)	1.1 (0.7 – 1.8)	1.1 (0.7 – 1.7)	1.1 (0.8 – 1.8)	0.460[d]
Uric acid (mg/dL)	4.2 ± 1.2	4.0 ± 0.8	4.4 ± 2.1	4.6 ± 0.5	0.219[c]
TC (mg/dL)	185 ± 38.8	180.5 ± 20.3	199.3 ± 37.5	182.6 ± 12.5	0.071[c]
LDL (mg/dL)	106 (54.0 – 182.0)	92 (64.0 – 151.0)	120 (54.1 – 181.6)	97 (71.8 – 129.0)	**0.006**[d*]
HDL (mg/dL)	52.9 ± 8.4	62.8 ± 5.8	59.0 ± 14.7	61.3 ± 5.1	**0.004**[c*]
ñ-HDL (mg/dL)	132.1 ± 38.3	117.7 ± 21.1	140.3 ± 33.5	121.3 ± 13.7	**0.020**[c*]
TG (mg/dL)	112.4 (36.0 – 229.0)	97 (57.0 – 146.0)	92.5 (43.0 – 279.0)	103.4 (44.0 – 168.0)	0.310[d]
RS (%)	2.37 ± 1.23	1.75 ± 0.86	4.6 ± 2.23	3.91 ± 0.99	0.107[c]

%BF – Body Fat; AC – Abdominal circumference; SBP – Systolic Blood Pressure; BMI – Body Mass Index; DBP – Diastolic Blood Pressure; FBS– Fasting Blood Sugar; HbA1c – Glycated Hemoglobin; TSH – Thyroid-stimulating hormone; T4 – Thyroxine; Anti TPO - Antiperoxidase; Anti TG – Antithyroglobulin; TC - Total Cholesterol; LDL– c– Low Density Lipoprotein Cholesterol; HDL–c – High Density Lipoproteic Cholesterol; Ñ HDL–c – No - High Density Lipoproteic Cholesterol; VLDL– c – Very low density lipoprotein; TG – Triglycerides; RS – Risk score. cANOVA: Age – G2>G1 p<0.0001; GC2>G1 p<0.0001; G2>GC1 p<0.0001; GC2>GC1 p<0.0001/ GJ – G2>G1 p<0.0001; G1>GC1 p<0.0001; GC2>G1 p<0.0001; G2>GC1 p<0.0001; G2>GC2 p<0.0001; GC2>GC1 P<0.0001. dKruskal Wallis: C.A – G2>GC1 p=0.002 / %GC – GC2>GC1 p=0.04; HbA1c – G1>GC1 p<0.0001; G2>GC1 p<0.0001; GC2>GC1 p<0.02 / Insulin - G4>G2 p=0.03; GC2>GC1 p=0.01 / HOMA-IR – GC2>GC1 p= 0.04. *p<0.05.

Table 2. Clinical and biochemical characteristics between groups, Uberaba, 2020.

Variables	Classification	G1 No. (%)	GC1 No. (%)	G2 No. (%)	GC2 No. (%)	*p*[a]
BMI	Low weight	2 (8)	0	1 (3.2)	1 (3.6)	0.215
	Eutrophic	9 (36)	15 (60)	10 (33.2)	15 (53.6)	
	Overweight/Obesity	14 (56)	10 (40)	20 (63.6)	12 (42.8)	
AC	Normal	9 (36)	14 (56)	3 (9.7)	13 (46.4)	**0.002***
	Altered	16 (64)	11 (44)	28 (90.3)	15 (53.6)	
%BF	Below average	0	1 (4)	0	0	0.044
	Average	3 (12)	6 (24)	1 (3.2)	0	
	Above average	8 (32)	6 (24)	7 (22.6)	7 (25)	
	Risk associated with obesity	14 (56)	12 (48)	23 (74.2)	21 (75)	
SBP	Normal	23 (92)	24 (96)	24 (77.4)	26 (92.9)	0.105
	Altered	2 (8)	1 (4)	7 (22.6)	2 (7.1)	
FBS	Normal	20 (80)	25 (100)	23 (74.2)	26 (92.8)	**0.022***
	Altered	5 (20)	0	8 (25.8)	2 (7.2)	
HbA1c	Normal	19 (76)	25 (100)	24 (77.4)	25 (89.3)	**0.047***
	Altered	6 (24)	0	7 (22.6)	3 (10.7)	
Insulin	Normal	22 (88)	25 (100)	29 (93.5)	28 (100)	0.115
	Altered	3 (12)	0	2 (6.5)	0	
Homa-IR	Normal	17 (68)	20 (80)	20 (64.5)	13 (46.4)	0.081
	Altered	8 (32)	5 (20)	11 (35.5)	15 (53.6)	
Uric acid	Normal	23 (92)	25 (100)	26 (83.9)	27 (96.4)	0.107
	Altered	2 (8)	0	5 (16.1)	1 (3.6)	
TC	Good	16 (64)	23 (92)	16 (48.4)	25 (89.3)	0.168
	Borderline	7 (28)	2 (8)	12 (41.9)	3 (10.7)	
	High	2 (8)	0	3 (9.7)	0	
LDL-c	Great	10 (40)	17 (68)	7 (22.6)	19 (67.8)	0.357
	Good	8 (32)	6 (24)	12 (38.7)	9 (32.2)	
	Borderline	6 (24)	2 (8)	10 (32.4)	0	
	High	1 (4)	0	2 (6.3)	0	
HDL-c	Good	6 (30)	19 (76)	13 (41.9)	21 (75)	0.251
	Borderline	17 (68)	6 (24)	17 (54.8)	7 (25)	
	Low	2 (8)	0	1 (3.3)	0	
Ñ-HDL-c	Great	14 (56)	19 (76)	13 (41.9)	21 (75)	**0.005***
	Good	4 (16)	4 (16)	9 (29)	7 (25)	
	High	6 (24)	2 (8)	8 (25.8)	0	
	Very high	1 (4)	0	1 (3.3)	0	
VLDL	Good	22 (88)	25 (100)	26 (83.9)	25 (89.3)	0.244
	High	3 (12)	0	5 (16.1)	3 (10.7)	
TG	Good	22 (88)	25 (100)	24 (77.6)	25 (89.3)	0.259
	Borderline	3 (12)	0	5 (16.1)	3 (10.7)	
	High	0	0	2 (6.3)	0	
	Very high	0	0	0	0	

