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Is oxidative stress a factor in the pathogenesis of subacute thyroiditis?

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Abstract

Introduction: In a performed study, selenium levels were detected to be lower in subacute thyroiditis (SAT). This outcome suggests that the oxidant-antioxidant system may play a role in the aetiopathogenesis of SAT, as is the case for many other diseases. The aim of the present study was to detect whether any association exists between SAT and oxidative stress, and to determine the factors of a possible association.

Material and methods: Twenty-five patients who were newly diagnosed with SAT and 30 healthy volunteers were enrolled in the study. Total antioxidant status (TAS), total oxidant status (TOS), oxidative stress index (OSI), paraoxonase 1 (PON1), and dynamic thiol/disulphide [native thiol (NT), total thiol (TT), disulphide (DS), DS/TT, DS/NT, and NT/TT] levels of the participants were evaluated.

Results: Total thiol and NT levels were found to be lower in the SAT group ($p < 0.001$). DS/NT and DS/TT levels were significantly higher in the patients with SAT, whereas NT/TT levels were lower ($p < 0.05$). A negative correlation was detected between C-reactive protein (CRP) and TAS, whereas a positive correlation was detected between CRP and OSI. There was a negative association between TSH and TAS only in the partial correlation analysis by adjusting for age, white blood cell count, neutrophil (Neu) level, CRP, and erythrocyte sedimentation rate (ESR) ($r = -0.481$, $p = 0.043$).

Conclusions: Thiol levels are significantly decreased and thiol/disulphide homeostasis is disrupted in patients with SAT. The present study has presented for the first time that there may be an association between SAT and oxidative stress. (*Endokrynol Pol* 2022; 73 (1): 64–70)

Key words: subacute thyroiditis; pathogenesis; oxidative stress; inflammation; dynamic thiol/disulphide

Introduction

Subacute thyroiditis (SAT) is a condition presenting with local or generalized inflammation of the thyroid gland. The main symptoms include fever appearing with inflammation, pain, and tenderness of the neck. Although the aetiology is not clear, there is a history of upper respiratory tract infection, which appears 2 to 8 weeks before thyroiditis. Therefore, SAT is thought to be related to a viral infection or post-viral inflammation. Autoimmunity does not play a primary role in the progress of the disease. However, a strong association with HLA-B35 molecules was revealed in many ethnic groups. Therefore, some authors suggest that SAT may develop due to transmission of viral infection in individuals with a genetic tendency [1].

Oxidative stress appears as a result of the over-expression of free oxygen radicals and the deficiency of antioxidant defence systems. The reactive oxygen radicals that appear cause tissue damage [2, 3]. There are many molecules reflecting the oxidant and antioxi-

nant status of an organism. For instance, total oxidant status (TOS) and total antioxidant status (TAS) reflect the general condition of oxidative stress in the body. Paraoxonase 1 (PON1) is an enzyme that protects low-density lipoprotein (LDL) against oxidative damage and is closely related to high-density lipoprotein (HDL) [4]. Thiols are the compounds including sulphhydryl groups connected to carbon atoms. Total thiol (TT) is an antioxidant that provides protection against tissue and cell damage by reacting with free oxygen radicals. Oxygen radicals oxidize the thiol groups of the proteins consisting of amino acids including sulphur and create disulphide (DS) bonds. Such disulphide bonds are the earliest indicators of protein oxidation, and these bonds are reversible. Reduction of reversible disulphide bonds provides the protection of dynamic thiol/disulphide homeostasis [5–8]. Homeostasis of dynamic thiol/disulphide plays a key role in cellular activities including antioxidant defence, signal transmission, detoxification, cell proliferation, and apoptosis. When thiol/disulphide homeostasis is disrupted as a result



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of oxidative stress and the balance slides towards disulphide, functional disorders appear in the aforesaid cellular activities. Therefore, abnormal thiol/disulphide homeostasis is expected to be associated with the aetiopathogenesis of many acute or chronic diseases [9].

