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## Atherogenic index and coronarian risk – comparative assessment regarding the particularities of chronic autoimmune thyroiditis presence

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### ABSTRACT

**Objectives:** Assessment of autoimmune cause hypothyroidism and dyslipidemia involvement in the apparition of major vascular complications. **Methods:** A total of 152 patients were investigated appreciating in comparison to a healthy control lot the hormone serum level, the presence of antimicrosomal thyroid antibodies and the serum levels of lipids. Atherogenic index and coronarian risk were calculated and correlated with the incidence of coronarian and cerebral vascular accidents. **Results:** Among the patients with goiter it was noted a high incidence of a subclinical hypothyroidism (31,58%). Thyroid autoimmunity was involved in 94,4% of the patients with clinical hypothyroidism, in 93,7 % with subclinical hypothyroidism and 100% in the patients with thyrotoxicosis. Low serum level of HDL-cholesterol was identified in 66,6% of patients with clinical hypothyroidism and 64,5% patients with subclinical hypothyroidism. The assessment of atherogenic index and coronarian risk was significantly higher ( $p<0,01$ ) in patients with hypothyroidism in comparison to healthy control subjects. The incidence of vascular accidents was significantly higher ( $p<0,01$ ) among the hypothyroid patients ( 19,7%/ 10,8%), of masculine gender (12,7%) where the main cause of

hypothyroidism was autoimmunity. **Conclusions:** The atherogenic index and coronarian risk were higher in patients with hypothyroidism associated to thyroid autoimmunity resulting in an increased probability in producing vascular accidents.

**Keywords:** hypothyroidism, dyslipidemia, atherogenic index, coronarian risk, antimicrosomal thyroid antibodies.

### Introduction

Thyroid functional impairment presents an important metabolic risk with major cardiovascular impact.[1; 2; 3; 4; 5; 6] Associating thyroid autoimmunity amplifies this risk.[3; 7]

Vascular impairment becomes an additional effect for thyroid hormone deficit and even if still unclear, for the presence of thyroid autoantibodies, known as “aggressive” on brain microcirculation, which created the concept of Hashimoto’s “encephalitis”.

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## Methods

The study included a total of 152 patients with goiter (OMS classification) and a control group of 252 healthy persons in terms of thyroid function, without known personal or family history regarding thyroid pathology.

The parameters studied were:

1. Ultrasound: thyroid volume and echogenicity
2. Evaluation of thyroid function (ECL): TSH, Free-T4, Free-T3.
3. Lipidic profile: HDL-cholesterol, LDL-cholesterol, triglycerides (TG)
4. TPOAb serum level (ECL) defined pathological as a value  $> 35$  UI/L.
5. The incidence of vascular cerebral and/or coronary accidents based on medical documents presented by patient.
6. Atherogenic index prediction (AI) (LDL-c/HDL-c report), considered normal if  $< 3.5$ ; the value of this index was considered to influence the coronary risk (CR) being inversely correlated with serum HDL-cholesterol level (Table I).

Table I- Coronary risk (FRIEDWALD) [2]

The Coronarian Risk	Females		Males	
	HDL – cholesterol			
	g / l	mmol / l	g / l	mmol / l
0,5	0,70	1,81	0,60	1,55
1,0	0,55	1,42	0,45	1,16
1,5	0,45	1,16	0,35	0,90
2,0	0,35	0,90	0,25	0,64
> 2	< 0,35	< 0,90	< 0,25	< 0,64

## Results and discussions

The structure of the two study groups according to their gender and age was as follows (Table II and Table III).

Table II: Patients with goiter

	19 – 30 years	31 – 45 years	46 – 53 years
<b>F (n = 88 )</b>	21(13,8%)	35 (25%)	32 (21%)
<b>M (n = 64 )</b>	12 (7,9%)	27 (17,7%)	25 (16,4%)
	33 (21,7%)	62 (40,7%)	57 (37,4%)

Table III: Healthy controls in witness lot

	19 – 30 years	31 – 45 years	46 – 53 years
<b>F (n = 148 )</b>	51 (20,2%)	54 (21,4%)	43 (17%)
<b>M (n = 104 )</b>	30 (11,9%)	27 (10,7%)	47 (18,6%)
	81 (32,1%)	81 (32,1%)	90 (35,6%)

The mean thyroid volume measured in patients with goiter was higher in males, having no statistical significance ( $p = 0,5$ ) (Table IV).