AC – Abdominal circumference; BMI – Body Mass Index; %BF – Body Fat; SBP – Systolic Blood Pressure; FBS – Fasting Blood Sugar; HbA1c – Glycated Hemoglobin; TSH – Thyroid-stimulating hormone; T4L – Thyroxine; Anti TPO - Antiperoxidase; Anti TG – Antithyroglobulin; CT – Total Cholesterol; LDL– c– Low Density Lipoprotein Cholesterol; HDL–c – High Density Lipoproteic Cholesterol; No HDL–c – No - High Density Lipoproteic Cholesterol; VLDL– c – Very low density lipoprotein; TG – Triglycerides. aChi square test. *p<0.05.

In Table 3, the patients were analyzed according to the presence of criteria for the diagnosis of MS. The percentages were higher in G1 compared to the comparative group and, when comparing the frequencies between the two groups, there was a statistical difference, with the frequency of women in CG1 without risk factors being significantly higher than in G1. The same occurred in G2 in relation to CG2 and, when comparing frequencies between the two groups, there was a difference, with the frequency of women in CG2 without risk factors being significantly higher than in G2, while the frequency of women in G2 with metabolic syndrome was significantly higher than in GC2.

Table 3. Comparison of the frequencies of risk factors in women with chronic autoimmune thyroiditis (AIT) and women in the comparative groups, Uberaba, 2020.

Groups	No risk factor No. (%)	1 risk factor No. (%)	Methabolic Syndrome No. (%)	*p-Value*[a] (G1&GC1)	*p-Value*[a] (G2&GC2)
G1	7 (28)	9 (36)	9 (36)	**0.003***	**0.002***
GC1	14 (56)	11 (44)	0		
G2	3 (9.7)	12 (38.7)	16 (51.6)		
GC2	12 (42.9)	12 (42.9)	4 (14.2)		

[a]Chi-Square test; *p<0.05

Table 4 shows the values of the correlation coefficient for the relationships between clinical and laboratory variables and lipid profile of premenopausal participants. Note that, in G1, FBS, Insulin concentrations and HOMA-IR index were significantly correlated with BMI and %BF. HOMA-IR further correlated with AC and HDL-c. Inverse correlations occurred between HbA1c and HDL-c, and direct correlations between AU and T4 with TG. Correlations between clinical data and lipid profile were not demonstrated. In GC1, FBS, HbA1c, insulin, HOMA-IR index, AU and lipid profile (except HDL-c) were directly correlated with adiposity indexes (BMI, AC and %BF). FBS still correlated significantly with ñ-HDL-c and TG, insulin with TG and HOMA-IR positively with TC and inversely with HDL-c. AU was positively correlated with TC and ñ-HDL-c and TSH with AC, HbA1c was inversely correlated with HDL-c and directly correlated with ñ-HDL-c and TG.

Table 5 shows the values of the correlation coefficient for the relationships between clinical and laboratory variables and lipid profile of postmenopausal participants. Note that, in G2, fewer correlations were significant between biochemical variables and anthropometric data. Insulin concentrations showed weak but significant correlations with BMI, AC, moderate with TG and inverse with HDL-c. HbA1c significantly correlated with AC, %BF and inverse correlation with TC. TSH was inversely correlated with ñ-HDL-c. The lipid profile was inversely correlated with anthropometric variables. And in GC2, FBS correlated positively and significantly with AC and TG and negatively with HDL-c. HOMA-IR correlated positively and significantly with ñ-HDL-c and TG and negatively with HDL-c.