The most important mechanisms in aetiopathogenesis appear to be genetic predisposition and viral infections; however, the exact cause has not been revealed yet. New hypotheses and studies are therefore needed to clarify the causes and risk factors for SAT. In a previous study performed within this scope, selenium levels were detected to be lower [10]. This outcome suggests that the oxidant-antioxidant system may play a role in the aetiopathogenesis of SAT, as is the case for many other diseases.

However, to the best of our knowledge, no previous study has indicated the association between SAT and oxidative stress directly. We therefore planned the present study to detect whether any association exists between SAT and oxidative stress and the determinant factors that affect such a possible association.

Materials and methods

The study was approved Ethics Committee of Clinical Research at Keçiören Education and Research Hospital, University of Health Sciences (Project No: 2012-KAEK-15/1701) before the onset of the study. The study was carried out in accordance with the Helsinki Declaration, and verbal and written consent was obtained from all participants.

Forty-three patients who had been referred as endocrinology outpatients between 15 June 2018 and 1 May 2019, and had been diagnosed with SAT were enrolled in the study. The exclusion criteria were diabetes mellitus, hypertension, cardiovascular or cerebrovascular disease, acute or chronic kidney or liver disease, any findings for acute or chronic infection, any rheumatologic disease or malignancy, and the use of any antioxidants, lipid-lowering drugs, vitamin supplements, tobacco, or alcohol. A total of 18 individuals with at least one exclusion criterion were excluded. The present study was thus completed with 25 patients who were newly diagnosed and had not received any treatment, as well as 30 healthy volunteers (Fig. 1).

SAT was diagnosed by history (pain on the anterior side of the neck, pain radiating to the ear, fever), physical exam (tenderness

of the thyroid compartment), laboratory findings (thyrotoxicosis, increased erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and/or leukocyte values), and ultrasound findings (focal or diffuse heterogeneous, hypoechoic thyroid parenchyma with decreased vascularization) [1].

Venous blood samples of the participants were collected after a fasting period of at least 10 hours. Blood samples of the patient group were collected at the time of diagnosis, before the administration of any non-steroidal anti-inflammatory drug or steroid treatment. The blood samples were centrifuged at 1500 rpm for 10 minutes, and serum and plasma were separated. The serum was transferred in Eppendorf tubes and stored at -80°C . All oxidative stress parameters were analysed once for the same serum sample.

The serum samples collected for CRP were analysed by the nephelometric method with a Beckman Coulter device (IMAGE Immunochemistry Systems, Ireland). White blood cell (WBC) and neutrophil (Neu) counts were analysed with an LH 750 Analyzer (Beckman Coulter, UK). Thyroid-stimulating hormone (TSH) (normal range: 0.6–4 mIU/mL), free T4 (fT4) (normal range: 0.8–1.7 ng/dL), and free T3 (fT3) (normal range: 2–3.9 ng/dL) were measured by electrochemiluminescence immunoassay method with a Cobas e 601 analyser (Roche Diagnostics Corp., USA).

Serum TOS level was measured with a commercial kit (Rel Assay Diagnostics, Turkey; Ref. No: RL0024, Lot No: JE 14048Og) via colorimetric method with CV% of 10 and linearity of 0–33.5 mmol/L. The results are expressed in micromolar H_2O_2 equivalents per litre (mmol/L H_2O_2 equivalent/L) (normal range: 0–4 IU/mL).

Serum TAS level was measured with a commercial kit (Rel Assay Diagnostics, Turkey; Ref. No: RL0017, Lot No: JE 14042A) via colorimetric method with CV% of 10 and linearity of 0–2.75 mmol/L. The results are expressed in mmol Trolox equivalents/L (mmol Trolox equivalent/L).

The oxidative stress index (OSI) value was calculated according to the following formula: $\text{OSI (arbitrary unit)} = \text{TOS (mmol } \text{H}_2\text{O}_2 \text{ equivalent/L)} / \text{TAS (mmol Trolox equivalent/L)}$ [4].