Table IV – Mean thyroid volume in patients with goiter

Sex	Thyroid mean volume (ml)	19 – 30 years	31 0 45 years	46 – 53 years
<b>F</b>	$24 \pm 1,2$	$23 \pm 1,1$	$24 \pm 0,8$	$28 \pm 1,8$
<b>M</b>	$26 \pm 2,2$	$26 \pm 2,1$	$24 \pm 2,3$	$26,8 \pm 1,4$

Thyroid echogenicity was appreciated as being normal/low. In subjects with thyroid hypoechogeny serum levels of antimicrosomal antibodies (TPOAb) were dosed (Table V).

Table V - : Incidence of chronic autoimmune thyroiditis in patients with thyroid hypoechogeny

	Negative TPOAb	Pathologic TPOAb
<b>F (n = 50)</b>	18 (18,6%)	32 (33%)
<b>M (n = 47)</b>	23 (23,7%)	24 (24,7%)
	41 (42,3%)	56 (57,7%)

The obtained data reveals an increased incidence of chronic autoimmune thyroiditis in females compared to men. However, it is noted that values of TPOAb considered non-pathological in patients with hypoechogenic thyroid were significantly ( $p < 0,01$ ) more frequent (64,7%/32,6%) among patients selected according to ultrasound criteria. Under functional aspect the patients were investigated

by dosage of serum level of TSH, FT4 and FT3 (Table VI).

Table VI – Thyroid function

	Normal	Clinical hypothyroidism	Subclinical hypothyroidism	Thyrotoxicosis
Study group (n = 152)	84 (55,26%)	18 (11,8%)	48 (31,5%)	2 (1,3 %)
Control group (n = 252)	240 (95,23 %)	0	12 (4,76 %)	0

Among the patients with goiter associating thyroid functional disorders was found a high incidence of subclinical hypothyroidism [n=48(31,58%)]. Patients with thyroid functional disorders (n=68) were characterized under the aspect of registered serum level of TPOAb (Table VII).

Table VII: Autoimmunity involvement in achieving thyroid functional disorders

Patients	Pathologic TPOAb (n)	Negative TPOAb (n)
Clinical hypothyroidism (n = 18)	17 94, 4 %	1 5,5 %
Subclinical hypothyroidism (n = 48)	45 93,7 %	3 6,2 %
Thyrotoxicosis (n = 2)	2 100 %	-

Subjects in control group presenting a hormonal profile characteristic to subclinical hypothyroidism (SCHT) showed the following characteristics (Table VIII)

Table VIII: Patients with subclinical hypothyroidism – Witness lot

	Pathologic TPOAb (n)	Negative TPOAb (n)	AGE (years)	Gender	
				F	M
Patients SCHT (n = 12)	9	3	49 ± 4	12	-

SCHT patients presenting pathological values of serum TPOAb level were considered having “asymptomatic” chronic autoimmune thyroiditis, but with evolutionary potential.

Lipid profile was achieved measuring the

following constants: HDL-cholesterol, LDL- cholesterol and TG. Significant pathological differences were found according to hormonal changes (Table IX).

Table IX – Lipid profile

	Thyroid function	HDL cholesterol			LDL cholesterol			Triglycerins		
		↑	N	↓	↑	N	↓	↑	N	↓
Study group n=152	Normal (n=84)	11	30	43	46	30	8	41	35	8
	Subclinical hypothyroidism (n = 48)	2	15	31	29	16	3	25	20	3
	Clinically manifested hypothyroidism (n= 18)	2	4	12	15	3	-	14	3	1
	Thyrotoxicosis (n = 2)	-	-	2	-	-	2	-	-	2
	%	9.8	32.2	57.8	59.2	32.2	8.5	52.6	38.1	9.2

Considering a low serum level of HDL-cholesterol in order of calculating the vascular risk, this parameter was rated separately (Table X).

Table X. – Patients with low serum HDL-cholesterol

Study group (n = 152)	Thyroid function	HDL ↓	%
	Normal (n = 84)	43	51,1 %
	Subclinical hypothyroidism (n = 48)	31	64,5 %
	Clinically manifested hypothyroidism (n = 18)	12	66,6 %

The percentage of low serum levels prevailed among hypothyroid patients.

Rating atherogenic index (AI) and coronary risk (CR) found pathological values distribution by the type of thyroid functional disorders (Table XI).