Table 4. Correlations between clinical and metabolic variables of participants with AIT in pre-menopausal (G1) and comparative group (CG1). Uberaba-MG, 2020.

Variables	Age		BMI		AC		%BF		TC		LDL-c		HDL-c		Ñ-HDL-c		TG	
	G1	GC1	G1	GC1	G1	GC1	G1	GC1	G1	GC1	G1	GC1	G1	GC1	G1	GC1	G1	GC1
FBS	0.147	0.162	**0.474[1]***	**0.7961***	0.365	**0.794#***	**0.472[#]***	**0.764#***	0.277	**0.412[1]***	0.337	0.356	-0.058	-0.332	0.288	**0.487[1]***	0.120	**0.391[#]***
HbA1c	0.198	0.323	0.263	**0.695#***	0.310	**0.741#***	0.327	**0.563#***	-0.193	0.395	-0.036	0.392	**-0.491[#]***	**-0.418[#]***	-0.127	**0.534[#]***	-0.285	**0.487[#]***
Insulin	-0.053	0.039	**0.428[#]***	**0.657#***	0.366	**0.632#***	**0.686[#]***	**0.472#***	0.146	0.158	0.208	0.178	-0.201	-0.266	0.142	0.178	0.121	**0.396[#]***
Homa-IR	0.041	0.133	**0.409[1]***	**0.664[1]***	**0.455[#]***	**0.720#***	**0.716[#]***	**0.565#***	0.160	0.133	0.242	0.207	**-0.453[1]***	-0.306	0.255	0.212	0.142	**0.400[#]***
AU	-0.145	0.184	0.333	**0.595[1]***	0.196	**0.577#***	0.149	**0.562#***	0.320	**0.411[1]***	0.333	0.300	-0.063	-0.385	0.338	**0.501[1]***	**0.520[#]***	0.384
TSH	-0.314	0.251	-0.114	0.350	0.022	**0.409#***	-0.055	0.312	-0.260	-0.005	-0.350	-0.109	0.390	-0.337	-0.288	0.087	-0.051	0.294
T4L	0.041	-0.158	0.002	0.133	0.067	0.032	0.197	0.074	0.027	0.150	0.104	0.322	0.107	0.016	0.009	0.246	**0.410[#]***	-0.167
TC	0.017	0.021	0.088	**0.5611***	0.132	**0.502#***	0.247	**0.461#***										
LDL-c	0.102	0.094	0.172	**0.520#***	0.140	**0.499#***	0.289	**0.461#***										
HDL-c	-0.044	-0.071	-0.267	-0.355	-0.336	-0.388	-0.341	0.262										
ñ-HDL-c	0.026	0.041	0.144	**0.6371***	0.173	**0.596#***	0.272	**0.602#***										
TG	-0.161	0.119	0.252	**0.496#***	0.169	**0.514#***	0.135	**0.410#***										

[1]Pearson Test; [#]Spearman Test; *p<0.05.

Table 5. Correlations between clinical and metabolic variables of participants with AIT treated in postmenopause (G2) and comparative group (CG2). Uberaba-MG, 2020.

Variables	Age		BMI		AC		%GC		TC		LDL-c		HDL-c		Ñ-HDL-c		TG	
	G2	GC2	G2	GC2	G2	GC2	G2	GC2	G2	GC2	G2	GC2	G2	GC2	G2	GC2	G2	GC2
FBS	-0.040	0.103	0.234	0.220	0.039	**0.405**[#*]	0.328	0.228	-0.062	0.219	-0.155	0.017	-0.037	**-0.389**[1*]	-0.053	0.352	0.054	**0.420**[#*]
HbA1c	0.150	0.228	0.349	0.282	**0.369**[#*]	0.332	**0.411**[#*]	0.243	**-0.407**[#*]	0.014	**-0.252**	0.097	-0.322	-0.264	-0.267	0.152	-0.084	-0.080
Insulin	0.212	0.152	**0.378**[#*]	0.317	**0.370**[#*]	0.231	0.269	-0.036	-0.144	0.241	-0.073	0.188	**-0.397**[#*]	-0.289	-0.035	0.339	0.267	**0.549**[#*]
Homa-IR	0.170	0.179	0.260	0.990	0.301	0.307	**0.370**[#*]	0.041	-0.133	0.243	-0.079	0.142	**-0.363**[1*]	**-0.523**[1*]	0.009	**0.427**[1*]	0.204	**0.597**[#*]
AU	0.240	-0.211	0.409	0.030	0.340	-0.003	**0.284**	0.055	-0.029	0.081	0.104	0.267	**-0.392**[1*]	**-0.388**[1*]	0.139	0.228	0.088	0.086
TSH	-0.119	0.373	0.210	0.244	**0.355**	0.218	0.100	0.237	-0.330	-0.165	-0.320	-0.269	0.014	0.119	**-0.376**[1*]	-0.196	-0.091	0.314
T4L	0.292	-0.101	0.041	0.018	-0.098	-0.056	-0.157	0.300	-0.187	0.321	-0.087	0.321	-0.034	-0.008	-0.202	0.286	-0.186	0.027
TC	-0.007	0.0	-0.053	0.101	-0.036	0.114	-0.045	0.332										
LDL-c	-0.318	-0.089	0.058	0.070	0.072	0.0	0.100	0.244										
HDL-c	**-0.544**[1*]	0.088	**-0.499**[1*]	0.059	**-0.501**[#*]	0.064	**-0.384**[#*]	0.085										
ñ-HDL-c	-0.140	-0.035	0.159	0.067	0.138	0.182	0.123	0.336										
TG	0.079	0.201	0.325	0.330	0.335	**0.457**[3*]	0.265	0.246										