Serum PON1 level was measured with a commercial kit (Rel Assay Diagnostics, Turkey; Ref. No: RL0031, Lot No: JE14028P) via colorimetric method with CV% of 5 and linearity of 0–750 U/L. PON1 activity was expressed as U/L of serum.

Thiol/disulphide homeostasis tests were performed as described by Erel and Neselioglu [11]. Briefly, disulphide bonds were first reduced to form free functional thiol groups. Unused reducer sodium borohydride was consumed and removed with formaldehyde, including reduced and native thiol (NT); all thiol groups were determined after reaction with 5,5'-dithiobis-2-nitrobenzoic acid. The dynamic disulphide (DS) amount was calculated by determining half of the difference between the total thiol (TT) and the native thiol. After the native thiol, total thiol, and disulphide amounts were determined, the ratios of disulphide/total thiol (DS/TT), native thiol/total thiol (NT/TT), and disulphide/native thiol (DS/NT) were calculated [11].

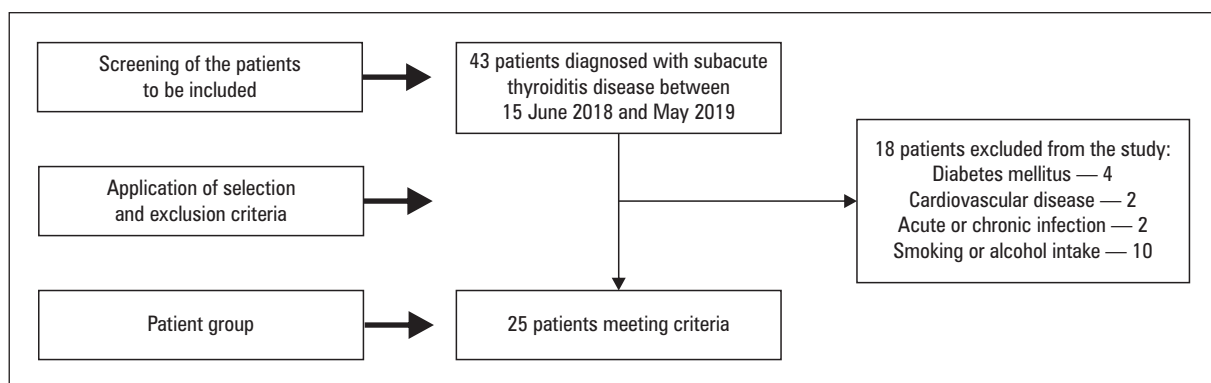


Figure 1. Determination of patient groups

Statistical analysis

Data obtained from the present study were evaluated with the IBM SPSS Statistics 22 program (IBM Corp., USA). Kolmogorov-Smirnov/Shapiro-Wilk tests and distributions of the data in histogram graphics were used to decide whether the data were distributed normally. Normally distributed data were expressed as mean \pm standard deviation, whereas non-normally distributed data were expressed as median (minimum–maximum). Categorical variables were expressed as percentages, and statistical analyses were conducted with the chi-square test. Student's t-test and the Mann-Whitney U test were used to assess the differences between the groups. Analysis of the associations between the variables was conducted with Spearman and Pearson correlation tests as well as partial correlation analysis. In the case of $p < 0.05$, a statistically significant difference/association was considered.

Results

The SAT and control groups were similar in terms of age and sex. The WBC count, Neu level, CRP, ESR, and ft3

and ft4 levels were significantly higher in the patient group, whereas the TSH level was significantly lower in the patient group ($p < 0.05$) (Tab. 1).

Evaluation of the patient and control groups in terms of oxidative stress parameters revealed no significant difference between the groups in terms of TAS, TOS, OSI, and PON1 levels. However, TT and NT levels were lower in the SAT group than in the control group ($p < 0.001$). DS levels were similar. DS/NT and DS/TT levels were significantly higher in the SAT group, whereas NT/TT levels were lower. A comparison of both groups for oxidative stress parameters is presented in Table 2.