Table XI- Correlation of IA/IRC/ thyroid functional status

Thyroidian function	AI			CR		
	Study group	Control group	p	Study group	Control group	p
Normal	3.22	2.68	< 0.01	2.18	1.23	< 0.01
Clinical hypothyroidism	4.84					
Subclinical hypothyroidism	4.73	3.87	< 0.01	3.42	2.67	< 0.01
Tyrotoxicosis	2.4			1.3		

Overall cardiovascular risk is markedly increased in patients with goiter compared to the control group (p<0,01). Statistical significance is maintained among patients with subclinical hypothyroidism, for those with goiter existing additional risks linked to the period and intensity of thyroid autoimmunity process evolution.

The incidence of stroke and coronary accidents was different in the two study groups (Table XII).

Table XII - Incidence of vascular accidents

	Nr. of vascular accid.	19 – 30 years		31 – 45 years		46 – 53 years		M		F	
		M	F	M	F	M	F	Study group	Control group	Study group	Control group
Study group	19 (12.5%)	1	-	3	2	8	5				
Control group	13 (5.16%)	1	-	2	1	6	3				
		0.5%		2%		5.4%		7.9%	3.5%	4.6%	1.6%

Findings for each study group by gender, age and thyroid functional level, regarding the incidence of strokes registered significant differences (Table XIII).

A high incidence of vascular accidents was found in men from the maximum age group and also among hypothyroid patients ( $p < 0,01$ ).

The association of hypothyroidism with thyroid autoantibodies represents a potential additional risk factor in the development of degenerative vascular pathology.

## Conclusions

1. Autoimmune thyropathy is associated frequently to thyroid functional disorders.

2. The presence of hypothyroidism increases the vascular risk and the atherogenic index.

3. The increased frequency of strokes is priorly found in hypothyroid patients group with present thyroid autoantibodies.

4. Early identification of potential hypothyroidism (“sub-subclinical”) characterized only by the presence of thyroid autoantibodies, of subclinical and patent hypothyroidism represents an activity of preventive care.

## References

1. Ichiki, T. (2010). Thyroid hormone and atherosclerosis. *Vascul Pharmacol*, 52(3-4), 151-156. doi: 10.1016/j.vph.2009.09.004
2. Singh, S., Duggal, J., Molnar, J., Maldonado, F., Barsano, C. P., & Arora, R. (2008). Impact of subclinical thyroid disorders on coronary heart disease, cardiovascular and all-cause mortality: a meta-analysis. *Int J Cardiol*, 125(1), 41-48. doi: 10.1016/j.ijcard.2007.02.027
3. Ciccone, M.M., De Pergola, G., Porcelli, M. T., Scicchitano, P., Caldarola, P., Iacoviello, M. & Favale, S. (2010). Increased carotid IMT in overweight and obese women affected by Hashimoto's thyroiditis: an adiposity and autoimmune linkage? *BMC Cardiovasc Disord*, 10, 22. doi: 10.1186/1471-2261-10-22
4. Toruner, F., Altinova, A. E., Karakoc, A., Yetkin,

Table XIII - The incidence of strokes in patients with normothyroidism (NT) and hypothyroidism (HT) correlated to their gender and age.

		Nr. of vascular accid		19 – 30 years		31 – 50 years		51 – 70 years		Males				Females			
				M	F	M	F	M	F	Study group		Control group		Study lot		Witness	
NT	Study group	2	3.1%	-	-	1	-	1	-	N	H	N	H	N	H	N	H
	Control group	5	2.9%	-	1	1	-	2	1								
HT	Study group	17	19.7%	2	-	4	3	5	3								
	Control group	8	10.8%	-	-	2	1	3	2								
%				0.7		3		4.3		3.1	12.7	1.7	6.7	-	7	1	4

- I., Ayvaz, G., Cakir, N. & Arslan, M. (2008). Risk factors for cardiovascular disease in patients with subclinical hypothyroidism. *Adv Ther*, 25(5), 430-437. doi: 10.1007/s12325-008-0053-7
5. Valentina, V. N., Marijan, B., Chedo, D. & Branka, K. (2011). Subclinical hypothyroidism and risk to carotid atherosclerosis. *Arq Bras Endocrinol Metabol*, 55(7), 475-480.
6. Palmieri, E. A., Fazio, S., Lombardi, G. & Biondi, B. (2004). Subclinical hypothyroidism and cardiovascular risk: a reason to treat? *Treat Endocrinol*, 3(4), 233-244.
7. Thvilum, M., Brandt, F., Brix, T. H. & Hegedus, L. (2012). A review of the evidence for and against increased mortality in hypothyroidism. *Nat Rev Endocrinol*, 8(7), 417-424. doi: 10.1038/nrendo.2012.29