[1]Pearson Test; [#]Spearman Test; *p<0.05.

DISCUSSION

The present research analyzed cardiometabolic, clinical and laboratory risk factors in women with AIT treated in pre and post-menopause, and aimed to answer the main question, namely: whether women with AIT who had hypothyroidism at diagnosis, but who are currently in regular treatment with L-thyroxine, behave in relation to the clinical and metabolic profile in a similar way to women without thyroid-related pathologies.

As expected, in the selection, the ages of G1 and CG1 were significantly lower than G2 and CG2, because they followed the age and hormonal status criteria; that is, groups with regular menstrual cycles and groups with already onset of menopause.

Most women in G1 had overweight/obesity BMI (56%), and AC (64%) above 80 cm, although there was no difference when compared to GC1, suggesting that these data are not due only to presence of AIT, but are also associated with a higher prevalence of overweight and obesity in the general population. As in other countries, obesity in Brazil has been considered a growing epidemic[16], with its etiology being complex and multifactorial, resulting from the interaction of genes, emotional, environmental, cultural and lifestyle factors[17].

Likewise, in G2, participants also had higher percentages of overweight/obesity BMI (63.6%), but in general there was no statistical difference between the groups. However, the AC was above 80 cm in 90.2% of the participants in G2, showing a difference in relation to CG2, although even in this group, 53.6% of the women had AC above 80 cm, suggesting the sum of factors such as the presence of AIT, the increase in overweight/obesity in the general and climacteric population, in G2 and in its comparative group, the last two factors could be blamed[9,11].

The comparison between groups of adiposity indices did not show a significant difference in BMI, but AC in G2 was higher when compared to young women (CG1), as well as the frequency already mentioned, higher in G2, in which three conditions were associated: age, climacteric and TCA. The %BF was higher in CG2 than in CG1, also suggesting the relevance of age and climacteric factor in the accumulation of subcutaneous fat. With advancing age and the onset of menopause, the prevalence of overweight/obesity increases, there is a decrease in lean mass, redistribution of body fat to the central type, insulin resistance and metabolic syndrome[9,11].

AIT affects the thyroid, but the immunological alterations of affected individuals present systemic repercussions with production and secretion of pro-inflammatory cytokines, especially interleukin 6 (IL-6), also produced by adipocytes and macrophages in adipose tissue. Elevated IL-6 concentrations have been related to increased atherosclerotic risk, and serum concentrations of inflammatory cytokines have been found in patients with ACT, suggesting that even in euthyroid status, they would be characterized by a pro-inflammatory state[11] capable of interfering with distribution of body fat, thus justifying the percentages found and higher AC values in groups G1 and G2, although the statistical significance was demonstrated only in G2.

An investigation that evaluated postmenopausal women with subclinical hypothyroidism found results similar to those of this study in relation to AC, associating its findings with autoimmunity alterations, as patients who presented reactive anti-thyroid autoantibodies were the most affected[11]. In a research that proposed to evaluate women with AIT in euthyroid status, as in this research, and the finding found in relation to AC was the same, women with AIT treated had higher AC compared to the control group[18].

A study carried out with postmenopausal men and women observed that the accumulation of trunk body fat in postmenopausal euthyroid women is related to an increase in the concentration of free T3[19]. In the present research, all participants were treated and in euthyroidism, but it is not routine for the evaluation of the treatment to perform T3 measurement. In clinical practice, a patient with TSH and T4 at reference values is considered

to be well treated, but T4 is considered a T3 prohormone, and its blood concentrations may not express what actually occurs at the tissue level and molecular[20].