In the correlation analysis performed on the whole study population, age was negatively correlated with TT and NT; however, a positive correlation was detected between age and PON1. Furthermore, NT and TT were

Table 1. Demographic characteristics and laboratory findings of the study population

	Control (n=30)	Subacute Thyroiditis (n=25)	p
Gender, n (%)			NS
Female	24 (80)	20 (80)	
Male	6 (20)	5 (20)	
Age [years]	35 (21–59)	38 (29–55)	NS
WBC [n/mm ³]	6885 (4500–10300)	8440 (4000–14,000)	0.003
Neu [n/mm ³]	3945 (2190–6690)	5280 (2510–9760)	< 0.001
CRP [mg/L]	0.14 (0.01–0.49)	4.5 (0.5–13.47)	< 0.001
ESR [mm/h]	11.5 (2–29)	37 (9–62)	< 0.001
ft3 [ng/dL]	2.76 (2.08–3.85)	5.09 (2.96–12.12)	0.001
ft4 [ng/dL]	1.1 (0.85–1.6)	2.24 (1.07–3.78)	< 0.001
TSH [mIU/mL]	1.82 (0.67–3.95)	0.01 (0–0.59)	< 0.001

WBC — white blood cell; Neu — neutrophil; CRP — C-reactive protein; ESR — erythrocyte sedimentation rate; ft3 — free triiodothyronine; ft4 — free thyroxine; TSH — thyroid-stimulating hormone; NS — nonsignificant

Table 2. Oxidative stress parameters of the study population

	Control (n = 30)	Subacute thyroiditis (n = 25)	p
TAS [mmol Trolox equivalent/L]	1.54 (1.3–2.24)	1.58 (1.18–1.88)	NS
TOS [mmol/L H ₂ O ₂ equivalent/L]	8.76 (3.41–18.43)	8.83 (4.91–14.55)	NS
OSI [arbitrary unit]	5.9 (2.76–11.46)	5.95 (2.91–11.3)	NS
PON1 [U/L]	292.3 (76.5–1019.1)	241.6 (105.7–664.3)	NS
NT [μ mol/L]	419.45 (332.8–522.5)	366 (239.4–501.9)	< 0.001
TT [μ mol/L]	447.5 (367.3–549.8)	384.1 (258.2–538.3)	< 0.001
DS [μ mol/L]	15.47 (8.25–21.75)	15.45 (9.05–28)	NS
DS/NT (%)	3.6 (1.71–5.55)	4.13 (2.41–8.59)	0.02
DS/TT (%)	3.35 (1.66–4.99)	3.82 (2.3–7.33)	0.02
NT/TT (%)	93.28 (90.01–96.69)	92.36 (85.34–95.4)	0.02

TAS — total antioxidant status; TOS — total oxidant status; OSI — oxidative stress index; PON1 — paraoxonase 1; NT — native thiol; TT — total thiol; DS — disulphide; NS — nonsignificant

negatively correlated with WBC count, Neu level, CRP, ESR, and fT4 and positively correlated with TSH level (Tab. 3). The partial correlation analysis performed by adjusting age, WBC count, Neu, ESR, and CRP level revealed a negative correlation between fT3 and TOS, OSI, DS, DS/NT, and DS/TT and a positive correlation between fT3 and NT/TT (Tab. 3).

A significant and negative association was detected between age and TT level only in the correlation analysis conducted on SAT patients ($r = -0.442$, $p = 0.027$). Furthermore, a negative correlation was found between CRP level and TAS, whereas a positive correlation was detected between CRP level and OSI. There was a negative association between TSH and TAS only in the partial correlation analysis adjusting the age, WBC count, Neu level, CRP, and ESR ($r = -0.481$, $p = 0.043$) (Tab. 3).

