SERUM LEVELS OF THE SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS ARE REDUCED IN CHILDREN WITH HASHIMOTO'S THYROIDITIS

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Background

Advanced Glycation End Products (AGEs) increase oxidative stress and promote inflammation, by interacting with their receptor (RAGE) on cell membrane. By contrast, the soluble form of RAGE (sRAGE), that is proteolytically cleaved from cell surface receptor via matrix metalloproteinases, sequester RAGE ligands and exerts cytoprotective and anti-inflammatory effects. Recently, increased levels of AGEs, as a specific marker of oxidative stress, have been reported in adult individuals suffering from Hashimoto's thyroiditis (HT).

Objective

Aim of the present study is to evaluate any change in serum levels of sRAGE and oxidative stress parameters in pediatric euthyroid HT patients, since no data are available from the literature.

Materials and Methods

- **19 HT pediatric patients** (3 M, 16 F; median age 12.44, range 6.54 - 15.81)
- **18 age- and sex-matched healthy controls** (6 M, 12 F; median age 12.71, range 5.68 - 15.07).
- **Exclusion criteria**: autoimmune, inflammatory and infection comorbidities; current or previous LT-4 therapy; altered thyroid function tests.
- **sRAGE** levels were measured by ELISA (kit sRAGE Elisa, R&D System, Minneapolis, USA; minimum detectable dose 3 pg/ml).
- **AGEs and Advanced Oxidation Protein Products (AOPPs)**, compounds formed by the transformation of proteins, were determined on spectrophotometric detection, as markers of oxidative stress.

Results

sRAGE levels were significantly lower in HT patients than in controls (**Figure 1**), whilst no differences emerged with regard to serum AGEs, as well as AOPPs (**Table 1**).

Patients did not differ significantly from controls with regard to lipid and glucidic profile neither for anthropometric parameters (data not shown).

sRAGE levels were negatively correlated with **BMI SDS** (**Figure 2**) and **anti-thyroid peroxidase antibodies (TPO-Ab) levels**, even if adjusted for BMI SDS (**Figures 3 and Table 2**). **AGE/sRAGE ratio** was positively correlated with **FT4 levels** (**Figure 4**).

Figure 1. Comparison of sRAGE in HT patients and controls.

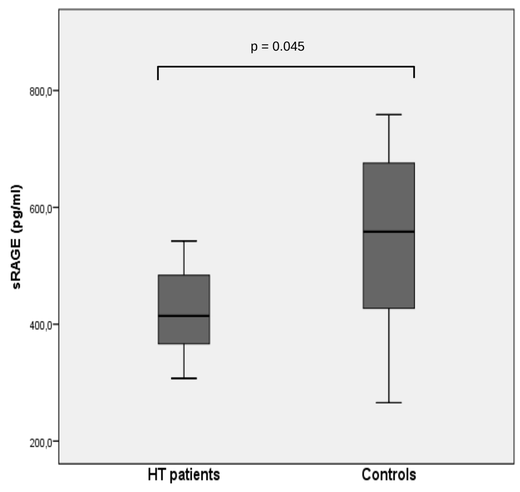

Figure 2. Inverse correlation between sRAGE and BMI in HT pts

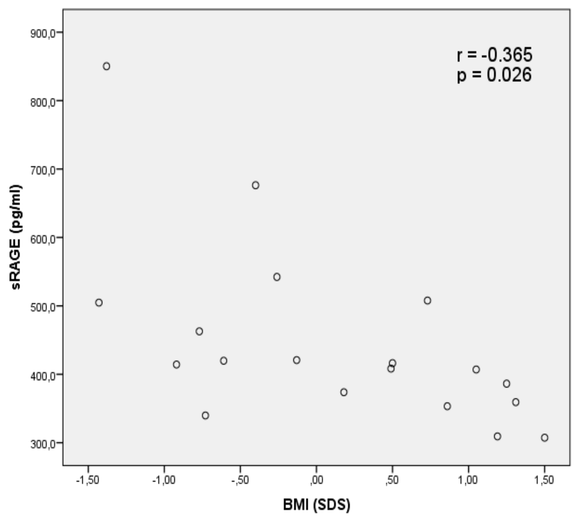

Table 1. Comparison of thyroid function tests and oxidative stress parameters (median and range) in HT patients and controls.