Thyroid hormones, especially T3, are extremely important for maintaining basal metabolism, modulating appetite and food intake, facilitating adaptive thermogenesis and regulating body weight. Together with leptin, they regulate signaling in the arcuate nucleus of the hypothalamus and reflect changes in energy stores. In patients with hypothyroidism, observed before and after treatment, high levels of leptin were found, which correlated with BMI and concentrations of TSH[20]. In the present research, the condition of euthyroidism presupposes that there are no abnormalities in these levels of regulation. However, the evaluation was cross-sectional and we did not investigate whether, over time or over the duration of treatment, patients had absolute regularity of treatment.

The analysis of the glycemic profile showed that in G2 the FBS, even within the reference values, was higher than in all groups. On the other hand, it was higher in GC2 than in G1 and GC1. It is expected that, with aging, the functions and mass of beta cells are compromised, decreasing insulin release and increasing plasma glucose[21] shifting the intermediary metabolism to neoglycogenesis, glycogenolysis, abdominal fat accumulation and increased AC. In addition, there are other factors to be considered in the context of AIT and menopause in group G2, AIT in G1 and increased population obesity in all. Likewise, HbA1c was also higher in the affected groups than in the comparative groups (G1>CG1; G2>CG1) and even between the comparative groups, in CG2 it was significantly higher than in CG1, reinforcing the justification.

Regarding insulin concentrations, in this study, CG2 was higher than GC1 and G2, reflecting on the HOMA-IR index, which was also higher in CG2 compared to CG1, while there was no difference between the other groups. These variables were expected to be smaller in the comparative groups; however, the patients were matched for age and hormonal status and not for anthropometric variables, so such alterations express altered adiposity indices in the general population[22,23]. There is a scarcity of studies on the analysis of patients with AIT in euthyroid status and metabolic variables, but some studies[1,11] did not observe a difference in the concentration of FBS, while another[18] showed significant differences in relation to the concentration of FBS. Regarding the HOMA-IR index, a difference was observed between patients with AIT[1], and an association was observed between central obesity, higher HBA1c, altered HOMA-IR index, abnormal lipid concentrations and the presence of metabolic syndrome[24].

As in other studies[25,26], in CG1, positive correlations were found between the anthropometric variables (BMI, AC and %BF) with the metabolic profile variables, in addition to a positive correlation between TSH and AC. In CG2, the correlations between anthropometric data and metabolic profile were not so clear, being significant only in relation to FBS and AC, showing a direct relationship between AC and insulin resistance, both being risk factors for MS[22,23].

Considering the lipid profile, there was a correlation between AC and TG. Excessive consumption of foods high in lipids increases the caloric density of the diet and increases obesity in the abdominal region and, consequently, the AC[27], especially in postmenopausal women, who already have a tendency to accumulate fat in this region[9,11].

In G1, there were significant correlations between some variables of the glycemic profile and anthropometric variables, which suggests a direct association between adiposity indices and body fat distribution with metabolic variables. Differently from CG1, in G1 there was no correlation between TSH or T4 and adiposity indices. And, in G2, positive correlations between HbA1c, AC and %BF, insulin concentrations with BMI, AC, HOMA-IR index and %BF indicate connections between mean glucose concentrations, insulin resistance, nutritional status and fat distribution, which is a consensus in another study, in which insulin resistance is present in obesity and in individuals with greater accumulation of abdominal fat[25]. Also in this group, significant correlations were observed between uric acid and BMI and between TSH and AC, as

shown in other studies[11]. Considering the lipid profile, inverse correlations of HDL-c with anthropometric variables were observed, which is within the context of insulin resistance and metabolic syndrome most commonly found in these patients.

In general, there was a predominance of borderline and high values in the affected groups (G1 and G2) in relation to the lipid profile as a whole. Assessing lipid parameters and excess lipoprotein (a) in a subgroup of women with AIT in euthyroidism, an increase in TC, LDL-c and TG concentrations compared to controls was verified[28]. The data corroborate those of this study[28], although it did not assess HDL-c. In turn, another study found no statistical difference in relation to the lipid profile (TC, TG, HDL-c and LDL-c) between participants with TCA in euthyroidism and the control group, but they demonstrated that concentrations of thyroid hormones correlated positively with TC, TG, LDL-c and HOMA-IR, concluding that patients with AIT are at increased risk of developing disorders in lipid metabolism[1].

In addition, in CG1 there was a positive correlation between the anthropometric variables and the lipid profile, except for the HDL-c variable. And positive and significant correlations, in addition to being expected, between some variables of the lipid profile and the glycemic profile, suggesting that IR is strongly related to an unfavorable lipid profile. With excessive production of fatty acids by the liver, there is a reduction in insulin sensitivity in muscle tissue, production of interleukins, growth factors and other cytokines by adipose tissue, and there may also be hyperinsulinemia that increases sodium reabsorption and the activity of the sympathetic system. TG and HDL-C concentrations have a good ability to identify IR in clinical practice, as they correlated strongly[29]. In the analysis between glycemic profile and lipid profile in CG2, some significant correlations were also observed, so even the analysis of the comparative groups suggests a spectrum of correlations over time, as the two groups basically differ in age and hormonal status.