Discussion

We found that NT, TT, and NT/TT values were significantly lower, and DS/NT and DS/TT values were significantly higher, in the SAT group when compared with the control group. Furthermore, we detected significant correlations between thiol levels and inflammatory markers as well as thyroid hormones. We thereby demonstrated a possible association between SAT and oxidative stress.

The aetiopathogenesis of SAT has not been clarified yet. However, it is generally accepted that the disease may present a genetic transition [1]. In particular, the presence of HLA-B35 was detected in two-thirds of the patients, and family series were identified rarely in the literature [1, 12, 13]. Another important determinant is viral factors. It is thought that the disease may develop due to many viral factors such as mumps, rubella, influenza, adenovirus, coxsackie virus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lately [1, 14]. One argument claims that both factors are responsible in the aetiopathogenesis, and the antigens appearing due to viral factors form a complex with HLA-B35 and activate cytotoxic T lymphocytes. Activated T lymphocytes cause damage in thyroid follicle cells, resulting in inflammation [15]. Hernik et al. showed that iron homeostasis and hepcidin also play an important role in the aetiology of SAT [16].

It is known that oxidative stress is related to inflammation and increases in inflammation, and it is also associated with many acute and chronic diseases [4, 9, 17–21]. Previous studies demonstrated that oxidative stress increases in autoimmune thyroid diseases progressing with chronic inflammation such as Hashimoto thyroiditis and Graves' disease, and there may be a cause-and-effect relationship between these diseases and oxidative stress [4, 5, 21–23]. These data suggest the

possible association of SAT involving viral factors and immune reactions with inflammation in the pathogenesis with oxidative stress. Furthermore, Moncayo et al. detected lower levels of selenium, which plays a key role in thyroid functions, in patients with SAT [10]. Briefly, the oxidative stress process that appears with the decrease of antioxidant radicals and/or the increase of direct oxidant radicals probably plays a key role in the pathogenesis of SAT.

We did not detect any significant increase in disulphide levels among oxidative stress parameters in SAT patients. However, significantly lower levels of antioxidant parameters (TT and NT) when compared to the control group and significantly higher DS/NT and DS/TT ratios indicate that thiol/disulphide homeostasis is disrupted by oxidative stress. Dynamic thiol/disulphide homeostasis plays a role in many critical mechanisms, and disruption of that balance disrupts some vital cell functions [2, 3, 11, 24]. Organelle pathologies appear due to oxidative stress [5]. Thiols are accepted as essential antioxidant buffers because they have constant interactions with almost all physiological oxidants [20]. One of the major thiol components of the body is glutathione. The glutathione peroxidase enzyme converts glutathione into glutathione disulphide and protects the thyroid gland from oxidative damage by hydrogen peroxide (H_2O_2), which acts during hormone synthesis [25]. Glutathione peroxidase is a selenium-dependent selenoprotein. Lower selenium levels have already been shown in patients with SAT [10]. Furthermore, it is also known that selenium deficiency increases the virulence of some infectious agents [26]. It is suggested that selenium deficiency may trigger SAT development after viral infection in genetically predisposed individuals. When all these mechanisms and study data are evaluated together, it may be considered that lower thiol levels play a role in the aetiopathogenesis of SAT with a similar mechanism. The main factor may be glutathione in this mechanism. Another finding supporting the hypothesis that dynamic thiol/disulphide homeostasis may play a role in the aetiopathogenesis of SAT is the similarity of other oxidant and antioxidant mechanisms (TAS, TOS, OSI, and PON1); the oxidative imbalance in SAT patients may be caused by inflammation and thyrotoxicosis due to the disease. Thyroid hormones regulate oxidative metabolism and play a role in free radical production [23, 27]. These hormones play a role in the synthesis and degradation of some enzymes including superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase, as well as some non-enzymatic antioxidants such as vitamins E and C, glutathione, uric acid, ferritin, transferrin, and ceruloplasmin. The changes in these enzymes