	HT (n = 19)	Controls (n = 18)	*p*
TSH (uUI/ml)	3.61 (1.15 – 4.97)	2.01 (1.25 - 4.89)	***0.033****
fT4 (pmol/L)	11.83 (8.34 - 16.85)	11.01 (9.11 - 12.97)	*0.136*
fT3 (pg/ml)	4.32 (3.64 - 5.40)	4.23 (3.36 - 5.94)	*0.763*
sRAGE (pg/ml)	414.3 (307.3 - 850.3)	558.3 (265.8 - 1132.3)	***0.045 ****
AGE (AU/gr)	124.25 (71.98 - 186.72)	139.26 (94.06 - 251.05)	*0.346*
AOPP (nmol/ml)	1.12 (0.62 - 1.83)	1.18 (0.76 - 2.27)	*0.254*
AGE/sRAGE ratio	0.289 (0.16 - 0.51)	0.26 (0.08 - 0.61)	*0.543*

Fig.3 Inverse correlation (adjusted for BMI SDS) between sRAGE and Ab-TPO in HT pts

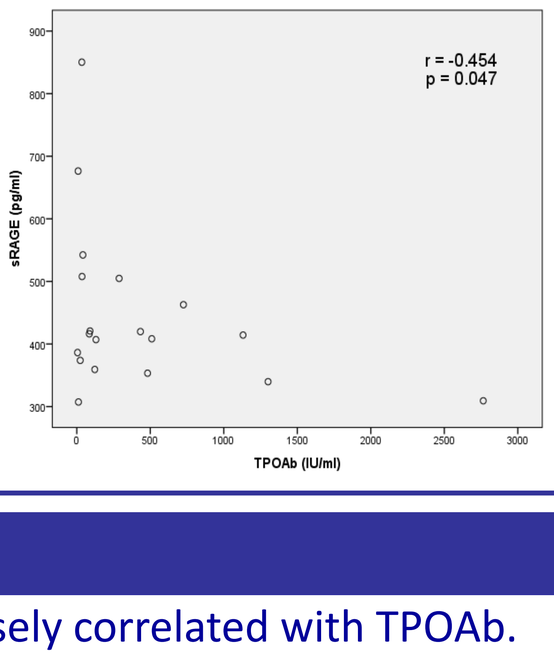

Figure 4. Positive correlation (adjusted for BMI SDS) between fT4 and AGE/sRAGE ratio in HT pts

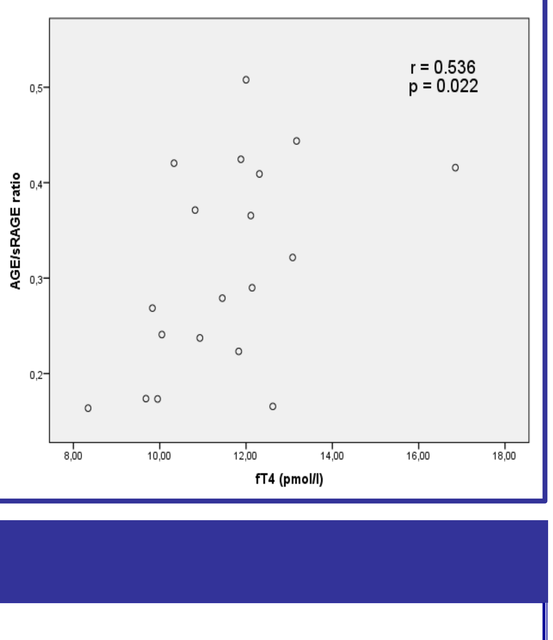

Table 2. Partial Spearman's rank correlation coefficients after adjustment for BMI in HT pts.

	AGE (AU/gr)		sRAGE (pg/ml)		AOPP (nmol/ml)		AGE/sRAGE ratio	
	r	*P*	r	*P*	r	*P*	r	*P*
TSH (uUI/ml)	0.069	*0.784*	-0.111	*0.662*	0.031	*0.902*	0.149	*0.556*
FT4 (pmol/L)	0.476	***0.046****	-0.141	*0.576*	-0.228	*-0.363*	0.536	***0.022****
TPOAb (IU/ml)	-0.166	*0.511*	-0.454	***0.047****	-0.159	*0.529*	0.190	*0.451*
TGAb (IU/ml)	0.116	*0.648*	-0.259	*0.299*	0.197	*0.434*	0.199	*0.428*

Conclusions

- sRAGE levels were decreased in HT children/adolescents and inversely correlated with TPOAb.
- Autoimmunity *per se* seems to play an important role in such a reduction of sRAGE, irrespective of any functional alteration.
- Given the protective effects of sRAGE, children and adolescents suffering from HT may exhibit increased susceptibility to oxidative damage, even when in euthyroid status.