In G1, a significant and negative correlation was found between HbA1c and HDL-c, and between HOMA-IR and HDL-c, and positive correlations between uric acid and TG and between T4 and TG. An association between insulin resistance expressed by altered HOMA-IR and HbA1c abnormalities and also with lower concentrations of HDL-c is expected. Furthermore, the interference of thyroid hormones in lipid metabolism has been described, but the positive correlation found between T4 and TG does not make any sense. And, when correlating the metabolic profile with the lipid profile in G2, an inverse correlation was observed between HbA1c and TC and between insulin, HOMA-IR, uric acid and HDL-c, indicating that metabolic and lipid alterations have associations in the aforementioned context.

High concentrations of TC and LDL-c and low levels of HDL-c play a relevant role in the genesis of atherosclerosis and cardiovascular disease[30]. A study suggests that dyslipidemia secondary to hypothyroidism is reversible with treatment, but subclinical hypothyroidism is a risk factor to be considered[20], and the present research suggests that numerous other factors persist even in compensated AIT.

When analyzing cardiometabolic risk factors, 72% of patients in G1 had 1 or more risk factors, and 36% had criteria for metabolic syndrome. In the comparative group (CG1), most participants were normal or had only 1 risk factor (44%). Regarding G2, 90.3% of patients have 1 or more risk factors, and 51.6% have metabolic syndrome. In CG2, most participants had no risk factor (42.9%) or had only 1 (42.9%), while only 14.3% met criteria for metabolic syndrome. Therefore, among patients with AIT, risk factors are added to age and menopause, adding to criteria for the diagnosis of MS. In a study carried out with postmenopausal women, the prevalence of MS was also higher in patients with thyroid autoimmunity[11]. In the research presented here, the G2 group surpassed the GC2, indicating the interference of AIT, in addition to age and menopause.

A study showed that higher levels of TSH can predict MS[6], however other studies observed MS both in women with euthyroid AIT (47%) and in women with subclinical hypothyroidism (49%), that is, regardless of TSH concentrations[11]. On the other hand, there

was an association between obesity, AC, waist-hip ratio, systolic blood pressure and HOMA-IR index in patients with anti-thyroid antibody concentrations, suggesting the involvement of thyroid autoimmune factors that have some common characteristics with the condition of inflammation low-grade found in overweight/obesity and that result in IR and prediabetes, evolutionary stages that may or may not progress to DM or cardiovascular disease.

CONCLUSION

The results of the metabolic profile suggest the presence of insulin resistance in both groups, being G1, G2 and GC2 with higher rates, however, whether this is due to AIT or obesity, the study design did not allow us to conclude. For this purpose, a future study should select patients with AIT and comparatives with normal BMI.

In the lipid profile, in both affected groups the results were more unfavorable in relation to their comparative groups. AIT is an independent risk factor for atherosclerosis, and special attention should be paid to the concentrations of cholesterol, lipid fractions and triglycerides when monitoring these patients.

The inclusion criteria and the regularity of treatment limited the number of people selected, but it is believed that the information collected will be essential to direct the conduct of outpatient care for patients with a diagnosis of AIT, with attention directed not only to the aspect of hormone replacement with thyroid hormones, but also in the therapeutic approach to each of these cardiovascular risk factors, which can be quantified on an outpatient basis.

REFERENCES

1. Lei Y, Yang J, Li H, Zhong H, Wan Q. Changes in glucose-lipid metabolism, insulin resistance, and inflammatory factors in patients with autoimmune thyroid disease. J Clin Lab Anal. [Internet]. 2019 [cited in 13 Jan 2020]; 33(7):e22929. DOI: https://doi.org/10.1002/jcla.22929

2. Moreira JN. Estudo dos fatores de risco cardiometabólicos em mulheres com tireoidite crônica autoimune. [dissertation]. Uberaba, MG: Universidade Federal do Triângulo Mineiro/UFTM; 2017. 94p.