Table 3. Factors related with oxidative stress parameters

Variables	TAS		TOS		OSI		PONI		NT		TT		DS		DS/NT		DS/TT		NT/TT		
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	
All participants																					
Age	-.094	.497	-.107	.436	-.035	.801	.375	.005*	-.383	.004*	-.375	.005*	-.061	.658	.169	.218	.169	.217	-.172	.210	
WBC	-.275	.042*	-.240	.078	-.098	.475	.061	.657	-.357	.008*	-.331	.014*	-.133	.333	.055	.689	.057	.682	-.056	.686	
Neu	-.294	.029*	-.148	.279	-.005	.972	-.071	.606	-.331	.013*	-.302	.025*	-.046	.738	.125	.364	.125	.365	-.124	.366	
CRP	-.142	.303	.039	.777	.100	.466	-.047	.736	-.521	.000*	-.500	.000*	.119	.387	.362	.007*	.362	.007*	-.362	.007*	
ESR	-.183	.181	-.098	.478	.021	.881	-.078	.572	-.400	.002*	-.407	.002*	-.090	.512	.090	.512	.091	.508	-.092	.504	
fT3	.138	.475	-.331	.080	-.326	.084	-.100	.606	-.176	.360	-.201	.297	-.294	.122	-.236	.218	-.236	.218	.235	.219	
fT4	.079	.565	.118	.390	.126	.358	-.196	.151	-.394	.003*	-.368	.006*	.114	.408	.325	.016*	.324	.016*	-.324	.016*	
TSH	-.008	.952	-.055	.688	-.080	.562	.057	.680	.363	.006*	.346	.010*	-.047	.735	-.228	.094	-.228	.094	.228	.095	
fT3*	.224	.317	-.578	.005*	-.624	.002*	.066	.771	-.035	.878	-.112	.619	-.535	.010*	-.512	.015*	-.507	.016*	.507	.016*	
fT4*	.224	.127	-.009	.954	-.130	.380	-.152	.303	-.197	.179	-.210	.151	-.116	.432	-.054	.718	-.038	.800	.038	.799	
TSH*	-.275	.059	-.094	.527	.036	.810	.116	.432	.016	.917	.013	.933	-.018	.904	.024	.874	.015	.917	-.015	.921	
All patients																					
Age	.059	.781	.083	.693	.000	1.000	.227	.275	-.395	.051	-.442	.027*	-.139	.509	.123	.558	.123	.558	-.129	.539	
WBC	-.093	.658	-.130	.537	.032	.881	.268	.196	-.101	.632	-.014	.946	-.121	.565	.073	.728	.073	.728	-.068	.748	
Neu	-.197	.345	-.124	.555	.066	.753	.206	.323	-.096	.648	-.005	.983	-.074	.726	.060	.776	.060	.776	-.056	.790	
CRP	-.550	.004*	.226	.276	.451	.024*	.030	.885	-.276	.182	-.207	.322	.247	.235	.321	.118	.321	.118	-.320	.119	
ESR	-.306	.137	-.288	.162	-.020	.923	-.048	.821	.003	.990	-.009	.966	-.112	.595	-.133	.527	-.133	.527	.131	.533	
fT3	.124	.554	-.064	.760	-.084	.690	-.048	.821	-.094	.655	-.115	.583	-.113	.590	-.103	.624	-.103	.624	.103	.625	
fT4	-.003	.990	-.094	.654	.022	.917	-.048	.818	-.232	.264	-.212	.310	-.040	.848	.044	.834	.044	.834	-.045	.832	
TSH	-.326	.112	-.211	.312	.022	.918	-.028	.895	-.112	.595	-.110	.600	.003	.989	.112	.596	.112	.596	-.115	.583	
fT3*	.235	.349	-.316	.201	-.379	.121	.148	.559	-.149	.556	-.186	.459	-.307	.215	-.258	.301	-.246	.325	.246	.326	
fT4*	.222	.376	-.248	.322	-.318	.199	-.055	.829	-.176	.484	-.190	.449	-.155	.540	-.108	.670	-.088	.727	.088	.727	
TSH*	-.481	.043*	-.029	.910	.171	.497	.122	.630	-.026	.918	-.046	.856	-.146	.563	-.102	.687	-.112	.658	.111	.660	