3. Antonelli A, Ferrari SMF, Corrado A, Di-DomenicantoniO A, Fallahi P. Autoimmune thyroid disorders. Autoimmun Rev. [Internet]. 2015 [cited in 13 Jan 2020]; 14(2):174-80. Available from: https://core.ac.uk/download/pdf/80258257.pdf

4. Jabrocka-Hybel A, Skalniak A, Piatkowski J, Turek-JabrockA R, Vyhouskaya P, Ludwig-SlomczyskA A, *et al.* How much of the predisposition to Hashimoto's thyroiditis can be explained based on previously reported associations? J Endocrinol Invest. [Internet]. 2018 [cited in 13 Jan 2020]; 41(12):1409-16. Available from: https://link.springer.com/article/10.1007/s40618-018-0910-4

5. Merril SJ, Minucci SB. Chapter six- Thyroid autoimmunity: an interplay of factors. Vitam Horm [Internet]. 2018 [cited in 02 Feb 2020]; 106:129-45. DOI: https://doi.org/10.1016/bs.vh.2017.07.001

6. Delitala AP, Scuteri A, Fiorillo E, Lakatta EG, Schlessinger D, Cucca F. Role of adipokines in the association between thyroid hormone and components of the metabolic syndrome. J Clin Med. [Internet]. 2019 [cited in 15 Mar 2020]; 8(6):764-74. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6617115/

7. Vieira EC, Peixoto MRG, Silveira EA. Prevalência e fatores associados à síndrome metabólica em idosos usuários do Sistema Único de Saúde. Rev Bras Epidemiol. [Internet]. 2014 [cited in 10 June 2020]; 17(4):805-17. DOI: http://dx.doi.org/10.1590/1809-4503201400040001

8. Phing CH, Saad HA, Yusof BNM, Taib N. Effectiveness of physical activity intervention among government employees with metabolic syndrome. J Exerc Sci Fit. [Internet]. 2017 [cited in 15 Mar 2020]; 15(2):55-62. Available from: https://www.sciencedirect.com/science/article/pii/S1728869X17300886?via%3Dihub

9. Pereira DCL, Lima SMRR. Prevalência e sobrepeso e obesidade em mulheres após a menopausa. Arq Med Hosp Fac Ciênc Med Santa Casa São Paulo [Internet]. 2015 [cited in 05 Feb 2020]; 60:1-6. Available from http://arquivosmedicos.fcmsantacasasp.edu.br/index.php/AMSCSP/article/view/158/168
10. Karakose M, KarbeK B, Sahin M, Arslan MS, TopaloglU O, Erden G, *et al.* The association of autoimmune thyroiditis and non-functional adrenal incidentalomas with insulin resistance. Arch Endocrinol Metab. [Internet]. 2015 [cited in 15 Jan 2020]; 59(1):42-6.Available from: https://www.scielo.br/scielo.php?pid=S2359-39972015000100042&script=sci_arttext
11. Sieminska L, Woojciechowska C, Walczak K, Borowski A, Marek B, Nowak M, *et al.* Associations between metabolic syndrome, serum thyrotropin, and thyroid antibodies status in postmenopausal women, and the role of interleukin-6. Endokrynol Pol. [Internet]. 2015 [cited in 16 June 2020]; 66(5):394-403. Available from: https://journals.viamedica.pl/endokrynologia_polska/article/view/EP.2015.0049/29962
12. Sociedade Brasileira de Cardiologia. 7ª Diretriz Brasileira de Hipertensão Arterial. Arq Bras Cardiol. [Internet]. 2016 [cited in 01 Oct 2021]; 107(Supl3):1-83. Available from: http://publicacoes.cardiol.br/2014/diretrizes/2016/05_HIPERTENSAO_ARTERIAL.pdf
13. Sociedade Brasileira de Diabetes. Diretrizes da Sociedade Brasileira de Diabetes. São Paulo: Clannad; 2019-2020. 491p.
14. International DiabeteS Federation. The IDF consensus worldwide definition of metabolic syndrome [Internet]. Brussels, Belgium: IDF; 2006 [cited in 01 Oct 2021]. 24p. Available from: https://www.idf.org/e-library/consensus-statements/60-idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html
15. Sociedade Brasileira de Cardiologia. Atualização da V Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose. Arq Bras Cardiol. [Internet]. 2017 [cited in 01 Oct 2021]; 109(2 Supl1):1-76. Available from: http://publicacoes.cardiol.br/2014/diretrizes/2017/02_DIRETRIZ_DE_DISLIPIDEMIAS.pdf
16. Martins-Silva T, Vaz JS, Mola CL, Assunção MCF, Tovo-Rodrigues L. Prevalência de obesidade em zonas rurais e urbanas no Brasil: Pesquisa Nacional de Saúde, 2013. Rev Bras Epidemiol. [Internet]. 2019 [cited in 13 Jan 2020]; 22:E190049. DOI: https://doi.org/10.1590/1980-549720190049
17. Marques DSM, Siqueira HGR, Cruz MA, Vieira MSV, Apolônio RSPT, Esteves AVS. A relação entre pré-eclâmpsia e obesidade: uma revisão integrativa. Rev Cad Med UNIFESO [Internet]. 2019 [cited in 13 June 2020]; 2(2):56-61. Available from: http://www.revista.unifeso.edu.br/index.php/cadernosdemedicinaunifeso/article/view/1394/608
18. Biyikli HH, Arduc A, Isik S, Azuguz U, Caner S, Dogru F, et al. Assessing the relationship between serum ghrelin levels and metabolic parameters and autoimmunity in patients with euthyroid Hashimoto's thyroiditis. Endocr Pract. [Internet]. 2014 [cited in 29 Jan 2020]; 20(8):818-24. DOI: https://doi.org/10.4158/EP13469.OR
19. Nie X, Xu Y, Ma X, Shen Y, Wang Y, Bao Y. Trunk fat and leg fat in relation to free triiodothyronine in euthyroid postmenopausal women. Endoc Conect.[Internet]. 2019 [cited in 29 Jan 2020]; 8(10):1425-32. Available from: https://ec.bioscientifica.com/view/journals/ec/8/10/EC-19-0394.xml
20. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev. [Internet]. 2014 [cited in 15 Jan 2020]; 94(2):355-82. Available from: https://journals.physiology.org/doi/full/10.1152/physrev.00030.2013?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org
21. Wan XM, Zhang M, Zhang P, Xie ZS, Xu FG, Zhou P, et. al. Jiawei Erzhiwan improves menopausal metabolic syndrome by enhancing insulin secretion in pancreatic β cells. Chin. J Nat Med. [Internet]. 2016 [cited in 02 Mar 2020]; 14(11):823-34. DOI: https://doi.org/10.1016/S1875-5364(16)30099-1