*Age and WBC, Neu, CRP, and ESR levels were adjusted (the analysis used partial correlation); *p < 0.05. WBC — white blood cell; Neu — neutrophil; CRP — C-reactive protein; ESR — erythrocyte sedimentation rate; fT3 — free triiodothyronine; fT4 — free thyroxine; TSH — thyroid-stimulating hormone; TAS — total antioxidant status; TOS — total oxidant status; OSI — oxidative stress index; PONI — Paraoxonase 1; DS — disulphide; NT — native thiol; TT — total thiol

and non-enzymatic substances affect the redox balance of the body. Enzymatic feedback mechanisms thereby regulate thyroid functions. One of the most important effects of thyroid hormones is increasing mitochondrial respiration. This causes up-regulation of reactive oxygen radicals and oxidative damage of membrane lipids. In other words, oxidative stress is known to be associated with thyroid functions both in hypothyroidism and hyperthyroidism [23, 27, 28]. The increase of free radicals along with increased cellular metabolic rate was shown in hyperthyroidism [29, 30]. There are different studies addressing the findings that antioxidant enzymes both increase and decrease [31, 32]. All patients enrolled in the present study had thyrotoxicosis. However, there was no increase in oxidative parameters (TOS, OSI, and DS). Furthermore, thiol levels, including glutathione, only decreased among antioxidant mechanisms. TAS and PON1 levels were normal, and there was no association between thyroid functions and total and native thiol levels in partial correlation analysis conducted by excluding the inflammation parameters and age in the patients with SAT. These findings suggest that the effect of thyroid hormones on oxidative stress is minimal.

Inflammation increases oxidative stress [4]. The oxidative balance may be disrupted both in chronic and acute inflammation [4,18]. However, an increase in levels of oxidative parameters such as TOS and DS is expected in oxidative stress appearing due to inflammation [4, 20]. In the present study, a negative correlation of NT and TT was detected with WBC count, Neu level, CRP, and ESR level in the whole study population. There was no such association in the patients with SAT. In other words, there was no association between inflammation severity and thiol levels. Maehira et al. showed a negative association between selenium levels and CRP and such a mechanism appears for NF- κ B [33]. A negative association was also shown between selenium levels and IL-6 [34]. These data reveal that lower thiol levels might be associated with an increase in inflammation markers and inflammation in patients with SAT. The expected inflammation-induced increase in oxidant parameters may not always be detected because the patients enrolled in the study were diagnosed early. Reversible thiol/disulphide homeostasis is the earliest stage of protein oxidation, and antioxidant parameters may start to decrease first with such a balance [5].

In consideration of all data obtained in the present study as well as the information in the literature, we believe that the dynamic thiol/disulphide balance may play a role in the aetiopathogenesis of SAT. However, we are aware of the necessity of other data to support this claim. The present study has some limitations at this stage. The most important limitation of our study

is its cross-sectional design. After complete recovery of inflammation and thyrotoxicosis findings, re-evaluation of oxidative stress parameters would provide a better understanding. Another limitation is the lack of glutathione, glutathione peroxidase, and selenium analyses. Furthermore, viral factors, HLA, and thyroid antibodies, which may act in the aetiopathogenesis of SAT, were not evaluated.

Conclusions

The present study has presented for the first time that there may be an association between SAT and oxidative stress; thiol levels are significantly decreased and thiol/disulphide homeostasis is disrupted in patients with SAT. The possible benefits of antioxidant therapies for the treatment and prevention of the disease and recurrence in patients with SAT should be considered. Large-scale studies are still required to reveal this association exactly.

Conflict of interest

The authors declare that they have no conflict of interest.

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