22. Santos ML, Martiniano SREG, Tavares RE. Avaliação de circunferência abdominal, razão cintura/quadril e IMC em adultos saudáveis. Rev Campo Saber [Internet]. 2017 [cited in 05 Jan 2020]; 3(3):14. Available fromm: https://periodicos.iesp.edu.br/index.php/campodosaber/article/view/100/81
23. Fonseca EJNC. Síndrome metabólica e resistência insulínica pelo HOMA-IR no climatério. Int J Cardiovasc. [Internet]. 2018 [cited in 15 Jan 2020]; 31(3):201-8. Available from: https://www.scielo.br/pdf/ijcs/v31n3/pt_2359-4802-ijcs-31-03-0201.pdf
24. Chen Y, Chunfang Z, Yingchao C, Ningjian W, Quin L, Bing H, et al. Are thyroid autoimmune diseases associated with cardiometabolic risks in a population with normal thyroid-stimulating hormone? Mediat Inflamm. [Internet]. 2018 [cited in 13 Nov 2020]; 2018:1856137. DOI: https://doi.org/10.1155/2018/1856137
25. Asghar A, Sheikh N. Role of immune cells in obesity induced low grade inflammation and insulin resistance. Cell Immunol. [Internet]. 2017 [cited in 03 Mar 2020]; 315:18-26. DOI: https://doi.org/10.1016/j.cellimm.2017.03.001
26. Park YM, ZhanG J, Steck SE, Fung TT, Hazlett LJ, Han K, et al. Obesity mediates the association between mediterranean diet consumption and insulin resistance and inflammation in US adults. J Nutr. [Internet]. 2017 [cited in 15 Jan 2020]; 147(4):563-71. Available from: https://academic.oup.com/jn/article/147/4/563/4584819
27. Deon RG, Rosa RD, Zanardo VPS, Closs VE, Schwanke CHA. Consumo de alimentos dos grupos que compõem a pirâmide alimentar americana por idosos brasileiros: uma revisão. Ciênc Saúde [Internet]. 2015 [cited in 15 June 2020]; 8(1):26-34. DOI: https://doi.org/10.15448/1983-652X.2015.1.18065
28. Yetkin DO, Dogantekin, B. The lipid parameters and lipoprotein(a) excess in Hashimoto Thyroiditis. Int J Endocrinol. [Internet]. 2015 [cited in 02 Feb 2020]; 2015:952729. DOI: https://doi.org/10.1155/2015/952729
29. Pereira, R. A relação entre dislipidemia e diabetes mellitus tipo 2. Cad UniFOA [Internet]. 2011 [cited in 15 Jan 2020]; 6(17):89-94. Available from: http://revistas.unifoa.edu.br/index.php/cadernos/article/view/1087/938
30. Schiavo M, Lunardelli A, Oliveira JR. Influência da dieta na concentração sérica de triglicerídeos. J Bras Patol Med Lab. [Internet]. 2003 [cited in 06 Feb 2020]; 39(4):283-8. DOI: https://doi.org/10.1590/S1676-24442003000400004

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CONTRIBUTIONS

Marina Destefano Prezotto and **Maria de Fátima Borges** contributed to the design, collection and analysis of data and writing. **Adriana Paula da Silva** participated in the data analysis, writing and reviewing. **Elvi Cristina Rojas Fonseca** and **Priscila de Melo Franciscon** collaborated in data collection and reviewing.

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